LIBRA JOURNAL CLUB

29 May-12 JUNE 2022

Our legal office confirmed that articles NOT OPEN ACCESS cannot be distributed to the members of the list. Thus, we will transmit only the titles of articles.

ABSTRACTS of almost all these articles are available from PubMed, and full papers can be obtained through your institutions' library.

OPEN ACCESS articles are available by accessing the articles from PubMed using just the PMID for the search (eg PMID: 35514131 without . at the end)

THIS TIME NEW FORMAT, LESS ELEGANT FORMAT BUT SIMPLER AND INCLUDES ABSTRACT AND INFO RE OPEN ACCESS ARTICLES. PLEASE CONFIRM WHETHER YOU LIKE IT! LMF

COPD

1

Review

Arch Gerontol Geriatr

. 2022 Jun 6;102:104746.

doi: 10.1016/j.archger.2022.104746. Online ahead of print.

Impact of integrated health care on elderly population: A systematic review of Taiwan's experience

Tai-Li Chen [1], Yun-Hsuan Feng [2], Sheng-Lun Kao [3], Jing-Wun Lu [4], Ching-Hui Loh [5]

Affiliations expand

- PMID: 35691276

- DOI: 10.1016/j.archger.2022.104746

Abstract

Background: Care fragmentation in the elderly population prompted the need for integrated health care systems. However, evidence regarding the impact of the integrated care system in Taiwan is unclear. We aimed to conduct a systematic review to evaluate the impact of Taiwan's integrated health care programs on geriatric population.

Methods: We searched bibliographic databases MEDLINE, Embase, Web of Science, and Airiti Library for relevant publications throughout May 2022. Studies investigating the effectiveness of Taiwan's integrated care programs were included. We used the critical appraisal skills programme (CASP) checklist, to assess the risk of bias of included studies.

Results: Thirty-four studies, with a total of 838,026 study subjects, were assessed. The systematic review on 11 subthemes (diabetes mellitus, chronic kidney disease, hepatitis C virus, fractures, cancer, dementia, atrial fibrillation, chronic obstructive pulmonary disease, mechanical ventilation, terminal illness, outpatients and community-dwelling patients), demonstrated that the implementation of integrated health care could not only provide benefits on survival, self-care ability, health quality, physical, and functional rehabilitation outcomes, but also significantly reduce medical utilization and expenditures.

Conclusion: The integrated health care system for multiple morbidities benefits the Taiwanese geriatric population in physical and functional outcomes. The thematic synthesis provides references for future rigorous clinical trials.

Keywords: Elderly; Integrated health care system; National health insurance program; Systematic review; Taiwan.

. 2022 Jun 8;S1076-6332(22)00311-7.

doi: 10.1016/j.acra.2022.05.009. Online ahead of print.

Quantitative CT Lung Imaging and Machine Learning Improves Prediction of Emergency Room Visits and Hospitalizations in COPD

Amir Moslemi[1], Kalysta Makimoto[1], Wan C Tan[2], Jean Bourbeau[3], James C Hogg[2], Harvey O Coxson[2], Miranda Kirby[4], Canadian Cohort of Obstructive Lung Disease

Affiliations expand

- PMID: 35690537

- DOI: 10.1016/j.acra.2022.05.009

Abstract

Rationale: Predicting increased risk of future healthcare utilization in chronic obstructive pulmonary disease (COPD) patients is an important goal for improving patient management.

Objective: Our objective was to determine the importance of computed tomography (CT) lung imaging measurements relative to other demographic and clinical measurements for predicting future health services use with machine learning in COPD.

Materials and methods: In this retrospective study, lung function measurements and chest CT images were acquired from Canadian Cohort of Obstructive Lung Disease study participants from 2010 to 2017 (https://clinicaltrials.gov, NCT00920348). Up to two follow-up visits (1.5- and 3-year follow-up) were performed and participants were asked for details related to healthcare utilization. Healthcare utilization was defined as any COPD hospitalization or emergency room visit due to respiratory problems in the 12 months prior to the follow-up visits. CT analysis was performed (VIDA Diagnostics Inc.); a total of 108 CT quantitative emphysema, airway and vascular measurements were investigated. A hybrid feature selection method with support vector machine classifier was used to predict healthcare utilization. Performance was determined using accuracy, F1-measure and area under the receiver operating characteristic curve (AUC) and Matthews's correlation coefficient (MC).

Results: Of the 527 COPD participants evaluated, 179 (35%) used healthcare services at follow-up. There were no significant differences between the participants with or without healthcare utilization at follow-up for age ($p = 0.50$), sex ($p = 0.44$), BMI ($p = 0.05$) or pack-years ($p = 0.76$). The accuracy for predicting subsequent healthcare utilization was 80% ± 3% (F1-measure = 74%, AUC = 0.80, MC = 0.6) when all measurements were considered, 76% ± 6% (F1-measure = 72%, AUC = 0.77, MC = 0.55) for CT measurements alone and 65% ± 5% (F1-measure = 60%, AUC = 0.67, MC = 0.34) for demographic and lung function measurements alone.

Conclusion: The combination of CT lung imaging and conventional measurements leads to greater prediction accuracy of subsequent health services use than conventional measurements alone, and may provide needed prognostic information for patients suffering from COPD.

Keywords: COPD; Computed tomography; Hospitalization; Machine learning; Quantitative imaging.

SUPPLEMENTARY INFO

Associated dataexpand

Proceed to details

Cite

Share

3

BMC Geriatr

. 2022 Jun 11;22(1):501.

doi: 10.1186/s12877-022-03169-2.

Effect of inpatient rehabilitation treatment ingredients on functioning, quality of life, length of stay, discharge destination, and mortality among older adults with unplanned admission: an overview review

K Lambe [1], S Guerra [1], G Salazar de Pablo [2], S Ayis [1], I D Cameron [3], N E Foster [4,5], E Godfrey [1,6], C L Gregson [7], F C Martin [1], C Sackley [1], N Walsh [8], K J Sheehan [9]

Affiliations expand

- PMID: 35689181

- PMCID: PMC9188066

- DOI: 10.1186/s12877-022-03169-2

Free PMC article

Abstract

Background: To synthesise the evidence for the effectiveness of inpatient rehabilitation treatment ingredients (versus any comparison) on functioning, quality of life, length of stay, discharge destination, and mortality among older adults with an unplanned hospital admission.

Methods: A systematic search of Cochrane Library, MEDLINE, Embase, PsychInfo, PEDro, BASE, and OpenGrey for published and unpublished systematic reviews of inpatient rehabilitation interventions for older adults following an unplanned admission to hospital from database inception to December 2020. Duplicate screening for eligibility, quality assessment, and data extraction including extraction of treatment components and their respective ingredients employing the Treatment Theory framework. Random effects meta-analyses were completed overall and by treatment ingredient. Statistical heterogeneity was assessed with the inconsistency-value (I^2).

Results: Systematic reviews (n = 12) of moderate to low quality, including 44 non-overlapping relevant RCTs were included. When incorporated in a rehabilitation intervention, there was a large effect of endurance exercise, early intervention and shaping knowledge on walking endurance after the inpatient stay versus comparison. Early intervention, repeated practice activities, goals and planning, increased medical care and/or discharge planning increased the likelihood of discharge home versus comparison. The evidence for activities of daily living (ADL) was conflicting. Rehabilitation interventions were not effective for functional mobility, strength, or quality of life, or reduce length of stay or mortality. Therefore, we did not explore the potential role of treatment ingredients for these outcomes.

Conclusion: Benefits observed were often for subgroups of the older adult population e.g., endurance exercise was effective for endurance in older adults with chronic obstructive pulmonary disease, and early intervention was effective for endurance for those with hip fracture. Future research should determine whether the effectiveness of these treatment ingredients observed in subgroups, are generalisable to older adults more broadly. There is a need for more transparent reporting of intervention components and ingredients according to established frameworks to enable future synthesis and/or replication.

Trial registration: PROSPERO Registration CRD42018114323 .

Keywords: Acute care; Exercise; Geriatrics; Hospital; Illness; Injury; Physiotherapy; Trauma.

Conflict of interest statement

KS received a grant from UK Research & Innovation Future Leaders Fellowship to support this work. This funding provides salary support for KS, KL, and SG. KS also received funding from the National Institutes of Health Research (NIHR) and Chartered Society of Physiotherapy Charitable Trust for hip fracture health services research. CS, NEF, NW and EG receive funding from the National Institute for Health Research (NIHR). CS and NEF are NIHR Senior Investigators. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care. CLG receives funding from Versus Arthritis (ref 22086). GSdP, SA, IDC, and FCM have no competing interests to declare.

- 67 references
- 2 figures

Review

Clin Respir J

. 2022 Jun 10.

doi: 10.1111/crj.13514. Online ahead of print.

Osteoporosis in COPD patients: Risk factors and pulmonary rehabilitation

Yujuan Li[1], Hongchang Gao[1], Lei Zhao[1], Jinrui Wang[1]

Affiliations expand

- PMID: 35688435

- DOI: 10.1111/crj.13514

Abstract

Objectives: To present a review on the pathogenesis, risk factor and treatment of chronic obstructive pulmonary disease complicated with osteoporosis and provide new ideas for the diagnosis and treatment.

Data source: A systematic search is carried out using keywords as chronic obstructive pulmonary disease, osteoporosis, risk factors, and pulmonary rehabilitation.

Results: Patients with chronic obstructive pulmonary disease have a high prevalence of osteoporosis and a high risk of fracture. The mechanisms of osteoporosis in COPD patients are associated with general risk factors, such as smoking, reduced physical activity, low weight, and disease-specific risk factors, such as systemic inflammatory, Vitamin D deficiency, use of glucocorticoid, anemia, hypoxemia, and hypercapnia. The treatment of osteoporosis in COPD

emphasizes comprehensive intervention, which mainly include basic treatment and anti-osteoporosis drugs. Noticeably, pulmonary rehabilitation program is an important part of treatment.

Conclusions: This work summarizes the pathogenesis, risk factor, prevention, and treatment of chronic obstructive pulmonary disease complicated with osteoporosis, and the latest progress of studies on chronic obstructive pulmonary disease and osteoporosis is discussed.

Keywords: chronic obstructive pulmonary disease; fracture; osteoporosis; prevalence; pulmonary rehabilitation; risk factors.

- 114 references

SUPPLEMENTARY INFO

Publication types, Grant supportexpand

FULL TEXT LINKS

WILEY Full Text Article

Proceed to details

Cite

Share

5

J Clin Med

-
-
-

. 2022 Jun 2;11(11):3181.

doi: 10.3390/jcm11113181.

Health-Screening-Based Chronic Obstructive Pulmonary Disease and Its Effect on Cardiovascular Disease Risk

Sang-Jun Lee[1 2 3], Sung-Soo Yoon[1 2 3], Myeong-Hoon Lee[1 2 3], Hye-Jun Kim[1 2 3], Yohwan Lim[1 2 3], Hyewon Park[1 2 3], Sun Jae Park[4], Seogsong Jeong[1 2 3], Hyun-Wook Han[1 2 3 5]

Affiliations expand

- PMID: 35683565

- PMCID: PMC9181412

- DOI: 10.3390/jcm11113181

Free PMC article

Abstract

Chronic obstructive pulmonary disease (COPD) is considered a major cause of death worldwide, and various studies have been conducted for its early diagnosis. Our work developed a scoring system by predicting and validating COPD and performed predictive model implementations. Participants who underwent a health screening between 2017 and 2020 were extracted from the Korea National Health and Nutrition Examination Survey (KNHANES) database. COPD individuals were defined as aged 40 years or older with prebronchodilator forced expiratory volume in 1 s/forced vital capacity (FEV1/FVC < 0.7). The logistic regression model was performed, and the C-index was used for variable selection. Receiver operating characteristic (ROC) curves with area under the curve (AUC) values were generated for evaluation. Age, sex, waist circumference and diastolic blood pressure were used to predict COPD and to develop a COPD score based on a multivariable model. A simplified model for COPD was validated with an AUC value of 0.780 from the ROC curves. In addition, we evaluated the association of the derived score with cardiovascular disease (CVD). COPD scores showed significant performance in COPD prediction. The developed score also showed a good effect on the diagnostic ability for CVD risk. In the future, studies comparing the diagnostic accuracy of the derived scores with standard diagnostic tests are needed.

Keywords: cardiovascular disease; chronic obstructive pulmonary disease; score system; self-diagnosis.

Conflict of interest statement

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

- 37 references
- 2 figures

SUPPLEMENTARY INFO

Grant supportexpand

FULL TEXT LINKS

FULL TEXT OPEN ACCESS MDPI

Review

J Clin Med

. 2022 Jun 2;11(11):3180.

doi: 10.3390/jcm11113180.

Hypercapnia in COPD: Causes, Consequences, and Therapy

Balázs Csoma [1], Maria Rosaria Vulpi [2], Silvano Dragonieri [2], Andrew Bentley [3], Timothy Felton [3], Zsófia Lázár [1], Andras Bikov [3]

Affiliations expand

- PMID: 35683563
- PMCID: PMC9181664
- DOI: 10.3390/jcm11113180

Free PMC article

Abstract

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disorder that may lead to gas exchange abnormalities, including hypercapnia. Chronic hypercapnia is an independent risk factor of mortality in COPD, leading to epithelial dysfunction and impaired lung immunity. Moreover, chronic hypercapnia affects the cardiovascular physiology, increases the risk of cardiovascular morbidity and mortality, and promotes muscle wasting and musculoskeletal abnormalities. Noninvasive ventilation is a widely used technique to remove carbon dioxide, and several studies have investigated its role in COPD. In the present review, we aim to summarize the causes and effects of chronic hypercapnia in COPD. Furthermore, we discuss the use of domiciliary

noninvasive ventilation as a treatment option for hypercapnia while highlighting the controversies within the evidence. Finally, we provide some insightful clinical recommendations and draw attention to possible future research areas.

Keywords: airway immunity; chronic obstructive pulmonary disease; hypercapnia; noninvasive ventilation.

Conflict of interest statement

The authors declare no conflict of interest.

- 153 references
- 3 figures

SUPPLEMENTARY INFO

Publication types, Grant supportexpand

FULL TEXT LINKS

FULL TEXT OPEN ACCESS MDPI

Proceed to details

Cite

Share

7

Respir Res

-
-
-

. 2022 Jun 8;23(1):148.

doi: 10.1186/s12931-022-02072-z.

Blocking P2X purinoceptor 4 signalling alleviates cigarette smoke induced pulmonary inflammation

Sven Schneider [1], Irmgard Merfort [2], Marco Idzko [3], Andreas Zech [4]

Affiliations expand

- PMID: 35676684

- PMCID: PMC9175376

- DOI: 10.1186/s12931-022-02072-z

Free PMC article

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is associated with elevated ATP levels in the extracellular space. Once released, ATP serves as danger signal modulating immune responses by activating purinergic receptors. Accordingly, purinergic signalling has been implicated in respiratory inflammation associated with cigarette smoke exposure. However, the role of P2X4-signalling has not been fully elucidated yet.

Methods: Here, we analysed the P2X4 mRNA expression in COPD patients as well as cigarette smoke-exposed mice. Furthermore, P2X4-signalling was blocked by either using a specific antagonist or genetic depletion of P2rx4 in mice applied to an acute and prolonged model of cigarette smoke exposure. Finally, we inhibited P2X4-signalling in macrophages derived from THP-1 before stimulation with cigarette smoke extract.

Results: COPD patients exhibited an increased P2X4 mRNA expression in cells isolated from the bronchoalveolar lavage fluid and peripheral mononuclear cells. Similarly, P2rx4 expression was elevated in lung tissue of mice exposed to cigarette smoke. Blocking P2X4-signalling in mice alleviated cigarette smoke induced airway inflammation as well as lung parenchyma destruction. Additionally, human macrophages derived from THP-1 cells released reduced concentrations of proinflammatory cytokines in response to cigarette smoke extract stimulation when P2X4 was inhibited.

Conclusion: Taken together, we provide evidence that P2X4-signalling promotes innate immunity in the immunopathologic responses induced by cigarette smoke exposure.

Conflict of interest statement

The authors declare that they have no competing interests.

- 48 references
- 4 figures

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS

Read free full text at BMC

Respir Med

. 2022 May 31;106895.

doi: 10.1016/j.rmed.2022.106895. Online ahead of print.

Non-respiratory symptom dominance is associated with depression in patients with chronic obstructive pulmonary disease

Yoko Hamakawa [1], Susumu Sato [2], Naoya Tanabe [3], Chin Kook Rhee [4], Ki-Suck Jung [5], Kwang Ha Yoo [6], Kazuya Tanimura [7], Shigeo Muro [8], Toyohiro Hirai [9]

Affiliations expand

- PMID: 35672183

- DOI: 10.1016/j.rmed.2022.106895

Abstract

Introduction: Depression is a common and important comorbidity in patients with chronic obstructive pulmonary disease (COPD). Depressive status is associated with a high COPD assessment test (CAT) total score, but it is difficult to distinguish patients with depression from those with severe symptomatic COPD. We hypothesized that a non-respiratory symptom-dominant elevation in CAT score is associated with depression in patients with COPD.

Methods: A total of 226 patients in the KYOTO cohort in Japan and 924 patients in the Korea COPD Subgroup Study (KOCOSS) cohort in the Republic of Korea were analyzed. Depression was diagnosed based on a PHQ-9 (patient health questionnaire-9) ≥5 in the KYOTO cohort and a BDI-II (Beck Depression Inventory-II) ≥17 in the KOCOSS cohort. Sums of respiratory symptoms (Q1-Q4; Q1234) and non-respiratory symptoms (Q5-Q8; Q5678) from CAT items were analyzed.

Results: Fifty-three (23.5%) patients in the KYOTO cohort and 111 (11.2%) patients in the KOCOSS cohort were identified as having depression. Fifty-five patients (24.3%) in the KYOTO cohort and 249 patients (26.9%) in the KOCOSS cohort showed non-respiratory symptom dominance (Q1234 ≤ Q5678), and they had a significantly higher prevalence of depression than did patients with respiratory symptom dominance (Q1234 > Q5678). Multivariable logistic regression

analysis showed that both the CAT total score and Q1234 ≤ Q5678 were significantly associated with depression in both cohorts. Moreover, even in symptomatic patients (CAT total score ≥10), these significant associations were preserved.

Conclusion: Non-respiratory symptom dominance in CAT is a suspicious feature for depression in patients with COPD.

Radiology

. 2022 Jun 7;212071.

doi: 10.1148/radiol.212071. Online ahead of print.

Deep Learning Prediction of Survival in Patients with Chronic Obstructive Pulmonary Disease Using Chest Radiographs

Ju Gang Nam[#1], Hye-Rin Kang[#1], Sang Min Lee[1], Hyungjin Kim[1], Chanyoung Rhee[1], Jin Mo Goo[1], Yeon-Mok Oh[1], Chang-Hoon Lee[#1], Chang Min Park[#1]

Affiliations expand

- PMID: 35670713

- DOI: 10.1148/radiol.212071

Abstract

Background Preexisting indexes for predicting the prognosis of chronic obstructive pulmonary disease (COPD) do not use radiologic information and are impractical because they involve complex history assessments or exercise tests. Purpose To develop and to validate a deep learning-based survival prediction model in patients with COPD (DLSP) using chest radiographs, in addition

to other clinical factors. Materials and Methods In this retrospective study, data from patients with COPD who underwent postbronchodilator spirometry and chest radiography from 2011-2015 were collected and split into training (n = 3475), validation (n = 435), and internal test (n = 315) data sets. The algorithm for predicting survival from chest radiographs was trained (hereafter, $DLSP_{CXR}$), and then age, body mass index, and forced expiratory volume in 1 second (FEV_1) were integrated within the model (hereafter, $DLSP_{integ}$). For external test, three independent cohorts were collected (n = 394, 416, and 337). The discrimination performance of $DLSP_{CXR}$ was evaluated by using time-dependent area under the receiver operating characteristic curves (TD AUCs) at 5-year survival. Goodness of fit was assessed by using the Hosmer-Lemeshow test. Using one external test data set, $DLSP_{integ}$ was compared with four COPD-specific clinical indexes: BODE, ADO, COPD Assessment Test (CAT), and St George's Respiratory Questionnaire (SGRQ). Results $DLSP_{CXR}$ had a higher performance at predicting 5-year survival than FEV_1 in two of the three external test cohorts (TD AUC: 0.73 vs 0.63 [P = .004]; 0.67 vs 0.60 [P = .01]; 0.76 vs 0.77 [P = .91]). $DLSP_{CXR}$ demonstrated good calibration in all cohorts. The $DLSP_{integ}$ model showed no differences in TD AUC compared with BODE (0.87 vs 0.80; P = .34), ADO (0.86 vs 0.89; P = .51), and SGRQ (0.86 vs 0.70; P = .09), and showed higher TD AUC than CAT (0.93 vs 0.55; P < .001). Conclusion A deep learning model using chest radiographs was capable of predicting survival in patients with chronic obstructive pulmonary disease. © RSNA, 2022 *Online supplemental material is available for this article.*

Respiration

. 2022 Jun 3;1-7.

doi: 10.1159/000524845. Online ahead of print.

Reversibility of Hypercapnia after an Acute Exacerbation of COPD

Jens Bräunlich [1,2], Kristin Turba [2], Hubert Wirtz [2]

Affiliations expand

- PMID: 35665699

- DOI: 10.1159/000524845

Free article

Abstract

Background: After an episode of hypercapnic AECOPD, some patients show reversible, prolonged or persistent hypercapnic respiratory failure. However, at the time of patient discharge, it is uncertain whether patients will remain hypercapnic or may return to a physiologic gas status.

Methods: Data were retrospectively collected from COPD patients with an acute hypercapnic exacerbation (AECOPD). Out of 143 total COPD inpatients, complete data set was available for 82 patients in stable condition. According to the first available capillary or arterial pCO2, patients were divided into those with persistent hypercapnia (PHG) and those with reversible hypercapnia.

Results: In this study, 51% of patients with acute hypercapnic AECOPD and follow-up (FUP) visits developed normocapnia after a time period of several weeks. These patients were characterized by lower carbon dioxide partial pressure (PaCO2), HCO3-, and BE levels prior to the AECOPD event, at discharge and at FUP. pH was higher at discharge and FUP in this group. Greater disease severity and lower forced vital capacity were prominent in patients with PHG. Binary logistic regression revealed GOLD D and higher PaCO2 at discharge as predicting factors for PHG.

Conclusions: A large percentage of patients has prolonged hypercapnia following acute hypercapnic COPD exacerbation. The risk profile of patients with irreversible hypercapnia should be carefully evaluated following AECOPD in order to choose selected patients for home-noninvasive ventilation.

Keywords: Chronic obstructive pulmonary disease; Exacerbations; Noninvasive ventilation; Respiratory muscles.

. 2022 Jun 4;1-6.

doi: 10.1007/s00063-022-00934-4. Online ahead of print.

Relationship between clinical anxiety and patient outcomes in patients with chronic obstructive lung disease exacerbation in the emergency department

Mehmet Furkan Yaldizkaya [1], Nurettin Özgür Doğan [1], İbrahim Ulaş Özturan [2], Elif Yaka [1], Serkan Yilmaz [1], Murat Pekdemir [1]

Affiliations expand

- PMID: 35661228

- PMCID: PMC9166224

- DOI: 10.1007/s00063-022-00934-4

Free PMC article

Abstract

in English, German

Purpose: Anxiety is a comorbidity that is not routinely addressed in patients with chronic obstructive lung disease (COPD) exacerbation in the emergency department (ED). Anxiety in patients with COPD exacerbation can be related with negative outcomes. The Generalized Anxiety Disorder 7 (GAD-7) score is an easy-to-use tool to determine anxiety. This study aimed to investigate the relationship between GAD-7 score and patient outcomes in patients with COPD exacerbation in the ED.

Methods: A prospective, cross-sectional study was conducted in a tertiary academic ED between July 2019 and January 2021. Patients admitted to the ED with COPD exacerbation were included. A GAD-7 score of ≥ 10 was defined as clinically significant anxiety. Negative outcomes were defined as a composite outcome that included recurrent ED visits, intensive care unit admission, and mortality. The relationship between clinically significant anxiety and negative outcomes within 30 days was determined.

Results: A total of 92 patients were assessed for eligibility and 80 were included in the study. Thirty-seven patients (46.3%) experienced negative outcomes. Although no significant difference was detected in median GAD-7 scores between patients with positive and negative outcomes, negative outcomes were significantly higher in patients who had a GAD-7 score of ≥ 10 (n = 25, p = 0.03). A sensitivity of 43.2%, specificity of 79.1%, positive likelihood ratio of 2.1 and negative likelihood ratio of 0.7 were determined for GAD-7 score in predicting negative outcome.

Conclusion: In patients with COPD exacerbation in the ED, a GAD-7 score of ≥ 10 was associated with 30-day negative outcomes.

Keywords: COPD exacerbation; Chronic obstructive pulmonary disease; Emergency department; GAD-7; Generalized anxiety disorder.

Conflict of interest statement

M.F. Yaldizkaya, N.Ö. Doğan, İ.U. Özturan, E. Yaka, S. Yilmaz and M. Pekdemir declare that they have no competing interests.

- 18 references
- 2 figures

doi: 10.1164/rccm.202201-0206OC. Online ahead of print.

Clinical Trial of Losartan for Pulmonary Emphysema: Pulmonary Trials Cooperative LEEP Trial

Robert A Wise [1], Janet T Holbrook [2], Robert H Brown [3], Gerard J Criner [4], Mark T Dransfield [5], Jiaxian He [6], Robert J Henderson [7], David A Kaminsky [8], Robert J Kaner [9], Stephen C Lazarus [10], Barry J Make [11], Meredith C McCormack [12], Enid R Neptune [13], Loretta G Que [14], American Lung Association Airways Clinical Research Centers and Pulmonary Trials Cooperative

Affiliations expand

- PMID: 35649189

- DOI: 10.1164/rccm.202201-0206OC

Abstract

Rationale: There are no pharmacologic agents that modify emphysema progression in patients with chronic obstructive pulmonary disease (COPD).

Objective: Evaluate the efficacy of losartan, an angiotensin receptor blocker (ARB), to reduce emphysema progression.

Methods: The trial was a multicenter randomized placebo-controlled trial, conducted between May 2017 and January 2021. Eligible participants were age ≥40, had moderate to severe airflow obstruction, ≥10 pack-years smoking, mild-moderate emphysema on high-resolution computed tomography (HRCT), and no medical indication for or intolerance of ARBs. Treatment with losartan, 100 mg daily, or matching placebo (1:1) was randomly assigned. The primary outcome was emphysema progression on HRCT over 48 weeks. Secondary outcomes included St George's Respiratory Questionnaire (SGRQ), modified Medical Research Council dyspnea scale, COPD Assessment Test, Physical Function-Short Form 20a (PROMIS 20a).

Results: 220 participants were enrolled; 58% were men, 19% were African American; and 24% current smokers. The medians (interquartile ranges) for age were as 65 (61, 73) years, and 48 (36, 59) for percent predicted FEV1 post-bronchodilator. The mean (95% confidence interval) percent emphysema progression was 1.35% (0.67, 2.03) in the losartan group vs 0.66% (0.09, 1.23) in placebo (P = NS).

Conclusions: Losartan did not prevent emphysema progression in people with COPD with mild-moderate emphysema. Clinical trial registration available at www.

Clinicaltrials: gov, ID: NCT02696564.

Keywords: Angiotensin Receptor Blocker; Emphysema; clinical trial; losartan; quantitative image analysis.

13

Editorial

Ann Am Thorac Soc

. 2022 Jun;19(6):897-899.

doi: 10.1513/AnnalsATS.202202-152ED.

Comorbid Chronic Obstructive Pulmonary Disease and Heart Failure: Shared Risk Factors and Opportunities to Improve Outcomes

Sadiya S Khan[1,2], Ravi Kalhan[2,3]

Affiliations expand

- PMID: 35648080
- PMCID: PMC9169135
- DOI: 10.1513/AnnalsATS.202202-152ED

Free PMC article

No abstract available

Comment on

- Differences in Outcomes between Heart Failure Phenotypes in Patients with Coexistent Chronic Obstructive Pulmonary Disease: A Cohort Study.
  Gulea C, Zakeri R, Quint JK. Ann Am Thorac Soc. 2022 Jun;19(6):971-980. doi: 10.1513/AnnalsATS.202107-823OC. PMID: 34905461

- 14 references
- 2 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

FULL TEXT LINKS

Am J Respir Crit Care Med

. 2022 Jun 1;205(11):P22-P24.

doi: 10.1164/rccm.20511P22.

Sudden Breathlessness

Ann Schneidman, Lynn Reinke, DorAnne Donesky, Virginia Carrieri-Kohlman

- PMID: 35647927

- DOI: 10.1164/rccm.20511P22

No abstract available

. 2022 Jun 7;1-9.

doi: 10.1080/02770903.2022.2082307. Online ahead of print.

Nebulizer versus metered dose inhaler with space chamber (MDI spacer) for acute asthma and chronic obstructive pulmonary disease exacerbation: attitudes of patients and healthcare providers in the COVID-19 era

Rayan Alsuwaigh [1], Yan Cao [2], Youxin Puan [1], Anthony Yii [1], Soyah Binti Mohamed Noor [2], Hui Ye [2], Haijuan Chen [2], Xiao Ling Li [2], Norlidah Binte Mohd Noor [2], Jason Liew [1], Tunn Ren Tay [1]

Affiliations expand

- PMID: 35608065

- DOI: 10.1080/02770903.2022.2082307

Abstract

Objective: Short-acting bronchodilators for asthma and chronic obstructive pulmonary disease (COPD) exacerbations are commonly delivered by nebulizers although administration using metered dose inhaler with space chamber (MDI spacer) has been shown to be equally efficacious. There are few studies examining patients' and healthcare providers' attitudes on the two administration methods in adults. This study explores patients' and healthcare providers' attitudes on the use of nebulizer versus MDI spacer for acute asthma and COPD exacerbations in adults.**Method**s: Patients admitted for asthma or COPD exacerbations, doctors, and nurses in a university-affiliated hospital were surveyed from 1 April 2021 to 30 September 2021 regarding their views on the effectiveness, ease of use, preparation and administration, side effects, and infection risk of the two administration methods.

Results: Ninety-nine patients, 103 doctors, and 650 nurses completed the survey. 60.6% of patients perceived nebulizer to be more effective. Patients who found nebulizer more comfortable were more likely to prefer nebulizer (OR 43.97, $p = 0.01$), while those who associated it with a greater infection risk were less likely to prefer nebulizer (OR 0.15, $p = 0.03$). 49.5% of doctors and 49.1% of nurses perceived nebulizer to be more effective, compared to 10.7% and 34.5%, respectively, for MDI spacer. Effectiveness and patient comfort influenced doctors' and nurses' preference for nebulizer while ease of preparation and administration influenced nurses' preference only.

Conclusions: Patients and healthcare providers perceived nebulizer to be more effective. Factors unique to each group influenced their preference for nebulizer.

Keywords: Bronchodilator; administration; attitude; infection risk; preference.

Respir Care

. 2022 Jun;67(6):750-755.

doi: 10.4187/respcare.10059.

The Changing Definition and Perception of COPD

David M Mannino [1]

Affiliations expand

- PMID: 35606006

- DOI: 10.4187/respcare.10059

Abstract

COPD remains one of the leading causes of death worldwide. The impact of smoking and air pollution remain important causative factors. Traditional classification of COPD includes the overlap of emphysema, chronic bronchitis and asthma. More recently the COPDGene definition includes the terms possible, probable and definite COPD. These are supported by findings from exposures, symptoms, spirometry and radiologic imaging. This new approach can lead to earlier diagnosis and modification of risk factors, earlier therapeutic intervention and improved treatments of established disease.

Keywords: COPD; definition; epidemiology; outcomes.

Conflict of interest statement

Dr Mannino discloses relationships with GlaxoSmithKline and the COPD Foundation.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

Proceed to details

Cite

Share

17

Intern Emerg Med

-
-
-

. 2022 Jun;17(4):953-955.

doi: 10.1007/s11739-022-02964-4. Epub 2022 May 17.

Persistent asthma hospitalisations and deaths require a national asthma prevention plan

Bianca Beghé [1], Leonardo Fabbri [2], Enrico Clini [3]

Affiliations expand

- PMID: 35578148

- DOI: 10.1007/s11739-022-02964-4

No abstract available

Keywords: Allergy; Anaphylaxixs; Bronchitis; Chronic obstructive pulmonary disease; Emphysema.

- 21 references

SUPPLEMENTARY INFO

MeSH termsexpand

Lancet Digit Health

. 2022 Jun;4(6):e445-e454.

doi: 10.1016/S2589-7500(22)00045-0. Epub 2022 May 10.

Predicting hospitalisation for heart failure and death in patients with, or at risk of, heart failure before first hospitalisation: a retrospective model development and external validation study

Joshua Bradley [1], Erik B Schelbert [2], Laura J Bonnett [3], Gavin A Lewis [1], Jakub Lagan [1], Christopher Orsborne [1], Pamela F Brown [1], Josephine H Naish [4], Simon G Williams [1], Theresa McDonagh [5], Matthias Schmitt [1], Christopher A Miller [6]

Affiliations expand

- PMID: 35562273

- DOI: 10.1016/S2589-7500(22)00045-0

Free article

Abstract

Background: Identifying people who are at risk of being admitted to hospital (hospitalised) for heart failure and death, and particularly those who have not previously been hospitalised for heart failure, is a priority. We aimed to develop and externally validate a prognostic model involving contemporary deep phenotyping that can be used to generate individual risk estimates of hospitalisation for heart failure or all-cause mortality in patients with, or at risk of, heart failure, but who have not previously been hospitalised for heart failure.

Methods: Between June 1, 2016, and May 31, 2018, 3019 consecutive adult patients (aged ≥16 years) undergoing cardiac magnetic resonance (CMR) at Manchester University National Health Service Foundation Trust, Manchester, UK, were prospectively recruited into a model development cohort. Candidate predictor variables were selected according to clinical practice and literature review. Cox proportional hazards modelling was used to develop a prognostic model. The final model was validated in an external cohort of 1242 consecutive adult patients undergoing CMR at the University of Pittsburgh Medical Center Cardiovascular Magnetic Resonance Center, Pittsburgh, PA, USA, between June 1, 2010, and March 25, 2016. Exclusion criteria for both cohorts included previous hospitalisation for heart failure. Our study outcome was a composite of first hospitalisation for heart failure or all-cause mortality after CMR. Model performance was evaluated in both cohorts by discrimination (Harrell's C-index) and calibration (assessed graphically).

Findings: Median follow-up durations were 1118 days (IQR 950-1324) for the development cohort and 2117 days (1685-2446) for the validation cohort. The composite outcome occurred in 225 (7·5%) of 3019 patients in the development cohort and in 219 (17·6%) of 1242 patients in the validation cohort. The final, externally validated, parsimonious, multivariable model comprised the predictors: age, diabetes, chronic obstructive pulmonary disease, N-terminal pro-B-type natriuretic peptide, and the CMR variables, global longitudinal strain, myocardial infarction, and myocardial extracellular volume. The median optimism-adjusted C-index for the externally validated model across 20 imputed model development datasets was 0·805 (95% CI 0·793-0·829) in the development cohort and 0·793 (0·766-0·820) in the external validation cohort. Model calibration was excellent across the full risk profile. A risk calculator that provides an estimated risk of hospitalisation for heart failure or all-cause mortality at 3 years after CMR for individual patients was generated.

Interpretation: We developed and externally validated a risk prediction model that provides accurate, individualised estimates of the risk of hospitalisation for heart failure and all-cause mortality in patients with, or at risk of, heart failure, before first hospitalisation. It could be used to direct intensified therapy and closer follow-up to those at increased risk.

Funding: The UK National Institute for Health Research, Guerbet Laboratories, and Roche Diagnostics International.

Conflict of interest statement

Declaration of interests EBS serves as an adviser for HAYA Therapeutics and consults for PureTech Health. PFB was in receipt of a Joint Alliance Medical and University Hospital of South Manchester Fellowship Salary Support Grant. JHN has a part-time appointment at Bioxydyn. TM serves as the clinical lead for the National Heart Failure Audit and has received speaker fees from Novartis, AstraZeneca, and Vifor. CAM has served on advisory boards for Novartis, Boehringer Ingelheim and Lilly Alliance, and AstraZeneca; serves as an adviser for HAYA Therapeutics and PureTech Health; and has received research support from Amicus Therapeutics, Guerbet Laboratories, Roche, and Univar Solutions (none are relevant to the contents of this Article, except where described in the Role of the funding source). All other authors declare no competing interests.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

ELSEVIER
OPEN ACCESS

Proceed to details

Cite

Share

19

Review

Lancet

-
-
-

. 2022 Jun 11;399(10342):2227-2242.

doi: 10.1016/S0140-6736(22)00470-6. Epub 2022 May 6.

Chronic obstructive pulmonary disease

Stephanie A Christenson[1], Benjamin M Smith[2], Mona Bafadhel[3], Nirupama Putcha[4]

Affiliations expand

- PMID: 35533707

- DOI: 10.1016/S0140-6736(22)00470-6

Abstract

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity, mortality, and health-care use worldwide. COPD is caused by exposure to inhaled noxious particles, notably tobacco smoke and pollutants. However, the broad range of factors that increase the risk of development and progression of COPD throughout the life course are increasingly being recognised. Innovations in omics and imaging techniques have provided greater insight into disease pathobiology, which might result in advances in COPD prevention, diagnosis, and treatment. Although few novel treatments have been approved for COPD in the past 5 years, advances have been made in targeting existing therapies to specific subpopulations using new biomarker-based strategies. Additionally, COVID-19 has undeniably affected individuals with COPD, who are not

only at higher risk for severe disease manifestations than healthy individuals but also negatively affected by interruptions in health-care delivery and social isolation. This Seminar reviews COPD with an emphasis on recent advances in epidemiology, pathophysiology, imaging, diagnosis, and treatment.

Conflict of interest statement

Declaration of interests SAC reports grant funding paid to her institution from the National Institutes of Health (NIH) and Merck; consulting fees paid from AstraZeneca, GlaxoSmithKline, and Glenmark Pharmaceuticals; payment and honoraria paid from AstraZeneca, Sanofi/Regeneron, Genentech, and Sunovion; and participation in advisory boards or Data and Safety Monitoring Boards (DSMBs) for AstraZeneca, GlaxoSmithKline, Sanofi/Regeneron, and Glenmark Pharmaceuticals. BMS reports grants paid to their institution from NIH, Canadian Institutes of Health Research, Canadian Lung Association, Quebec Respiratory Health Research Network, and McGill University Health Centre Foundation, and leadership as director for the Centre for Outcomes and Research Evaluation of the McGill University Health Centre Research Institute. MB reports grants paid to their institution from AstraZeneca and Roche; consulting fees paid to their institution from AstraZeneca and GlaxoSmithKline; honoraria paid to their institution from AstraZeneca, Boehringer Ingelheim, and GlaxoSmithKline; and participation in advisory boards or DSMBs with fees paid to their institution from AstraZeneca and GlaxoSmithKline. NP reports research funding paid to their institution from NIH and CSL Behring, and participation in advisory boards for CSL Behring and Pharmacosmos.

. 2022 Jun;197:106857.

doi: 10.1016/j.rmed.2022.106857. Epub 2022 Apr 22.

Relationship between prior inhaled corticosteroid use and benefits ofbudesonide/glycopyrronium/formoterol fumarate dihydrate on exacerbations, symptoms, health-related quality of life, and lung function in patients with chronic obstructive pulmonary disease: Analyses from the ETHOS study

Dave Singh [1], Klaus F Rabe [2], Fernando J Martinez [3], Matthias Krüll [4], Martin Jenkins [5], Mehul Patel [5], Paul Dorinsky [6]

Affiliations expand

- PMID: 35512458

- DOI: 10.1016/j.rmed.2022.106857

Free article

Abstract

Background: In the Phase III ETHOS study (NCT02465567), budesonide/glycopyrronium/formoterol fumarate dihydrate (BGF) triple therapy at two inhaled corticosteroid (ICS) doses reduced moderate/severe exacerbation rates and improved symptoms, health-related quality of life (HRQoL), and lung function versus glycopyrronium/formoterol fumarate dihydrate (GFF) or budesonide/formoterol fumarate dihydrate (BFF) dual therapy in patients with moderate-to-very-severe chronic obstructive pulmonary disease (COPD). Here, we assessed whether the benefit for BGF versus GFF was driven by patients who received ICS before randomization to GFF.

Methods: ETHOS was a 52-week, randomized, double-blind, multicenter, parallel-group study in symptomatic patients with COPD and ≥1 moderate/severe exacerbation in the previous year. Patients received BGF 320/14.4/10 μg, BGF 160/14.4/10 μg, GFF 14.4/10 μg, or BFF 320/10 μg twice daily via a single metered dose Aerosphere™ inhaler. In these subgroup analyses, efficacy and safety were assessed in patients with or without prior ICS use in the 30 days before screening.

Results: The modified intent-to-treat population comprised 8509 patients (prior ICS use, n = 6810 [80%]; no prior ICS use, n = 1699 [20%]). Moderate/severe exacerbation rates were reduced by 24% and 23% in patients with and without prior ICS use, respectively, with BGF 320 versus GFF. Benefits of BGF 320 versus GFF were also similar in patients with and without prior ICS use across other endpoints relating to exacerbations, symptoms, HRQoL, lung function, and safety. Trends were similar for BGF 160 versus GFF.

Conclusion: Benefits on exacerbations, symptoms, HRQoL, and lung function with BGF versus GFF were observed, irrespective of prior ICS use in the 30 days before screening.

Keywords: Budesonide/glycopyrronium/formoterol fumarate dihydrate; Chronic obstructive pulmonary disease; Inhaled corticosteroids; Triple therapy.

Respir Care

. 2022 Jun;67(6):667-675.

doi: 10.4187/respcare.09446. Epub 2022 May 3.

Multidisciplinary Care and Prognosis in Patients With COPD and Interstitial Lung Disease Prescribed Long-Term Oxygen Therapy

Amelia Ca Harrison [1], Julien F Robinson [1], Laura Tu [2], Christine F McDonald [3], Yet Hong Khor [4]

Affiliations expand

- PMID: 35504724

- DOI: 10.4187/respcare.09446

Abstract

Background: Home oxygen therapy is prescribed for patients with advanced lung disease based on the criteria established in landmark trials in subjects with COPD. In clinical practice, its use has been extrapolated to other diseases, including interstitial lung disease (ILD). Patients with COPD and ILD experience a high symptom burden and require access to specialized multidisciplinary

care. We aimed to evaluate the health-related outcomes and supportive care needs of patients with COPD and ILD receiving home oxygen therapy.

Methods: This was a retrospective cohort study using the oxygen database of a quaternary metropolitan teaching hospital. Patients with a diagnosis of COPD or ILD who were prescribed home oxygen therapy between January 2012-December 2018 were identified. Demographic information, results of physiologic testing, comorbidities, hospitalizations, and mortality data were collected.

Results: Three hundred and eighty-four subjects were included for analysis, of whom 56% were male. The median age was 75 y. The majority (59%) had a diagnosis of COPD. Long-term oxygen therapy (LTOT) was prescribed for 187 (48.7%), with no significant demographic differences between those with COPD or ILD. Another 187 were prescribed ambulatory oxygen alone, with 55 transitioning to LTOT during the study period. Most subjects (65.4%) were referred for pulmonary rehabilitation; however, palliative care referrals were generally low (22.9%). Referrals to other medical specialties and allied health were common (82%). Transplant-free survival after commencement of LTOT was poor, with 38% of subjects surviving at 5 y. The 5-y survival of subjects with ILD after commencing on LTOT was 10% compared to 52% for those with COPD. Multivariable Cox regression analyses showed that the only predictor of survival after commencing LTOT was the principal respiratory diagnosis.

Conclusions: This study found that subjects prescribed LTOT had poor transplant-free survival after initiation, which was significantly worse for those with ILD compared to those with COPD. Despite their poor overall survival, worse than many cancers, only a minority were referred for palliative care input. Referrals to pulmonary rehabilitation were also suboptimal. This patient population had complex care needs requiring multidisciplinary management. Appropriate and early referrals to palliative care and improved care coordination for this complex group of patients are key areas for improvement in clinical practice.

Keywords: COPD; ambulatory oxygen therapy; interstitial lung disease; long-term oxygen therapy.

Conflict of interest statement

Dr Khor discloses relationships with Air Liquide Healthcare, Boehringer Ingelheim, and Roche. Dr McDonald discloses relationships with Air Liquide Healthcare and Menarini. The remaining authors have disclosed no conflicts of interest.

Geriatr Gerontol Int

-
-
-

. 2022 Jun;22(6):471-476.

doi: 10.1111/ggi.14390. Epub 2022 Apr 29.

Development and validation of a predictive risk model for frailty in elderly patients with multimorbidity

Fengmei Huang[#1], Xiaoling Yang[#1], Li Yuan[1], Miye Wang[2,3], Rao Li[1], Ziwei Ye[1], Jing Lv[1], Ting He[1]

Affiliations expand

- PMID: 35485599

- DOI: 10.1111/ggi.14390

Abstract

Aims: This study aimed to investigate the influencing factors of frailty in elderly patients with multimorbidity and to develop a predictive risk model for frailty in elderly patients with multimorbidity.

Methods: In total, 3836 elderly patients with multimorbidity who were admitted to the medical wards of five grade A tertiary hospitals in Sichuan Province from March 2020 to June 2021 were selected. Based on the general data of patients with multimorbidity, the independent risk factors for frailty were obtained using logistic analysis, and a risk prediction model of frailty was developed.

Results: Independent risk factors for frailty in patients with multimorbidity were age, types of medication, and comorbidity with chronic heart failure (CHF), chronic obstructive pulmonary disease (COPD) and chronic cerebrovascular disease (CCVD); and the protective factors for frailty were body mass index (BMI), exercise and education level. The expression of the model was Z = -2.054 + 0.016 × age - 0.029 × BMI - 0.153 × education level-1.059 × exercise + 0.203 × types of medication + 0.788 × comorbidity with CHF + 0.950 × comorbidity with COPD + 0.363 × comorbidity with CCVD.

Conclusion: Age, BMI, education level, exercise, types of medication, and comorbidity with CHF, COPD and CCVD can affect frailty risk in elderly patients with multimorbidity, which may be helpful to predict the frailty risk of elderly patients with multimorbidity. Geriatr Gerontol Int 2022; 22: 471-476.

Keywords: elderly; frailty; multimorbidity; prediction; risk model.

- 29 references

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

FULL TEXT LINKS

Proceed to details

Cite

Share

23

Respir Med

-
-
-

. 2022 Jun;197:106807.

doi: 10.1016/j.rmed.2022.106807. Epub 2022 Mar 18.

Adherence and persistence to once-daily single-inhaler versus multiple-inhaler triple therapy among patients with chronic obstructive pulmonary disease in the USA: A real-world study

David Mannino [1], Michael Bogart [2], Benjamin Wu [3], Guillaume Germain [4], François Laliberté [5], Sean D MacKnight [6], Young Jung [7], Marjorie Stiegler [8], Mei Sheng Duh [9]

Affiliations expand

- PMID: 35429764

- DOI: 10.1016/j.rmed.2022.106807

Free article

Abstract

Background: Triple therapy comprising an inhaled corticosteroid, long-acting muscarinic antagonist, and long-acting β_2 agonist (ICS/LAMA/LABA) is recommended for chronic obstructive pulmonary disease (COPD) patients at risk of exacerbation. Multiple-inhaler triple therapy (MITT) is associated with poor adherence and persistence; however, these outcomes have not been evaluated for single-inhaler fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI).

Methods: This retrospective analysis of the IQVIA PharMetrics Plus claims database identified patients with COPD initiating triple therapy between 18 September 2017 and 30 June 2019. The first date of single-inhaler FF/UMEC/VI dispensing, or first day of overlapping ICS, LAMA, and LABA medications for MITT users, defined the index date. Patients were ≥40 years, had ≥12 months of continuous insurance coverage pre-index (baseline) and ≥6 months' coverage post-index; those with MITT during baseline were excluded. Inverse probability weighting was used to balance baseline characteristics. Adherence was assessed using proportion of days covered (PDC) and was evaluated using linear and log-binomial models. Persistence (non-persistence identified as >30-day gap between fills) was evaluated using Cox models.

Results: 9942 patients (FF/UMEC/VI: 2782; MITT: 7160) were included. Adherence was significantly higher for FF/UMEC/VI versus MITT users (mean PDC, 0.66 vs. 0.48; $p < 0.001$), and FF/UMEC/VI users were twice as likely to be adherent (PDC ≥0.8) than MITT users (46.5% vs. 22.3%; risk ratio [95% CI]: 2.08 [1.85-2.30]; $p < 0.001$). After 12 months, significantly more FF/UMEC/VI users persisted on therapy than MITT users (35.7% vs. 13.9%; hazard ratio [95% CI]: 1.91 [1.81-2.01]; $p < 0.001$).

Conclusions: COPD patients initiating single-inhaler FF/UMEC/VI had significantly improved adherence and persistence compared with MITT.

Keywords: Chronic obstructive pulmonary disease; Medication adherence; Multiple-inhaler triple therapy; Persistence; Single-inhaler triple therapy.

. 2022 Jun;197:106833.

doi: 10.1016/j.rmed.2022.106833. Epub 2022 Apr 7.

Chronic obstructive pulmonary disease is associated with a higher risk of functional gastrointestinal disorders

Yu-Chi Chiu [1], Wei-Pin Chang [2], Gau-Jun Tang [3], Tzuo-Yun Lan [4], Kang-Yun Lee [5], Vincent Yi-Fong Su [6]

Affiliations expand

- PMID: 35427844

- DOI: 10.1016/j.rmed.2022.106833

Abstract

Rationale: The association between chronic obstructive pulmonary disease (COPD) and functional gastrointestinal disorders (FGIDs) remains unclear.

Methods: Using Taiwan's National Health Insurance Research Database, we conducted a nationwide population-based study to explore the relationship of COPD and future FGIDs development. The COPD cohort consisted of 4107 patients with COPD between 2000 and 2005. For a comparison cohort, 12,321 age- and gender-matched patients without COPD were randomly selected. The two cohorts were tracked for 5 year and observed for occurrence of FGIDs. The operational definition of COPD in the Korean Health Insurance Review and Assessment Service database was used to validate the results. The validation study confirmed the accuracy of definitions of COPD (83.5% sensitivity).

Results: The adjusted hazard ratios (aHR) of FGIDs in patients with COPD was higher (aHR: 1.63; 95% confidence interval (CI): 1.45-1.83; P < .001) than that of the comparison patients. In our secondary analysis in which FGIDs was divided into gastroesophageal reflux disease, irritable bowel syndrome and functional dyspepsia. Patients with COPD also had higher risk for all three subtypes of FGIDs: irritable bowel syndrome (aHR: 1.55; 95% confidence interval (CI): 1.27-1.90; P < .001), gastroesophageal reflux disease (aHR: 2.10; 95% confidence interval (CI): 1.76-2.49; P < .001), and functional dyspepsia (aHR: 1.34; 95% confidence interval (CI): 1.11-1.62; P = .003). The results in validated COPD group were consistent with those in unvalidated COPD group.

Conclusion: Patients with COPD appeared to be at higher risk for future FGIDs.

Keywords: COPD; Functional gastrointestinal disorders; Gastroesophageal reflux disease; Irritable bowel syndrome and functional dyspepsia.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

ELSEVIER FULL-TEXT ARTICLE

Proceed to details

Cite

Share

25

Respir Med

-
-
-

. 2022 Jun;197:106850.

doi: 10.1016/j.rmed.2022.106850. Epub 2022 Apr 9.

The effectiveness of pulmonary rehabilitation on chronic obstructive pulmonary disease patients with concurrent presence of comorbid depression and anxiety

Abebaw M Yohannes [1], Richard Casaburi [2], Sheila Dryden [3], Nicola A Hanania [4]

Affiliations expand

- PMID: 35427843

- DOI: 10.1016/j.rmed.2022.106850

Abstract

Background: We examined the prevalence of comorbid depression and anxiety in patients with chronic obstructive pulmonary disease (COPD) and their response to eight-weeks of pulmonary rehabilitation (PR).

Methods: Seven hundred thirty four patients with clinically stable COPD completed an eight-week outpatient multidisciplinary PR, comprising 2-h (1-h exercise and 1-h education) per/week. Depression and anxiety, exercise capacity, quality of life (QOL), and dyspnea were measured pre- and post-PR by the incremental shuttle walk test (ISWT), St. George's Respiratory Questionnaire (SGRQ), and modified Medical Research Council (mMRC) scale, respectively. The Depression

Anxiety Stress Scale (DASS-21) was completed and patients classified as having clinically significant comorbid anxiety and depression, anxiety alone, depression alone, or with neither.

Results: The mean (SD) age of patients was 71 (8.8) years, and 51% were men. Prevalence of pre-PR comorbid depression and anxiety was 34%, anxiety alone 20%, depression alone 5% and neither 41%. The prevalence of stress was 59%. In patients with anxiety and depressive symptoms, total SGRQ score improved from 64.9 (13.8) pre-PR to 50.1 (17.2) post PR ($p < 0.001$), mMRC score improved from 3.4(1.0) pre-PR to 2.8 (1.1) post PR ($p < 0.001$), and ISWT distance walked increased from 188.6 (117.6) pre-PR to 248.6 (149.1) post PR, $p < 0.001$.

Conclusion: One in three patients with COPD suffer from comorbid depression and anxiety with a high level of disease burden, reflected by symptoms of elevated dyspnea and impaired QOL. PR improves QOL and exercise capacity, and reduces dyspnea in patients with COPD and comorbid depression and anxiety.

Keywords: COPD; Depression and anxiety; Exercise capacity; Pulmonary rehabilitation; Quality of life; Stress.

J Hosp Palliat Nurs

. 2022 Jun 1;24(3):E101-E107.

doi: 10.1097/NJH.0000000000000858. Epub 2022 Mar 25.

Clinician Perspectives on How to Hold Earlier Discussions About Palliative and End-of-Life Care With Chronic Obstructive Pulmonary Disease Patients: A Qualitative Study

Nuno Tavares, Nikki Jarrett, Tom Wilkinson, Katherine Hunt

- PMID: 35334479

- DOI: 10.1097/NJH.0000000000000858

Abstract

Chronic obstructive pulmonary disease is associated with progressive symptoms and increased treatment burden, especially at the end of life. However, most patients do not receive palliative care until late in their lives or discuss their end-of-life preferences with clinicians. This study explored clinicians' perspectives on the timing and nature of palliative care discussions. Qualitative interviews were conducted with 7 physicians and 7 nurses working in primary and secondary care settings. Data were analyzed using a thematic analysis. Participants advocated for early, gradual, and informed palliative and future care discussions, because these discussions were thought to be less traumatic and better accepted by patients. Despite this, patient- and clinician-related barriers severely affected clinicians' ability to start discussions at earlier stages. Participants felt many patients were not ready for these discussions and feared damaging hope if the subject was broached. Therefore, clinicians delayed discussions until patients approached the end of life. Stand-alone conversations about and near the end of life were described as current practice; however, clinicians believed these discussions reduced patients' hope and were potentially upsetting. Instead, individualized early, regular, and gradual discussions about immediate and long-term care plans were thought to be less negative and be better accepted.

Conflict of interest statement

The authors have no conflicts of interest to disclose.

- 24 references

27

J Allergy Clin Immunol Pract

. 2022 Jun;10(6):1587-1597.

doi: 10.1016/j.jaip.2022.02.032. Epub 2022 Mar 8.

Risk Factors for Persistent Chronic Cough During Consecutive Years: A Retrospective Database Analysis

Robert S Zeiger [1], Michael Schatz [2], Yichen Zhou [3], Fagen Xie [4], Vishal Bali [5], Jonathan Schelfhout [5], Amar Das [5], Julie A Stern [4], Wansu Chen [4]

Affiliations expand

- PMID: 35272071

- DOI: 10.1016/j.jaip.2022.02.032

Abstract

Background: The identification of patients at high risk for diseases provides clinicians essential information to better manage such patients. Persistent chronic cough (PCC) is a condition with high clinical burden and limited knowledge of the risk factors that drive the persistent symptoms.

Objective: To understand the risk factors of PCC in patients with CC diagnosed by specialists.

Methods: In this retrospective study, adults aged 18 to 85 years diagnosed with CC by a pulmonologist, allergist, otolaryngologist, or gastroenterologist in the period 2011 to 2016 were identified. PCC was defined by another CC code or at least 2 cough events at least 8 weeks but no more than 4 months apart in each of the 2 consecutive years beginning 1 year after the original CC diagnosis. Unadjusted and adjusted risk ratios with 95% CI for patient characteristics at baseline in relationship to PCC were estimated by Poisson regression models with robust error variance.

Results: Of the adults with CC, 3270 (27.4%) had PCC and 5302 (44.5%) did not have CC during follow-up; 3341 (28.1%) had CC in only 1 follow-up year and were excluded from the analysis. Compared with patients without PCC, patients with PCC were noted to have significantly increased adjusted risk ratios for the following baseline features: (1) demographic characteristics (elderly, females, and less educated); (2) comorbidities (chronic obstructive pulmonary disease, chronic sinusitis, bronchiectasis, pulmonary fibrosis, hypertension, depression, and cough complications); (3) medication dispensed (inhaled corticosteroids/long-acting beta-agonists, leukotriene modifiers, nasal corticosteroids, nasal short-acting muscarinic antagonists, proton pump inhibitors, antitussives with narcotics, and neuromodulators); and (4) specialist care, particularly with pulmonologists.

Conclusions: Knowledge of the independent risk factors associated with PCC should aid clinicians in identifying such patients and improve their management.

Keywords: Antitussives; Chronic cough; Comorbidities; Cough; Persistent chronic cough.

Arch Rehabil Res Clin Transl

. 2022 Jun;4(2):100185.

doi: 10.1016/j.arrct.2022.100185. Epub 2022 Feb 24.

COVID-19 Postacute Sequela Rehabilitation: A Look to the Future Through the Lens of Chronic Obstructive Pulmonary Disease and Pulmonary Rehabilitation

Shweta Gore [1], Julie Keysor [1]

Affiliations expand

- PMID: 35229076

- PMCID: PMC8868001

- DOI: 10.1016/j.arrct.2022.100185

Free PMC article

Abstract

Post-COVID-19 condition is characterized by a myriad of persistent symptoms experienced up to 60 days after the acute infection, not only in those hospitalized, but also in patients with mild to moderate acute symptoms. The overwhelming evidence on multisystem involvement in post-COVID-19 condition brings to attention the need for integrated delivery models to address health

care needs of this population. The World Health Organization recently highlighted critical gaps in adequately providing the level of integrative care required to address the multisystem needs of this population in current health care delivery models and recommended development of new innovative models of delivery. This article presents a novel approach to addressing these gaps from a rehabilitation perspective.

Keywords: COPD, chronic obstructive pulmonary disease; CORF, comprehensive outpatient rehabilitation facility; COVID-19; Delivery of health care, integrated; PR, pulmonary rehabilitation; Pulmonary disease, chronic obstructive; Rehabilitation; Telerehabilitation.

- 64 references
- 1 figure

Review

Am J Respir Crit Care Med

-
-
-

. 2022 Jun 1;205(11):1271-1280.

doi: 10.1164/rccm.202110-2389CI.

A Pandemic Lesson for Global Lung Diseases: Exacerbations Are Preventable

William Cookson [1], Miriam Moffatt [1], Garth Rapeport [1], Jennifer Quint [1]

Affiliations expand

- PMID: 35192447

- DOI: 10.1164/rccm.202110-2389CI

Abstract

A dramatic global reduction in the incidence of common seasonal respiratory viral infections has resulted from measures to limit the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during the pandemic. This has been accompanied by falls reaching 50% internationally in the incidence of acute exacerbations of preexisting chronic respiratory diseases that include asthma, chronic obstructive pulmonary disease, and cystic fibrosis. At the same time, the incidence of acute bacterial pneumonia and sepsis has fallen steeply worldwide. Such findings demonstrate the profound impact of common respiratory viruses on the course of these global illnesses. Reduced transmission of common respiratory bacterial pathogens and their interactions with viruses appear also as central factors. This review summarizes pandemic changes in exacerbation rates of asthma, chronic obstructive pulmonary disease, cystic fibrosis, and pneumonia. We draw attention to the substantial body of knowledge about respiratory virus infections in these conditions, and that it has not yet translated into clinical practice. Now that the large scale of benefits that could be gained by managing these pathogens is unmistakable, we suggest that the field merits substantial academic and industrial investment. We consider how pandemic-inspired measures for prevention and treatment of common infections should become a cornerstone for managing respiratory diseases.

Keywords: COPD; SARS-CoV-2 pandemic; asthma; nonpharmaceutical interventions; pneumonia.

. 2022 Jun;27(4):319-324.

doi: 10.1080/1354750X.2022.2043443. Epub 2022 Feb 24.

Free lung desmosine: a potential biomarker for elastic fiber injury in pulmonary emphysema

Michael Fagiola[1,2], George Gu[1], Joseph Avella[2], Jerome Cantor[1]

Affiliations expand

- PMID: 35170389

- DOI: 10.1080/1354750X.2022.2043443

Abstract

Introduction: Desmosine and isodesmosine (DID) are biomarkers for elastic fibre damage in pulmonary emphysema. However, current methods for measuring lung DID involve tissue hydrolysis and lack specificity for those fibres undergoing breakdown. To address this limitation, free (nonpeptide-bound) DID content in unhydrolyzed tissues was evaluated as a more accurate biomarker in an animal model of pulmonary emphysema.

Methods: Hamsters were treated with either cigarette smoke and lipopolysaccharide (LPS), room air and LPS, or room air alone (controls). Free DID levels in fresh and formalin-fixed lungs were measured by LC-MS/MS and correlated with the mean linear intercept (MLI) measure of airspace size.

Results: There was no significant difference in free DID between fresh and formalin-fixed lungs. Animals treated with smoke and LPS had significantly higher levels of free DID than the LPS only group (359 vs. 93.1 ng/g wet lung, respectively; $p = 0.0012$) and room air controls (undetectable levels; $p = 0.0002$). There was a significant positive correlation between free DID and MLI ($p < 0.0001$).

Conclusions: The results support the hypothesis that free lung DID is a sensitive indicator of alveolar wall injury that may be used to study the development of pulmonary emphysema in both animal models and post-mortem human lung tissue.

Keywords: Desmosine; cigarette smoke; elastin; lipopolysaccharide; pulmonary emphysema.

J Clin Sleep Med

. 2022 Jun 1;18(6):1491-1501.

doi: 10.5664/jcsm.9890.

Sleep problems and associations with cardiovascular disease and all-cause mortality in asthma-chronic obstructive pulmonary disease overlap: analysis of the National Health and Nutrition Examination Survey (2007-2012)

Lynn M Baniak[1,2], Paul W Scott[2], Eileen R Chasens[2], Christopher C Imes[2], Bomin Jeon[2], Xiaojun Shi[2], Patrick J Strollo[1,3], Faith S Luyster[2]

Affiliations expand

- PMID: 35040430

- DOI: 10.5664/jcsm.9890

Abstract

Study objectives: The impact of sleep problems (ie, sleep duration and presence of sleep disorders) on cardiovascular morbidity and all-cause mortality in adults with asthma-chronic obstructive pulmonary disease overlap (ACO) is unknown.

Methods: Using the National Health and Nutrition Examination Survey database (2007-2012 cycles) and National Death Index data, we identified 398 persons with ACO. Data on self-reported physician-diagnosed sleep disorders and cardiovascular disease were collected. Sleep duration in hours was categorized as short (≤ 5 hours), normal (6-8 hours), and long (≥ 9 hours). Associations between sleep duration and presence of sleep disorders and cardiovascular disease and all-cause mortality were analyzed in regression models adjusted for age, sex, race, smoking status, and body mass index.

Results: Presence of sleep disorders was more commonly reported in the ACO group (24.7%) compared to all other groups. The ACO group had a higher proportion of short sleepers (27.6%) compared to controls (11.7%) and chronic obstructive pulmonary disease (19.2%) and a higher proportion of long sleepers (6.9%) compared to chronic obstructive pulmonary disease (5.5%). Presence of sleep disorders was associated with increased risk for cardiovascular disease (odds ratio = 2.48; 95% confidence interval, 1.65-3.73) and death (hazard ratio = 1.44; 95% confidence interval, 1.03-2.02); risk did not vary between groups. A stronger association existed between sleep

duration and increased risk for cardiovascular and all-cause mortality in ACO compared to chronic obstructive pulmonary disease and controls.

Conclusions: These results suggest that persons with ACO may represent a high-risk group that should be targeted for more aggressive intervention for sleep problems, a modifiable risk factor.

Citation: Baniak LM, Scott PW, Chasens ER, et al. Sleep problems and associations with cardiovascular disease and all-cause mortality in asthma-chronic obstructive pulmonary disease overlap: analysis of the National Health and Nutrition Examination Survey (2007-2012). *J Clin Sleep Med*. 2022;18(6):1491-1501.

Keywords: COPD; asthma; mortality; sleep disorder; sleep duration.

Thorax

. 2022 Jun;77(6):616-620.

doi: 10.1136/thoraxjnl-2020-216807. Epub 2022 Jan 13.

Inhaled corticosteroids reduce senescence in endothelial progenitor cells from patients with COPD

Koralia Paschalaki[1], Christos Rossios[#2], Charis Pericleous[#2], Mairi MacLeod[2], Stephen Rothery[2], Gavin C Donaldson[2], Jadwiga A Wedzicha[2], Vassilis Gorgoulis[3 4 5 6], Anna M Randi[2], Peter J Barnes[2]

Affiliations expand

- PMID: 35027472
- PMCID: PMC9120381
- DOI: 10.1136/thoraxjnl-2020-216807

Free PMC article

Abstract

Cellular senescence contributes to the pathophysiology of chronic obstructive pulmonary disease (COPD) and cardiovascular disease. Using endothelial colony-forming-cells (ECFC), we have demonstrated accelerated senescence in smokers and patients with COPD compared with non-smokers. Subgroup analysis suggests that ECFC from patients with COPD on inhaled corticosteroids (ICS) (n=14; eight on ICS) exhibited significantly reduced senescence (Senescence-associated-beta galactosidase activity, $p21^{CIP1}$), markers of DNA damage response (DDR) and IFN-γ-inducible-protein-10 compared with patients with COPD not on ICS. In vitro studies using human-umbilical-vein-endothelial-cells showed a protective effect of ICS on the DDR, senescence and apoptosis caused by oxidative stress, suggesting a protective molecular mechanism of action of corticosteroids on endothelium.

Keywords: COPD pharmacology.

Conflict of interest statement

Competing interests: Part of this work was funded by an academic AstraZeneca AB Project Grant.

- 10 references
- 2 figures

SUPPLEMENTARY INFO

MeSH terms, Substances, Grant supportexpand

FULL TEXT LINKS

BMJ Open Access Full Text

Proceed to details

Cite

Am J Med Sci

. 2022 Jun;363(6):502-510.

doi: 10.1016/j.amjms.2021.10.025. Epub 2022 Jan 5.

Sudden cardiac arrest in patients with chronic obstructive pulmonary disease: trends and outcomes from the national inpatient sample

Muhammad Zia Khan [1], Muhammad Bilal Munir [2], Muhammad U Khan [2], Sudarshan Balla [2]

Affiliations expand

- PMID: 34995573

- DOI: 10.1016/j.amjms.2021.10.025

Abstract

Background: The outcomes of patients with sudden cardiac arrest (SCA) and chronic obstructive pulmonary disease (COPD) are largely unknown. The purpose of this study was to assess mortality, trends, predictors, and outcomes in patients of SCA and COPD from a large inpatient administrative database.

Methods: Data from the National Inpatient Sample (NIS) was used from January 2002 to December 2014. Patients were identified by applying relevant International Classification of Diseases, Ninth Revision, Clinical Modification codes. Propensity score matching was applied for adjustment of cofounders. Binomial multiple logistic regression analysis was used to assess for predictors of mortality.

Results: In total 59,610 were identified with sudden cardiac arrest in which 13,195 (22.1%) patients had COPD. The mean age was 65.6 years. 37.8% were females. In the propensity match cohort, Mortality was 44.4% in patients with SCA without COPD when compared to 47.6% in SCA patients with COPD ($p < 0.01$). COPD was independently associated with higher mortality (OR, 1.121 [95% CI; 1.070-1.175] $p < 0.01$). Comorbidities like, diabetes mellitus and liver disease were associated with higher mortality. Female sex, racial and ethnic minorities were independent predictors for higher mortality.

Conclusions: SCA in settings of COPD may have high mortality when compared to patients with SCA and no concomitant COPD. Further research delving into potential mechanisms for SCA in COPD patients is warranted.

Keywords: Chronic obstructive pulmonary disease; Disparities sex and racial; Mortality; National sample; Sudden cardiac arrest.

Conflict of interest statement

Declaration of Competing Interest Author declare that there are no conflicts of interests.

Ann Am Thorac Soc

. 2022 Jun;19(6):971-980.

doi: 10.1513/AnnalsATS.202107-823OC.

Differences in Outcomes between Heart Failure Phenotypes in Patients with Coexistent Chronic Obstructive Pulmonary Disease: A Cohort Study

Claudia Gulea[1,2], Rosita Zakeri[3], Jennifer K Quint[1,2]

Affiliations expand

- PMID: 34905461

- DOI: 10.1513/AnnalsATS.202107-823OC

Abstract

Rationale: Differences in clinical presentation and outcomes between heart failure (HF) phenotypes in patients with chronic obstructive pulmonary disease (COPD) have not been assessed. **Objectives:** The aim of this study was to compare clinical outcomes and healthcare resource use between patients with COPD and HF with preserved ejection fraction (HFpEF), mildly reduced ejection fraction (HFmEF), and reduced ejection fraction (HFrEF). **Methods:** Patients with COPD and HF were identified in the U.S. administrative claims database OptumLabs DataWarehouse between 2008 and 2018. All-cause and cause-specific (HF) hospitalization, acute exacerbation of COPD (AECOPD, severe and moderate combined), mortality, and healthcare resource use were compared between HF phenotypes. **Results:** From 5,419 patients with COPD, 70% had HFpEF, 20% had HFrEF, and 10% had HFmEF. All-cause hospitalization did not differ across groups; however, patients with COPD and HFrEF had a greater risk of HF-specific hospitalization (hazard ratio [HR], 1.54; 95% confidence interval [CI], 1.29-1.84) and mortality (HR, 1.17; 95% CI, 1.03-1.33) than patients with COPD and HFpEF. Conversely, patients with COPD and HFrEF had a lower risk of AECOPD than those with COPD and HFpEF (HR, 0.75; 95% CI, 0.66-0.87). Rates of long-term stays (in skilled-nursing facilities) and emergency room visits were lower for those with COPD and HFrEF than for those with COPD and HFpEF. **Conclusions:** Outcomes in patients with comorbid COPD and HFpEF are largely driven by COPD. Given the paucity in treatments for HFpEF, better differentiation between cardiac and respiratory symptoms may provide an opportunity to reduce the risk of AECOPD. Risk of death and HF hospitalization were highest among patients with COPD and HFrEF, emphasizing the importance of optimizing guideline-recommended HFrEF therapies in this group.

Keywords: COPD; heart failure; hospitalization; mortality.

Comment in

- Comorbid Chronic Obstructive Pulmonary Disease and Heart Failure: Shared Risk Factors and Opportunities to Improve Outcomes.
  Khan SS, Kalhan R.Ann Am Thorac Soc. 2022 Jun;19(6):897-899. doi: 10.1513/AnnalsATS.202202-152ED.PMID: 35648080 **Free PMC article.** No abstract available.

. 2022 Jun 9;59(6):2102184.

doi: 10.1183/13993003.02184-2021. Print 2022 Jun.

Tiotropium treatment for bronchiectasis: a randomised, placebo-controlled, crossover trial

Lata Jayaram[1,2], Alain C Vandal[3,4], Catherina L Chang[5], Chris Lewis[6], Cecilia Tong[4], Christine Tuffery[5], Jill Bell[4], Wendy Fergusson[6], Gene Jeon[4], David Milne[6,7], Stuart Jones[4], Noel Karalus[5], Sandra Hotu[6], Conroy Wong[4,7,8]

Affiliations expand

- PMID: 34795034

- PMCID: PMC9178212

- DOI: 10.1183/13993003.02184-2021

Free PMC article

Abstract

Background: Tiotropium *via* the HandiHaler device is an established long-acting, anticholinergic bronchodilator that prevents exacerbations and improves lung function in patients with chronic obstructive pulmonary disease. We hypothesised that tiotropium would reduce pulmonary exacerbations and improve lung function in patients with stable bronchiectasis and airflow limitation, and assessed the effect of tiotropium on these outcomes.

Methods: In a randomised, double-blind, two-period crossover trial, we recruited adult patients from three hospitals in New Zealand. Patients were excluded if they had a smoking history of >20 pack-years. Patients were assigned to either the tiotropium-placebo or placebo-tiotropium sequence in a 1:1 ratio, using randomly permuted blocks stratified by centre. Participants and investigators were masked to treatment allocation. Eligible patients received tiotropium 18 µg *via* HandiHaler daily for 6 months followed by 6 months of placebo, or *vice versa*, with a washout period of 4 weeks. The primary end-point was rate of event-based exacerbations during the 6-month period. Primary analyses were carried out in an intention-to-treat set.

Results: 90 patients were randomly assigned and 85 completed both treatment cycles. The rate of exacerbations was 2.17 per year under the tiotropium treatment and 2.27 per year under placebo (rate ratio 0.96, 95% CI 0.72-1.27; p=0.77). Tiotropium, compared with placebo, improved forced expiratory volume in 1 s by 58 mL (95% CI 23-92 mL; p=0.002). Adverse events were similar under both treatments.

Conclusions: Tiotropium *via* HandiHaler over 6 months significantly improved lung function but not frequency of exacerbations. Further research is required to understand the clinical context and significance of these findings.

Conflict of interest statement

Conflict of interest: All authors have no conflicts of interest to declare.

Comment in

- Bronchodilators in bronchiectasis: there is light but it is still too dim.
  Cazzola M, Martínez-García MÁ, Matera MG.Eur Respir J. 2022 Jun 9;59(6):2103127. doi: 10.1183/13993003.03127-2021. Print 2022 Jun.PMID: 35680152 No abstract available.

J Clin Psychol Med Settings

. 2022 Jun;29(2):310-317.

doi: 10.1007/s10880-021-09828-7. Epub 2021 Oct 7.

Affective Comorbidity Associated with Symptoms, Lung Function, and Differences Between Patients with COPD for Biomass and Tobacco Smoke Exposure

Andrea Hernández-Pérez[1,2], Inés Vargas-Núñez[3], Bernardo Moreno-Jiménez[4], Rogelio Pérez-Padilla[5,3], Alejandra Ramírez-Venegas[5]

Affiliations expand

- PMID: 34618283

- DOI: 10.1007/s10880-021-09828-7

Abstract

Anxiety and depression are common entities in patients diagnosed with Chronic Obstructive Pulmonary Disease (COPD). This study aimed to determine the prevalence of affective comorbidity (depression and anxiety) associated with lung function, functional capacity, dyspnea, and quality of life; as well as the differences between groups of patients diagnosed with COPD associated with biomass (COPD-BE) and patients with COPD secondary to tobacco (COPD-TS). Comparative cross-sectional observational study. Multiple hierarchical regression models, analysis of variance, and covariance were carried out. A total of 291 COPD patients were evaluated, symptoms of depression were found to be higher in patients with COPD-BE than in patients with COPD-TS (5.3 ± 4.2 versus 4.2 ± 4, 1, p = 0.016), as well as anxiety complications (4.1 ± 3.8 versus 3.8 ± 3.3, p = 0.095), although with anxiety it was not statistically significant, being adjusted for age and FEV1. Patients with COPD-BE had higher prevalence of depression, compared to COPD-TS (41.2% versus 27.7%, p = 0.028). In the multivariate regression models, the variables of dyspnea and quality of life were associated with depression and anxiety, explaining 25% and 24% of the variability, respectively. Depression is higher in COPD-BE patients compared to COPD-TE patients, it is necessary to consider affective comorbidity in routine evaluation and provide a comprehensive intervention to prevent the effects on other clinical conditions of the disease.

Keywords: Anxiety; Chronic obstructive pulmonary disease; Comorbidity; Depression.

- 33 references

Proceed to details

Cite

Share

37

Thorax

-
-
-

. 2022 Jun;77(6):530-531.

doi: 10.1136/thoraxjnl-2021-217930. Epub 2021 Sep 23.

Inhaled corticosteroids in COPD: risk and benefits

Christer Janson [1]

Affiliations expand

- PMID: 34556555

- DOI: 10.1136/thoraxjnl-2021-217930

No abstract available

Keywords: COPD pharmacology.

Conflict of interest statement

Competing interests: CJ has served in an advisory board and/or served as a speaker and/or participated in education arranged from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis, Chiesi, and TEVA. KL has served in an advisory board and/or served as a speaker and/or participated in education arranged by AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis and Pfizer.

Thorax

-
-
-

. 2022 Jun;77(6):573-580.

doi: 10.1136/thoraxjnl-2021-217160. Epub 2021 Aug 26.

Use of inhaled corticosteroids and risk of acquiring *Pseudomonas aeruginosa* in patients with chronic obstructive pulmonary disease

Josefin Eklöf [1], Truls Sylvan Ingebrigtsen [2], Rikke Sørensen [3], Mohamad Isam Saeed [4], Imane Achir Alispahic [4], Pradeesh Sivapalan [4 2], Jonas Bredtoft Boel [5], Jette Bangsborg [5], Christian Ostergaard [6], Ram Benny Dessau [7], Ulrich Stab Jensen [7], Ejvind Frausing Hansen [8], Therese Sophie Lapperre [9], Howraman Meteran [4], Torgny Wilcke [4], Niels Seersholm [4], Jens-Ulrik Stæhr Jensen [4 10 11]

Affiliations expand

- PMID: 34446524

- PMCID: PMC9120392

- DOI: 10.1136/thoraxjnl-2021-217160

Free PMC article

Abstract

Background: Inhaled corticosteroids (ICS) are commonly used to treat COPD and are associated with increased risk of pneumonia. The aim of this study was to assess if accumulated use of ICS is associated with a dose-dependent risk of a positive airway culture with *Pseudomonas aeruginosa* in patients with COPD.

Methods: We conducted a multiregional epidemiological cohort study including Danish COPD patients followed in outpatient clinics during 2010-2017. ICS use was categorised based on accumulated prescriptions redeemed 365 days prior to cohort entry. Cox proportional hazard regression model was used to estimate the risk of acquiring *P. aeruginosa*. Propensity score matched models were used as sensitivity analyses.

Results: A total of 21 408 patients were included in the study, of which 763 (3.6%) acquired *P. aeruginosa* during follow-up. ICS use was associated with a dose-dependent risk of *P. aeruginosa* (low ICS dose: HR 1.38, 95% CI 1.03 to 1.84, p=0.03; moderate ICS dose: HR 2.16, 95% CI 1.63 to 2.85, p<0.0001; high ICS dose: HR 3.58, 95% CI 2.75 to 4.65, p<0.0001; reference: no ICS use). A propensity matched model confirmed the results (high ICS dose compared with no/low/moderate ICS dose: HR 2.05, 95% CI 1.76 to 2.39, p p<0.0001).

Conclusion: Use of ICS in patients with COPD followed in Danish outpatient clinics was associated with a substantially increased and dose-dependent risk of acquiring *P. aeruginosa*. Caution should be taken when administering high doses of ICS in severely ill patients with COPD. These results should be confirmed in comparable cohorts and other settings.

Keywords: COPD epidemiology; respiratory infection.

Conflict of interest statement

Competing interests: RBD reports grants and personal fees from Roche, outside the submitted work. TSI reports personal fees from AstraZeneca, outside the submitted work. PS reports non-financial support from Novartis and personal fees from Boehringer Ingelheim, outside the submitted work. HM is a member of ALK-Abelló Nordic A/S advisory board.

Review

Int J Environ Health Res

-
-
-

. 2022 Jun;32(6):1403-1417.

doi: 10.1080/09603123.2021.1887460. Epub 2021 Feb 12.

Chronic obstructive pulmonary disease (COPD) in women due to indoor biomass burning: a meta analysis

Ritul Kamal [1,2], Anup Kumar Srivastava [1], Chandrasekharan Nair Kesavachandran [1], Vipin Bihari [1], Amarnath Singh [1]

Affiliations expand

- PMID: 33573386

- DOI: 10.1080/09603123.2021.1887460

Abstract

Chronic Obstructive Pulmonary Disease (COPD) is attributable to household air pollution and is known to increase the Disability Adjusted Life Years (DALYs), morbidity and mortality and women are most susceptible groups for the exposure. In order to understand the global risk among women with COPD due to exposure of household air pollutants, an evidence-based systematic review and meta-analysis was conducted. Meta regression analysis was carried out to identify potential sources of heterogeneity. The summary estimates of the included studies showed higher prevalence of COPD due to biomass fuel exposure in women. Clinical diagnosis has shown more risk of COPD prevalence compared to diagnosis based on spirometer test alone. However, the data between included studies for both clinical and spirometry-based studies showed higher heterogeneity. The present meta-data analysis has shown that household air pollutants may be a factor associated with increased risk of COPD in women.

Keywords: COPD; biomass; meta-analysis; systematic review; women.

Review

J Pharm Pract

. 2022 Jun;35(3):445-454.

doi: 10.1177/0897190020969286. Epub 2020 Dec 3.

The Role of the Pharmacist in Optimizing Outcomes With Roflumilast, a PDE4 Inhibitor for the Treatment of COPD

Dennis Williams [1,2]

Affiliations expand

- PMID: 33267721
- PMCID: PMC9161436
- DOI: 10.1177/0897190020969286

Free PMC article

Abstract

Purpose: The pharmacology of roflumilast, recent dosing revisions, and the integral roles of pharmacists in effective chronic obstructive pulmonary disease (COPD) management are reviewed here.

Summary: COPD is characterized by progressive airflow limitation and intermittent acute exacerbations of symptoms, which contribute to disease progression, worsening of comorbidities, and reduced health-related quality of life. Patients with COPD may use a variety of pharmacotherapies (in combination with nonpharmacological modalities) to prevent exacerbations, reduce the impact of symptoms, and reduce or prevent COPD progression. Given the complex and multifaceted nature of disease management, pharmacists are uniquely positioned to collaborate with other clinicians to improve treatment adherence and efficacy via a number of diverse avenues in patients with COPD. Central to this endeavor is patient education and counseling regarding their treatment regimen.

Conclusion: Recent findings from a phase 3 clinical trial demonstrate improved tolerability and reduced treatment discontinuation resulting from the use of an uptitration regimen in patients with severe COPD who initiate therapy with roflumilast. Pharmacists have a central role in effective COPD management, especially with respect to patient education about treatments.

Keywords: COPD; chronic obstructive pulmonary disease; dosing; pharmacist; roflumilast.

Conflict of interest statement

Declaration of Conflicting Interests: The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Dennis Williams reports that his spouse owns stock in GlaxoSmithKline.

- 41 references
- 3 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

Proceed to details

Cite

Share

41

Meta-Analysis

J Telemed Telecare

-
-
-

. 2022 Jun;28(5):342-359.

doi: 10.1177/1357633X20937573. Epub 2020 Aug 20.

The use of wearable devices in chronic disease management to enhance adherence and improve telehealth outcomes: A systematic review and meta-analysis

Tomoko Kamei[1], Takuya Kanamori[2], Yuko Yamamoto[3], Sisira Edirippulige[4]

Affiliations expand

- PMID: 32819184

- DOI: 10.1177/1357633X20937573

Abstract

Introduction: Wearable device (WD) interventions are rapidly growing in chronic disease management; nevertheless, the effectiveness of these technologies to monitor telehealth outcomes has not been adequately discussed. This study aims to evaluate the effects of WDs in adherence and other health outcomes for people with chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), and cardiac disease (CD).

Methods: CINAHL, PsycINFO, CENTRAL, and EMBASE were searched for randomized controlled trials (RCTs) and non-RCTs from 1937 to February 2020. Studies comparing interventions with the use of WD were assessed for quality in RCTs and a meta-analysis was performed.

Results: Eleven studies were included in this review. All of the interventions involved WD use with educational support such as goal setting, virtual social support, e-health program, real-time feedback, written information, maintain diary, and text messaging. The meta-analysis showed no difference in adherence (p = .38). The DM group showed effects of more than a 2% reduction in weight when WDs were implemented for three months (risk ratio = 2.20; 95% confidence interval (CI) 1.38 to 3.50; p = .0009), as well as blood glucose (mean difference (MD) = -32.39; 95% CI = -48.07 to -16.72; p < .0001), haemoglobin A_{1c} (MD = -0.69; 95% CI = -1.28 to -0.10; p = .02), and physical exercise time in the CD group (MD = 9.53; 95% CI = 0.59 to 18.47; p = .04).

Discussion: WD with educational support may be particularly useful for people with DM and CD to enhance support beyond usual care. The results of this review showed insufficient evidence to support the use of WD for COPD to enhance telehealth outcomes for disease management.

Keywords: Wearable device; cardiac disease; chronic obstructive pulmonary disease; diabetes; meta-analysis; systematic review.

ASTHMA

World Allergy Organ J

. 2022 Jun 1;15(6):100655.

doi: 10.1016/j.waojou.2022.100655. eCollection 2022 Jun.

Revisiting differences between atopic and non-atopic asthmatics: When age is shaping airway inflammatory profile

Sara Gerday [1], Florence Schleich [1 2], Monique Henket [1], Françoise Guissard [1], Virginie Paulus [1], Renaud Louis [1 2]

Affiliations expand

- PMID: 35694004

- PMCID: PMC9163576

- DOI: 10.1016/j.waojou.2022.100655

Abstract

Background: Atopic asthma is one of the most common asthma phenotypes and is generally opposed to the non-atopic counterpart. There have been very few large-scale studies comparing atopic and non-atopic asthmatics in terms of systemic and airway inflammation across the age spectrum.

Methods: Here, we have undertaken a retrospective study investigating 1626 patients (924 atopic and 702 non-atopic asthmatics) recruited from our university asthma clinic who underwent extensive clinical investigations including induced sputum. Atopy was defined by any positive specific IgE to common aeroallergens (>0,35 kU/L). We performed direct comparisons between the groups and sought to appreciate the influence of age on the airway and systemic inflammatory components. The study was approved by the ethics committee of the University Hospital of Liege (Ref. 2016/276). Informed consents were obtained from healthy subjects.

Results: Atopic asthmatics were younger *(P* < .001), had a higher male/female ratio *(P* < .001), an earlier disease onset *(P* < .001) and a greater proportion of treated rhinitis *(P* < .001) while non-atopic asthmatics had greater smoke exposure *(P* < .001), lower FEV_1/FVC ratio (*P* = .01) and diffusing capacity (*P* < .001). There was no difference between the 2 groups regarding FEV_1 (% predicted), asthma control, asthma quality of life and exacerbations in the previous 12 months. Regarding inflammation, atopic patients had higher FeNO levels (median = 28 ppb, *P* < .001), were more eosinophilic both in blood (median = 2.8%, *P* < .001) and in sputum (median = 2.2%, *P* < .001) while non-atopic patients displayed greater blood (median = 57%, *P* = .01) and sputum (median = 58.8%, *P* = .01) neutrophilic inflammation. However, stratifying patients by age showed that non-atopic asthmatics above 50 years old became equally eosinophilic in the sputum *(P* = .07), but not in the blood, as compared to atopic patients. Likewise, FeNO rose in non-atopic patients after 50 years old but remained, however, lower than in atopic patients.

Conclusions: We conclude that, while sharing many features, atopic group still differentiates from non-atopic asthmatics by demographics, functional and inflammatory profiles. When atopic asthmatics showed a constant eosinophilic pattern across the age spectrum, non-atopic asthmatics were found to be neutrophilic before the age of 50 but eosinophilic above 50 years old.

Keywords: Atopic asthma; Eosinophils; Neutrophils; Non-atopic asthma; Sputum.

Conflict of interest statement

SG, FG, VP, MH: no competing interests. FS reports grants from GSK, Astrazeneca, Teva, Chiesi and Novartis; consulting fees from GSK, Astrazeneca, Amgen, Chiesi and Novartis; lecture payments from GSK, Astrazeneca, Teva, Chiesi and Novartis, outside the submitted work. RL reports grants from GSK, AZ, Novartis, Chiesi and Teva; royalties from patent AU2016328384, CA2997506, EP 3337393, US2020345266; consulting fees and lecture payments from GSK, AZ, Novartis, Sanofi and Chiesi, outside the submitted work.

Review

Respirology

. 2022 Jun 12.

doi: 10.1111/resp.14312. Online ahead of print.

Bronchial thermoplasty: State of the art

Muhammad Daniyal Hashmi[1], Asad Khan[2], Majid Shafiq[3]

Affiliations expand

- PMID: 35692074

- DOI: 10.1111/resp.14312

Abstract

Since the publication of a sham-controlled, randomized trial (AIR2) and subsequent marketing approval by the US Food and Drug Administration, we have significantly advanced our understanding of bronchial thermoplasty (BT)'s scientific basis, long-term safety, clinical efficacy and cost-effectiveness. In particular, the last 2 years have witnessed multiple research publications on several of these counts. In this review, we critically appraise our evolving understanding of BT's biologic underpinnings and clinical impact, offer an evidence-based patient workflow guide for the busy pulmonologist and highlight both current challenges as well as potential solutions for the researcher and the clinician.

Keywords: bronchial thermoplasty; cost-effectiveness; efficacy; mechanism of action; safety; severe asthma.

- 60 references

SUPPLEMENTARY INFO

Publication typesexpand

Proceed to details

Cite

Share

3

J Allergy Clin Immunol Pract

-
-
-

. 2022 Jun 8;S2213-2198(22)00575-X.

doi: 10.1016/j.jaip.2022.05.026. Online ahead of print.

Clinical deterioration and lung function change in patients with concomitant asthma and bronchiectasis

Na Young Kim [1], Chang-Hoon Lee [1], Kwang Nam Jin [2], Hyun Woo Lee [3], Eun Young Heo [3], Deog Kyeom Kim [3], Jung-Kyu Lee [3]

Affiliations expand

- PMID: 35690367

- DOI: 10.1016/j.jaip.2022.05.026

Abstract

Background: Only limited data are available regarding the effects of bronchiectasis on the clinical course of asthma.

Objective: This study evaluated longitudinal clinical outcomes according to bronchiectasis status in patients with asthma.

Methods: This retrospective study included patients with asthma who underwent chest computed tomography and pulmonary function tests between January 2013 and December 2019. The annual incidence of episodes of moderate-to-severe acute clinical deterioration (exacerbations) and longitudinal changes in lung function were evaluated.

Results: Of 667 patients with asthma, 251 had bronchiectasis. Patients with bronchiectasis had significantly more history of tuberculosis and non-tuberculous mycobacterial lung disease, and lower forced expiratory volume in 1 s and forced vital capacity, compared with patients without bronchiectasis, although there was no difference in smoking intensity and inhaled corticosteroid treatment. Bronchiectasis was significantly associated with higher annual rates of severe and moderate-to-severe acute exacerbations; it was also associated with greater risk of acute exacerbation during follow-up. The severity and progression of bronchiectasis were independent risk factors for acute exacerbation. There were no significant differences in annual decline of lung function according to bronchiectasis status or bronchiectasis progression.

Conclusions: In patients with asthma, the presence and progression of bronchiectasis were significantly associated with increased risk of moderate-to-severe acute exacerbation, but they were not associated with longitudinal changes in lung function.

Keywords: Asthma; Bronchiectasis; Exacerbation; Lung function.

Am J Respir Crit Care Med

. 2022 Jun 10.

doi: 10.1164/rccm.202112-2745OC. Online ahead of print.

The Impact of Insulin Resistance on Loss of Lung Function and Response to Treatment in Asthma

Michael C Peters [1], Mark Schiebler [2], Juan Carlos Cardet [3], Mats W Johansson [4 5], Ronald Sorkness [6], Mark D DeBoer [7], Eugene R Bleecker [8], Deborah A Meyers [9], Mario Castro [10], Kaharu Sumino [11], Serpil C Erzurum [12], Matthew C Tattersall [13], Joe G Zein [14], Annette T Hastie [15], Wendy

Moore[16], Bruce D Levy[17], Elliot Israel[18], Melody Duvall[19], Brenda R Phillips[20], David T Mauger[21], Sally E Wenzel[22,23], Merritt L Fajt[24,25], Suneil K Koliwad[26], Loren C Denlinger[27], Prescott G Woodruff[28], Nizar N Jarjour[13], John V Fahy[29], National Heart Lung and Blood Institute Severe Asthma Research Program-3

Affiliations expand

- PMID: 35687105

- DOI: 10.1164/rccm.202112-2745OC

Abstract

Rationale: The role of obesity-associated insulin resistance (IR) in airflow limitation in asthma is uncertain.

Objectives: Using data in the Severe Asthma Research Program 3 (SARP-3), we evaluated relationships between homeostatic measure of IR (HOMA-IR), lung function (cross sectional and longitudinal analyses) and treatment responses to bronchodilators and corticosteroids.

Methods: HOMA-IR values was categorized as without (< 3.0), moderate (3.0-5.0), or severe (>5.0). Lung function included forced expired volume in one second (FEV1) and forced vital capacity (FVC) measured before and after treatment with inhaled albuterol and intramuscular triamcinolone acetonide (TA) and yearly for 5 years.

Measurements and main results: Among 307 participants in SARP-3, 170 (55%) were obese and 140 (46%) had IR. Compared to patients without IR, those with IR had significantly lower values for forced expired volume in one second (FEV1) and forced vital capacity (FVC), and these lower values were not attributable to obesity effects. Compared to patients without IR, those with IR had lower FEV1 responses to beta adrenergic agonists and systemic corticosteroids. The annualized decline in FEV1 was significantly greater in patients with moderate IR (-41 mLs/year) and severe IR (-32 mLs/year,) than in patients without IR (-13mLs/year, p< 0.001 for both comparisons).

Conclusion: IR is common in asthma and is associated with lower lung function, accelerated loss of lung function, and suboptimal lung function responses to bronchodilator and corticosteroid treatments. Clinical trials in patients with asthma and IR are needed to determine if improving IR might also improve lung function.

Keywords: asthma; insulin resistance; lung function; obesity.

Share

5

Review

J Asthma Allergy

. 2022 Jun 3;15:749-765.

doi: 10.2147/JAA.S275039. eCollection 2022.

Targeting TSLP in Asthma

Jane R Parnes[1], Nestor A Molfino[1], Gene Colice[2], Ubaldo Martin[2], Jonathan Corren[3], Andrew Menzies-Gow[4]

Affiliations expand

- PMID: 35685846
- PMCID: PMC9172920
- DOI: 10.2147/JAA.S275039

Free PMC article

Abstract

Thymic stromal lymphopoietin (TSLP) is an epithelial cell-derived cytokine implicated in the initiation and persistence of inflammatory pathways in asthma. Released in response to a range of epithelial insults (eg, allergens, viruses, bacteria, pollutants, and smoke), TSLP initiates multiple downstream innate and adaptive immune responses involved in asthma inflammation. Inhibition of TSLP is postulated to represent a novel approach to treating the diverse phenotypes and endotypes of asthma. Tezepelumab, the TSLP inhibitor farthest along in clinical development, is a human monoclonal antibody (IgG2λ) that binds specifically to TSLP, preventing interactions with its heterodimeric receptor. Results of recently published phase 2 and 3 studies, reviewed in this article, provide evidence of the safety and efficacy of tezepelumab that builds on initial findings. Tezepelumab is safe, well tolerated, and provides clinically meaningful improvements in asthma control, including reduced incidence of exacerbations and hospitalizations in patients with severe asthma. Clinical benefits were associated with reductions in levels of a broad spectrum of cytokines

(eg, interleukin [IL]-5, IL-13) and baseline biomarkers (eg, blood eosinophils, immunoglobulin [Ig]E, fractional exhaled nitric oxide [FeNO]) and were observed across a range of severe asthma phenotypes (ie, eosinophilic and non-eosinophilic). These data strengthen the notion that anti-TSLP elicits broad inhibitory effects on pathways that are key to asthma inflammation rather than on narrower inhibition of individual downstream factors. This review presents the rationale for targeting TSLP to treat asthma, as well as the clinical effects of TSLP blockade on asthma outcomes, biomarkers of disease activity, airway inflammation, lung physiology, and patient symptoms.

Keywords: TSLP; anti-TSLP; asthma; exacerbation rates; thymic stromal lymphopoietin.

Conflict of interest statement

Jane R Parnes reports a patent Treatment of asthma with anti-TSLP antibody: US-10828365-B2 issued to Assigned to Amgen and AstraZeneca. Jane R. Parnes and Nestor A. Molfino are employees and stockholders of Amgen Inc. Gene Colice and Ubaldo Martin are employees and stockholders of AstraZeneca. Jonathan Corren has received grant support, consulting fees, fees for a speakers bureau, and advisory board fees from AstraZeneca and Regeneron; grant support, advisory board fees, and fees for a speakers bureau from Genentech; and grant support from Sanofi, Teva Pharmaceutical Industries, and OptiNose. Andrew Menzies-Gow has received grants, advisory board fees, lecture fees, and consulting fees from AstraZeneca; advisory board fees from GlaxoSmithKline; advisory board fees and lecture fees from Novartis; advisory board fees, lecture fees, and travel expenses from Teva; advisory board fees, lecture fees, and consulting fees from Sanofi. The authors report no other conflicts of interest in this work.

- 76 references
- 5 figures

SUPPLEMENTARY INFO

Publication types, Grant supportexpand

FULL TEXT LINKS

FREE full-text article Dovepress

Proceed to details

Cite

Share

6

Review

Cells

-
-
-

. 2022 May 29;11(11):1781.

doi: 10.3390/cells11111781.

Cellular Senescence in Aging Lungs and Diseases

Arbi Aghali[1], Maunick Lefin Koloko Ngassie[2,3], Christina M Pabelick[1,4], Y S Prakash[1,4]

Affiliations expand

- PMID: 35681476

- PMCID: PMC9179897

- DOI: 10.3390/cells11111781

Free PMC article

Abstract

Cellular senescence represents a state of irreversible cell cycle arrest occurring naturally or in response to exogenous stressors. Following the initial arrest, progressive phenotypic changes define conditions of cellular senescence. Understanding molecular mechanisms that drive senescence can help to recognize the importance of such pathways in lung health and disease. There is increasing interest in the role of cellular senescence in conditions such as chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis (IPF) in the context of understanding pathophysiology and identification of novel therapies. Herein, we discuss the current knowledge of molecular mechanisms and mitochondrial dysfunction regulating different aspects of cellular senescence-related to chronic lung diseases to develop rational strategies for modulating the senescent cell phenotype in the lung for therapeutic benefit.

Keywords: COPD; aging; asthma; lung diseases; mitochondrial dysfunction; pulmonary fibrosis; remodeling; senescence.

Conflict of interest statement

The authors declare no conflict of interest.

- 152 references
- 3 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

FULL TEXT LINKS

Proceed to details

Cite

Share

7

Published Erratum

Eur Respir J

-
-
-

. 2022 Jun 9;59(6):1362020.

doi: 10.1183/13993003.62020-2013. Print 2022 Jun.

"International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma." Kian Fan Chung, Sally E. Wenzel, Jan L. Brozek, *et al. Eur Respir J* 2014; 43: 343–373

No authors listed

- PMID: 35680153

- DOI: 10.1183/13993003.62020-2013

No abstract available

Erratum for

- International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, Adcock IM, Bateman ED, Bel EH, Bleecker ER, Boulet LP, Brightling C, Chanez P, Dahlen SE, Djukanovic R, Frey U, Gaga M, Gibson P, Hamid Q, Jajour NN, Mauad T, Sorkness RL, Teague WG.Eur

Respir J. 2014 Feb;43(2):343-73. doi: 10.1183/09031936.00202013. Epub 2013 Dec 12.PMID: 24337046

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

Full text at ersjournals.com

Proceed to details

Cite

Share

8

Review

Eur Respir Rev

-
-
-

. 2022 Jun 7;31(164):210278.

doi: 10.1183/16000617.0278-2021. Print 2022 Jun 30.

Biologics in severe asthma: the role of real-world evidence from registries

Giovanni Paoletti[1,2], Jack Pepys[2], Marta Casini[2], Danilo Di Bona[3], Enrico Heffler[1,2], Celine Y Y Goh[4,5], David B Price[4,5,6], Giorgio Walter Canonica[7,2]

Affiliations expand

- PMID: 35675922

- DOI: 10.1183/16000617.0278-2021

Free article

Abstract

Asthma is one of the most common noncommunicable diseases; in the majority of patients it is well controlled with inhaled bronchodilators and inhaled corticosteroids, but the management of severe asthma has been a significant challenge historically. The introduction of novel biologic drugs in the past few decades has revolutionised the field, presenting physicians with a variety of biologic drugs with different mechanisms for the treatment of severe asthma.It is of crucial importance to evaluate the effectiveness of these drugs by following their "real-life" effectiveness rather than relying solely on their efficacy, established in carefully designed clinical trials, which therefore do not necessarily match the profile of the real-life patient. Understanding the actual effectiveness of the specific drugs in real-life patients is a crucial part of tailoring the right drugs to the right patients. Registries serve as an important tool in obtaining real-life evidence, since they are in effect observational studies, following the entire patient population.

Conflict of interest statement

Conflict of interest: G. Paoletti reports no conflict of interest. Conflict of interest: J. Pepys reports no conflict of interest. Conflict of interest: M. Casini reports no conflict of interest. Conflict of interest: D. Di Bona reports no conflict of interest. Conflict of interest: E. Heffler reports personal fees from AstraZeneca, Sanofi, Novartis, Teva, GSK, Circassia, Boehringer Ingelheim, Valeas, and Nestlè Purina, outside the submitted work. Conflict of interest: C.Y.Y. Goh reports no conflicts of interest. Conflict of interest: D.B. Price has board membership with Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, Circassia, Viatris, Mundipharma, Novartis, Regeneron Pharmaceuticals, Sanofi Genzyme, Teva Pharmaceuticals, and Thermofisher; consultancy agreements with Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Viatris, Mundipharma Novartis, Pfizer, Teva Pharmaceuticals, and Theravance; grants and unrestricted funding for investigator-initiated studies (conducted through Observational and Pragmatic Research Institute Pte Ltd) from AstraZeneca, Boehringer Ingelheim, Chiesi, Circassia, Viatris, Mundipharma, Novartis, Pfizer, Regeneron Pharmaceuticals, Sanofi Genzyme, Teva Pharmaceuticals, Theravance, and UK National Health Service; payment for lectures/speaking engagements from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, Viatris, Mundipharma, Novartis, Pfizer, Regeneron Pharmaceuticals, Sanofi Genzyme, and Teva Pharmaceuticals; payment for travel/accommodation/meeting expenses from AstraZeneca, Boehringer Ingelheim, Circassia, Mundipharma, Novartis, Teva Pharmaceuticals, and Thermofisher; funding for patient enrolment or completion of research from Novartis; stock/stock options from AKL Research and Development Ltd which produces phytopharmaceuticals; owns 74% of the social enterprise Optimum Patient Care Ltd (Australia and UK) and 74% of Observational and Pragmatic Research Institute Pte Ltd (Singapore); 5% shareholding in Timestamp which develops adherence monitoring technology; is peer reviewer for grant committees of the Efficacy and Mechanism Evaluation programme, and Health Technology Assessment; and was an expert witness for GlaxoSmithKline. Conflict of interest: G.W. Canonica has received grants and consultancy fees from A. Menarini, ALK-Abelló, Allergy Therapeutics, AstraZeneca-Medimmune, Boehringer Ingelheim, Chiesi Farmaceutici, Genentech, Guidotti-Malesci, GlaxoSmithKline, Hal Allergy, Merck Sharp & Dohme, Mundipharma, Novartis, Orion, Sanofi-Aventis, Sanofi Genzyme/Regeneron, Stallergenes Greer, Uriach Pharma, Teva, Valeas and Vifor Pharma.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

Respirology

. 2022 Jun 7.

doi: 10.1111/resp.14302. Online ahead of print.

Pathways linked to unresolved inflammation and airway remodelling characterize the transcriptome in two independent severe asthma cohorts

Stephany Sánchez-Ovando[1], Stelios Pavlidis[2], Nazanin Zounemat Kermani[2], Katherine Joanne Baines[1], Daniel Barker[3], Peter G Gibson[1 4], Lisa G Wood[1], Ian M Adcock[5], Kian Fan Chung[5], Jodie Louise Simpson[1], Peter A B Wark[1 4]

Affiliations expand

- PMID: 35673765

- DOI: 10.1111/resp.14302

Abstract

Background and objective: Severe asthma (SA) is a heterogeneous disease. Transcriptomic analysis contributes to the understanding of pathogenesis necessary for developing new therapies. We sought to identify and validate mechanistic pathways of SA across two independent cohorts.

Methods: Transcriptomic profiles from U-BIOPRED and Australian NOVocastrian Asthma cohorts were examined and grouped into SA, mild/moderate asthma (MMA) and healthy controls (HCs). Differentially expressed genes (DEGs), canonical pathways and gene sets were identified as central to SA mechanisms if they were significant across both cohorts in either endobronchial biopsies or induced sputum.

Results: Thirty-six DEGs and four pathways were shared across cohorts linking to tissue remodelling/repair in biopsies of SA patients, including SUMOylation, NRF2 pathway and oxidative stress pathways. MMA presented a similar profile to HCs. Induced sputum demonstrated IL18R1 as a shared DEG in SA compared with healthy subjects. We identified enrichment of gene sets related to corticosteroid treatment; immune-related mechanisms; activation of $CD4^+$ T cells, mast cells and IL18R1; and airway remodelling in SA.

Conclusion: Our results identified differentially expressed pathways that highlight the role of $CD4^+$ T cells, mast cells and pathways linked to ongoing airway remodelling, such as IL18R1, SUMOylation and NRF2 pathways, as likely active mechanisms in the pathogenesis of SA.

Keywords: airway remodelling; biopsies; gene expression; inflammation; pathogenesis; severe asthma; sputum; transcriptome.

Improving Medication Adherence in Asthma

Patrick J Kerr[1,2], Vincent Brennan[1], Elaine Mac Hale[1], Frank Doyle[3], Richard W Costello[1,4]

Affiliations expand

- PMID: 35672007

- DOI: 10.1055/s-0042-1749636

Abstract

In little over a generation, the ingenuity of scientists and clinician researchers has developed inhaled medications and pathway-specific biological agents that control the inflammation and physiology of asthma. Unfortunately, whether it is because of cost or difficulty understanding why or how to use inhaled medications, patients often do not take these medications. The consequences of poor treatment adherence, loss of control and exacerbations, are the same as if the condition remained untreated. Furthermore, poor adherence is difficult to detect without direct measurement. Together this means that poor treatment adherence is easily overlooked and, instead of addressing the cause of poor adherence, additional medicines may be prescribed. In other words, poor treatment adherence is a risk for the patient and adds cost to healthcare systems. In this article, we discuss the rationale for and the delivery of successful interventions to improve medication adherence in asthma. We contextualize these interventions by describing the causes of poor treatment adherence and how adherence is assessed. Finally, future perspectives on the design of new interventions are described.

Conflict of interest statement

None declared.

Clin Ophthalmol

-
-
-

. 2022 May 30;16:1675-1695.

doi: 10.2147/OPTH.S358066. eCollection 2022.

Impact of Inhaled and Intranasal Corticosteroids Exposure on the Risk of Ocular Hypertension and Glaucoma: A Systematic Review and Meta-Analysis

Anastasiya Vinokurtseva[1], Matthew Fung[1], Erica Ai Li[2], Richard Zhang[1], James J Armstrong[1 2], Cindy M L Hutnik[1 2 3]

Affiliations expand

- PMID: 35669010
- PMCID: PMC9165658
- DOI: 10.2147/OPTH.S358066

Free PMC article

Abstract

Purpose: Starting in 2019, the Global Initiative for Asthma recommended the use of inhaled corticosteroids (ICS) as part of reliever combination therapy in patients 12 years of age and older, thus dramatically increasing the population exposure to ICS. ICS and intranasal corticosteroids (INS) are commonly used for a variety of respiratory diseases. Chronic steroid use is a well-known risk factor for elevated intraocular pressure (IOP) and glaucoma regardless of route of administration. This study aimed to determine the reported risk of glaucoma, ocular hypertension (OHT) and IOP elevation associated with ICS and INS use.

Materials and methods: Systematic literature search in MEDLINE, EMBASE, Cochrane, CINAHL, BIOSIS, and Web of Science databases from the date of inception identified studies that assess ocular outcomes related to glaucoma in ICS and INS users. Study selection, risk of bias assessment and data extraction were done independently in duplicate. Meta-analysis assessed glaucoma incidence, OHT incidence and IOP changes in patients using ICS and INS. Study adhered to PRISMA guidelines. Study protocol was registered with PROSPERO: CRD42020190241.

Results: Qualitative and quantitative analyses included 65 and 41 studies, respectively. Incidence of glaucoma was not significantly different in either ICS or INS users compared to control over 45,457 person-years of follow-up. Similarly, no significant difference in OHT incidence over 4431 person-years was detected. In studies reporting IOP, a significantly higher IOP was observed (0.69 mmHg) in 857 ICS or INS users compared to 615 controls. However, no significant increase in IOP was observed within ICS or INS users when compared to pre-treatment baseline.

Conclusion: Overall, use of ICS or INS does not significantly increase the incidence of glaucoma or OHT. However, ICS and INS patients had significantly higher IOPs compared to untreated patients. Awareness of these findings is significant in care of patients with additional risk factors for glaucoma.

Keywords: asthma; corticosteroids; glaucoma; inhalation; intranasal.

Conflict of interest statement

The authors report no conflicts of interest in this work.

- 102 references
- 6 figures

Syst Rev

. 2022 Jun 7;11(1):115.

doi: 10.1186/s13643-022-01975-8.

Risk factors for asthma exacerbation during pregnancy: protocol for a systematic review and meta-analysis

Marleen P Bokern [#1], Annelies L Robijn [#2 3 4], Megan E Jensen [2 3 4], Daniel Barker [3 4], Katherine J Baines [2 3 4], Vanessa E Murphy [5 6 7]

Affiliations expand

- PMID: 35668513
- PMCID: PMC9172055
- DOI: 10.1186/s13643-022-01975-8

Free PMC article

Abstract

Background: Asthma is the most common medical condition to affect pregnancy. Asthma exacerbations occur in up to 45% of pregnant women and have been associated with adverse perinatal and infant outcomes. Conflicting literature exists regarding the risk factors for exacerbations, and no synthesis of the literature currently exists. Therefore, this systematic review and meta-analysis aims to determine risk factors for asthma exacerbations during pregnancy among pregnant women with asthma.

Methods: This protocol has been reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis protocols checklist. A systematic search will be conducted in the electronic MEDLINE, Embase, CINAHL and Cochrane Clinical Trials Register databases (from January 2000 onwards). Eligibility of each publication will be determined based on predefined selection criteria. Prospective cohort studies, retrospective cohort studies, case-control studies and randomised controlled trials (RCTs) will be included. Quality of included studies will be determined using the Newcastle Ottawa Scale and the Cochrane Risk of Bias tool. Pooled relative risk will be computed using random-effects meta-analyses. Heterogeneity will be assessed using the chi-squared test and the I^2 parameter. Publication bias will be assessed by inspecting a funnel plot for asymmetry and with the Egger's test of analyses including ten studies or more.

Discussion: The results of this systematic review and meta-analysis will discuss the potential risk factors for asthma exacerbations during pregnancy. This may aid healthcare professionals in early identification of pregnant women with asthma at risk of poor outcomes, providing the opportunity to implement early interventions in order to avoid deterioration of asthma symptoms during pregnancy.

Systematic review registration: PROSPERO CRD42020196190.

Keywords: Asthma; Pregnancy; Risk factors.

Conflict of interest statement

The authors declare that they have no competing interests.

- 34 references

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

Read free full text at BMC

Proceed to details

Cite

Pediatr Pulmonol

-
-
-

. 2022 Jun 6.

doi: 10.1002/ppul.26033. Online ahead of print.

Dupilumab in children with moderate-to-severe asthma: A cost utility analysis

Jefferson A Buendía [1], Diana G Patiño [1]

Affiliations expand

- PMID: 35668042

- DOI: 10.1002/ppul.26033

Abstract

Introduction: Dupilumab is an effective and safe medicine for the management of severe asthma. Due to its high cost, concerns are generated regarding its cost-effectiveness. This study aimed to estimate the cost-utility of dupilumab plus standard of care (SoC) versus SoC alone in children between 6 and 11 years old with severe asthma and eosinophilic phenotype.

Methods: A Markov-type model was developed to estimate costs and health outcomes of a simulated cohort of pediatric patients with persistent asthma treated over a 6-year period. To determine the robustness of the model deterministic and probabilistic sensitivity analyses were conducted.

Results: The quality-adjusted life-years (QALYs) per patient estimated were 0.85 with dupilumab and 0.84 with SoC. The total mean of discounted costs per patient per cycle were US$ 379 for dupilumab and US$ 19 for SoC. The incremental cost-effectiveness ratio estimated was $24 660 US$ per QALY CONCLUSION: Dupilumab is not cost-effective in Colombia in children between 6 and 11 years old with severe asthma and eosinophilic phenotype. Our evidence should motivate regulatory agencies to improve negotiations for new drugs with better information and evidence.

Keywords: health economics; healthcare; public health.

- 29 references

PeerJ

. 2022 May 30;10:e13444.

doi: 10.7717/peerj.13444. eCollection 2022.

IL-4/IL-13 axis as therapeutic targets in allergic rhinitis and asthma

Siti Muhamad Nur Husna[1], Norasnieda Md Shukri[2], Noor Suryani Mohd Ashari[1], Kah Keng Wong[1]

Affiliations expand

- PMID: 35663523

- PMCID: PMC9161813

- DOI: 10.7717/peerj.13444

Free PMC article

Abstract

Allergic rhinitis (AR) is a common disorder of the upper airway, while asthma is a disease affecting the lower airway and both diseases are usually comorbid. Interleukin (IL)-4 and IL-13 are critical cytokines in the induction of the pathogenic Th2 responses in AR and asthma. Targeting the IL-4/IL-13 axis at various levels of its signaling pathway has emerged as promising targeted therapy in both AR and asthma patient populations. In this review, we discuss the biological characteristics of IL-4 and IL-13, their signaling pathways, and therapeutic antibodies against each cytokine as well as their receptors. In particular, the pleiotropic roles of IL-4 and IL-13 in orchestrating Th2

responses in AR and asthma patients indicate that dual IL-4/IL-13 blockade is a promising therapeutic strategy for both diseases.

Keywords: Allergic rhinitis; Asthma; IL-13; IL-13Rα1; IL-4; IL-4Rα; Therapeutic antibodies.

Conflict of interest statement

The authors declare there are no competing interests.

- 103 references
- 2 figures

Review

Nat Rev Immunol

-
-
-

. 2022 Jun 1;1-14.

doi: 10.1038/s41577-022-00735-y. Online ahead of print.

Role of thymic stromal lymphopoietin in allergy and beyond

Risa Ebina-Shibuya[1], Warren J Leonard[2]

Affiliations expand

- PMID: 35650271

- PMCID: PMC9157039

- DOI: 10.1038/s41577-022-00735-y

Free PMC article

Abstract

Thymic stromal lymphopoietin (TSLP) is a pleiotropic cytokine that acts on multiple cell lineages, including dendritic cells, T cells, B cells, neutrophils, mast cells, eosinophils and innate lymphoid cells, affecting their maturation, survival and recruitment. It is best known for its role in promoting type 2 immune responses such as in allergic diseases and, in 2021, a monoclonal antibody targeting TSLP was approved for the treatment of severe asthma. However, it is now clear that TSLP has many other important roles in a variety of settings. Indeed, several genetic variants for TSLP are linked to disease severity, and chromosomal alterations in TSLP are common in certain cancers, indicating important roles of TSLP in disease. In this Review, we discuss recent advances in TSLP biology, highlighting how it regulates the tissue environment not only in allergic disease but also in infectious diseases, inflammatory diseases and cancer. Encouragingly, therapies targeting the TSLP pathway are being actively pursued for several diseases.

Conflict of interest statement

W.J.L. is an inventor on NIH patents related to thymic stromal lymphopoietin (TSLP). R.E-S. declares no competing interests.

- 189 references
- 4 figures

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

nature publishing group

Proceed to details

Cite

Share

Semin Respir Crit Care Med

. 2022 Jun 1.

doi: 10.1055/s-0042-1747939. Online ahead of print.

Endoscopic Options for Moderate COPD, Chronic Bronchitis, and Uncontrolled Asthma

Felix J F Herth[1,2], Konstantina Kontogianni[1,2], Judith Brock[1,2]

Affiliations expand

- PMID: 35649430

- DOI: 10.1055/s-0042-1747939

Abstract

Until now, interventional therapies for patients with chronic obstructive pulmonary disease have been available in the form of lung volume reduction procedures as end-stage options. Currently, the range of indications is expanding to include earlier stages of the diseases. Lung denervation is available for moderate COPD, and patients with chronic bronchitis are being evaluated for endoscopic goblet cell ablation. Rheoplasty, metered spray cryo technique, and Karakoca resector balloon are used for this indication. But also, for patients with severe uncontrolled asthma, several techniques are available today. In addition to thermoplasty as a long-proven procedure, new and currently under investigation is the targeted lung denervation.Most of these techniques are currently being tested in large pivotal trials and it will soon become clear in which phenotype which technique will be used in the different forms and stages of obstructive diseases. The current paper presents the techniques and the currently available literature.

Conflict of interest statement

None declared.

Cite

Share

17

J Allergy Clin Immunol Pract

. 2022 May 28;S2213-2198(22)00532-3.

doi: 10.1016/j.jaip.2022.05.022. Online ahead of print.

Factors related to biologic adherence and outcomes among moderate-to-severe asthma patients

Oyomoare L Osazuwa-Peters [1], Melissa A Greiner [1], Amber Oberle [2], Megan Oakes [1], Sheila M Thomas [3], Hayden Bosworth [4]

Affiliations expand

- PMID: 35640790

- DOI: 10.1016/j.jaip.2022.05.022

Abstract

Background: Adherence barriers to asthma biologics may not be uniform across administration settings for moderate-to-severe asthma patients.

Objective: To examine differences in asthma biologic adherence and associated factors, as well as association with 1-year all-cause emergency department (ED) visit, across administration settings.

Methods: A retrospective study of biologic naïve moderate-to-severe asthma patients with initial biologic therapy between 01/01/2016 and 04/30/2020 in the Optum Clinformatics Data Mart was performed. Three administration settings were identified: Clinic-only (outpatient office/infusion center), Home (self-administration), and Hybrid setting (mixture of clinic and self-administration). Asthma biologic adherence was the proportion of observed over expected biologic dose administrations received within 6 months from initial therapy. Factors associated with adherence were identified by administration setting, using Poisson regression analyses. Relationship between 1-year all-cause ED visit and adherence was assessed for each administration setting using Cox regression analyses.

Results: Study cohort was 3,932 patients. Biologics adherence was 0.75 [0.5, 1] in Clinic setting, the most common administration setting, and 0.83 [0.5, 1] in both Home and Hybrid settings. Specialist access was consistently associated with better biologic adherence while Black race,

Hispanic ethnicity, lower education, Medicare only insurance and higher patient out-of-pocket cost were associated with worse biologic adherence in some settings. In the Hybrid setting, hazard for 1-year all-cause ED visit decreased with biologics adherence.

Conclusion: Asthma biologic adherence varied by administration setting. Efforts to improve asthma biologic adherence should consider promoting self-administration when beneficial, improving prior specialist access, and targeting patients with higher risk of sub-optimal adherence particularly black and Hispanic patients.

Keywords: Administration setting; asthma biologics; health care use; medication adherence; social determinants.

Ann Allergy Asthma Immunol

. 2022 May 28;S1081-1206(22)00493-8.

doi: 10.1016/j.anai.2022.05.025. Online ahead of print.

Predictors of nonresponse to dupilumab in patients with atopic dermatitis: A machine learning analysis

Jashin J Wu [1], H Chih-Ho Hong [2], Joseph F Merola [3], David Gruben [4], Erman Güler [5], Claire Feeney [6], Ankur Bhambri [7], Daniela E Myers [7], Marco DiBonaventura [8]

Affiliations expand

- PMID: 35640774

- DOI: 10.1016/j.anai.2022.05.025

Abstract

Background: Many patients with atopic dermatitis (AD) have a suboptimal response to systemic therapy.

Objective: This study assessed predictors of nonresponse to dupilumab in patients with AD.

Methods: Data (April 2017 through June 2019) for patients aged ≥12 years with AD (ICD-9/10-CM: 691.8/L20.x) who initiated dupilumab on or after April 1, 2017 (index date) were collected from an electronic health record and insurance claims database. Nonresponse indicators (dupilumab discontinuation, addition of another systemic therapy or phototherapy, addition of a high-potency topical corticosteroid, AD-related hospital visit, AD-related emergency room visit, incident skin infection) were predicted from available demographic and clinical variables using machine learning.

Results: Among 419 patients (mean age: 45 years), 145 (35%) experienced ≥1 indicator of nonresponse in the 6-month post-index period. In patients with ≥1 indicator, the most common was dupilumab discontinuation (47% [68/145]). Of note, this analysis could not capture nonmedical reasons of dupilumab discontinuation (eg, cost, access). The most common predictors of nonresponse were a claim for ibuprofen (in 69% of patients with a nonresponse indicator) and Quan-Charlson Comorbidity Index value of 3-4 (59%).

Conclusion: Systemic dupilumab therapy for AD can be associated with a relatively high prevalence of nonresponse indicators. Factors associated with these indicators -ie, predictors of nonresponse- may be used to optimize disease management.

Keywords: atopic dermatitis; claims data; discontinuation; dupilumab; machine learning; nonresponse.

J Asthma

. 2022 Jun 7;1-9.

doi: 10.1080/02770903.2022.2082307. Online ahead of print.

Nebulizer versus metered dose inhaler with space chamber (MDI spacer) for acute asthma and chronic obstructive pulmonary disease exacerbation: attitudes of patients and healthcare providers in the COVID-19 era

Rayan Alsuwaigh [1], Yan Cao [2], Youxin Puan [1], Anthony Yii [1], Soyah Binti Mohamed Noor [2], Hui Ye [2], Haijuan Chen [2], Xiao Ling Li [2], Norlidah Binte Mohd Noor [2], Jason Liew [1], Tunn Ren Tay [1]

Affiliations expand

- PMID: 35608065

- DOI: 10.1080/02770903.2022.2082307

Abstract

Objective: Short-acting bronchodilators for asthma and chronic obstructive pulmonary disease (COPD) exacerbations are commonly delivered by nebulizers although administration using metered dose inhaler with space chamber (MDI spacer) has been shown to be equally efficacious. There are few studies examining patients' and healthcare providers' attitudes on the two administration methods in adults. This study explores patients' and healthcare providers' attitudes on the use of nebulizer versus MDI spacer for acute asthma and COPD exacerbations in adults.**Method**s: Patients admitted for asthma or COPD exacerbations, doctors, and nurses in a university-affiliated hospital were surveyed from 1 April 2021 to 30 September 2021 regarding their views on the effectiveness, ease of use, preparation and administration, side effects, and infection risk of the two administration methods.

Results: Ninety-nine patients, 103 doctors, and 650 nurses completed the survey. 60.6% of patients perceived nebulizer to be more effective. Patients who found nebulizer more comfortable were more likely to prefer nebulizer (OR 43.97, $p = 0.01$), while those who associated it with a greater infection risk were less likely to prefer nebulizer (OR 0.15, $p = 0.03$). 49.5% of doctors and 49.1% of nurses perceived nebulizer to be more effective, compared to 10.7% and 34.5%, respectively, for MDI spacer. Effectiveness and patient comfort influenced doctors' and nurses' preference for nebulizer while ease of preparation and administration influenced nurses' preference only.

Conclusions: Patients and healthcare providers perceived nebulizer to be more effective. Factors unique to each group influenced their preference for nebulizer.

Keywords: Bronchodilator; administration; attitude; infection risk; preference.

Share

20

Intern Emerg Med

. 2022 Jun;17(4):953-955.

doi: 10.1007/s11739-022-02964-4. Epub 2022 May 17.

Persistent asthma hospitalisations and deaths require a national asthma prevention plan

Bianca Beghé [1], Leonardo Fabbri [2], Enrico Clini [3]

Affiliations expand

- PMID: 35578148

- DOI: 10.1007/s11739-022-02964-4

No abstract available

Keywords: Allergy; Anaphylaxixs; Bronchitis; Chronic obstructive pulmonary disease; Emphysema.

- 21 references

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

SpringerLink FULL-TEXT ARTICLE

Proceed to details

Cite

Share

21

Clinical Trial

N Engl J Med

. 2022 Jun 2;386(22):2071-2083.

doi: 10.1056/NEJMoa2203163. Epub 2022 May 15.

Albuterol–Budesonide Fixed-Dose Combination Rescue Inhaler for Asthma

Alberto Papi[1], Bradley E Chipps[1], Richard Beasley[1], Reynold A Panettieri Jr[1], Elliot Israel[1], Mark Cooper[1], Lynn Dunsire[1], Allison Jeynes-Ellis[1], Eva Johnsson[1], Robert Rees[1], Christy Cappelletti[1], Frank C Albers[1]

Affiliations expand

- PMID: 35569035

- DOI: 10.1056/NEJMoa2203163

Abstract

Background: As asthma symptoms worsen, patients typically rely on short-acting β_2-agonist (SABA) rescue therapy, but SABAs do not address worsening inflammation, which leaves patients at risk for severe asthma exacerbations. The use of a fixed-dose combination of albuterol and budesonide, as compared with albuterol alone, as rescue medication might reduce the risk of severe asthma exacerbation.

Methods: We conducted a multinational, phase 3, double-blind, randomized, event-driven trial to evaluate the efficacy and safety of albuterol-budesonide, as compared with albuterol alone, as rescue medication in patients with uncontrolled moderate-to-severe asthma who were receiving inhaled glucocorticoid-containing maintenance therapies, which were continued throughout the trial. Adults and adolescents (≥12 years of age) were randomly assigned in a 1:1:1 ratio to one of three trial groups: a fixed-dose combination of 180 μg of albuterol and 160 μg of budesonide (with each dose consisting of two actuations of 90 μg and 80 μg, respectively [the higher-dose combination group]), a fixed-dose combination of 180 μg of albuterol and 80 μg of budesonide (with each dose consisting of two actuations of 90 μg and 40 μg, respectively [the lower-dose combination group]), or 180 μg of albuterol (with each dose consisting of two actuations of 90 μg [the albuterol-alone group]). Children 4 to 11 years of age were randomly assigned to only the lower-dose combination group or the albuterol-alone group. The primary efficacy end point was the first event of severe asthma exacerbation in a time-to-event analysis, which was performed in the intention-to-treat population.

Results: A total of 3132 patients underwent randomization, among whom 97% were 12 years of age or older. The risk of severe asthma exacerbation was significantly lower, by 26%, in the higher-dose combination group than in the albuterol-alone group (hazard ratio, 0.74; 95% confidence interval [CI], 0.62 to 0.89; P = 0.001). The hazard ratio in the lower-dose combination group, as compared with the albuterol-alone group, was 0.84 (95% CI, 0.71 to 1.00; P = 0.052). The incidence of adverse events was similar in the three trial groups.

Conclusions: The risk of severe asthma exacerbation was significantly lower with as-needed use of a fixed-dose combination of 180 μg of albuterol and 160 μg of budesonide than with as-needed use of albuterol alone among patients with uncontrolled moderate-to-severe asthma who were receiving a wide range of inhaled glucocorticoid-containing maintenance therapies. (Funded by Avillion; MANDALA ClinicalTrials.gov number, NCT03769090.).

Comment in

- Another Rescue Therapy Option for Patients with Moderate-to-Severe Asthma.
  Schatz M.N Engl J Med. 2022 Jun 2;386(22):2139-2140. doi: 10.1056/NEJMe2205717.PMID: 35648708 No abstract available.

Environ Int

. 2022 Jun;164:107241.

doi: 10.1016/j.envint.2022.107241. Epub 2022 Apr 12.

Long-term exposure to air pollution and mortality in a Danish nationwide administrative cohort study: Beyond mortality from cardiopulmonary disease and lung cancer

Rina So [1], Zorana J Andersen [2], Jie Chen [3], Massimo Stafoggia [4], Kees de Hoogh [5], Klea Katsouyanni [6], Danielle Vienneau [5], Sophia Rodopoulou [7], Evangelia Samoli [7], Youn-Hee Lim [2], Jeanette T Jørgensen [2], Heresh Amini [2], Tom Cole-Hunter [2], Seyed Mahmood Taghavi Shahri [2], Matija Maric [2], Marie Bergmann [2], Shuo Liu [2], Shadi Azam [2], Steffen Loft [2], Rudi G J Westendorp [8], Laust H Mortensen [9], Mariska Bauwelinck [10], Jochem O Klompmaker [11], Richard Atkinson [12], Nicole A H Janssen [13], Bente Oftedal [14], Matteo Renzi [15], Francesco Forastiere [16], Maciek Strak [17], Lau C Thygesen [18], Bert Brunekreef [3], Gerard Hoek [3], Amar J Mehta [9]

Affiliations expand

- PMID: 35544998

- DOI: 10.1016/j.envint.2022.107241

Free article

Abstract

Background: The association between long-term exposure to air pollution and mortality from cardiorespiratory diseases is well established, yet the evidence for other diseases remains limited.

Objectives: To examine the associations of long-term exposure to air pollution with mortality from diabetes, dementia, psychiatric disorders, chronic kidney disease (CKD), asthma, acute lower respiratory infection (ALRI), as well as mortality from all-natural and cardiorespiratory causes in the Danish nationwide administrative cohort.

Methods: We followed all residents aged ≥ 30 years (3,083,227) in Denmark from 1 January 2000 until 31 December 2017. Annual mean concentrations of fine particulate matter ($PM_{2.5}$), nitrogen dioxide (NO_2), black carbon (BC), and ozone (warm season) were estimated using European-wide hybrid land-use regression models (100 m × 100 m) and assigned to baseline residential addresses. We used Cox proportional hazard models to evaluate the association between air pollution and mortality, accounting for demographic and socioeconomic factors. We additionally applied indirect adjustment for smoking and body mass index (BMI).

Results: During 47,023,454 person-years of follow-up, 803,881 people died from natural causes. Long-term exposure to $PM_{2.5}$ (mean: 12.4 μg/m^3), NO_2 (20.3 μg/m^3), and/or BC (1.0×10^{-5}/m) was statistically significantly associated with all studied mortality outcomes except CKD. A 5 μg/m^3 increase in $PM_{2.5}$ was associated with higher mortality from all-natural causes (hazard ratio 1.11; 95% confidence interval 1.09-1.13), cardiovascular disease (1.09; 1.07-1.12), respiratory disease (1.11; 1.07-1.15), lung cancer (1.19; 1.15-1.24), diabetes (1.10; 1.04-1.16), dementia (1.05; 1.00-1.10), psychiatric disorders (1.38; 1.27-1.50), asthma (1.13; 0.94-1.36), and ALRI (1.14; 1.09-1.20). Associations with long-term exposure to ozone (mean: 80.2 μg/m^3) were generally negative but became significantly positive for several endpoints in two-pollutant models. Generally, associations were attenuated but remained significant after indirect adjustment for smoking and BMI.

Conclusion: Long-term exposure to $PM_{2.5}$, NO_2, and/or BC in Denmark were associated with mortality beyond cardiorespiratory diseases, including diabetes, dementia, psychiatric disorders, asthma, and ALRI.

Keywords: Cardiorespiratory disease; Dementia; Long-term exposure to air pollution; Mortality; Nationwide administrative cohort; Psychiatric disorders.

Randomized Controlled Trial

Pulm Pharmacol Ther

. 2022 Jun;73-74:102129.

doi: 10.1016/j.pupt.2022.102129. Epub 2022 May 4.

Pharmacokinetic profile of beclometasone dipropionate/formoterol fumarate administered through a novel dry-powder inhaler in Chinese healthy volunteers

Zhu Luo [1], Germano Lucci [2], Luigi Santoro [2], Eva Topole [2], Fabrizia Mariotti [2]

Affiliations expand

- PMID: 35525480

- DOI: 10.1016/j.pupt.2022.102129

Abstract

Introduction: An extrafine formulation of the inhaled corticosteroid beclometasone dipropionate (BDP) plus the long-acting β_2-agonist formoterol fumarate (FF) has been available for years via a pressurised metered-dose inhaler for the management of asthma and chronic obstructive pulmonary disease. More recently, the same extrafine BDP/FF formulation has become available in a multidose dry-powder inhaler (DPI) called the NEXThaler. The pharmacokinetics (PK) of BDP/FF via this DPI have previously been evaluated in a Caucasian population. The current study aimed to evaluate the PK profile of BDP/FF via DPI in healthy Chinese volunteers. The results were then compared to previous Caucasian data.

Methods: This open-label parallel group study randomised subjects to single-dose BDP/FF 200/12, 400/24, or 800/48 μg via DPI. Blood samples were taken up to 24 h post-dose for PK evaluation of BDP, beclometasone 17-monopropionate (B17MP, active metabolite of BDP) and formoterol. The primary objective of the study was to evaluate the PK of BDP/FF (BDP, B17MP and formoterol). The study is registered on the World Health Organization International Clinical Trials Registry Platform (ChiCTR1900021899).

Results: Of 36 subjects randomised, all completed the study. Following inhalation of all three doses, plasma concentration of formoterol and BDP increased rapidly, with peak mean values at the first post-dose timepoint (5 min), then rapidly decreasing; B17MP reached peak concentration slightly later. Plasma exposure to formoterol, BDP and B17MP increased broadly in a dose-proportional manner to BDP/FF dose, with t_{max} values similar across the dose range. All BDP/FF doses were generally well tolerated.

Conclusions: Therapeutic and supra-therapeutic doses of BDP/FF administered via DPI resulted in approximately dose-proportional plasma exposure in healthy Chinese subjects, with PK profiles that were comparable to previous data from Caucasian subjects.

Keywords: Asthma; Chronic obstructive pulmonary disease; Fixed-dose combination; Inhaled corticosteroid; Long-acting beta2-agonist.

24

Published Erratum

Pulm Pharmacol Ther

.
. 2022 Jun;73-74:102126.

doi: 10.1016/j.pupt.2022.102126. Epub 2022 Apr 11.

Corrigendum to "Dose bridging data for mometasone furoate in once-daily fixed-dose inhaled combinations of mometasone furoate/indacaterol and mometasone furoate/indacaterol/glycopyrronium in patients with asthma" [Pulm. Pharmacol. Therapeut. 70 (2021) 102068]

Roland Buhl[1], Ivan Nikolaev[2], Hanns-Christian Tillmann[3], Soniya Vaidya[4], Christian Bartels[2], Monish Jain[5], Juergen Jauernig[2], Huib A M Kerstjens[6]

Affiliations expand

- PMID: 35422377

- DOI: 10.1016/j.pupt.2022.102126

No abstract available

Erratum for

- Dose bridging data for mometasone furoate in once-daily fixed-dose inhaled combinations of mometasone furoate/indacaterol and mometasone furoate/ indacaterol/glycopyrronium in patients with asthma.
  Buhl R, Nikolaev I, Tillmann HC, Vaidya S, Bartels C, Jain M, Jauernig J, Kerstjens HAM.Pulm Pharmacol Ther. 2021 Oct;70:102068. doi: 10.1016/j.pupt.2021.102068. Epub 2021 Jul 28.PMID: 34329722 Review.

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

ELSEVIER FULL-TEXT ARTICLE

Proceed to details

Cite

Share

25

Nat Rev Endocrinol

. 2022 Jun;18(6):332.

doi: 10.1038/s41574-022-00678-3.

Metabolomic profiling of adrenal function in asthma

Shimona Starling[1]

Affiliations expand

- PMID: 35414021

- DOI: 10.1038/s41574-022-00678-3

No abstract available

- 1 reference

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

Proceed to details

Cite

Share

26

Lancet Respir Med

. 2022 Jun;10(6):526-527.

doi: 10.1016/S2213-2600(22)00053-4. Epub 2022 Apr 7.

Inhaled corticosteroids: not just for asthma, but for COVID-19?

Felicity Liew[1], Peter J M Openshaw[2]

Affiliations expand

- PMID: 35397799

- PMCID: PMC8989394

- DOI: 10.1016/S2213-2600(22)00053-4

Free PMC article

No abstract available

Conflict of interest statement

PJMO reports grants from the EU Innovative Medicines Initiative (IMI) 2 Joint Undertaking during the submitted work; grants from UK Medical Research Council, EU-IMI, UK National Institute for Health Research, and UK Research and Innovation-Department for Business, Energy and Industrial Strategy; and personal fees from Pfizer, Nestle, Janssen, and Sequris, outside the submitted work. FL declares no competing interests.

- 10 references
- 1 figure

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS

ELSEVIER FULL-TEXT ARTICLE

Proceed to details

Cite

Share

27

Editorial

Clin Exp Allergy

. 2022 Jun;52(6):732-734.

doi: 10.1111/cea.14141. Epub 2022 Apr 6.

Breathing exercises for adults with asthma

Verah Harper [1], James Trayer [2]

Affiliations expand

- PMID: 35388565

- DOI: 10.1111/cea.14141

No abstract available

Keywords: asthma; basic immunology; breathing exercises; pneumology.

- 9 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

WILEY Full Text Article

Proceed to details

Cite

Share

28

Am J Respir Cell Mol Biol

. 2022 Jun;66(6):648-660.

doi: 10.1165/rcmb.2021-0301OC.

CBX4 Regulates Long-Form Thymic Stromal Lymphopoietin-mediated Airway Inflammation through SUMOylation in House Dust Mite-induced Asthma

Shixiu Liang[1], Zicong Zhou[1], Zili Zhou[1], Jieyi Liu[1], Wufeng Huang[1], Hangming Dong[1], Fei Zou[2], Haijin Zhao[1], Changhui Yu[1], Shaoxi Cai[1]

Affiliations expand

- PMID: 35358396

- DOI: 10.1165/rcmb.2021-0301OC

Abstract

Thymic stromal lymphopoietin presents in two distinct isoforms: short-form (sfTSLP) and long-form (lfTSLP). lfTSLP promotes inflammation, whereas sfTSLP inhibits inflammation, in allergic asthma. However, little is known about the regulation of lfTSLP and sfTSLP during allergic attack in the asthma airway epithelium. Here, we report that small ubiquitin-like modifier (SUMOylation) was enhanced in house dust mite-induced allergic asthma airway epithelium. Inhibition of SUMOylation significantly alleviated airway T-helper cell type 2 inflammation and lfTSLP expression. Mechanistically, chromobox 4 (CBX4), a SUMOylation E3 ligase, enhanced lfTSLP mRNA translation, but not sfTSLP, through the RNA-binding protein muscle excess (MEX)-3B. MEX-3B promoted lfTSLP translation by binding the lfTSLP mRNA through its K homology domains. Furthermore, CBX4 regulated MEX-3B transcription in human bronchial epithelial cells through enhancing SUMOylation concentrations of the transcription factor TFII-I. In conclusion, we demonstrate an important mechanism whereby CBX4 promotes MEX-3B transcription through enhancing TFII-I SUMOylation and MEX-3B enhances the expression of lfTSLP through binding to the lfTSLP mRNA and promoting its translation. Our findings uncover a novel target of CBX4 for therapeutic agents for lfTSLP-mediated asthma.

Keywords: SUMOylation; TSLP; airway inflammation; asthma.

Comment in

- SUMO Wrestling in the Airway Epithelium: Does It Regulate Thymic Stromal Lymphopoietin?
  Gounni AS, Koussih L.Am J Respir Cell Mol Biol. 2022 Jun;66(6):591-592. doi: 10.1165/rcmb.2021-0558ED.PMID: 35364000 **Free PMC article.** No abstract available.

SUPPLEMENTARY INFO

MeSH terms, Substances, Grant supportexpand

FULL TEXT LINKS

Proceed to details

Cite

Share

29

J Asthma

-
-
-

. 2022 May 30;1-9.

doi: 10.1080/02770903.2022.2056048. Online ahead of print.

Long-term safety of once-daily indacaterol acetate/glycopyrronium bromide/mometasone furoate high-dose, and indacaterol acetate/mometasone furoate high-dose, in Japanese patients with inadequately controlled asthma: Results from two open-label, 52-week studies

Hironori Sagara [1], Peter D'Andrea [2], Ana-Maria Tanase [3], Abhijit Pethe [2], Yukina Tanaka [4], Kazutaka Matsuo [4], Motoi Hosoe [3], Yoichi Nakamura [5]

Affiliations expand

- PMID: 35348408

- DOI: 10.1080/02770903.2022.2056048

Abstract

Introduction: The 52-week long-term safety of once-daily indacaterol acetate/glycopyrronium bromide/mometasone furoate (IND/GLY/MF) high-dose (150/50/160 µg) and IND/MF high-dose (150/320 µg) was evaluated in two studies enrolling Japanese patients with inadequately controlled asthma.

Methods: Study 1 (IND/GLY/MF) and Study 2 (IND/MF) were 52-week, phase III, open-label, single-arm, multicenter studies conducted in Japanese adult patients with inadequately controlled asthma. The primary endpoint was incidence and severity of treatment-emergent adverse events (AEs) over 52-weeks.

Results: In Study 1, 94 patients received IND/GLY/MF high-dose and 84 (89.4%) patients completed the 52-week study treatment; in Study 2, 51 patients received IND/MF high-dose and 48 (94.1%) patients completed the 52-week study treatment. In Study 1, 68.1% and 6.4% of 94 patients reported ≥1 AE and ≥1 serious AE (SAE) respectively. In Study 2, 78.4% of 51 patients reported ≥1 AE; no patients reported SAEs. The most commonly reported AEs were asthma (exacerbation; 30.9% and 54.9%) and nasopharyngitis (18.1% and 29.4%) in Study 1 and Study 2, respectively. Severe AEs including asthma (exacerbation) were reported in 13.8% and 13.7% of patients in Study 1 and Study 2, respectively. In Study 1, 10 patients (10.6%) reported treatment-related AEs, of which dysphonia (9 patients [9.6%]) was the most commonly reported; no treatment-related AEs were reported in Study 2. In Study 1, one death (not study drug-related) was reported after study discontinuation (92 days after last dose of study medication).

Conclusions: Once-daily IND/GLY/MF and IND/MF high-dose were well-tolerated in Japanese patients with inadequately controlled asthma. No unexpected safety findings were observed.

Supplemental data for this article is available online at.

Keywords: Asthma control; Japan; long-acting β2-adrenergic agonist/inhaled corticosteroid (LABA/ICS); long-acting β2-adrenergic agonist/long-acting muscarinic antagonist/inhaled corticosteroid (LABA/LAMA/ICS); lung function; safety.

Review

Curr Nutr Rep

. 2022 Jun;11(2):311-317.

doi: 10.1007/s13668-022-00411-6. Epub 2022 Mar 26.

Vitamin D and Asthma: a Systematic Review of Clinical Trials

Itamar Nitzan[1,2], Francis B Mimouni[3,4], Alona Bin Nun[3,5], Yair Kasirer[3,5], Joseph Mendlovic[3,4,6]

Affiliations expand

- PMID: 35347665

- DOI: 10.1007/s13668-022-00411-6

Abstract

Purpose of the review: To perform a systematic review of prospective clinical trials to determine whether improving vitamin D status improves asthma control.

Recent findings: In cross sectional studies suboptimal viramin D status is often associated with poor asthma control. However, decreased 25-hydroxycholecalciferol (25 (OH) D) concentrations might not be causally associated with asthma control. We performed a systematic review until December 15, 2021 according to PRISMA guideline, searching MEDLINE, MEDLINE In-Process, Embase, Cochrane Database of Systematic Reviews, and Cochrane Central Register of Controlled Trials. Two searches were performed, the first using "vitamin D" and the second using "Vitamin D" or "ergocalciferol" or "cholecalciferol" and "Asthma". From 419 retrieved papers, after removal of duplicate and after using exclusion criteria, 28 full-text articles were eligible, of which 6 remained for quantitative analysis and 11 (9 studies) for qualitative analysis. From both analyses, prospective studies do not support that improving the vitamin D status of asthmatic children improves asthma control.

Keywords: Asthma; Vitamin D.

- 30 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

Proceed to details

Cite

Share

31

Review

Allergy

.
. 2022 Jun;77(6):1719-1735.

doi: 10.1111/all.15295. Epub 2022 Apr 2.

Allergen immunotherapy for asthma prevention: A systematic review and meta-analysis of randomized and non-randomized controlled studies

Mariana Farraia[1 2 3], Inês Paciência[1 2], Francisca Castro Mendes[1 2 3], João Cavaleiro Rufo[1 2], Mohamed Shamji[4 5], Ioana Agache[6], André Moreira[1 2 3 7]

Affiliations expand

- PMID: 35342949

- DOI: 10.1111/all.15295

Abstract

Background: Allergen immunotherapy (AIT) is a disease-modifying treatment for IgE-mediated diseases. Randomized controlled trials (RCTs) support AIT's potential role in asthma prevention but evidence from non-randomized studies of interventions (NRSI) and longitudinal observational studies has been poorly addressed. Therefore, we aimed to conduct a systematic review and meta-analysis to assess clinical data from all study types to evaluate quantitatively the preventive role of AIT in asthma onset.

Methods: We search three databases. Studies were screened, selected and evaluated for quality using risk-of-bias (ROB) tools. Data were descriptively summarized and meta-analysed using random effects. We performed a sensitivity, influence and subgroup analyses. Publication bias and heterogeneity were assessed.

Results: From the 4549 identified studies, 24 (12 RCTs and 12 NRSI) were included in the qualitative synthesis and 18 underwent meta-analysis. One study was at low ROB, seven had moderate ROB, and 15 were proven of high ROB. Random-effects analysis showed a significant decrease in the risk of developing asthma following AIT by 25% (RR, 95% CI: 0.75, 0.64-0.88). This effect was not significant in the sensitivity analysis. Publication bias raised concerns, together with the moderate heterogeneity between studies (I^2 = 58%). Subgroup analysis showed a remarkable preventive effect of AIT in children (RR, 95% CI: 0.71, 0.53-0.96), when completing 3 years of therapy (RR, 95% CI: 0.64, 0.47-0.88), and in mono-sensitized patients (RR, 95% CI: 0.49, 0.39-0.61).

Conclusions: Our findings support a possible preventive effect of AIT in asthma onset and suggest an enhanced effect when administered in children, mono-sensitized, and for at least 3 years, independently of allergen type.

Keywords: allergen immunotherapy; allergy treament; asthma; prevention; rhinitis.

- 50 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

FULL TEXT LINKS

WILEY Full Text Article

Proceed to details

Cite

Share

32

Review

Am J Prev Med

-
-
-

. 2022 Jun;62(6):953-960.

doi: 10.1016/j.amepre.2022.01.015. Epub 2022 Mar 23.

Association Between E-Cigarettes and Asthma in Adolescents: A Systematic Review and Meta-Analysis

Xuechao Li [1], Yi Zhang [2], Rongqiang Zhang [3], Fei Chen [4], Lihua Shao [5], Li Zhang [6]

Affiliations expand

- PMID: 35337694

- DOI: 10.1016/j.amepre.2022.01.015

Free article

Abstract

Introduction: Numerous studies have revealed the relationship between E-cigarettes and asthma but have shown inconsistent results. This study systematically evaluated the potential association between E-cigarette use and asthma in adolescents.

Methods: PubMed, Embase (Ovid), Cochrane Library, and the China Biological Medicine Database were searched for relevant articles published between database inception and February 28, 2021. The quality of included studies was evaluated using the Agency for Healthcare Research and Quality assessment, and a quantitative meta-analysis was conducted to pool outcomes of ORs with 95% CIs.

Results: A total of 10 cross-sectional studies incorporating a total of 483,948 participants were included. All the study participants were middle- and high-school students with a mean age of 15-16 years. The median prevalence of ever E-cigarette use was 11.2% (range=2.2%, 45%), and that of current use was 7.5% (range=2.7%, 25%). Overall, E-cigarette use was associated with significantly higher odds of having asthma (pooled OR=1.31, 95% CI=1.22, 1.42) than nonuse, and both current use (OR=1.36, 95% CI=1.26, 1.48) and ever use (OR=1.20, 95% CI=1.12, 1.28) showed similar associations.

Discussion: This study shows that both current and ever E-cigarette use have significant associations with asthma in adolescents. This knowledge might provide potential evidence for developing primary prevention strategies and serve as a reference for public health policy.

Arch Bronconeumol

. 2022 Jun;58(6):471-473.

doi: 10.1016/j.arbres.2022.02.003. Epub 2022 Feb 12.

Small Airway Disease in Asthma: Why is it so Important?

[Article in English, Spanish]

F Baraldi[1], F Alfano[1], M Contoli[1], A Papi[2]

Affiliations expand

- PMID: 35305860

- DOI: 10.1016/j.arbres.2022.02.003

No abstract available

doi: 10.1016/j.jaip.2022.02.040. Epub 2022 Mar 15.

An Online Weight Loss Intervention for People With Obesity and Poorly Controlled Asthma

Olivia Johnson [1], Lynn B Gerald [2], Jean Harvey [3], Gem Roy [4], Heather Hazucha [4], Chelsey Large [5], Alyce Burke [4], Meredith McCormack [6], Robert A Wise [6], Janet T Holbrook [4], Anne E Dixon [7]

Affiliations expand

- PMID: 35304842

- PMCID: PMC9188993

- DOI: 10.1016/j.jaip.2022.02.040

Free PMC article

Abstract

Background: Weight loss might improve asthma control in people with obesity. However, people with asthma might have particular challenges losing weight and the amount of weight loss needed to improve asthma control is not clear.

Objectives: To pilot-test an online weight loss intervention and to estimate the impact of weight loss on asthma control.

Methods: We performed a 6-month, single-arm, futility trial of an online weight loss intervention at 2 centers. To reject the assumption of futility, 9 or more participants had to lose at least 5% of their body weight. We also assessed the association between weight loss (≥5%) and asthma outcomes.

Results: Forty-three participants (85% women) started the weight loss intervention. The median and interquartile range for the body mass index was 40.3 kg/m^2 (range 34.7-46.8 kg/m^2), and 14 (range 12-17 kg/m^2) for the Asthma Control Test score. At 6 months, 10 participants (23%; 95% CI 12%-39%) lost at least 5% of their initial weight. Weight loss of at least 5% was associated with a clinically and statistically significant improvements in their Asthma Control Test (median [interquartile range] increase of 3 [1 to 7]; P < .05), Marks Asthma Quality of Life Score (-9.5 [-18 to -3]; P = .008), and their general health-related quality of life score (RAND-36; improved by 9.4 [2.8 to 22.5]; P =.014).

Conclusions: An online weight loss intervention has the potential to meet U.S. Food and Drug Administration guidance for product evaluation (at least a 5% weight loss in 35% of people) for treating obesity, and is associated with a clinically significant improvement in asthma control, quality of life, and overall health-related quality of life.

Keywords: Asthma control; Asthma quality of life; Diet; Exercise; Lung function.

J Allergy Clin Immunol Pract

. 2022 Jun;10(6):1515-1526.

doi: 10.1016/j.jaip.2022.02.026. Epub 2022 Mar 6.

Dupilumab Demonstrates Rapid Onset of Response Across Three Type 2 Inflammatory Diseases

G Walter Canonica[1], Arnaud Bourdin[2], Anju T Peters[3], Martin Desrosiers[4], Claus Bachert[5], Stephan Weidinger[6], Eric L Simpson[7], Nadia Daizadeh[8], Zhen Chen[9], Siddhesh Kamat[9], Asif H Khan[10], Jingdong Chao[9], Neil M H Graham[9], Elizabeth Laws[11], Ana B Rossi[8], Marius Ardeleanu[9], Leda P Mannent[10], Nikhil Amin[9], Benjamin Ortiz[9], Yamo Deniz[9], Michel Djandji[8], Paul J Rowe[11]

Affiliations expand

- PMID: 35259535

- DOI: 10.1016/j.jaip.2022.02.026

Free article

Abstract

Background: Type 2 inflammatory diseases often coexist in patients. Dupilumab targets type 2 inflammation and has demonstrated treatment benefits in patients with atopic dermatitis (AD), asthma, and chronic rhinosinusitis with nasal polyps (CRSwNP) with an acceptable safety profile.

Objective: This post hoc analysis across five phase 3 studies in patients with moderate to severe AD or asthma, or severe CRSwNP, evaluated time of onset and duration of the treatment response.

Methods: Patients received subcutaneous dupilumab 200/300 mg or placebo. Assessments included the Eczema Area and Severity Index, Peak Pruritus Numerical Rating Scale, and Dermatology Life Quality Index in AD; pre-bronchodilator FEV_1, daily morning peak expiratory flow, and symptom scores in asthma; and University of Pennsylvania Smell Identification Test, daily nasal congestion, and loss of smell scores in CRSwNP.

Results: At week 2 after the initiation of dupilumab versus placebo, 67.8% versus 36.5% of AD patients achieved a clinically meaningful benefit (Eczema Area and Severity Index: 50% or greater improvement; Peak Pruritus Numerical Rating Scale: 3 point or greater improvement; or Dermatology Life Quality Index: 4 point or greater improvement) ($P < .001$). Moreover, 61.6% versus 39.9% of asthma patients achieved improvements in pre-bronchodilator FEV_1 of 100 mL or greater and 48.8% versus 26.3% achieved 200 mL or greater improvement (both $P < .001$); 33.2% versus 5.6% of CRSwNP patients regained a sense of smell ($P < .001$). Treatment effects further improved or were sustained to the end of treatment.

Conclusions: Clinically meaningful responses were achieved rapidly after the first dupilumab dose in AD, asthma, or CRSwNP and were sustained throughout treatment (see Video in this article's Online Repository at www.jaci-inpractice.org).

Keywords: Anti-IL-13; Anti-IL-4; Asthma; Dupilumab; Rapid onset.

J Allergy Clin Immunol Pract

. 2022 Jun;10(6):1562-1568.

doi: 10.1016/j.jaip.2022.02.022. Epub 2022 Mar 5.

As-Needed Use of Short-Acting β ₂-Agonists Alone Versus As-Needed Use of Short-Acting β ₂-Agonists Plus Inhaled Corticosteroids in Pediatric Patients With Mild Intermittent (Step 1) Asthma: A Cost-Effectiveness Analysis

Carlos E Rodríguez-Martínez [1], Monica P Sossa-Briceño [2], Jefferson Antonio Buendia [3]

Affiliations expand

- PMID: 35259534

- DOI: 10.1016/j.jaip.2022.02.022

Abstract

Background: Although the efficacy of the as-needed use of short-acting β_2-agonists (SABAs) plus inhaled corticosteroids (ICS) for treating children with mild intermittent asthma has been demonstrated, evidence of its cost-effectiveness is scarce.

Objectives: The aim of the present study was to compare the cost-effectiveness of the as-needed use of SABAs alone versus the as-needed use of SABAs plus ICS in children 5 to 11 years old with mild intermittent (step 1) asthma but suffering from an exacerbation of asthma symptoms.

Methods: A decision-analysis model was adapted. Effectiveness parameters were obtained from a randomized clinical trial. Cost data were obtained from hospital bills and from the national manual of drug prices in Colombia. The study was carried out from the perspective of the national health care system in Colombia. The main outcome of the model was a first course of prednisone for an asthma exacerbation (AE).

Results: Compared with the use of SABAs alone, the as-needed use of SABAs plus ICS was associated with lower overall treatment costs (US$17.99 vs US$27.94 mean cost per patient) and a higher probability of a lack of a requirement for a first course of prednisone (0.6500 vs 0.5100), thus showing dominance.

Conclusions: In Colombia, compared with the use of albuterol alone, the use of beclomethasone dipropionate added to albuterol as needed for symptom relief is cost-effective in children 5 to 11 years old with mild intermittent (step 1) asthma, because it involves a higher probability of a lack of a requirement for prednisone for AE at lower total treatment costs.

Keywords: Acute asthma; Children; Cost-effectiveness; Inhaled corticosteroids.

J Allergy Clin Immunol Pract

. 2022 Jun;10(6):1545-1553.e2.

doi: 10.1016/j.jaip.2022.02.020. Epub 2022 Mar 5.

Longitudinal Impact of Sputum Inflammatory Phenotypes on Small Airway Dysfunction and Disease Outcomes in Asthma

Mustafa Abdo [1], Frauke Pedersen [2], Anne-Marie Kirsten [3], Vera Veith [4], Heike Biller [4], Frederik Trinkmann [5], Erika von Mutius [6], Matthias Kopp [7], Gesine Hansen [8], Klaus F Rabe [4], Thomas Bahmer [9], Henrik Watz [3], ALLIANCE study group

Affiliations expand

- PMID: 35257957

- DOI: 10.1016/j.jaip.2022.02.020

Free article

Abstract

Background: Little is known about the relationship between airway inflammatory phenotypes and some important asthma features such as small airway dysfunction (SAD).

Objective: To describe the longitudinal impact of airway inflammatory phenotypes on SAD and asthma outcomes.

Methods: We measured eosinophil and neutrophil counts in induced sputum at baseline and 1 year later to stratify 197 adult patients with asthma into 4 inflammatory phenotypes. We conducted a comprehensive assessment of lung function using spirometry, body plethysmography, impulse oscillometry, and inert gas single and multiple breath washouts. We compared lung function, asthma severity, exacerbation frequency, and symptom control between the phenotypes. We studied the longitudinal impact of persistent sputum inflammatory phenotypes and the change of sputum cell counts on lung function.

Results: Patients were stratified into eosinophilic (23%, n = 45), neutrophilic (33%, n = 62), mixed granulocytic (22%, n = 43), and paucigranulocytic (24%, n = 47) phenotypes. Patients with eosinophilic and mixed granulocytic asthma had higher rates of airflow obstruction and severe exacerbation as well as poorer symptom control than patients with paucigranulocytic asthma. All SAD measures were worse in patients with eosinophilic and mixed asthma than in those with paucigranulocytic asthma (all P values <.05). Eosinophilic asthma also indicated worse distal airflow obstruction, increased ventilation inhomogeneity (all P values <.05), and higher tendency for severe exacerbation (P = .07) than neutrophilic asthma. Longitudinally, persistent mixed granulocytic asthma was associated with the worst follow-up measures of SAD compared with persistent neutrophilic, persistent paucigranulocytic, or nonpersistent asthma phenotypes. In patients with stable forced expiratory volume in 1 second (FEV1), the mean increase in small airway resistance (R5-20) was greater in patients with persistent mixed granulocytic asthma (+103%) than in patients with persistent neutrophilic (+26%), P = .040, or persistent paucigranulocytic asthma (-41%), P = .028. Multivariate models adjusted for confounders and treatment with inhaled or oral corticosteroids or antieosinophilic biologics indicated that the change of sputum eosinophil rather than neutrophil counts is an independent predictor for the longitudinal change in FEV1, forced expiratory flow at 25% to 75% of forced vital capacity, specific effective airway resistance, residual lung volume, and lung clearance index.

Conclusions: In asthma, airway eosinophilic inflammation is the main driver of lung function impairment and poor disease outcomes, which might also be aggravated by the coexistence of airway neutrophilia to confer a severe mixed granulocytic asthma phenotype. Persistent airway eosinophilia might be associated with dynamic SAD even in patients with stable FEV1.

Keywords: Airway inflammation; Eosinophilic asthma; Mixed granulocytic asthma; Small airway dysfunction.

Ann Allergy Asthma Immunol

. 2022 Jun;128(6):669-676.e6.

doi: 10.1016/j.anai.2022.02.017. Epub 2022 Mar 2.

Real-world effectiveness of benralizumab: Results from the ZEPHYR 1 Study

Yen Chung[1], Rohit Katial[1], Fan Mu[2], Erin E Cook[3], Joshua Young[3], Danni Yang[3], Keith A Betts[3], Donna D Carstens[1]

Affiliations expand

- PMID: 35247595

- DOI: 10.1016/j.anai.2022.02.017

Free article

Abstract

Background: Real-world evidence characterizing the clinical outcomes and economic impact on patients with severe eosinophilic asthma treated with benralizumab is limited.

Objective: To characterize patients with severe asthma treated with benralizumab and assess its clinical and economic impact in the United States.

Methods: A pre-post benralizumab comparison was performed using a large US insurance claims database between November 2016 and November 2019. The primary cohort included patients with asthma aged 12 years or more with 2 or more records of benralizumab. Secondary cohorts included persistent users (6 or more records of benralizumab), patients switching to benralizumab from mepolizumab or omalizumab, and stratified by Medicaid vs non-Medicaid. Exacerbations, concomitant medications, and exacerbation-related health care resource utilization (HCRU) and costs were compared in the 12-month periods pre- and post-benralizumab initiation (index).

Results: Of the 204 patients in the primary cohort, mean age at index was 45.3 years and 68.6% were of female sex. The patients experienced a significant 55% reduction in rates of exacerbations post-benralizumab initiation (3.25 pre-index vs 1.47 post-index per person-year; $P < .001$), and 41% of the patients had no exacerbations post-benralizumab initiation. The proportion of oral corticosteroid-dependent patients decreased from 82% to 50% ($P < .001$). Reductions in HCRU were 42%, 46%, and 57% for asthma exacerbation-related inpatient hospitalizations, emergency department, and outpatient visits, respectively (all $P < .001$). Exacerbation-related costs decreased by $6439 ($13,559 vs $7120; $P < .001$). Similar results for all outcomes were observed for the persistent cohort, switch cohorts, and Medicaid vs non-Medicaid cohorts.

Conclusion: Patients with severe asthma treated with benralizumab experienced clinical and economic benefits in the real world, as demonstrated by the reduction in exacerbations and HCRU.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

J Allergy Clin Immunol Pract

. 2022 Jun;10(6):1534-1544.e4.

doi: 10.1016/j.jaip.2022.02.014. Epub 2022 Feb 22.

Benralizumab Effectiveness in Severe Asthma Is Independent of Previous Biologic Use

David J Jackson [1], Hassan Burhan [2], Andrew Menzies-Gow [3], Paul Pfeffer [4], Alexandra Nanzer [5], Esther Garcia Gil [6], Tamsin Morris [7], Trung N Tran [8], Ian Hirsch [9], Sabada Dube [7]

Affiliations expand

- PMID: 35202871

- DOI: 10.1016/j.jaip.2022.02.014

Free article

Abstract

Background: Benralizumab is an IL-5 receptor alpha-directed cytolytic mAb that depletes eosinophils, reducing exacerbations and oral corticosteroid (OCS) use, and improves asthma control for patients with severe eosinophilic asthma (SEA). Data on response in patients previously treated with other biologic therapies are limited.

Objective: To describe real-world clinical outcomes with benralizumab for patients with and without prior biologic use for uncontrolled SEA.

Methods: This retrospective study compared clinical outcomes before and after benralizumab initiation in adults with uncontrolled SEA with 3 or more asthma exacerbations in the previous 12

months or on maintenance OCS treatment. Outcomes included exacerbations, OCS use, patient-reported outcomes, and health care resource utilization, including emergency department visits and hospitalizations.

Results: In all, 208 patients were enrolled, including 90 (43.3%) with previous experience with an alternate biologic for SEA. Benralizumab led to an 81% reduction in exacerbation rate, with 48% of patients with previous exacerbations experiencing none after 48 weeks. Overall, 67% of patients requiring baseline maintenance OCS achieved greater than or equal to 50% reduction in daily OCS dosage, and 53% eliminated maintenance OCS. Clinically meaningful improvements in patient-reported outcomes were seen, with response at 4 weeks predicting longer-term benefits. Health care resource utilization also decreased. Improvements were observed irrespective of previous biologic experience, fractional exhaled nitric oxide concentrations, atopic status, or other baseline characteristics.

Conclusions: In a multicenter real-world setting, patients with uncontrolled SEA achieved substantial improvements in all clinical outcome measures with benralizumab irrespective of previous biologic use, atopic status, or baseline fractional exhaled nitric oxide concentration.

Keywords: Atopy; Benralizumab; Biologic; Fractional exhaled nitric oxide; Oral corticosteroids; Patient-reported outcomes; Real-world study; Severe eosinophilic asthma.

Randomized Controlled Trial

Chest

-
-
-

. 2022 Jun;161(6):1456-1464.

doi: 10.1016/j.chest.2022.02.025. Epub 2022 Feb 22.

Azithromycin for Poorly Controlled Asthma in Children: A Randomized Controlled Trial

Jagat Jeevan Ghimire [1], Kana Ram Jat [2], Jhuma Sankar [1], Rakesh Lodha [1], Venkat K Iyer [3], Hitender Gautam [4], Seema Sood [4], S K Kabra [1]

Affiliations expand

- PMID: 35202621

- DOI: 10.1016/j.chest.2022.02.025

Abstract

Background: Azithromycin has immunomodulatory actions, and its beneficial effects have been demonstrated in asthmatic adults. Data on children are limited.

Research question: Does the addition of oral azithromycin to standard therapy in children with poorly controlled asthma improve asthma control compared with standard treatment alone?

Study design and methods: This open-label randomized controlled trial included children (5-15 years of age) with poorly controlled asthma defined by Asthma Control Test (ACT) and Childhood Asthma Control Test (CACT) score of ≤ 19. They were randomized to receive azithromycin (10 mg/kg) three times weekly for 3 months along with standard treatment or standard treatment alone. The primary outcome was the ACT and CACT scores at 3 months. Secondary outcomes were asthma control according to Global Initiative for Asthma (GINA) guidelines, the number of exacerbations, change in spirometry parameters, change in fractional exhaled nitric oxide (Feno) level, positive throat swab results, and side effects.

Results: The trial included 120 children (89 boys; 60 in each group). The mean ± SD age was 9.9 ± 3 years. The baseline parameters were similar between the groups. Mean ± SD ACT and CACT scores (available for 115 children) at 3 months of intervention were 21.71 ± 2.17 vs 18.33 ± 2.19 ($P < .001$) in the azithromycin and control groups, respectively. The numbers of children with well-controlled asthma according to GINA guidelines were 41 of 56 vs 10 of 56 in the azithromycin and control groups, respectively ($P < .001$). The median number of exacerbations requiring emergency visit and steroid use were fewer in the azithromycin group: 0 (interquartile range [IQR], 3) vs 1 [IQR, 6]; $P < .001$). No difference was found in Feno level, spirometry parameters, positive throat swab results, and adverse effects between the groups.

Interpretation: The use of azithromycin in children with poorly controlled asthma resulted in improved asthma control and reduced exacerbations.

Trial registry: Clinical Trials Registry - India; No.: CTRI/2019/06/019727; URL: www.ctri.nic.in.

Keywords: azithromycin; poorly controlled childhood asthma.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

ELSEVIER FULL-TEXT ARTICLE

Proceed to details

Cite

Share

41

Review

Am J Respir Crit Care Med

. 2022 Jun 1;205(11):1271-1280.

doi: 10.1164/rccm.202110-2389CI.

A Pandemic Lesson for Global Lung Diseases: Exacerbations Are Preventable

William Cookson [1], Miriam Moffatt [1], Garth Rapeport [1], Jennifer Quint [1]

Affiliations expand

- PMID: 35192447

- DOI: 10.1164/rccm.202110-2389CI

Abstract

A dramatic global reduction in the incidence of common seasonal respiratory viral infections has resulted from measures to limit the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during the pandemic. This has been accompanied by falls reaching 50% internationally in the incidence of acute exacerbations of preexisting chronic respiratory diseases that include asthma, chronic obstructive pulmonary disease, and cystic fibrosis. At the same time, the incidence of acute bacterial pneumonia and sepsis has fallen steeply worldwide. Such findings demonstrate the profound impact of common respiratory viruses on the course of these global illnesses. Reduced transmission of common respiratory bacterial pathogens and their interactions with viruses appear also as central factors. This review summarizes pandemic changes in

exacerbation rates of asthma, chronic obstructive pulmonary disease, cystic fibrosis, and pneumonia. We draw attention to the substantial body of knowledge about respiratory virus infections in these conditions, and that it has not yet translated into clinical practice. Now that the large scale of benefits that could be gained by managing these pathogens is unmistakable, we suggest that the field merits substantial academic and industrial investment. We consider how pandemic-inspired measures for prevention and treatment of common infections should become a cornerstone for managing respiratory diseases.

Keywords: COPD; SARS-CoV-2 pandemic; asthma; nonpharmaceutical interventions; pneumonia.

J Allergy Clin Immunol Pract

. 2022 Jun;10(6):1497-1505.

doi: 10.1016/j.jaip.2022.01.040. Epub 2022 Feb 5.

Targeting Downstream Type 2 Cytokines or Upstream Epithelial Alarmins for Severe Asthma

Rory Chan[1], Kirsten Stewart[1], Rasads Misirovs[1], Brian J Lipworth[2]

Affiliations expand

- PMID: 35131510

- DOI: 10.1016/j.jaip.2022.01.040

Free article

Abstract

Biologics, including omalizumab, mepolizumab, benralizumab, and dupilumab, targeting downstream IgE, cytokines IL-5, and IL-4/13, respectively, have shown promising effects in terms of reduction in annualized asthma exacerbation rates (AER), oral corticosteroid-sparing effects, improvements in forced expiratory volume in 1 second, and improved Asthma Control Questionnaire scores. However, despite these welcome advances, approximately 30% of patients with severe asthma receiving biologics tailored to their specific downstream type 2 biomarkers, including total IgE, peripheral blood eosinophils, and fractional exhaled nitric oxide, do not experience meaningful improvements in their AER. Instead of blocking downstream cytokines, targeting upstream epithelial alarmins, including IL-33, thymic stromal lymphopoietin, and IL-25, has been proposed to tackle the immunologic heterogeneity of asthma. This review article aims to pragmatically summarize the latest key clinical data on antialarmin therapies in severe asthma and put these findings into context with regard to currently available downstream cytokine blockers.

Keywords: Antialarmins; Biologics; Brodalumab; Cytokines; Itepekimab; Severe asthma; Tezepelumab.

Intern Emerg Med

. 2022 Jun;17(4):1107-1113.

doi: 10.1007/s11739-021-02923-5. Epub 2022 Feb 1.

Hospitalization and mortality for acute exacerbation of asthma: an Italian population-based study

Ombretta Para [1], Andrea Montagnani [2], Stefano Guidi [3], Lorenza Bertù [4], Dario Manfellotto [5], Mauro Campanini [6], Andrea Fontanella [7], Francesco Dentali [4], FADOI-Epidemiological Study Group

Affiliations expand

- PMID: 35103927

- DOI: 10.1007/s11739-021-02923-5

Abstract

Asthma is an ever-increasing disease with a highly variable prevalence among different ethnic groups. Information on hospital admission for acute exacerbation of asthma in adult patients and data regarding short-term prognosis of these patients are limited. We, thus, performed an epidemiological study on hospital admission for asthma acute exacerbation in Italy using hospital discharge database records derived from all Italian hospitals. Patients > 15 years old were identified using clinical Modification (ICD-9-CM) codes. Information on baseline characteristics, vital status at discharge, duration of hospitalization, and up to five secondary discharge diagnoses was collected. Comorbidity was evaluated using the Charlson comorbidity index (CCI). During the observation period (2013-2014), 20,056 patients with asthma acute exacerbation were hospitalized. Median length of hospitalization was 7.9 days (interquartile range 4-10) and mean in-hospital mortality was 0.8%. In-hospital mortality and length of hospitalization varied among different regions (from 0 to 2.9% and from 6.5 to 8.9 days, respectively). Old age, invasive and non-invasive mechanical ventilation, and CCI resulted as significantly associated with higher in-hospital mortality. Our study results, on a large sample of patients, confirm that hospitalization for asthma acute exacerbation is not uncommon among Italian current population. Older age, high CCI, and use of ventilator support were associated with a higher mortality rate. These findings should be analyzed to set up appropriate health care policies on patients with asthma.

Keywords: Asthma; Clinical modification codes; Exacerbation.

Adv Ther

. 2022 Jun;39(6):2365-2378.

doi: 10.1007/s12325-021-02025-w. Epub 2022 Jan 24.

A Review of the Unique Drug Development Strategy of Indacaterol Acetate/Glycopyrronium Bromide/Mometasone Furoate: A First-in-Class, Once-Daily, Single-Inhaler, Fixed-Dose Combination Treatment for Asthma

Dominic Brittain [1], Peter D'Andrea [2], Emilie Gruen [3], Motoi Hosoe [3], Devendra Jain [3], Juergen Jauernig [3], Abhijit Pethe [2], Emil Scosyrev [2], Ana-Maria Tanase [3], Hanns-Christian Tillmann [4]

Affiliations expand

- PMID: 35072888

- PMCID: PMC9122880

- DOI: 10.1007/s12325-021-02025-w

Free PMC article

Abstract

A novel, once-daily (o.d.), fixed-dose combination (FDC) of indacaterol acetate (IND), glycopyrronium bromide (GLY), and mometasone furoate (MF), delivered by the inhaler Breezhaler® device, is the first long-acting beta2-adrenergic agonist/long-acting muscarinic antagonist/inhaled corticosteroid (LABA/LAMA/ICS) therapy to be approved for maintenance treatment of asthma in adults inadequately controlled on LABA/ICS. The approval of IND/GLY/MF in the European Union (EU) also included an optional electronic sensor and smartphone (or other suitable device) application, making it the first "digital companion" that can be prescribed with an asthma medication. As a result, the European Medicines Agency included this approval as one of the "outstanding contributions to public health" (for Pneumology/Allergology) in their 2020 highlights report. Alongside IND/GLY/MF, an o.d. LABA/ICS FDC, IND/MF, was also developed and approved. This review outlines the unique strategy used in the accelerated development of IND/GLY/MF that combined various approaches: (1) selecting individual components with established efficacy/safety, (2) bridging doses to optimize efficacy/safety of IND/GLY/MF and IND/MF delivered via the Breezhaler® device, (3) developing IND/GLY/MF and IND/MF in parallel, and (4) submission for regulatory approval before formal completion of the pivotal phase III studies. IND/GLY/MF and IND/MF were combined in a single-development plan (PLATINUM program), which comprised four phase III studies: QUARTZ and PALLADIUM

evaluated IND/MF while IRIDIUM and ARGON evaluated IND/GLY/MF. A unique feature was the inclusion of two LABA/ICS comparators in the pivotal IRIDIUM study-IND/MF as an internal comparator, and high-dose salmeterol xinafoate/fluticasone propionate (SAL/FLU) as a marketed comparator. In the ARGON study, IND/GLY/MF was compared against o.d. tiotropium (via Respimat®) plus twice-daily (b.i.d.) high-dose SAL/FLU (via Diskus®). As a result of this development strategy, the development and approval of IND/GLY/MF was accelerated by ca. 4 years as against what would be expected from a traditional approach, novel data were generated, and a unique optional digital companion was approved in the EU. A Video Abstract by Dr Dominic Brittain, Global Drug Development, Novartis. (MP4 228293 kb).

Keywords: Accelerated development strategy; Asthma; Digital companion; Indacaterol acetate/glycopyrronium bromide/mometasone furoate; LABA/LAMA/ICS; Once daily; Single inhaler.

- 42 references
- 4 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

SpringerLink FULL-TEXT ARTICLE

Proceed to details

Cite

Share

45

J Allergy Clin Immunol

. 2022 Jun;149(6):1970-1980.

doi: 10.1016/j.jaci.2021.12.761. Epub 2022 Jan 13.

Refractory neutrophilic asthma and ciliary genes

Vamsi P Guntur [1], Laurie A Manka [2], Camille M Moore [3], Elizabeth Wynn [4], Eszter K Vladar [5], Rafeul Alam [6], Tuyet-Hang Pham [7], Tasha E Fingerlin [8], Richard J Martin [2]

Affiliations expand

- PMID: 35034774

- DOI: 10.1016/j.jaci.2021.12.761

Abstract

Background: Refractory asthma (RA) remains poorly controlled, resulting in high health care utilization despite guideline-based therapies. Patients with RA manifest higher neutrophilia as a result of increased airway inflammation and subclinical infection, the underlying mechanisms of which remain unclear.

Objective: We sought to characterize and clinically correlate gene expression differences between refractory and nonrefractory (NR) asthma to uncover molecular mechanisms driving group distinctions.

Methods: Microarray gene expression of paired airway epithelial brush and endobronchial biopsy samples was compared between 60 RA and 30 NR subjects. Subjects were hierarchically clustered to identify subgroups of RA, and biochemical and clinical traits (airway inflammatory molecules, respiratory pathogens, chest imaging) were compared between groups. Weighted gene correlation network analysis was used to identify coexpressed gene modules. Module expression scores were compared between groups using linear regression, controlling for age, sex, and body mass index.

Results: Differential gene expression analysis showed upregulation of proneutrophilic and downregulation of ciliary function genes/pathways in RA compared to NR. A subgroup of RA with downregulated ciliary gene expression had increased levels of subclinical infections, airway neutrophilia, and eosinophilia as well as higher chest imaging mucus burden compared to other RA, the dominant differences between RA and NR. Weighted gene correlation network analysis identified gene modules related to ciliary function, which were downregulated in RA and were associated with lower pulmonary function and higher airway wall thickness/inflammation, markers of poorer asthma control.

Conclusions: Identification of a novel ciliary-deficient subgroup of RA suggests that diminished mucociliary clearance may underlie repeated asthma exacerbations despite adequate treatment, necessitating further exploration of function, mechanism, and therapeutics.

Keywords: Refractory asthma; asthma pathogenesis; ciliary gene expression; neutrophilic asthma.

Randomized Controlled Trial

Allergy

. 2022 Jun;77(6):1786-1796.

doi: 10.1111/all.15197. Epub 2022 Feb 9.

Baseline type 2 biomarker levels and response to tezepelumab in severe asthma

Jonathan Corren [1], Tuyet-Hang Pham [2], Esther Garcia Gil [3], Kinga Sałapa [4], Pin Ren [5], Jane R Parnes [6], Gene Colice [7], Janet M Griffiths [2]

Affiliations expand

- PMID: 34913186

- DOI: 10.1111/all.15197

Abstract

Background: Tezepelumab is a human monoclonal antibody that blocks activity of thymic stromal lymphopoietin (TSLP). In the phase IIb PATHWAY study (NCT02054130), tezepelumab significantly reduced annualized asthma exacerbation rates (AAERs) versus placebo in adults with severe, uncontrolled asthma. We evaluated the effects of tezepelumab in reducing type 2 (T2) inflammatory biomarker levels in the PATHWAY population, and the relationship between baseline T2 biomarker levels and AAER.

Methods: Adults with severe, uncontrolled asthma (n = 550) were randomized to tezepelumab (70 mg or 210 mg every 4 weeks, or 280 mg every 2 weeks) or placebo for 52 weeks. Blood eosinophil count, fractional exhaled nitric oxide (FeNO), and serum total immunoglobulin (Ig)E, interleukin (IL)-5, IL-13, periostin, thymus and activation-regulated chemokine (TARC), and TSLP were

measured at baseline and over 52 weeks. AAERs were analyzed by baseline threshold (high/low) biomarker levels.

Results: Positive correlations were observed between T2 inflammatory biomarkers (blood eosinophil count, FeNO, IL-5, IL-13 and periostin) at baseline. At Week 52, treatment with tezepelumab 210 mg reduced all biomarker levels measured from baseline versus placebo. Exacerbations were reduced by 55-83% in the pooled tezepelumab cohort versus placebo, irrespective of baseline blood eosinophil count, FeNO, or serum total IgE, IL-5, IL-13, periostin, TARC, or TSLP, when these biomarkers were assessed individually.

Conclusion: At baseline, positive correlations between specific T2 inflammatory biomarkers were observed. Tezepelumab reduced multiple T2 inflammatory biomarkers, which indicates decreased airway inflammation, and reduced exacerbations irrespective of baseline T2 biomarker profiles in patients with severe asthma.

Keywords: asthma; biomarkers; inflammation.

doi: 10.1016/j.arbres.2021.11.003. Epub 2021 Nov 16.

Treating Neutrophilic Inflammation in Airways Diseases

Merete B Long [1], James D Chalmers [2]

Affiliations expand

- PMID: 34866748

- PMCID: PMC8626223

- DOI: 10.1016/j.arbres.2021.11.003

No abstract available

- 28 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Ann Am Thorac Soc

-
-
-

. 2022 Jun;19(6):907-915.

doi: 10.1513/AnnalsATS.202012-1562OC.

Long-Term Natural History of Severe Asthma Exacerbations and Their Impact on the Disease Course

Tae Yoon Lee [1], John Petkau [2], Mohsen Sadatsafavi [1]

Affiliations expand

- PMID: 34797732
- PMCID: PMC9169129
- DOI: 10.1513/AnnalsATS.202012-1562OC

Free PMC article

Abstract

Rationale: The long-term natural history of asthma in terms of successive severe exacerbations and the influence of each exacerbation on the course of the disease is not well studied. **Objectives:** To investigate the long-term natural history of asthma among patients who are hospitalized for asthma for the first time in terms of the risk of future severe exacerbations and heterogeneity in this risk across patients. **Methods:** Using the administrative health databases of British Columbia, Canada (January 1, 1997 to March 31, 2016), we created an incident cohort of patients with at least one asthma exacerbation that required inpatient care. We estimated the 5-year cumulative incidence of severe exacerbations after successive numbers of previous events. We used a joint frailty model to investigate the extent of between-individual variability in exacerbation risk and the associations of each exacerbation with the rate of subsequent events. Analyses were conducted separately for pediatric (<14 years old) and adult (⩾14 years old) patients. **Results:** Analyses were based on 3,039 pediatric (mean age at baseline, 6.4; 35% female) and 5,442 (mean age at baseline, 50.8; 68% female) adult patients. The 5-year rates of severe exacerbations after the first three events were 0.16, 0.29, and 0.35 for the pediatric group, and 0.14, 0.33, and 0.49 for the adult group. Both groups exhibited substantial variability in patient-specific risks of exacerbation: the mid-95% interval of 5-year risk of experiencing a severe exacerbation ranged from 11% to 24% in pediatric patients and from 8% to 40% in adult patients. After controlling for potential confounders, the first follow-up exacerbation was associated with an increase of 79% (95% confidence interval [CI], 11-189%) in the rate of subsequent events in the pediatric group, whereas this increase was 188% (95% CI, 35-515%) for the adult group. The effects of subsequent exacerbations were not statistically significant. **Conclusions:** After the first severe exacerbation, the risk of subsequent events is substantially different among patients. The number of previous severe exacerbations carries nuanced prognostic information about future risk. Our results suggest that severe exacerbations in the early course of asthma detrimentally affect the course of the disease and risk of subsequent exacerbations.

Keywords: asthma; exacerbation; frailty model; prognosis; recurrent events.

- 55 references

- 4 figures

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

FULL TEXT LINKS

AnnalsATS Final Version

Proceed to details

Cite

Share

49

Eur Respir J

. 2022 Jun 9;59(6):2100731.

doi: 10.1183/13993003.00731-2021. Print 2022 Jun.

Childhood asthma: pathogenesis and phenotypes

Mariëlle W Pijnenburg [1], Urs Frey [2], Johan C De Jongste [3], Sejal Saglani [4]

Affiliations expand

- PMID: 34711541

- DOI: 10.1183/13993003.00731-2021

Abstract

In the pathogenesis of asthma in children there is a pivotal role for a type 2 inflammatory response to early life exposures or events. Interactions between infections, atopy, genetic susceptibility and environmental exposures (such as farmyard environment, air pollution and tobacco smoke exposure) influence the development of wheezing illness and the risk of progression to asthma. The immune system, lung function and the microbiome in gut and airways develop in parallel, and dysbiosis of the microbiome may be a critical factor in asthma development. Increased infant weight gain and preterm birth are other risk factors for development of asthma and reduced lung function. The complex interplay between these factors explains the heterogeneity of asthma in

children. Subgroups of patients can be identified as phenotypes, based on clinical parameters, or endotypes, based on a specific pathophysiological mechanism. Paediatric asthma phenotypes and endotypes may ultimately help to improve diagnosis of asthma, prediction of asthma development and treatment of individual children, based on clinical, temporal, developmental or inflammatory characteristics. Unbiased, data-driven clustering, using a multidimensional or systems biology approach may be needed to better define phenotypes. The present knowledge on inflammatory phenotypes of childhood asthma has now been successfully applied in the treatment with biologicals of children with severe therapy-resistant asthma, and it is to be expected that more personalised treatment options may become available.

Conflict of interest statement

Conflict of interest: M.W. Pijnenburg has nothing to disclose. Conflict of interest: U. Frey has nothing to disclose. Conflict of interest: J.C. De Jongste has nothing to disclose. Conflict of interest: S. Saglani has nothing to disclose.

Thorax

. 2022 Jun;77(6):552-562.

doi: 10.1136/thoraxjnl-2021-217343. Epub 2021 Oct 6.

Blood eosinophil cationic protein and eosinophil-derived neurotoxin are associated with different asthma expression and evolution in adults

Vanessa Granger[1,2], Farid Zerimech[3,4,5], Jinan Arab[6], Valerie Siroux[7,8], Patricia de Nadai[9], Anne Tsicopoulos[9], Régis Matran[3,4,5], Zeina Akiki[10], Rachel Nadif[11]

Affiliations expand

- PMID: 34615736

- DOI: 10.1136/thoraxjnl-2021-217343

Abstract

Background: Eosinophil-derived neurotoxin (EDN) and eosinophil cationic protein (ECP) are proteins released by activated eosinophils whose role in adult asthma remains unclear.

Objective: To study associations between ECP, EDN and various asthma characteristics in adults from the Epidemiological Study on the Genetics and Environment of Asthma (EGEA).

Methods: Plasma ECP and EDN levels were measured by ELISA. Cross-sectional analyses were performed in 941 adults (43±16 years old, 39% with asthma) at EGEA2 (2003-2007). Longitudinal analyses investigated the associations between EDN level at EGEA2 and changes in asthma characteristics between EGEA2 and EGEA3 (2011-2013, n=817). We used generalised estimated equations adjusted for age, sex, smoking status and body mass index to take into account familial dependence.

Results: At EGEA2, both high ECP and EDN levels were associated with current asthma (adjusted OR (aOR) (95% CI): 1.69 (1.35-2.12) and 2.12 (1.76-2.57)). Among asthmatics, high EDN level was associated with asthma attacks (aOR: 1.50 (1.13-1.99)), wheezing and breathlessness (aOR: 1.38 (1.05-1.80)), use of asthma treatments (aOR: 1.91 (1.37-2.68)) and bronchial hyper-responsiveness (aOR: 2.03 (1.38-2.97)), even after further adjustment on ECP. High ECP level was associated with high neutrophil count and tended to be associated with chronic bronchitis. High EDN level at EGEA2 was associated with persistent asthma (aOR: 1.62 (1.04-2.52)), nocturnal symptoms (aOR from 2.19 to 3.57), worsening wheezing and breathlessness (aOR: 1.97 (1.36-2.85)) and nocturnal shortness of breath (aOR: 1.44 (1.04-1.98)) between EGEA2 and EGEA3.

Conclusions: EDN and ECP were associated with different asthma expression in adults. EDN could be a potential biomarker to monitor asthma evolution in adults.

Keywords: asthma; eosinophil biology.

Conflict of interest statement

Competing interests: AT reports grant from Santelys, personal fees from ALK-Abello and non-financial support from AstraZeneca outside the submitted work.

- Cited by 1 article

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS

BMJ Full Text

Proceed to details

Cite

Share

51

Meta-Analysis

Thorax

. 2022 Jun;77(6):563-572.

doi: 10.1136/thoraxjnl-2021-217124. Epub 2021 Sep 30.

Epinephrine (adrenaline) compared to selective beta-2-agonist in adults or children with acute asthma: a systematic review and meta-analysis

Christina Baggott[1], Jo Katherine Hardy[1], Jenny Sparks[1], Doñah Sabbagh[1], Richard Beasley[1,2], Mark Weatherall[3], James Fingleton[4,2,3]

Affiliations expand

- PMID: 34593615

- DOI: 10.1136/thoraxjnl-2021-217124

Abstract

Background: International asthma guidelines recommend against epinephrine (adrenaline) administration in acute asthma unless associated with anaphylaxis or angio-oedema. However, administration of intramuscular epinephrine in addition to nebulised selective β_2-agonist is recommended for acute severe or life-threatening asthma in many prehospital guidelines. We conducted a systematic review to determine the efficacy of epinephrine in comparison to selective β_2-agonist in acute asthma.

Methods: We included peer-reviewed publications of randomised controlled trials (RCTs) that enrolled children or adults in any healthcare setting and compared epinephrine by any route to selective β_2-agonist by any route for an acute asthma exacerbation. The primary outcome was treatment failure, including hospitalisation, need for intubation or death.

Results: Thirty-eight of 1140 studies were included. Overall quality of evidence was low. Seventeen studies contributed data on 1299 participants to the meta-analysis. There was significant statistical heterogeneity, I^2=56%. The pooled Peto's OR for treatment failure with epinephrine versus selective β_2-agonist was 0.99 (0.75 to 1.32), p=0.95. There was strong evidence that recruitment age group was associated with different estimates of the odds of treatment failure; with studies recruiting adults-only having lower odds of treatment failure with epinephrine. It was not possible to determine whether epinephrine in addition to selective β_2-agonist improved outcomes.

Conclusion: The low-quality evidence available suggests that epinephrine and selective β_2-agonists have similar efficacy in acute asthma. There is a need for high-quality double-blind RCTs to determine whether addition of intramuscular epinephrine to inhaled or nebulised selective β_2-agonist improves outcome.

Prospero registration number: CRD42017079472.

Keywords: asthma; asthma guidelines; critical care; emergency medicine; paediatric asthma.

Conflict of interest statement

Competing interests: None declared.

. 2022 Jun;85:100969.

doi: 10.1016/j.mam.2021.100969. Epub 2021 Jun 3.

Corticosteroid resistance in asthma: Cellular and molecular mechanisms

Gaetano Caramori [1], Francesco Nucera [2], Sharon Mumby [3], Federica Lo Bello [2], Ian M Adcock [4]

Affiliations expand

- PMID: 34090658

- DOI: 10.1016/j.mam.2021.100969

Abstract

Inhaled glucocorticoids (GCs) are drugs widely used as treatment for asthma patients. They prevent the recruitment and activation of lung immune and inflammatory cells and, moreover, have profound effects on airway structural cells to reverse the effects of disease on airway inflammation. GCs bind to a specific receptor, the glucocorticoid receptor (GR), which is a member of the nuclear receptor superfamily and modulates pro- and anti-inflammatory gene transcription through a number of distinct and complementary mechanisms. Targets genes include many pro-inflammatory mediators such as chemokines, cytokines, growth factors and their receptors. Inhaled GCs are very effective for most asthma patients with little, if any, systemic side effects depending upon the dose. However, some patients show poor asthma control even after the administration of high doses of topical or even systemic GCs. Several mechanisms relating to inflammation have been considered to be responsible for the onset of the relative GC resistance observed in these patients. In these patients, the side-effect profile of GCs prevent continued use of high doses and new drugs are needed. Targeting the defective pathways associated with GC function in these patients may also reactivate GC responsiveness.

Keywords: Asthma; Glucocorticoids; Inflammation; Resistance.

- Cited by 1 article

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

FULL TEXT LINKS

ELSEVIER FULL-TEXT ARTICLE

Postgrad Med J

. 2022 Jun;98(1160):461-465.

doi: 10.1136/postgradmedj-2020-139511. Epub 2021 Feb 15.

Audit of oxygen administration to achieve a target oxygen saturation range in acutely unwell medical patients

James Harper[1 2 3], Nethmi Kearns[4 2], Grace Bird[4 2 3], Robert McLachlan[4 2], Allie Eathorne[4], Mark Weatherall[5], Richard Beasley[4 2 3]

Affiliations expand

- PMID: 33589491

- DOI: 10.1136/postgradmedj-2020-139511

Abstract

Purpose of the study: To evaluate documentation of a target oxygen saturation (SpO_2) range and ability to achieve this range in acutely unwell inpatients.

Study design: In this single-centre audit, patients with discharge diagnoses of pneumonia, heart failure and exacerbation of asthma or COPD admitted to Wellington Regional Hospital, New Zealand between 1 June 2019 and 31 August 2019 who received oxygen were identified. In those with a documented target SpO_2 range, the proportion of SpO_2 measurements in the observation chart which were within, above and below range were determined as well as the maximum and minimum SpO_2. Regression analysis was performed to determine whether these outcomes were influenced by the prescribed range, high-dependency care or the number of adjustments to oxygen administration.

Results: 268 admissions were screened. Of the 100 eligible admissions who received oxygen, a target SpO_2 range was documented in 62. The mean (SD) proportion of SpO_2 measurements within range was 56.2 (30.6)%. A hypercapnic target SpO_2 range was

associated with a higher probability of an SpO_2 above range; multivariate OR 5.34 (95% CI 1.65 to 17.3, p=0.006) and a lower probability of an SpO_2 below range; multivariate OR 0.25 (95% CI 0.08 to 0.80) p=0.02. The mean (SD) maximum SpO_2 was similar in those with a target range of 92%-96% versus a hypercapnic range; 96.2 (3.0)% and 95.2 (3.4)%, respectively.

Conclusions: Oxygen prescription and delivery in this clinical setting was suboptimal. SpO_2 values above the designated range are common, particularly in patients with a hypercapnic target range.

Keywords: audit.

Conflict of interest statement

Competing interests: RB reports a grant from Fisher and Paykel Healthcare outside the submitted work. JH reports personal fees from Fisher and Paykel Healthcare outside the submitted work.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS

BMJ Full Text

RHINITIS

1

PeerJ

-
-
-

. 2022 May 30;10:e13444.

doi: 10.7717/peerj.13444. eCollection 2022.

IL-4/IL-13 axis as therapeutic targets in allergic rhinitis and asthma

Siti Muhamad Nur Husna [1], Norasnieda Md Shukri [2], Noor Suryani Mohd Ashari [1], Kah Keng Wong [1]

Affiliations expand

- PMID: 35663523
- PMCID: PMC9161813
- DOI: 10.7717/peerj.13444

Free PMC article

Abstract

Allergic rhinitis (AR) is a common disorder of the upper airway, while asthma is a disease affecting the lower airway and both diseases are usually comorbid. Interleukin (IL)-4 and IL-13 are critical cytokines in the induction of the pathogenic Th2 responses in AR and asthma. Targeting the IL-4/IL-13 axis at various levels of its signaling pathway has emerged as promising targeted therapy in both AR and asthma patient populations. In this review, we discuss the biological characteristics of IL-4 and IL-13, their signaling pathways, and therapeutic antibodies against each cytokine as well as their receptors. In particular, the pleiotropic roles of IL-4 and IL-13 in orchestrating Th2 responses in AR and asthma patients indicate that dual IL-4/IL-13 blockade is a promising therapeutic strategy for both diseases.

Keywords: Allergic rhinitis; Asthma; IL-13; IL-13Rα1; IL-4; IL-4Rα; Therapeutic antibodies.

Conflict of interest statement

The authors declare there are no competing interests.

- 103 references
- 2 figures

SUPPLEMENTARY INFO

Grant supportexpand

FULL TEXT LINKS

Int J Tuberc Lung Dis

. 2022 Jun 1;26(6):544-549.

doi: 10.5588/ijtld.21.0603.

Parental TB associated with offspring asthma and rhinitis

J P López-Cervantes [1], R Shigdel [2], S Accordini [3], T Mustafa [4], R J Bertelsen [2], S Makvandi-Nejad [1], M Lerm [5], W Horsnell [6], C Svanes [1]

Affiliations expand

- PMID: 35650692

- DOI: 10.5588/ijtld.21.0603

Abstract

BACKGROUND: Infections in early life are associated with asthma and allergies in one-generation settings; however, the link between parental infection and offspring phenotype is rarely investigated. We aim to study the association of parental TB before conception of the offspring with offspring asthma and rhinitis.**METHODS:** We included 2,965 offspring born in 1985-2004 and registered in the Norwegian prescription database to 1,790 parents born after 1960 with a history of TB, and included in the Norwegian TB registry. Offspring asthma (*n* = 582) and rhinitis (*n* = 929) were defined based on diagnosis, type of medication and prescribed medication ≥1 year. Associations of parental TB <8 years, ≥8 years but before offspring´s birth year and after birth (reference category) with offspring asthma and rhinitis were analysed using logistic regression.**RESULTS:** Asthma risk was higher in persons with parental TB in childhood (OR 1.73, 95% CI 1.20-2.50) or later preconception (OR 1.38, 95% CI 1.00-1.91) than in persons with parental TB after offspring´s birth; this was significant only in the maternal line (childhood: OR 1.95, 95% CI 1.13-3.37; later preconception: OR 1.74, 95% CI 1.08-2.80). Associations with rhinitis were not identified.**CONCLUSIONS:** Parental childhood TB was associated with higher asthma risk in future offspring. We speculate that TB impacts maternal immunity and dysregulates the offspring´s type

2 immunity, and that TB-induced epigenetic reprograming of immune defences are transferred to the offspring.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

Proceed to details

Cite

Share

3

Am J Respir Crit Care Med

. 2022 Jun 1.

doi: 10.1164/rccm.202203-0608LE. Online ahead of print.

Allergen Immunotherapy Reverses Immune Response to SARS-CoV-2 Vaccine in Patients with Allergic Rhinitis: A Prospective Observational Trial

Yin Yao [1], Ao Huang [2], Yi-Ke Deng [3], Yan Liu [4], Hong-Yu Zhu [1], Nan Wang [1], Zhe-Zheng Wang [3], Rong-Fei Zhu [5], Di Yu [6], Zheng Liu [7]

Affiliations expand

- PMID: 35649178

- DOI: 10.1164/rccm.202203-0608LE

No abstract available

Keywords: Allergen immunotherapy; Allergic rhinitis; Humoral immune response; SARS-CoV-2; Vaccine.

FULL TEXT LINKS

Acta Otolaryngol

. 2022 May 28;1-7.

doi: 10.1080/00016489.2022.2078879. Online ahead of print.

Long-term efficacy of turbinoplasty compared with medical treatment in patients with allergic rhinitis

Shin Hyuk Yoo [1], Ji Hyeok Choi [1], Ji-Hun Mo [1]

Affiliations expand

- PMID: 35635012

- DOI: 10.1080/00016489.2022.2078879

Abstract

Background: The effectiveness of turbinate surgery has been proven in patients with allergic rhinitis (AR).

Objectives: This study evaluated the long-term efficacy of turbinoplasty in AR and to compare the results with those of medical treatment.

Methods: This study included 192 patients diagnosed with AR who underwent surgical or medical treatment. Medical records were reviewed to assess pre-treatment and 2-year post-treatment frequency and severity of AR symptoms, prescription frequency for AR medication, and satisfaction score for treatment. Parameters for 5-year post-treatment efficacy were acquired *via* a telephone survey. A total of 128 patients who had undergone turbinoplasty were defined as a 'turbinoplasty group,' and 64 patients who were treated only with medications were defined as a 'medication group'. Allergic symptom, medication, and satisfaction scores were compared.

Results: Patients in the turbinoplasty group demonstrated significant improvements in all allergic symptom scores, while those in the medication group showed significant symptom improvement only in nasal obstruction on long-term follow-up. Patients in the turbinoplasty group also showed a lower prescription frequency after treatment and higher subjective satisfaction scores than those in the medication group.

Conclusions: This long-term follow-up study demonstrated that turbinoplasty for AR appears to be an effective treatment option compared with medical therapy alone.

Keywords: Allergic rhinitis; efficacy; long-term; turbinoplasty.

Randomized Controlled Trial

Immunotherapy

. 2022 Jun;14(9):683-694.

doi: 10.2217/imt-2021-0353. Epub 2022 Apr 25.

Efficacy of subcutaneous house dust mite immunotherapy in patients with moderate to severe allergic rhinitis

Antonio Valero [1], Ethel Ibáñez-Echevarría [2], Carmen Vidal [3], Isabela Raducan [4], José Vicente Castelló Carrascosa [4], Jaime Sánchez-López [5]

Affiliations expand

- PMID: 35465692

- DOI: 10.2217/imt-2021-0353

Free article

Abstract

Aim: To evaluate the efficacy of subcutaneous immunotherapy (SCIT) for the treatment of allergy to house dust mites (HDM) in adults with moderate/severe allergic rhinitis (AR). **Methods:** Patients sensitized to HDM were randomized to SCIT plus rescue medication (Group A, n = 38) or rescue medication alone (Group B, n = 18), and assessed at baseline and 2, 6 and 12 months. **Results:** At month 12, Group A presented significant improvement with respect to baseline as evaluated by a visual analogue scale at three concentrations of antigen (0.1, 1 and 10 IR/ml; $p < 0.0001$). Group A presented significant decreases in symptom scores after 2 months of treatment, which were maintained after 1 year. After 12 months of treatment, Group A showed rescue medication consumption reductions ($p < 0.001$) and quality of life improvements ($p < 0.0001$). SCIT elicited a strong immunological response and was well tolerated. **Conclusion:** SCIT is efficacious for HDM allergy in patients with AR, generating a strong immunological response. Trial Registration Number: EUCTR2009-018155-16-ES (Cochrane Central Register of Controlled Trials).

Keywords: IgE; allergen immunotherapy; allergic rhinitis; house dust mites; subcutaneous immunotherapy.

Plain Language Summary

Allergic rhinitis is a common disease that can be treated by exposing the patient to small quantities of the agents triggering the allergy. In this study, allergic patients were injected with extracts of house dust mites over a period of 12 months, and the status of the patient was evaluated at the initiation of treatment and at 2, 6 and 12 months. The study showed that the allergic rhinitis symptoms improved after only 2 months of treatment with the extract and were sustained after 1 year. Also, other medication to treat the rhinitis was reduced with the treatment, and quality of life improved. Overall, the study suggests that treatment with injections of extracts of house dust mites can help patients with allergic rhinitis.

. 2022 Jun;10(6):1506-1514.e2.

doi: 10.1016/j.jaip.2022.01.005. Epub 2022 Jan 21.

Risk of Chronic Rhinosinusitis With Nasal Polyps in Endotypes of Dermatophagoides pteronyssinus-Induced Rhinitis

Sergio De Marchi [1], Emanuela Cecchin [2], Sergio Umberto De Marchi [2], Federico Iuri [2], Leonardo A Sechi [2]

Affiliations expand

- PMID: 35074602

- DOI: 10.1016/j.jaip.2022.01.005

Abstract

Background: Observation of the natural history of two emerging endotypes of allergic rhinitis, local-sensitization rhinitis (LAR) and dual-allergic rhinitis (DAR), compared with systemic-sensitization rhinitis (AR), could improve knowledge of the role of allergy in chronic rhinosinusitis with nasal polyps (CRSwNP).

Objective: To test the hypothesis that endotypes of Dermatophagoides pteronyssinus (DP)-induced rhinitis were risk factors for CRSwNP and adult-onset asthma and to investigate whether delayed hypersensitivity to DP, assessed by atopy patch test, could be a contributing factor.

Methods: We conducted a prospective observational study over 15 years on a cohort of 999 patients: 468 with AR, 333 with LAR, and 198 with DAR. The latter endotype was characterized by the coexistence of seasonal disease caused by systemic sensitization to pollen in patients with DP-induced LAR. The study design included a physical visit; ear, nose, and throat examination with anterior rhinoscopy; skin prick test; serum-specific IgE; DP-atopy patch test; nasal allergen provocation test with DP; paranasal sinuses computed tomography scan; nasal endoscopy; and spirometry.

Results: During 15 years of follow-up, 194 patients developed CRSwNP with a higher rate of LAR (28.2%) and DAR (22.2%) than AR (12%). For LAR and DAR, 7.5% and 10.6% of patients developed adult-onset asthma temporally linked to CRSwNP in 68% and 71.4% of cases, respectively. A total of 858 patients with rhinitis had delayed hypersensitivity to DP. Moreover, DP-ATP was an independent predictive factor for CRSwNP and had elevated positive and negative predictive values for localized allergic disease of the nasal mucosa.

Conclusions: Endotypes of DP-induced allergic rhinitis represent risk factors for CRSwNP. Patients with local-sensitization rhinitis and DAR are more at risk than those with AR. In these emerging

endotypes, progression toward CRSwNP is often associated with the development of adult-onset asthma. Chronic rhinosinusitis with nasal polyps shows several possible indicators for type 2 endotype. Delayed hypersensitivity to DP is an independent predictive factor for CRSwNP.

Keywords: Adult-onset asthma; Allergic rhinitis; Atopy patch test; Chronic rhinosinusitis; Dermatophagoides; Dual-allergic rhinitis; Dust mites; Local allergic rhinitis; Nasal allergen provocation test; Nasal polyps.

Int Forum Allergy Rhinol

. 2022 Jun;12(6):876-879.

doi: 10.1002/alr.22937. Epub 2022 Jan 5.

Comorbid chronic rhinosinusitis is not associated with worse asthma control test responses: A case-control study

Amarbir S Gill [1], Jorgen S Sumsion [2], Heather Howe [3], Jeremiah A Alt [1]

Affiliations expand

- PMID: 34914191

- DOI: 10.1002/alr.22937

No abstract available

Keywords: asthma; asthma control; chronic rhinosinusitis; comorbidities; quality of life.

- 9 references

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

Proceed to details

Cite

Share

8

Int Forum Allergy Rhinol

. 2022 Jun;12(6):886-888.

doi: 10.1002/alr.22934. Epub 2022 Jan 27.

Use of face masks and allergic rhinitis from ragweed: Why mention only total pollen count and not air pollution levels?

Gennaro Liccardi[1], Matteo Martini[2], Maria Beatrice Bilò[3], Manlio Milanese[4], Paola Rogliani[5]

Affiliations expand

- PMID: 34875142

- DOI: 10.1002/alr.22934

No abstract available

Keywords: COVID-19; SARS-CoV-2; air pollutants; allergic rhinitis; allergy; face masks; hypersensitivity; lockdown; personal protective equipment (PPE); pollen count; ragweed pollen.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

Int Forum Allergy Rhinol

. 2022 Jun;12(6):813-820.

doi: 10.1002/alr.22936. Epub 2022 Jan 5.

Economic Evaluation of Dupilumab Versus Endoscopic Sinus Surgery for the Treatment of Chronic Rhinosinusitis With Nasal Polyps

Arjun K Parasher[1], Matt Gliksman[1], Daniel Segarra[2], Theodore Lin[3], Luke Rudmik[4], Troy Quast[5]

Affiliations expand

- PMID: 34874120

- DOI: 10.1002/alr.22936

Abstract

Background: Dupilumab is a novel monoclonal antibody that recently received US Food and Drug Administration approval for the treatment of chronic rhinosinusitis with nasal polyps. Endoscopic sinus surgery (ESS) has been the mainstay of treatment for patients refractory to initial medical therapy. Data comparing the cost-effectiveness of these treatments are scarce. The objective of this study is to compare the cost-effectiveness of dupilumab and ESS treatment for patients with chronic rhinosinusitis with nasal polyps refractory to medical therapy.

Methods: A cohort-style Markov decision tree economic evaluation with 10-year time horizon was performed. The two comparative treatment strategies were dupilumab therapy or ESS followed by postoperative maintenance therapy. Patients with response to treatment continued with either maintenance or dupilumab therapy; patients with no response underwent ESS. The primary outcome measure was incremental cost per quality-adjusted life-year calculated from Sino-Nasal

Outcome Test (SNOT-22) scores. Sensitivity analyses were performed including discounting scenarios and a probabilistic sensitivity analysis.

Results: The dupilumab strategy cost $195,164 and produced 1.779 quality-adjusted life-years. The ESS strategy cost $20,549 and produced 1.526 quality-adjusted life-years. This implies an incremental cost of $691,691 for dupilumab for every 1-unit increase in quality-adjusted life-year compared with ESS. Probability sensitivity analysis indicated that ESS was more cost-effective than dupilumab in all iterations.

Conclusions: While dupilumab and ESS may demonstrate similar clinical effectiveness, ESS remains the most cost-effective treatment option and should remain the standard of care for patients with chronic rhinosinusitis with nasal polyps refractory to medical therapy.

Keywords: chronic rhinosinusitis; endoscopic sinus surgery; health care economics; medical therapy of chronic rhinosinusitis.

- 30 references

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS

WILEY Full Text Article

Proceed to details

Cite

Share

10

J Asthma

. 2022 Jun;59(6):1139-1147.

doi: 10.1080/02770903.2021.1897837. Epub 2021 Mar 15.

Nasal polyp eosinophilia and FeNO may predict asthma symptoms development after endoscopic sinus surgery in CRS patients without asthma

Ryota Kurokawa [1], Yoshihiro Kanemitsu [1], Kensuke Fukumitsu [1], Norihisa Takeda [1], Jennifer Maries Yap [1], Yoshiyuki Ozawa [2], Ayako Masaki [3], Junya Ono [4], Kenji Izuhara [5], Hirono Nishiyama [1], Satoshi Fukuda [1], Takehiro Uemura [1], Tomoko Tajiri [1], Hirotsugu Ohkubo [1], Ken Maeno [1], Yutaka Ito [1], Tetsuya Oguri [1], Masaya Takemura [1], Motohiko Suzuki [6], Akio Niimi [1]

Affiliations expand

- PMID: 33653221

- DOI: 10.1080/02770903.2021.1897837

Abstract

Background: Asthma is a significant comorbidity of eosinophilic chronic rhinosinusitis (CRS). Type2-driven biomarkers such as sinus tissue eosinophilia and fractional nitric oxide (FeNO) may be utilized to detect high risk patients who develop asthma symptoms after endoscopic sinus surgery (ESS) in CRS patients.

Methods: Thirty-six CRS patients without asthma who agreed to undergo ESS between October 2015 and December 2017 were prospectively observed for 12 months following ESS. They were monitored for the development of typical asthma symptoms including dyspnea, wheezes, and cough which responded to anti-asthma medication. Biomarkers were compared between patients who developed asthma symptoms after ESS (asthma symptoms group) and those who did not (non-asthma group). Biomarker changes following ESS intervention were also evaluated.

Results: Six patients were lost to follow after ESS. Thus, 30 CRS patients [16 with nasal polyps (NPs) proved by surgery] were followed. Seven (23%) newly complained of asthma symptoms during follow-up. Levels of FeNO and the prevalence of eosinophilic NPs (eosinophils ≥ 70/high power fields) were significantly higher in the asthma symptom group than in non-asthma group [50.7 ppb *vs* 22.4 ppb for FeNO levels, and 100% (n = 3) *vs* 23% (n = 3) for eosinophilic NP prevalence, both $p < 0.05$]. Levels of sputum periostin decreased significantly by ESS in the non-asthma group. However, changes of biomarkers after ESS were comparable between the two groups.

Conclusions: Eosinophils in NPs (≥70/high power fields) and preoperative FeNO may be significant biomarkers for predicting the development of asthma symptoms after ESS.

Keywords: Chronic rhinosinusitis; asthma; nasal polyps.

CHRONIC COUGH

1

Lung

.
. 2022 Jun 7.

doi: 10.1007/s00408-022-00543-0. Online ahead of print.

A Randomized, Placebo-Controlled Study to Investigate the Safety, Tolerability, and Pharmacokinetics of 3 Weeks of Orally Administered Gefapixant in Healthy Younger and Older Adults

Jesse Nussbaum [1,2], Azher Hussain [3], Anthony Ford [3], Peter Butera [3], Michael Kitt [3], Steve Smith [3], Aubrey Stoch [3], Marian Iwamoto [3]

Affiliations expand

- PMID: 35670873

- DOI: 10.1007/s00408-022-00543-0

Abstract

Purpose: Patients with chronic cough are typically female and have a mean age of ~ 60 years. However, initial pharmacokinetic (PK) characterization of the P2X3-receptor antagonist gefapixant, developed to treat refractory or unexplained chronic cough, was performed in healthy participants who were predominantly younger adult males. The objective of this Phase 1 study was to assess the safety, tolerability, and PK of gefapixant in younger (18-55 years) and older (65-80 years) males and females.

Methods: A randomized, double-blind, placebo-controlled study was conducted. Healthy adult participants were stratified into 4 cohorts by age and sex (younger males/females and older males/females) and randomized 4:1 (younger adults) or 3:1 (older adults) to receive gefapixant 300 mg twice daily (BID) for 1 week, followed by gefapixant 600 mg BID for 2 weeks or placebo. Safety, tolerability, and PK were assessed.

Results: Of 36 randomized and treated participants, 28 (100%) receiving gefapixant and 6 (75%) receiving placebo reported ≥ 1 adverse event (AE). The most common treatment-related AEs in the gefapixant group were taste related. Predefined renal/urologic AEs were reported by 7 (25%) participants receiving gefapixant (all mild to moderate in severity). Gefapixant exposure was generally lower in younger males compared with younger females and older adults; however, differences may have been due to estimated glomerular filtration rate.

Conclusion: The safety profile of gefapixant 300-600 mg BID was generally consistent with previous studies. Additional characterization of gefapixant PK as a function of age and sex using population PK modeling is warranted.

Keywords: Aged [MeSH]; Chronic cough; Gefapixant; Pharmacokinetics; Safety [MeSH]; Tolerability.

- 23 references

FULL TEXT LINKS

SpringerLink FULL-TEXT ARTICLE

Proceed to details

Cite

Share

2

ERJ Open Res

-
-
-

. 2022 May 30;8(2):00119-2022.

doi: 10.1183/23120541.00119-2022. eCollection 2022 Apr.

Impact of mental health and personality traits on the incidence of chronic cough in the Canadian Longitudinal Study on Aging

Imran Satia[1,2,3,4], Alexandra J Mayhew[3,4], Nazmul Sohel[3,4], Om Kurmi[1,2,3,5], Kieran J Killian[1], Paul M O'Byrne[1,2], Parminder Raina[3,4]

Affiliations expand

- PMID: 35651367
- PMCID: PMC9149388
- DOI: 10.1183/23120541.00119-2022

Free PMC article

Abstract

Background: Chronic cough is a common troublesome condition, but risk factors for developing chronic cough are poorly understood. The aim of this study was to understand the relationship between mental health disorders, personality traits and chronic cough.

Methods: The Canadian Longitudinal Study on Aging is a prospective, nationally generalisable, random sample of adults aged 45-85 years at baseline recruited between 2011 and 2015, and followed-up 3 years later. Chronic cough was defined as a daily cough over the last 12 months. Incident chronic cough was defined as those participants who reported new-onset chronic cough between baseline and follow-up 1. Current depressive symptoms and psychological distress were assessed using the Center for Epidemiologic Study Short Depression Scale (CESD-10) and Kessler Psychological Distress Scale (K-10), respectively. The "Big Five" personality traits were assessed using the Ten-Item Personality Inventory. Relative risks are reported using a multivariate mutually adjusted model.

Results: At follow-up 1, 2506 participants (11.1%) reported new-onset chronic cough during the ∼3-year interval. Depressive symptoms (CESD-10 ≥10: relative risk 1.22 (95% CI 1.03-1.44)) and psychological distress (K-10 ≥22: relative risk 1.20 (95% CI 1.07-1.36)) at baseline were both independent predictors of a higher risk of incident chronic cough. Prevalent and incident chronic cough were also independently associated with an increased risk of developing depressive symptoms and psychological distress. Personality traits did not influence the development of chronic cough but did increase the risk of depressive symptoms and psychological distress.

Conclusions: This study shows that there is a bidirectional relationship between chronic cough, and depressive symptoms and psychological distress, and personality traits do not independently influence the development of chronic cough.

Conflict of interest statement

Conflict of interest: I. Satia reports grants and personal fees from Merck during the conduct of the study; and grants and personal fees from GSK, personal fees from AstraZeneca and Genentech, grants from the E.J. Moran Campbell Early Career Award, and personal fees from Respiplus, outside the submitted work; he is an Associate Editor of this journal. Conflict of interest: A.J. Mayhew has nothing to disclose. Conflict of interest: N. Sohel has nothing to disclose. Conflict of interest: O. Kurmi has nothing to disclose. Conflict of interest: K.J. Killian has nothing to disclose. Conflict of interest: P.M. O'Byrne reports grants and personal fees from AstraZeneca, personal fees from GSK, grants from Novartis, grants and personal fees from Medimmune, and personal fees from Chiesi, outside the submitted work. Conflict of interest: P. Raina has nothing to disclose.

- 63 references
- 4 figures

FULL TEXT LINKS

Proceed to details

Cite

Share

3

Case Reports

J Med Case Rep

. 2022 May 28;16(1):208.

doi: 10.1186/s13256-022-03423-6.

Allergic shiners in a patient with cough-variant asthma: a case report

Mahsa Rekabi [1], Nasim Raad [2], Atefeh Abedini [2], Sepideh Darougar [3], Ali Akbar Velayati [2]

Affiliations expand

- PMID: 35624503

- PMCID: PMC9142182

- DOI: 10.1186/s13256-022-03423-6

Free PMC article

Abstract

Background: Chronic cough, with a duration of coughing of more than 8 weeks in adults, affects 5-10% of the general population. One of the most common causes of chronic cough is cough-variant asthma, which accounts for approximately one-third of cases. This phenotype of asthma is characterized by extreme sensitivity of the neuronal pathways mediating cough to environmental irritants, which results in an urge to cough. This case is an example of cough-variant asthma presenting with allergic shiners due to her severe cough.

Case presentation: A 38-year-old Iranian woman, who was well before the start of the coronavirus disease 2019 pandemic, presented with a nonproductive hacking cough that had begun after excessive use of antiseptic solutions. The only positive finding on physical examination was a reddish-purple rash on and around the eyelids mimicking a heliotrope rash, which had probably evolved due to the severity of the cough. The results of the pulmonary function test were within normal limits. Methacholine challenge test and chest x-ray were both normal. Chest high-resolution computed tomography revealed hyperinflation and tree-in-bud opacities. All other laboratory tests were normal. Because of the reversibility in her pulmonary function test, despite normal baseline parameters, asthma treatment was initiated, resulting in disappearance of the cough and the eye discoloration, being indicative of the correct diagnosis and proper treatment.

Conclusion: Patients with cough-variant asthma may often have no other classic symptoms of asthma other than cough.

Keywords: Allergic shiners; Asthma; Chronic cough; Cough-variant asthma.

Conflict of interest statement

The authors declare that they have no competing interests.

- 10 references
- 2 figures

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Clin Pharmacokinet

. 2022 May 28.

doi: 10.1007/s40262-022-01126-1. Online ahead of print.

Safety, Pharmacodynamics, and Pharmacokinetics of P2X3 Receptor Antagonist Eliapixant (BAY 1817080) in Healthy Subjects: Double-Blind Randomized Study

Christian Friedrich [1], Klaus Francke [2], Isabella Gashaw [2 3], Christian Scheerans [2], Stefan Klein [2], Lueder Fels [2], Jaclyn A Smith [4], Thomas Hummel [5], Alyn Morice [6]

Affiliations expand

- PMID: 35624408

- DOI: 10.1007/s40262-022-01126-1

Abstract

Background and objective: There is no licensed treatment for refractory chronic cough; off-label therapies have limited efficacy and can produce adverse effects. Excessive adenosine triphosphate signaling via P2X3 receptors is implicated in refractory chronic cough, and selective P2X3 receptor antagonists such as eliapixant (BAY 1817080) are under investigation. The objective of the study was to investigate the safety and tolerability of ascending repeated oral doses of eliapixant in healthy volunteers.

Methods: We conducted a repeated-dose, double-blind, randomized, placebo-controlled study in 47 healthy male individuals. Subjects received repeated twice-daily ascending oral doses of eliapixant (10, 50, 200, and 750 mg) or placebo for 2 weeks. The primary outcome was frequency and severity of adverse events. Other outcomes included pharmacokinetics and evaluation of taste disturbances, which have occurred with the less selective P2X3 receptor antagonist gefapixant.

Results: Peak plasma concentrations of eliapixant were reached 3-4 h after administration of the first and subsequent doses. With multiple dosing, steady-state plasma concentrations were reached after ~ 6 days, and plasma concentrations predicted to achieve ≥ 80% P2X3 receptor occupancy (the level required for efficacy) were reached at 200 and 750 mg. Increases in plasma concentrations with increasing doses were less than dose proportional. After multiple dosing, mean plasma concentrations of eliapixant showed low peak-trough fluctuations and were similar for 200- and 750-mg doses. Eliapixant was well tolerated with a low incidence of taste-related adverse events.

Conclusions: Eliapixant (200 and 750 mg) produced plasma concentrations that cover the predicted therapeutic threshold over 24 h, with good safety and tolerability. These results enabled eliapixant to progress to clinical trials in patients with refractory chronic cough.

Clinical trial registration: Clinicaltrials.gov: NCT03310645 (initial registration: 16 October, 2017).

Plain Language Summary

There are few effective treatments for patients with a long-term (chronic) cough. It is thought that chronic cough is caused by nerves becoming oversensitive, wrongly causing a cough when there is no need. We tested a new drug called eliapixant in 47 healthy men. Eliapixant reduces the excessive nerve signaling responsible for chronic cough. We looked for side effects of eliapixant and measured how it behaves in the body. In particular we looked for side effects relating to the sense of taste because gefapixant, a similar drug to eliapixant, can affect taste. Participants took one of four eliapixant doses or a placebo twice daily for 2 weeks. The highest levels of eliapixant in the blood were seen 3–4 h after taking the drug, and stable concentrations were seen after about 6 days. At the two highest doses, eliapixant reached concentrations in the body that should be high enough to work in patients with chronic cough. Side effects were generally similar between eliapixant and placebo. Taste-related side effects were mild and went away without needing treatment.

The positive results of this study meant that eliapixant could be tested in patients with chronic cough.

- 60 references

SUPPLEMENTARY INFO

Associated dataexpand

FULL TEXT LINKS

Proceed to details

Cite

Share

5

Arch Dis Child

-
-
-

. 2022 Jun;107(6):539.

doi: 10.1136/archdischild-2022-324318.

Chronic cough - over stimulation of C-fibres?

No authors listed

- PMID: 35589129

- DOI: 10.1136/archdischild-2022-324318

No abstract available

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

BMJ Full Text

Proceed to details

Cite

Share

6

Review

Mayo Clin Proc

. 2022 Jun;97(6):1164-1175.

doi: 10.1016/j.mayocp.2022.02.005. Epub 2022 Apr 26.

The Evolving Clinical Practice of Chronic Cough

Sumera R Ahmad [1], Vivek N Iyer [2]

Affiliations expand

- PMID: 35483988

- DOI: 10.1016/j.mayocp.2022.02.005

Abstract

Chronic cough, defined as a cough lasting for greater than 8 weeks, accounts for a substantial number of primary care and specialist consultations in the United States. Although cough can arise from a myriad number of serious respiratory diseases, attention has traditionally focused on diagnosing and treating gastroesophageal reflux, upper airway cough syndrome, and eosinophilic airway inflammation (asthma and nonasthmatic eosinophilic bronchitis) in patients with normal chest imaging. The newly described

paradigm and entity of cough hypersensitivity syndrome (CHS) becomes useful when the etiology of cough remains elusive or when the cough remains refractory despite appropriate therapy for underlying causes. We present an update on the evolving understanding of refractory chronic cough and/or unexplained chronic cough as manifestations of laryngeal hypersensitivity and CHS. This includes a focus on understanding the pathophysiology underlying current and novel therapeutics for CHS, while also ensuring that common causes of chronic cough continue to be evaluated and treated in a systematic multidisciplinary manner.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Proceed to details

Cite

Share

7

J Allergy Clin Immunol Pract

. 2022 Jun;10(6):1587-1597.

doi: 10.1016/j.jaip.2022.02.032. Epub 2022 Mar 8.

Risk Factors for Persistent Chronic Cough During Consecutive Years: A Retrospective Database Analysis

Robert S Zeiger [1], Michael Schatz [2], Yichen Zhou [3], Fagen Xie [4], Vishal Bali [5], Jonathan Schelfhout [5], Amar Das [5], Julie A Stern [4], Wansu Chen [4]

Affiliations expand

- PMID: 35272071

- DOI: 10.1016/j.jaip.2022.02.032

Abstract

Background: The identification of patients at high risk for diseases provides clinicians essential information to better manage such patients. Persistent chronic cough (PCC) is a condition with high clinical burden and limited knowledge of the risk factors that drive the persistent symptoms.

Objective: To understand the risk factors of PCC in patients with CC diagnosed by specialists.

Methods: In this retrospective study, adults aged 18 to 85 years diagnosed with CC by a pulmonologist, allergist, otolaryngologist, or gastroenterologist in the period 2011 to 2016 were identified. PCC was defined by another CC code or at least 2 cough events at least 8 weeks but no more than 4 months apart in each of the 2 consecutive years beginning 1 year after the original CC diagnosis. Unadjusted and adjusted risk ratios with 95% CI for patient characteristics at baseline in relationship to PCC were estimated by Poisson regression models with robust error variance.

Results: Of the adults with CC, 3270 (27.4%) had PCC and 5302 (44.5%) did not have CC during follow-up; 3341 (28.1%) had CC in only 1 follow-up year and were excluded from the analysis. Compared with patients without PCC, patients with PCC were noted to have significantly increased adjusted risk ratios for the following baseline features: (1) demographic characteristics (elderly, females, and less educated); (2) comorbidities (chronic obstructive pulmonary disease, chronic sinusitis, bronchiectasis, pulmonary fibrosis, hypertension, depression, and cough complications); (3) medication dispensed (inhaled corticosteroids/long-acting beta-agonists, leukotriene modifiers, nasal corticosteroids, nasal short-acting muscarinic antagonists, proton pump inhibitors, antitussives with narcotics, and neuromodulators); and (4) specialist care, particularly with pulmonologists.

Conclusions: Knowledge of the independent risk factors associated with PCC should aid clinicians in identifying such patients and improve their management.

Keywords: Antitussives; Chronic cough; Comorbidities; Cough; Persistent chronic cough.

Thorax

. 2022 Jun;77(6):621-624.

doi: 10.1136/thoraxjnl-2021-218403. Epub 2022 Jan 7.

Expression of interferon-γ and its effect on cough hypersensitivity in chronic refractory cough patients

Jiayang Sun [#1,2], Chen Zhan [#1], Zheng Deng [#1], Wei Luo [1], Qiaoli Chen [1], Mei Jiang [1], Nanshan Zhong [1], Kefang Lai [3]

Affiliations expand

- PMID: 34996851

- DOI: 10.1136/thoraxjnl-2021-218403

Abstract

Chronic refractory cough (CRC) is characterised by cough hypersensitivity. Interferon-γ (IFN-γ) has been reported to induce calcium influx, action potentials of vagal neurons in vitro and cough response in guinea pigs. While the effect of IFN-γ in CRC patients remains unknown. Here, via flow-cytometry and inhalation cough challenge, we found CRC patients had significantly increased levels of sputum IFN-γ^+CD4$^+$ T cells, IFN-γ^+CD8$^+$ T cells as well as supernatant of IFN-γ. The average number of coughs in CRC patients increased as the concentration of inhaled IFN-γ went up in IFN-γ cough challenge. Two or more coughs and five or more coughs elicited by inhaled IFN-γ in CRC patients occurred in 7 of 10 and 2 of 10, respectively. Preinhaled IFN-γ (100 µg/mL) increased the capsaicin cough sensitivity in CRC patients but not healthy volunteers. Targeting IFN-γ may be a potential effective anti-tussive strategy in CRC patients.

Keywords: cough/mechanisms/pharmacology.

Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS

Proceed to details

Cite

Share

9

Randomized Controlled Trial

Eur Respir J

. 2022 Jun 2;59(6):2100725.

doi: 10.1183/13993003.00725-2021. Print 2022 Jun.

Randomised trial of the P2X $_3$ receptor antagonist sivopixant for refractory chronic cough

Akio Niimi [1], Junpei Saito [2], Tadashi Kamei [3], Masaharu Shinkai [4], Hiroyuki Ishihara [5], Mitsuaki Machida [5], Sayaka Miyazaki [6]

Affiliations expand

- PMID: 34649978

- PMCID: PMC9176336

- DOI: 10.1183/13993003.00725-2021

Free PMC article

Abstract

Background: The purinoceptor subtype $P2X_3$ has been shown to have significant involvement in the cough reflex; the heterotrimer version of the purinoceptor ($P2X_{2/3}$) has been implicated in taste disturbance. The most advanced clinical candidate antagonist gefapixant has low selectivity among $P2X_3$ receptors and induced taste disturbance, whereas newly developed sivopixant has high selectivity towards $P2X_3$ *versus* $P2X_{2/3}$.

Methods: In a phase 2a, randomised, double-blind, placebo-controlled, crossover, multicentre study, adult patients with refractory or unexplained chronic cough received oral sivopixant 150 mg or placebo once daily for 2 weeks, followed by a 2-3-week washout period, and then crossed over to placebo or sivopixant for 2 weeks. Efficacy and safety of sivopixant were evaluated.

Results: Of 31 randomised patients, 15 in the sivopixant-first group and 15 in the placebo-first group completed the study. After 2 weeks of treatment, the placebo-adjusted ratios of the average hourly number of coughs to baseline during daytime (primary end-point) and over 24 h (secondary end-point) were -31.6% (p=0.0546) and -30.9% (p=0.0386), respectively. Sivopixant also improved health-related quality of life. Treatment-related adverse events occurred in 12.9% and 3.2% of patients during sivopixant and placebo administration, respectively. Mild taste disturbance occurred in two patients (6.5%) during sivopixant administration.

Conclusions: Sivopixant reduced objective cough frequency and improved health-related quality of life, with a low incidence of taste disturbance, among patients with refractory or unexplained chronic cough.

Conflict of interest statement

Conflict of interest: A. Niimi has nothing to disclose. Conflict of interest: J. Saito has nothing to disclose. Conflict of interest: T. Kamei has nothing to disclose. Conflict of interest: M. Shinkai has nothing to disclose. Conflict of interest: H. Ishihara is an employee and minor stockholder of Shionogi & Co., Ltd. Conflict of interest: M. Machida is an employee and minor stockholder of Shionogi & Co., Ltd. Conflict of interest: S. Miyazaki is an employee and minor stockholder of Shionogi & Co., Ltd.

- Cited by 1 article
- 30 references
- 3 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

Free full text at ersjournals.com

Proceed to details

Cite

Share

10

J Asthma

. 2022 Jun;59(6):1139-1147.

doi: 10.1080/02770903.2021.1897837. Epub 2021 Mar 15.

Nasal polyp eosinophilia and FeNO may predict asthma symptoms development after endoscopic sinus surgery in CRS patients without asthma

Ryota Kurokawa [1], Yoshihiro Kanemitsu [1], Kensuke Fukumitsu [1], Norihisa Takeda [1], Jennifer Maries Yap [1], Yoshiyuki Ozawa [2], Ayako Masaki [3], Junya Ono [4], Kenji Izuhara [5], Hirono Nishiyama [1], Satoshi Fukuda [1], Takehiro Uemura [1], Tomoko Tajiri [1], Hirotsugu Ohkubo [1], Ken Maeno [1], Yutaka Ito [1], Tetsuya Oguri [1], Masaya Takemura [1], Motohiko Suzuki [6], Akio Niimi [1]

Affiliations expand

- PMID: 33653221

- DOI: 10.1080/02770903.2021.1897837

Abstract

Background: Asthma is a significant comorbidity of eosinophilic chronic rhinosinusitis (CRS). Type2-driven biomarkers such as sinus tissue eosinophilia and fractional nitric oxide (FeNO) may be utilized to detect high risk patients who develop asthma symptoms after endoscopic sinus surgery (ESS) in CRS patients.

Methods: Thirty-six CRS patients without asthma who agreed to undergo ESS between October 2015 and December 2017 were prospectively observed for 12 months following ESS. They were monitored for the development of typical asthma symptoms including dyspnea, wheezes, and cough which responded to anti-asthma medication. Biomarkers were compared between patients who developed asthma symptoms after ESS (asthma symptoms group) and those who did not (non-asthma group). Biomarker changes following ESS intervention were also evaluated.

Results: Six patients were lost to follow after ESS. Thus, 30 CRS patients [16 with nasal polyps (NPs) proved by surgery] were followed. Seven (23%) newly complained of asthma symptoms during follow-up. Levels of FeNO and the prevalence of eosinophilic NPs (eosinophils ≥ 70/high power fields) were significantly higher in the asthma symptom group than in non-asthma group [50.7 ppb *vs* 22.4 ppb for FeNO levels, and 100% (n = 3) *vs* 23% (n = 3) for eosinophilic NP prevalence, both $p < 0.05$]. Levels of sputum periostin decreased significantly by ESS in the non-asthma group. However, changes of biomarkers after ESS were comparable between the two groups.

Conclusions: Eosinophils in NPs (≥70/high power fields) and preoperative FeNO may be significant biomarkers for predicting the development of asthma symptoms after ESS.

Keywords: Chronic rhinosinusitis; asthma; nasal polyps.