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COPD

Thorax

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. 2022 Jul 1;thoraxjnl-2021-218315.

doi: 10.1136/thoraxjnl-2021-218315. Online ahead of print.

The relationship between interstitial lung abnormalities, mortality, and multimorbidity: a cohort study

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Affiliations expand

- PMID: 35777957

- DOI: 10.1136/thoraxjnl-2021-218315

Abstract

Background: Interstitial lung abnormalities (ILAs) are associated with increased mortality. It is unclear whether multimorbidity accounts for the mortality association or how strongly ILA is associated with mortality relative to other common age-associated diseases. We determined the association of ILA with all-cause mortality adjusted for multimorbidity, compared mortality associated with ILA and prevalent cardiovascular disease (CVD), diabetes mellitus, chronic kidney disease, chronic obstructive pulmonary disease and cancer and also determined the association between ILA and these diseases.

Methods: We measured ILA (none, indeterminant, definite) using blinded reads of CT images, prevalent chronic diseases and potential confounders in two observational cohorts, the Framingham Heart Study (FHS) (n=2449) and Age, Gene/Environment Susceptibility - Reykjavik Study (AGES-Reykjavik) (n=5180). We determined associations with mortality using Cox proportional hazards models and between ILA and diseases with multinomial logistic regression.

Results: Over a median (IQR) follow-up of 8.8 (1.4) years in FHS and 12.0 (7.7) years in AGES-Reykjavik, in adjusted models, ILAs were significantly associated with increased mortality (HR, 95% CI 1.95, 1.23 to 3.08, p=0.0042, in FHS; HR 1.60, 1.41 to 1.82, p<0.0001, in AGES-Reykjavik) adjusted for multimorbidity. In both cohorts, the association of ILA with mortality was of similar magnitude to the association of most other diseases. In adjusted models, ILAs were associated only with prevalent kidney disease (OR, 95% CI 1.90, 1.01 to 3.57, p=0.0452) in FHS and with prevalent CVD (OR 1.42, 1.12 to 1.81, p=0.0040) in AGES-Reykjavik.

Conclusions: ILAs were associated with mortality adjusted for multimorbidity and were similarly associated with increased mortality compared with several common chronic diseases. ILAs were not consistently associated with the prevalence of these diseases themselves.

Keywords: clinical epidemiology; idiopathic pulmonary fibrosis; imaging/CT MRI etc.

Conflict of interest statement

Competing interests: JLS reports personal fees for consultancy from Apneo Therapeutics and Decimal.health, outside the submitted work. At the time of publication, JLS was employed by Vertex Pharmaceuticals. MN reports personal fees for consultancy from Daiichi Sankyo and AstraZeneca; honoraria from Roche; and grants from Merck, AstraZeneca, Canon Medical Systems and NIH (R01CA203636, U01CA209414, R01HL111024), outside the submitted work. HH reports grants from Canon Medical System Inc. and Konica-Minolta Inc., personal fees for consultancy from Mitsubishi Chemical Inc.

and personal fees for advisory board work from Canon Medical System Inc., outside the submitted work. JM reports fees to her institution on her behalf for guest lecture/consultant outside the submitted work from Merck. GMH reports personal fees from Genentech, Boehringer Ingelheim, The Gerson Lehrman Group and Mitsubishi Chemical, outside the submitted work.

Eur Respir J

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Adverse roles of mast cell chymase-1 in chronic obstructive pulmonary disease

Gang Liu[1], Andrew G Jarnicki[2], Keshav R Paudel[1], Wenying Lu[3], Ridhima Wadhwa[1], Ashleigh M Philp[1 4], Hannelore Van Eeckhoutte[5], Jacqueline E Marshall[1], Vamshikrishna Malyla[1], Angelica Katsifis[1], Michael Fricker[6], Nicole G Hansbro[1], Kamal Dua[1 7], Nazanin Z Kermani[8], Mathew S Eapen[3], Angelica Tiotiu[9 10], K Fan Chung[9], Gaetano Caramori[11], Ken Bracke[5], Ian M Adcock[9], Sukhwinder S Sohal[3], Peter A Wark[6], Brian G Oliver[12], Philip M Hansbro[13 6]

Affiliations expand

- PMID: 35777766

- DOI: 10.1183/13993003.01431-2021

Abstract

Background: COPD is the third leading cause of death worldwide. Cigarette smoke (CS)-induced chronic inflammation inducing airway remodelling, emphysema and impaired lung function is the primary cause. Effective therapies are urgently needed. Human chymase-1 (hCMA1) and it's ortholog mCMA1/mouse mast cell (MC) protease-5 (mMCP5) are

exocytosed from activated MCs and have adverse roles in numerous disorders, but their role in COPD is unknown.

Methods: We evaluated hCMA1 levels in lung tissues of COPD patients. We used *mmcp5*-deficient ($^{-/-}$) mice to evaluate this proteases' role and potential for therapeutic targeting in CS-induced experimental COPD. We also used *ex vivo/in vitro* studies to define mechanisms.

Results: The levels of hCMA1 mRNA and CMA1^{+} MCs were increased in lung tissues from severe compared to early/mild COPD patients, non-COPD smokers and healthy controls. Degranulated MC numbers and mMCP5 protein were increased in lung tissues of wild-type (WT) mice with experimental COPD. *mmcp5* $^{-/-}$ mice were protected against CS-induced inflammation and macrophage accumulation, airway remodelling, emphysema and impaired lung function in experimental COPD. CS extract challenge of co-cultures of MCs from WT but not *mmcp5* $^{-/-}$ mice with WT lung macrophages increased in TNF-α release. It also caused the release of CMA1 from human MCs, and recombinant hCMA-1 induced TNF-α release from human macrophages. Treatment with CMA1 inhibitor potently suppressed these hallmark features of experimental COPD.

Conclusion: CMA1/mMCP5 promotes the pathogenesis of COPD, in part, by inducing TNF-α expression and release from lung macrophages. Inhibiting hCMA1 may be a novel treatment for COPD.

SUPPLEMENTARY INFO

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Medicine (Baltimore)

. 2022 Jul 1;101(26):e29737.

doi: 10.1097/MD.0000000000029737.

Risk factors for in-hospital death in elderly patients over 65 years of age with dementia: A retrospective cross-sectional study

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Affiliations expand

- PMID: 35777004

- DOI: 10.1097/MD.0000000000029737

Abstract

As the population continues to age, dementia is becoming a huge social, economic, and healthcare burden. However, the risk factors for in-hospital death in elderly patients over 65 years of age with dementia are not well understood. Identifying factors that affect their prognosis could help clinicians with scientific decision-making. To examine the risk factors for in-hospital death in elderly patients over 65 years of age with dementia in the Geriatric Department of West China Hospital. In this retrospective, cross-sectional study, we analyzed inpatients aged ≥65 years with dementia between 2010 and 2016 using electronic medical records from the Information Center of West China Hospital. The risk factors for death were assessed using multivariable logistic regression. Out of a total of 2986 inpatients with dementia, 3.4% died. Patient deaths were related to digestive diseases, respiratory diseases, circulatory diseases, urinary diseases, and chronic obstructive pulmonary disease, whereas patient survival was associated with osteoporosis and Parkinson disease. Patients with a mean length of hospital stay of ≥60 days had an increased risk of death (all P <.05). In the multiple logistic regression analysis, age ≥80 years, digestive diseases, respiratory diseases, urinary diseases, diabetes, chronic obstructive pulmonary disease, and ≥7 comorbidities were risk factors for death. Mortality in hospitalized older patients with dementia is low, but some risk factors may be easily ignored. These findings could raise awareness among clinicians and caregivers about risk factors in hospitalized older patients, particularly hospitalized elderly patients with multiple comorbidities. Therefore, to reduce mortality, early prevention and management of potential risks are necessary.

Conflict of interest statement

The authors have no funding and conflicts of interest to disclose.

- 59 references

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Review

Thorax

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. 2022 Jun 30;thoraxjnl-2021-218333.

doi: 10.1136/thoraxjnl-2021-218333. Online ahead of print.

Cardiovascular disease in chronic obstructive pulmonary disease: a narrative review

Vishanna Balbirsingh[1], Andrea S Mohammed[1], Alice M Turner[2], Michael Newnham[3]

Affiliations expand

- PMID: 35772939

- DOI: 10.1136/thoraxjnl-2021-218333

Abstract

Patients with chronic obstructive pulmonary disease (COPD) are at increased risk of cardiovascular disease (CVD) and concomitant disease leads to reduced quality of life, increased hospitalisations and worse survival. Acute pulmonary exacerbations are an important contributor to COPD burden and are associated with increased cardiovascular

(CV) events. Both COPD and CVD represent a significant global disease impact and understanding the relationship between the two could potentially reduce this burden. The association between CVD and COPD could be a consequence of (1) shared risk factors (environmental and/or genetic) (2) shared pathophysiological pathways (3) coassociation from a high prevalence of both diseases (4) adverse effects (including pulmonary exacerbations) of COPD contributing to CVD and (5) CVD medications potentially worsening COPD and vice versa. CV risk in COPD has traditionally been associated with increasing disease severity, but there are other relevant COPD subtype associations including radiological subtypes, those with frequent pulmonary exacerbations and novel disease clusters. While the prevalence of CVD is high in COPD populations, it may be underdiagnosed, and improved risk prediction, diagnosis and treatment optimisation could lead to improved outcomes. This state-of-the-art review will explore the incidence/prevalence, COPD subtype associations, shared pathophysiology and genetics, risk prediction, and treatment of CVD in COPD.

Keywords: COPD epidemiology; COPD exacerbations; COPD pathology; COPD pharmacology.

Conflict of interest statement

Competing interests: AMT reports research grants from AstraZeneca and Chiesi, personal fees from GSK, Boehringer, CSL Behring, AstraZeneca and Chiesi.

. 2022 Jun 30;12(6):e059122.

doi: 10.1136/bmjopen-2021-059122.

Impact of COPD and asthma on in-hospital mortality and management of patients with heart failure in England and Wales: an observational analysis

Claudia Gulea[1,2], Rosita Zakeri[3], Constantinos Kallis[4,2], Jennifer K Quint[4,2]

Affiliations expand

- PMID: 35772828

- DOI: 10.1136/bmjopen-2021-059122

Free article

Abstract

Objective: To evaluate the association between having concomitant chronic obstructive pulmonary disease (COPD) or asthma, and in-patient mortality and post-discharge management among patients hospitalised for acute heart failure (HF).

Setting: Data were obtained from patients enrolled in the National Heart Failure Audit.

Participants: 217 329 patients hospitalised for HF in England-Wales between March 2012 and 2018.

Outcomes: In-hospital mortality, referrals to cardiology follow-up and prescriptions for HF medications were compared between patients with comorbid COPD (COPD-HF) or asthma (asthma-HF) versus HF-alone using mixed-effects logistic regression.

Results: Patients with COPD-HF were more likely to die during hospitalisation, and those with asthma-HF had a reduced likelihood of death, compared with patients who had HF-alone ((adjusted)OR_{adj}, 95% CI: 1.10, 1.06 to 1.14 and OR_{adj}, 95% CI: 0.84, 0.79 to 0.88). In patients who survived to discharge, referral to HF follow-up services differed between groups: patients with COPD-HF had reduced odds of cardiology follow-up (OR_{adj}, 95% CI 0.79, 0.77 to 0.81), while cardiology referral odds for asthma-HF were similar to HF-alone.

Overall, proportions of HF medication prescriptions at discharge were low for both COPD-HF and asthma-HF groups, particularly prescriptions for beta-blockers.

Conclusions: In this nationwide analysis, we showed that COPD and asthma significantly impact the clinical course in patients hospitalised for HF. COPD is associated with higher in-patient mortality and lower cardiology referral odds, while COPD and asthma are both associated with lower use of prognostic HF therapies on discharge. These data highlight therapeutic gaps and a need for better integration of cardiopulmonary services to improve healthcare provision for patients with HF and coexisting respiratory disease.

Keywords: epidemiology; heart failure; respiratory medicine (see Thoracic Medicine).

Conflict of interest statement

Competing interests: None declared.

Editorial

Ann Am Thorac Soc

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doi: 10.1513/AnnalsATS.202204-317ED.

Mind the Gap: Addressing Cardiovascular Disease in Chronic Obstructive Pulmonary Disease

J Michael Wells[1,2,3,4,5], Gregory A Payne[1,3,4,6,5]

Affiliations expand

- PMID: 35772101

- DOI: 10.1513/AnnalsATS.202204-317ED

No abstract available

Comment on

- Control of Cardiovascular Risk Factors in Patients with Chronic Obstructive Pulmonary Disease.
  Hawkins NM, Peterson S, Ezzat AM, Vijh R, Virani SA, Gibb A, Mancini GBJ, Wong ST.Ann Am Thorac Soc. 2022 Jul;19(7):1102-1111. doi: 10.1513/AnnalsATS.202104-463OC.PMID: 35007497

SUPPLEMENTARY INFO

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AnnalsATS Final Version

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. 2022 Jun 30.

doi: 10.1164/rccm.202201-0199OC. Online ahead of print.

Home High-Flow Nasal Cannula Oxygen Therapy for Stable Hypercapnic COPD: A Randomized Trial

Kazuma Nagata[1], Takeo Horie[2], Naohiko Chohnabayashi[3], Torahiko Jinta[4], Ryosuke Tsugitomi[3], Akira Shiraki[5], Fumiaki Tokioka[6], Toru Kadowaki[7], Akira Watanabe[8], Motonari Fukui[9], Takamasa Kitajima[9], Susumu Sato[10], Toru Tsuda[11], Nobuhito Kishimoto[12], Hideo Kita[13], Yoshihiro Mori[14], Masayuki Nakayama[15], Kenichi Takahashi[16], Tomomasa Tsuboi[17], Makoto Yoshida[18], Osamu Hataji[19], Satoshi Fuke[20], Michiko Kagajo[21], Hiroki Nishine[22], Hiroyasu Kobayashi[23], Hiroyuki Nakamura[24], Miyuki Okuda[25], Sayaka Tachibana[26], Shohei Takata[27], Hisayuki Osoreda[28], Kenichi Minami[29], Takashi Nishimura[30], Tadashi Ishida[6], Jiro Terada[31], Naoko Takeuchi[32], Yasuo Kohashi[33], Hiromasa Inoue[34], Yoko Nakagawa[35], Takashi Kikuchi[35], Keisuke Tomii[36], FLOCOP study investigators

Affiliations expand

- PMID: 35771533

- DOI: 10.1164/rccm.202201-0199OC

Abstract

Rationale: The long-term effects of high-flow nasal cannula for chronic hypercapnic respiratory failure due to chronic obstructive pulmonary disease remain unclear.

Objectives: To assess whether long-term high-flow nasal cannula reduces the number of exacerbations and improves other physiological parameters in patients with chronic hypercapnic respiratory failure due to chronic obstructive pulmonary disease.

Methods: We enrolled 104 participants (aged ≥40 years) with daytime hypercapnia (global initiative for chronic obstructive lung disease stages 2-4), receiving long-term oxygen therapy (≥16 h/day for ≥1 month), and randomly assigned them to high-flow nasal cannula/long-term oxygen therapy and long-term oxygen therapy groups. The primary endpoint was the moderate/severe exacerbation rate. We compared changes from baseline in arterial blood gas values, peripheral oxygen saturation, pulmonary function, health-related quality of life scores, and the 6-min walk test.

Measurements and main results: High-flow nasal cannula significantly reduced the rate of moderate/severe exacerbations (unadjusted mean count 1.0 vs. 2.5, a ratio of the adjusted mean count between groups [95% confidence interval] 2.85 [1.48-5.47]) and prolonged the duration without moderate/severe exacerbations. The median time to first moderate or severe exacerbation in the long-term oxygen therapy group was 25 (14.1-47.4) weeks; this was not reached in the high-flow nasal cannula/long-term oxygen therapy group. High-flow nasal cannula significantly improved health-related quality of life scores, peripheral oxygen saturation, and specific pulmonary function parameters. No safety concerns were identified.

Conclusions: High-flow nasal cannula is a reasonable therapeutic option for patients with stable hypercapnic chronic obstructive pulmonary disease and a history of exacerbations. Clinical trial registration available at www.

Clinicaltrials: gov, ID: NCT03282019.

Keywords: chronic obstructive; hypercapnia; oxygen inhalation therapy; pulmonary disease; respiratory insufficiency.

Review

Curr Opin Pulm Med

. 2022 Jul 1;28(4):296-302.

doi: 10.1097/MCP.0000000000000876.

Revealing the pathogenic and ageing-related mechanisms of the enigmatic idiopathic pulmonary fibrosis (and chronic obstructive pulmonary disease)

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Affiliations expand

- PMID: 35749794

- DOI: 10.1097/MCP.0000000000000876

Abstract

Purpose of review: Growing evidence suggests that ageing-associated alterations occur in both idiopathic pulmonary fibrosis (IPF) and chronic obstructive pulmonary disease (COPD). Here, we review the most recent literature on dysregulated ageing pathways in IPF and COPD and discuss how they may contribute to disease pathogenesis.

Recent findings: Recent studies have shown that alveolar epithelial type II (ATII) cells undergo premature senescence under stress and that senescent ATII cells promote lung fibrogenesis. Some studies have explored the role of mitochondrial dysfunction in IPF. They have provided evidence that dysfunctional mitochondria are important contributors to fibrogenesis through release of damaged DNA and excessive formation of reactive oxygen species, whereas restoration of mitochondrial homeostasis may attenuate lung fibrosis. Insufficient autophagy has been shown to promote epithelial-to-mesenchymal transition and aberrant epithelial-fibroblast crosstalk, suggesting that autophagy augmentation may represent a potential therapeutic strategy. A number of studies have also explored the role of cellular senescence, mitochondrial homeostasis and autophagy in COPD.

Summary: Several ageing mechanisms are dysregulated in the lungs of patients with IPF and COPD, although how they contribute to disease development and progression remains elusive. Genetic or pharmacologic attenuation of senescence-related pathways and elimination of senescent cells may represent a promising therapeutic strategy.

- 62 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Am J Respir Crit Care Med

. 2022 Jul 1;206(1):17-24.

doi: 10.1164/rccm.202201-0209PP.

Blood Eosinophils and Chronic Obstructive Pulmonary Disease: A Global Initiative for Chronic Obstructive Lung Disease Science Committee 2022 Review

Dave Singh[1], Alvar Agusti[2], Fernando J Martinez[3], Alberto Papi[4], Ian D Pavord[5], Jadwiga A Wedzicha[6], Claus F Vogelmeier[7], David M G Halpin[8]

Affiliations expand

- PMID: 35737975

- DOI: 10.1164/rccm.202201-0209PP

No abstract available

Review

Eur Respir Rev

. 2022 May 25;31(164):210259.

doi: 10.1183/16000617.0259-2021. Print 2022 Jun 30.

Antibiotic resistance in chronic respiratory diseases: from susceptibility testing to the resistome

Hélène Pailhoriès[1,2], Jean-Louis Herrmann[3,4], Lourdes Velo-Suarez[5], Claudie Lamoureux[6,7], Clémence Beauruelle[6,7], Pierre-Régis Burgel[8], Geneviève Héry-Arnaud[9,6,7]

Affiliations expand

- PMID: 35613743

- DOI: 10.1183/16000617.0259-2021

Free article

Abstract

The development of resistome analysis, *i.e.* the comprehensive analysis of antibiotic-resistance genes (ARGs), is enabling a better understanding of the mechanisms of antibiotic-resistance emergence. The respiratory microbiome is a dynamic and interactive network of bacteria, with a set of ARGs that could influence the response to antibiotics. Viruses such as bacteriophages, potential carriers of ARGs, may also form part of this respiratory resistome. Chronic respiratory diseases (CRDs) such as cystic fibrosis, severe asthma, chronic obstructive pulmonary disease and bronchiectasis, managed with long-term antibiotic therapies, lead to multidrug resistance. Antibiotic susceptibility testing provides a partial view of the bacterial response to antibiotics in the complex lung environment. Assessing the ARG network would allow personalised, targeted therapeutic strategies and suitable antibiotic stewardship in CRDs, depending on individual resistome and microbiome signatures. This review summarises the influence of pulmonary antibiotic protocols on the respiratory microbiome, detailing the variable consequences according to antibiotic class and duration of treatment. The different resistome-profiling methods are explained to clarify their respective place in antibiotic-resistance analysis in the lungs. Finally, this review details current knowledge on the respiratory resistome related to therapeutic strategies and provides insight into the application of resistome analysis to counter the emergence of multidrug-resistant respiratory pathogens.

Conflict of interest statement

Conflict of interest: P-R. Burgel reports grants or contracts from GSK, Boehringer Ingelheim and Vertex; consulting fees from AstraZeneca, Chiesi, GSK and Insmed; and payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Insmed, Novartis, Pfizer, Vertex and Zambon, all outside the submitted work. The remaining authors have nothing to disclose.

Review

Respir Med

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. 2022 Jul;198:106880.

doi: 10.1016/j.rmed.2022.106880. Epub 2022 May 13.

A systematic review of blood eosinophils and continued treatment with inhaled corticosteroids in patients with COPD

Dagmar Abelone Dalin[1], Anders Løkke[2], Pernille Kristiansen[3], Charlotte Jensen[4], Kirsten Birkefoss[5], Hanne Rolighed Christensen[6], Nina Skavlan Godtfredsen[7], Ole Hilberg[2], Jeanett Friis Rohde[8], Anja Ussing[9], Charlotte Vermehren[10], Mina Nicole Händel[8]

Affiliations expand

- PMID: 35599064

- DOI: 10.1016/j.rmed.2022.106880

Free article

Abstract

Inhaled corticosteroid (ICS) in patients with chronic obstructive pulmonary disease (COPD) has been debated for 20 years. In our systematic literature review and meta-analysis, we addressed the following: Should patients with COPD and a blood eosinophil count (EOS) of, respectively, a) < 150 cells/μl, b) 150-300 cells/μl, and c) > 300 cells/μl continue treatment with ICS? Protocol registered in PROSPERO (CRD42020178110) and funded by the Danish Health Authority. We searched Medline, Embase, CINAHL and Cochrane Central on 22nd July 2020 for randomized controlled trials (RCT) of ICS treatment in patients with COPD (≥40 years, no current asthma), which analyzed outcomes by EOS count and where >50% of patients used ICS prior. We used the GRADE method. Meta-analyzes for the outcomes were divided into EOS subgroups and analyzed for differences. We identified 11

RCTs with a total of 29,654 patients. A significant difference ($p < 0.00001$) between the three subgroups' reduction of risk of moderate to severe exacerbation was found. Rate ratios for EOS counts: <150 cells/μL was 0.88 (95%CI: 0.83, 0.94); 150-300 cells/μL was 0.80 (95%CI: 0.69, 0.94); >300 cells/μL was 0.57 (95%CI: 0.49, 0.66). Overall, the certainty of the effect estimates was low to very low due to risk of bias, unexplained heterogeneity, few RCTs, and wide confidence intervals. A clear correlation was demonstrated between effect of continued ICS treatment (number of exacerbations, lung function, and quality of life) and increasing EOS count. Our meta-analyses suggested that treatment with ICS seemed beneficial for everyone except patients with EOS count below 150 cells/μl.

Keywords: Blood eosinophils; Chronic obstructive pulmonary disease; Eosinophil; Inhaled corticosteroid.

Respir Med

. 2022 Jul;198:106879.

doi: 10.1016/j.rmed.2022.106879. Epub 2022 May 16.

Fractional exhaled nitric oxide and mortality in asthma and chronic

obstructive pulmonary disease in a national cohort aged 40 years and older

Isaac Ikwu [1], Louis Gardy Nicolas [2], Alem Mehari [3], Richard F Gillum [4]

Affiliations expand

- PMID: 35599063

- DOI: 10.1016/j.rmed.2022.106879

Abstract

Background: Little is known about Fractional concentration of exhaled Nitric Oxide (FeNO) as a predictor of mortality in persons with asthma or chronic obstructive pulmonary disease (COPD).

Objective: This study tested the hypotheses that FeNO level ≥ 25 ppb was associated with mortality in a national cohort of persons with asthma or COPD age ≥ 40 years.

Methods: In the 2007-2012 National Health and Nutrition Examination Survey (NHANES), FeNO was measured using an electrochemical sensor. Mortality was determined through 2015 using linkage to the National Death Index. Weighted Cox proportional hazards survival analysis was performed taking the complex survey design into account using STATA V.17.

Results: Among the 611 participants with current asthma, 5.16% died during the follow-up period. FeNO ≥ 25 ppb was associated with a hazard ratio (HR) of 0.20, (p = 0.006, 95% CI:0.068-0.618) alone or with little change after controlling for confounding variables. Due to effect modification, the analysis was repeated in persons with and without a history of emergency department (ED) visit for asthma in the previous year. In 522 persons without ED visits, FeNO ≥ 25 ppb was significantly associated with mortality HR 0.094, 95 CI 0.034-0.26, p < 0.001. In 83 persons with ED visits no significant association remained after controlling for all confounders. (Six persons were omitted from this analysis due to missing data on confounders in the extended regression model.) Among 614 with COPD, FeNO ≥ 25 ppb was not associated with mortality.

Conclusion: In persons with current asthma at baseline, FeNO ≥ 25 ppb was associated with reduced hazard of mortality during follow up among those with no history of ED visits in the previous year. No significant association of FeNO with mortality was seen in persons with COPD.

Keywords: Asthma; COPD; Fractional exhaled nitric oxide; Mortality.

Respir Med

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. 2022 Jul;198:106865.

doi: 10.1016/j.rmed.2022.106865. Epub 2022 May 7.

Depressive and anxiety symptoms in patients with COPD: A network analysis

Abebaw M Yohannes[1], Martino Belvederi Murri[2], Nicola A Hanania[3], Elizabeth A Regan[4], Anand Iyer[5], Surya P Bhatt[6], Victor Kim[7], Gregory L Kinney[8], Robert A Wise[9], Michelle N Eakin[9], Karin F Hoth[10], COPDGene Investigators

Affiliations expand

- PMID: 35576775

- DOI: 10.1016/j.rmed.2022.106865

Abstract

Background: Individuals with Chronic Obstructive Pulmonary Disease (COPD) often develop anxiety and depression, which worsen illness management and prognosis. Physical and psychological symptoms, contextual and illness-related factors display complex reciprocal interactions, which give rise to heterogeneous presentations. Examining the patterns of association between specific physical and psychological symptoms in patients with COPD may help to focus on the precision of the patient-centred care.

Research question: We used network analyses to examine the links between symptoms of COPD, depression and anxiety.

Methods: Data from 1587 individuals with COPD from the COPDGene study were included. We estimated a Bayesian Gaussian Graphical Model to highlight the unique associations between symptoms of COPD (assessed with the COPD Assessment Test), depression and anxiety (assessed with the Hospital Anxiety and Depression Scale (HADS), while examining the role of sociodemographic characteristics, lung function tests, and health status.

Results: Unique Variable Analysis reduced 14 HADS items to Tension/worry (chronic anxiety), Fear/panic (acute anxiety), Restlessness, Anhedonia, Sadness and Slowing. In network analyses, chest-tightness was related to acute anxiety, while cough and weakness were connected with core depressive symptoms (sadness and lack of pleasure). Chronic anxiety was linked with acute anxiety and depressive symptoms. Findings were confirmed accounting for the role of confounders, including lung function, sex, ethnicity and lifestyle factors. A simulation based on our model yielded distinct predictions about anxiety and depression in two participants with similar COPD severity, but different symptom profiles.

Conclusion: Network analyses highlighted specific associations between symptoms of COPD, depression and anxiety. Accounting for symptom-level interactions may help to promote personalized treatment approaches.

Keywords: Anxiety; COPD; Depression; Dyspnoea; Network analysis; Panic; Worries.

Sleep Med

. 2022 Jul;95:120-125.

doi: 10.1016/j.sleep.2022.04.017. Epub 2022 Apr 22.

Psychometric properties of the Insomnia Severity Index for people with chronic obstructive pulmonary disease

Jeehye Jun [1], Chang G Park [2], Mary C Kapella [3]

Affiliations expand

- PMID: 35569329

- DOI: 10.1016/j.sleep.2022.04.017

Abstract

Objective/background: Insomnia is one of the most commonly reported symptoms among people with chronic obstructive pulmonary disease (COPD). Prior research evaluated the psychometric properties of the Insomnia Severity Index (ISI) with various populations, but no studies have examined the measurement properties of the instrument in the COPD population. This study aimed to determine the reliability and validity of the ISI for the COPD population.

Patients/methods: This study included 96 people with COPD and insomnia. As psychometric properties, the ISI's internal consistency, factor structure, and criterion validity were examined with this sample. Exploratory factor analysis (EFA) and confirmatory factor analysis (CFA) were used to evaluate construct validity. Correlations between scores for the ISI and for measures of depression, anxiety, fatigue, and dyspnea were examined to determine criterion validity.

Results: The Cronbach's alpha value for the ISI was 0.79, indicating good internal consistency. In the EFA, a single ISI factor with an eigenvalue of 3.19 accounted for 45.6% of the variance. CFA indicated adequate construct validity, and interference of sleep problems with daytime functioning and level of distress caused by sleep difficulties showed the highest factor loadings (both 0.78). Criterion validity was supported by significant, weak to moderate correlations between scores for the ISI and for measures of depression, anxiety, fatigue, and dyspnea.

Conclusions: The results provide evidence that the ISI has good reliability and validity for measuring insomnia severity in the COPD population.

Keywords: Chronic obstructive pulmonary disease; Factor analysis; Insomnia; Insomnia Severity Index; Reliability; Validity.

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Adv Ther

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. 2022 Jul;39(7):3424.

doi: 10.1007/s12325-022-02175-5.

Correction to: Effects of High-Intensity Interval Training on Pulmonary Function and Exercise Capacity in Individuals with Chronic Obstructive Pulmonary Disease: A Meta-Analysis and Systematic Review

Min Gao[#1], Yangxi Huang[#1], Qianyi Wang[2], Kouying Liu[1,3], Guozhen Sun[4,5]

Affiliations expand

- PMID: 35556228

- DOI: 10.1007/s12325-022-02175-5

No abstract available

Erratum for

- Effects of High-Intensity Interval Training on Pulmonary Function and Exercise Capacity in Individuals with Chronic Obstructive Pulmonary Disease: A Meta-Analysis and Systematic Review.
  Gao M, Huang Y, Wang Q, Liu K, Sun G.Adv Ther. 2022 Jan;39(1):94-116. doi: 10.1007/s12325-021-01920-6. Epub 2021 Nov 18.PMID: 34792785 Review.

Review

Eur Respir Rev

. 2022 May 4;31(164):210196.

doi: 10.1183/16000617.0196-2021. Print 2022 Jun 30.

The impact of long-acting muscarinic antagonists on mucus hypersecretion and cough in chronic obstructive pulmonary disease: a systematic review

Luigino Calzetta[1], Beatrice Ludovica Ritondo[2], Maria Cristina Zappa[3], Gian Marco Manzetti[2], Andrea Perduno[2], Janis Shute[4], Paola Rogliani[2]

Affiliations expand

- PMID: 35508331

- DOI: 10.1183/16000617.0196-2021

Free article

Abstract

Patients suffering from chronic obstructive pulmonary disease (COPD) clinically manifest airway mucus hypersecretion as sputum expectoration and cough. Evidence accumulated in the past decade has shown that the cholinergic system not only regulates airway smooth muscle contraction but also the activity of inflammatory and airway epithelial cells, including goblet cells, and submucosal gland activity. Long-acting muscarinic antagonists (LAMAs) with the most favourable M_3/M_2 muscarinic acetylcholine (ACh) receptors residency properties are not only excellent bronchodilators but potentially also mucus-modifying agents, able to positively impact on mucus hypersecretion and cough. The aim of this systematic review was to investigate the impact of LAMAs on mucus hypersecretion and cough in COPD patients. The evidence confirmed that LAMAs, mainly tiotropium and

aclidinium, improved sputum production and cough in moderate to severe COPD. Thus, LAMAs not only antagonise the ACh-induced bronchoconstriction of the airways but also appear to limit the production of mucus secreted in response to ACh by airway goblet cells and/or submucosal glands. Further clinical studies are necessary to evaluate the impact of LAMAs exclusively on sputum symptoms and cough as primary end-points and to investigate whether LAMAs have a modulatory action on the rheological properties of mucus.

Conflict of interest statement

Conflict of interest: L. Calzetta reports grants and personal fees from Boehringer Ingelheim, grants and personal fees from Novartis, non-financial support from AstraZeneca, grants from Chiesi Farmaceutici, grants from Almirall, personal fees from ABC Farmaceutici, personal fees from Edmond Pharma, grants and personal fees from Zambon, personal fees from Verona Pharma, and personal fees from Ockham Biotech. Conflict of interest: B.L. Ritondo declares no conflict of interest. Conflict of interest: M.C. Zappa declares no conflict of interest. Conflict of interest: G.M. Manzetti. declares no conflict of interest. Conflict of interest: A. Perduno declares no conflict of interest. Conflict of interest: J. Shute is the Scientific Director of Ockham Biotech Ltd. Conflict of interest: P. Rogliani reports grants and personal fees from Boehringer Ingelheim, grants and personal fees from Novartis, personal fees from AstraZeneca, grants and personal fees from Chiesi Farmaceutici, grants and personal fees from Almirall, grants from Zambon, personal fees from Biofutura, personal fees from GlaxoSmithKline, personal fees from Menarini, and personal fees from Mundipharma.

. 2022 Jul 1;206(1):44-55.

doi: 10.1164/rccm.202106-1439OC.

Ambient Air Pollution and Dysanapsis: Associations with Lung Function and Chronic Obstructive Pulmonary Disease in the Canadian Cohort Obstructive Lung Disease Study

Jean Bourbeau[1,2], Dany Doiron[1], Sharmistha Biswas[1], Benjamin M Smith[2,3], Andrea Benedetti[1,2], Jeffrey R Brook[4,5], Shawn D Aaron[6], Kenneth R Chapman[7], Paul Hernandez[8], François Maltais[9], Darcy D Marciniuk[10], Denis O'Donnell[11], Don D Sin[12], Brandie Walker[13], Liesel Dsilva[14], Gilbert Nadeau[14], Valérie Coats[15], Chris Compton[16], Bruce E Miller[17], Wan C Tan[12], CanCOLD Collaborative Research Group and the Canadian Respiratory Research Network

Collaborators, Affiliations expand

- PMID: 35380941

- DOI: 10.1164/rccm.202106-1439OC

Abstract

Rationale: Outdoor air pollution is a potential risk factor for lower lung function and chronic obstructive pulmonary disease (COPD). Little is known about how airway abnormalities and lung growth might modify this relationship. **Objectives:** To evaluate the associations of ambient air pollution exposure with lung function and COPD and examine possible interactions with dysanapsis. **Methods:** We made use of cross-sectional postbronchodilator spirometry data from 1,452 individuals enrolled in the CanCOLD (Canadian Cohort Obstructive Lung Disease) study with linked ambient fine particulate matter ($PM_{2.5}$) and nitrogen dioxide (NO_2) air pollution estimates. Dysanapsis, or the ratio of the airway-to-lung volume calculated from thoracic computed tomography images, was used to examine possible interactions. **Measurements and Main Results:** In adjusted models, 101.7 ml (95% confidence interval [CI], -166.2 to -37.2) and 115.0 ml (95% CI, -196.5 to -33.4) lower FEV_1 were demonstrated per increase of 2.4 ug/m^3 $PM_{2.5}$ and 9.2 ppb NO_2, respectively. Interaction between air pollution and dysanapsis was not statistically significant when modeling the airway-to-lung ratio as a continuous variable. However, a

109.8 ml (95% CI, -209.0 to -10.5] lower FEV_1 and an 87% (95% CI, 12% to 213%) higher odds of COPD were observed among individuals in the lowest, relative to highest, airway-to-lung ratio, per 2.4 μg/m^3 increment of $PM_{2.5}$. **Conclusions:** Ambient air pollution exposure was associated with lower lung function, even at relatively low concentrations. Individuals with dysanaptic lung growth might be particularly susceptible to inhaled ambient air pollutants, especially those at the extremes of dysanapsis.

Keywords: air quality; chronic airflow obstruction; chronic obstructive pulmonary disease; computed tomography; pulmonary function test.

Comment in

- Small Airway Anatomy: An Indicator of Pollution Susceptibility in Adults?
  Chen K, Rice MB.Am J Respir Crit Care Med. 2022 Jul 1;206(1):2-4. doi: 10.1164/rccm.202203-0592ED.PMID: 35504004 No abstract available.

Am J Respir Crit Care Med

. 2022 Jul 1;206(1):25-33.

doi: 10.1164/rccm.202111-2630OC.

International Differences in the Frequency of Chronic Obstructive

Pulmonary Disease Exacerbations Reported in Three Clinical Trials

Peter M A Calverley[1], Fernando J Martinez[2], Jørgen Vestbo[3,4], Christine R Jenkins[5,6], Robert Wise[7], David A Lipson[8,9], Nicholas J Cowans[10], Julie Yates[11], Courtney Crim[11], Bartolome R Celli[12]

Affiliations expand

- PMID: 35363593

- DOI: 10.1164/rccm.202111-2630OC

Abstract

Rationale: Exacerbations of chronic obstructive pulmonary disease (COPD) are an important endpoint in multinational clinical treatment trials, but the observed event rate is often lower than anticipated and appears to vary between countries. **Objectives:** We investigated whether systematic differences in national exacerbation rates might explain this observed variation. **Methods:** We reviewed data from three large multicenter international randomized trials conducted over an 18-year period with different designs and clinical severities of COPD, comparing bronchodilator and/or inhaled corticosteroids with bronchodilators alone and/or placebo. Exacerbations were defined by antibiotic and/or oral corticosteroid use (moderate) or need for hospitalization (severe). We calculated crude exacerbation rates in the 30 countries contributing 30 or more patients to at least two trials. We grouped data by exacerbation rate based on their first study contribution. **Measurements and Main Results:** For the 29,756 patients in 41 countries analyzed, the mean exacerbation rate was two- to threefold different between the highest and lowest tertiles of the recruiting nations. These differences were not explained by demographic features, study protocol, or reported exacerbation history at enrollment. Of the 18 countries contributing to all trials, half of those in the highest and half in the lowest tertiles of exacerbation history remained in these groups across trials. Severe exacerbations showed a different rank order internationally. **Conclusions:** Countries contributing to COPD trials differ consistently in their reporting of healthcare-defined exacerbations. These differences help explain why large studies have been needed to show differences between treatments that decrease exacerbation risk.

Keywords: bronchodilators; chronic obstructive pulmonary disease; exacerbations; inhaled corticosteroids.

SUPPLEMENTARY INFO

Grant supportexpand

Editorial

Radiology

. 2022 Jul;304(1):193-194.

doi: 10.1148/radiol.220449. Epub 2022 Mar 15.

What Are the Long-term Pulmonary Sequelae of COVID-19 Infection?

Brett M Elicker[1]

Affiliations expand

- PMID: 35289668

- DOI: 10.1148/radiol.220449

No abstract available

Comment on

- Quantitative Chest CT Assessment of Small Airways Disease in Post-Acute SARS-CoV-2 Infection.
  Cho JL, Villacreses R, Nagpal P, Guo J, Pezzulo AA, Thurman AL, Hamzeh NY, Blount RJ, Fortis S, Hoffman EA, Zabner J, Comellas AP.Radiology. 2022 Jul;304(1):185-192. doi: 10.1148/radiol.212170. Epub 2022 Mar 15.PMID: 35289657

- Cited by 1 article

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Radiology FULL TEXT

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20

Infect Dis (Lond)

. 2022 Jul;54(7):508-513.

doi: 10.1080/23744235.2022.2050422. Epub 2022 Mar 14.

Mortality of COVID-19 is associated with comorbidity in patients with chronic obstructive pulmonary disease

Niklas Andreen[1,2], Lars-Magnus Andersson[1,2], Nicklas Sundell[1,2], Lars Gustavsson[1,2], Johan Westin[1,2]

Affiliations expand

- PMID: 35287524

- DOI: 10.1080/23744235.2022.2050422

Abstract

Background: The aim of this study was to compare the outcome of coronavirus disease 2019 (COVID-19) in hospitalised patients with chronic obstructive pulmonary disease (COPD) with the outcome in matched COVID-19 patients without COPD.

Methods: Sixty-three COPD patients hospitalised for acute COVID-19 from March through August 2020 were retrospectively identified and 63 hospitalised COVID-19 patients without COPD were selected and matched for age, gender and month of hospital admission.

Results: COPD patients had a higher rate of comorbidities, especially cardiovascular disease, and a trend towards a higher 30-day mortality than control patients (35% vs. 22%). In the COPD group, high Charlson comorbidity index (p = 0.03) and previous cerebrovascular disease (p = 0.04) were associated with 30-day mortality in univariate analysis. Inhaled corticosteroids maintenance therapy was not associated with lower mortality.

Conclusion: COPD patients hospitalised for acute COVID-19 disease had significantly more comorbidities and a high risk of severe outcome and death within 30 days. Comorbidity, especially cardiovascular diseases, was associated with mortality among COPD patients.

Keywords: COPD; COVID-19; Coronavirus infection; disease severity; inhaled corticosteroids; mortality.

. Jul-Aug 2022;28(4):284-296.

doi: 10.1016/j.pulmoe.2021.12.008. Epub 2022 Feb 10.

Issue 1 – "Update on adverse respiratory effects of outdoor air pollution". Part 1): Outdoor air pollution and respiratory diseases: A general update and an Italian perspective

S De Matteis[1], F Forastiere[2], S Baldacci[3], S Maio[3], S Tagliaferro[3], S Fasola[4], G Cilluffo[4], S La Grutta[4], G Viegi[5]

Affiliations expand

- PMID: 35153178

- DOI: 10.1016/j.pulmoe.2021.12.008

Free article

Abstract

Objective: to summarize the main updated evidence about the health effects of air pollution and to focus on Italian epidemiological experiences on the respiratory effects.

Results: the recent literature indicates that there is strong evidence for causal relationships between $PM_{2.5}$ air pollution exposure and all-cause mortality as well as mortality from acute lower respiratory infections, ischaemic heart disease, stroke, chronic obstructive pulmonary disease, and lung cancer. A growing body of evidence also suggests causal relationships with type II diabetes and impacts on neonatal mortality from low birth weight and short gestation as well as neurologic effects in both children and adults. Italy, a Southern European country, faces a more threatening air pollution challenge because of the effects of both anthropogenic pollutants and natural dust (particulate matter, PM). The 2020 Report of the European Environment Agency highlighted the number of premature deaths in Italy attributable to main pollutants: 52,300 for $PM_{2.5}$, 10,400 for NO_2 and 3,000 for O_3 in 2018. In Italy, original time series and analytical epidemiological studies showed increased

cardio-respiratory hospital admissions and mortality and increased risk of respiratory diseases in people living in urban areas.

Conclusions: adverse health effects of air pollutants, even at low levels, have been confirmed by recent epidemiological studies. Further studies should focus on the potential link between air pollution exposure and respiratory infections. This topic has become particularly important in the current SARS-COV-2 pandemic. Based on strong scientific evidence, the Italian government, which hosts the Global Alliance against Chronic Respiratory Diseases (GARD)-Italy at the Ministry of Health, the scientific respiratory societies and the patients' associations, as well as others in the health sector and civil society, must increase their engagement in advocacy for clean air policies, especially in light of the new Air Quality Guidelines of the World Health Organization.

Keywords: Air pollution; Air quality guidelines; Chronic respiratory diseases; Epidemiology; Italy; Meta-analysis.

Conflict of interest statement

Conflicts of interest None.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

Proceed to details

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22

Ann Am Thorac Soc

. 2022 Jul;19(7):1102-1111.

doi: 10.1513/AnnalsATS.202104-463OC.

Control of Cardiovascular Risk Factors in Patients with Chronic Obstructive Pulmonary Disease

Nathaniel M Hawkins[1], Sandra Peterson[2], Allison M Ezzat[3], Rohit Vijh[4], Sean A Virani[1], Andrew Gibb[2], G B John Mancini[1], Sabrina T Wong[2,5]

Affiliations expand

- PMID: 35007497

- DOI: 10.1513/AnnalsATS.202104-463OC

Abstract

Rationale: Cardiovascular disease accounts for one-third of deaths in patients with chronic obstructive pulmonary disease (COPD). Better control of cardiovascular risk factors in primary care could improve outcomes. **Objectives:** To define the prevalence, monitoring, treatment, and control of risk factors in patients with COPD. **Methods:** Repeated cross-sectional analysis of primary care electronic medical records for all patients with COPD in the Canadian Primary Care Sentinel Surveillance Network from 2013 to 2018 (n = 32,695 in 2018). A control group was matched 1:1 for age, sex, and rural residence (n = 32,638 in 2018). Five risk factors were defined using validated definitions including laboratory results: hypertension, dyslipidemia, diabetes, obesity, and smoking. **Results:** All risk factors were more common in patients with COPD compared with matched control subjects, including hypertension (52.3% vs. 44.9%), dyslipidemia (62.0% vs. 57.8%), diabetes (25.0% vs. 20.2%), obesity (40.8% vs. 36.8%), and smoking (40.9% vs. 11.4%), respectively. The mean Framingham risk score was 20.6% versus 18.6%, with 53.8% of patients with COPD being high risk (⩾20%). Monitoring of risk factors within the last year in patients with COPD in 2018 was suboptimal: 71.8% hypertension, 39.4% dyslipidemia, 74.5% diabetes, 52.3% obesity. Smoking status was infrequently recorded in the electronic record. In those monitored, guideline recommended targets were achieved in 60.8%, 46.6%, 57.4%, 10.6% and 12.0% for each risk factor. Cardiovascular therapies including angiotensin-converting enzyme inhibitors (69%), statins (69%), and smoking cessation therapies (27%) were underused. **Conclusions:** In patients with COPD, major cardiovascular risk factors are common, yet inadequately monitored, undertreated, and poorly controlled. Strategies are needed to improve comprehensive risk factor management proven to reduce cardiovascular morbidity and mortality.

Keywords: COPD; cardiovascular disease; cardiovascular risk factors.

Comment in

- Mind the Gap: Addressing Cardiovascular Disease in Chronic Obstructive Pulmonary Disease.
  Wells JM, Payne GA.Ann Am Thorac Soc. 2022 Jul;19(7):1093-1095. doi: 10.1513/AnnalsATS.202204-317ED.PMID: 35772101 No abstract available.

SUPPLEMENTARY INFO

Grant supportexpand

FULL TEXT LINKS

Proceed to details

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23

Thorax

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. 2022 Jul;77(7):641-642.

doi: 10.1136/thoraxjnl-2021-218296. Epub 2022 Jan 7.

Does impaired respiratory function lead to sudden cardiac death?

Rebecca F D'Cruz[1][2][3], Georgios Kaltsakas[4][2][3]

Affiliations expand

- PMID: 34996850

- DOI: 10.1136/thoraxjnl-2021-218296

No abstract available

Keywords: COPD; Lung function; Sudden cardiac death; asthma; clinical epidemiology; respiratory physiology.

Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

Ann Am Thorac Soc

. 2022 Jul;19(7):1213-1220.

doi: 10.1513/AnnalsATS.202108-930OC.

A Systematic Review of Published Algorithms for Selecting an Inhaled Delivery System in Chronic Obstructive Pulmonary Disease

David M G Halpin[1], Donald A Mahler[2,3]

Affiliations expand

- PMID: 34856108

- DOI: 10.1513/AnnalsATS.202108-930OC

Abstract

Rationale: Medication for treatment of chronic obstructive pulmonary disease (COPD) is available in many different delivery systems; however, national and international guidelines do not provide recommendations on how to select the optimal system for an individual patient. **Objectives:** To perform a systematic review of published algorithms for inhaler selection in outpatients with COPD. **Methods:** PubMed, EMBASE, PsycINFO, Cochrane, and Google Scholar were searched for articles on inhaler selection published between January 1, 1990, and March 10, 2021. The results were reviewed for articles containing an algorithm for inhaler selection. The quality of publications containing an algorithm was assessed using the Joanna Briggs Institute's System for the Unified Management, Assessment and Review of Information text and opinion critical appraisal checklist. Individual steps recommended in the algorithms and the order in which they were considered were extracted independently by the two authors using the Joanna Briggs Institute's text and opinion data extraction tool. Textual syntheses and a table of factors included were used to appraise and compare algorithms. **Results:** The search identified 1,016 publications. After removing duplicate studies (n = 409), 607 abstracts were examined. Nine different algorithms or hierarchical recommendations for device selection were identified. All nine publications were considered of good quality. Most algorithms contain only a few decision steps. There were significant differences between the algorithms. None of the algorithms have been validated. Three domains for factors included in the algorithms were identified: patient factors, device attributes, and healthcare professional (HCP) factors. Patient factors were considered most frequently (19 times) compared with device attributes (10 times) and HCP factors (7 times). Five specific attributes/factors with at least three rankings in different algorithms were identified as key factors for device selection: ability to perform the required inspiratory maneuver and handle device correctly, sufficient inspiratory flow for dry powder inhalers, availability of molecule(s) in the device, and continuity of device. **Conclusions:** Although the algorithms generally provide step-by-step approaches based on a literature review and/or the experiences of the different authors, none were developed using item generation/reduction methodology or included input from patients with COPD. However, the review identified key factors that should be considered by HCPs when selecting therapy. **Registration:** PROSPERO (CRD42021244475).

Keywords: COPD; device selection; inhaler.

Randomized Controlled Trial

Thorax

. 2022 Jul;77(7):643-651.

doi: 10.1136/thoraxjnl-2021-216934. Epub 2021 Oct 14.

Telerehabilitation for chronic respiratory disease: a randomised controlled equivalence trial

Narelle S Cox[1,2], Christine F McDonald[2,3,4], Ajay Mahal[5], Jennifer A Alison[6,7], Richard Wootton[8], Catherine J Hill[9], Paolo Zanaboni[8,10], Paul O'Halloran[11], Janet Bondarenko[12], Heather Macdonald[13], Kathryn Barker[14], Hayley Crute[13], Christie Mellerick[15], Bruna Wageck[15], Helen Boursinos[15], Aroub Lahham[15], Amanda Nichols[15], Pawel Czupryn[16], Monique Corbett[15], Emma Handley[15], Angela T Burge[15,2,12], Anne E Holland[15,2,12]

Affiliations expand

- PMID: 34650004

- DOI: 10.1136/thoraxjnl-2021-216934

Abstract

Rationale: Pulmonary rehabilitation is an effective treatment for people with chronic respiratory disease but is delivered to <5% of eligible individuals. This study investigated whether home-based telerehabilitation was equivalent to centre-based pulmonary rehabilitation in people with chronic respiratory disease.

Methods: A multicentre randomised controlled trial with assessor blinding, powered for equivalence was undertaken. Individuals with a chronic respiratory disease referred to pulmonary rehabilitation at four participating sites (one rural) were eligible and

randomised using concealed allocation to pulmonary rehabilitation or telerehabilitation. Both programmes were two times per week for 8 weeks. The primary outcome was change in Chronic Respiratory Disease Questionnaire Dyspnoea (CRQ-D) domain at end-rehabilitation, with a prespecified equivalence margin of 2.5 points. Follow-up was at 12 months. Secondary outcomes included exercise capacity, health-related quality of life, symptoms, self-efficacy and psychological well-being.

Results: 142 participants were randomised to pulmonary rehabilitation or telerehabilitation with 96% and 97% included in the intention-to-treat analysis, respectively. There were no significant differences between groups for any outcome at either time point. Both groups achieved meaningful improvement in dyspnoea and exercise capacity at end-rehabilitation. However, we were unable to confirm equivalence of telerehabilitation for the primary outcome ΔCRQ-D at end-rehabilitation (mean difference (MD) (95% CI) -1 point (-3 to 1)), and inferiority of telerehabilitation could not be excluded at either time point (12-month follow-up: MD -1 point (95% CI -4 to 1)). At end-rehabilitation, telerehabilitation demonstrated equivalence for 6-minute walk distance (MD -6 m, 95% CI -26 to 15) with possibly superiority of telerehabilitation at 12 months (MD 14 m, 95% CI -10 to 38).

Conclusion: telerehabilitation may not be equivalent to centre-based pulmonary rehabilitation for all outcomes, but is safe and achieves clinically meaningful benefits. When centre-based pulmonary rehabilitation is not available, telerehabilitation may provide an alternative programme model.

Trial registration number: ACtelerehabilitationN126160003604l5.

Keywords: exercise; pulmonary rehabilitation.

Conflict of interest statement

Competing interests: AEH, CFM, JAA, AM and RW, as the chief investigators, report grant funding from the National Health and Medical Research Council (NHMRC) (GNT1101616) for the conduct of this trial. NSC reports fellowship funding from the NHMRC (GNT1119970) to work on this trial. CFM reports fees paid to the institution from Menarini and AstraZeneca, and in-kind trial support from Air Liquide Healthcare—all unrelated to the present work.

Comment in

- Critically appraised paper: In people with chronic respiratory disease, telerehabilitation was equivalent to centre-based pulmonary rehabilitation at improving exercise capacity but may not be for dyspnoea.

Cavalheri V.J Physiother. 2022 Apr;68(2):143. doi: 10.1016/j.jphys.2022.02.005. Epub 2022 Apr 2.PMID: 35382996 No abstract available.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Thorax

. 2022 Jul;77(7):652-662.

doi: 10.1136/thoraxjnl-2020-215632. Epub 2021 Aug 20.

Airflow obstruction, impaired lung function and risk of sudden cardiac death: a prospective cohort study

Yun-Jiu Cheng[#1,2], Zhen-Guang Chen[#3], Feng-Juan Yao[#4], Li-Juan Liu[1,2], Ming Zhang[5], Su-Hua Wu[6,2]

Affiliations expand

- PMID: 34417352

- DOI: 10.1136/thoraxjnl-2020-215632

Abstract

Background: Growing evidence suggests that compromised lung health may be linked to cardiovascular disease. However, little is known about its association with sudden cardiac death (SCD).

Objectives: We aimed to assess the link between impaired lung function, airflow obstruction and risk of SCD by race and gender in four US communities.

Methods: A total of 14 708 Atherosclerosis Risk in Communities (ARIC) study participants who underwent spirometry and were asked about lung health (1987-1989) were followed. The main outcome was physician-adjudicated SCD. Fine-Gray proportional subdistribution hazard models with Firth's penalised partial likelihood correction were used to estimate the HRs.

Results: Over a median follow-up of 25.4 years, 706 (4.8%) subjects experienced SCD. The incidence of SCD was inversely associated with FEV_1 in each of the four race and gender groups and across all smoking status categories. After adjusting for multiple measured confounders, HRs of SCD comparing the lowest with the highest quintile of FEV_1 were 2.62 (95% CI 1.62 to 4.26) for white males, 1.80 (95% CI 1.03 to 3.15) for white females, 2.07 (95% CI 1.05 to 4.11) for black males and 2.62 (95% CI 1.21 to 5.65) for black females. The above associations were consistently observed among the never smokers. Moderate to very severe airflow obstruction was associated with increased risk of SCD. Addition of FEV_1 significantly improved the predictive power for SCD.

Conclusions: Impaired lung function and airflow obstruction were associated with increased risk of SCD in general population. Additional research to elucidate the underlying mechanisms is warranted.

Keywords: COPD epidemiology; critical care; emphysema; respiratory measurement.

Conflict of interest statement

Competing interests: None declared.

- Cited by 1 article

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

Clinical Trial

J Asthma

. 2022 Jul;59(7):1420-1432.

doi: 10.1080/02770903.2021.1938603. Epub 2021 Aug 1.

A randomized controlled trial of glycopyrrolate administered by metered dose inhaler in patients with uncontrolled asthma despite ICS/LABA treatment

Edward Kerwin[1], Paul Dorinsky[2], Mehul Patel[3], Kimberly Rossman[4], Colin Reisner[4], Andrea Maes[5], Patrick Darken[6], Dianne Griffis[2], Harald Fjällbrant[7]

Affiliations expand

- PMID: 34338132

- DOI: 10.1080/02770903.2021.1938603

Abstract

Objective: To evaluate the efficacy and safety of three doses of glycopyrrolate metered dose inhaler (GP MDI) in patients with uncontrolled asthma despite treatment with inhaled

corticosteroid/long-acting β_2-agonists (ICS/LABA) with or without tiotropium, to characterize the benefit of triple therapy.

Method: This phase II/III, double-blind study randomized patients to 24 weeks' treatment with twice-daily GP MDI 36 µg, 18 µg, 9 µg, or placebo MDI (all delivered *via* Aerosphere inhalers), or once-daily open-label tiotropium 2.5 µg. Patients continued their own ICS/LABA regimen throughout the study. The primary endpoint was change from baseline in forced expiratory volume in 1 s (FEV_1) area under the curve from 0 - 4 h (AUC_{0-4}) at Week 24. Secondary endpoints included patient questionnaires to measure asthma control or symptoms. Safety was also assessed.

Results: The primary analysis (modified intent-to-treat) population included 1066 patients. The primary study endpoint was not met (changes from baseline in FEV_1 AUC_{0-4} at Week 24 were 294 mL, 284 mL, 308 mL, 240 mL, and 347 mL for GP MDI 36 µg, GP MDI 18 µg, GP MDI 9 µg, placebo, and open-label tiotropium, respectively). There were no significant differences between treatment and placebo in secondary endpoints at Week 24. *Post-hoc* analyses using post-bronchodilator FEV_1 as the baseline measurement, or averaging values across multiple baseline visits, showed a dose-related response to GP MDI. The incidence of adverse events was low and similar across treatments.

Conclusion: Although this study did not meet its primary endpoint, *post hoc* analyses identified a dose-related response to GP MDI when alternative definitions of baseline FEV_1 were used in the analyses.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

ASTHMA

Allergy

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. 2022 Jul 1.

doi: 10.1111/all.15425. Online ahead of print.

Relationship between inflammatory status and microbial composition in severe asthma and during exacerbation

S Diver[1], K Haldar[1], P J McDowell[2], J Busby[2], V Mistry[1], C Micieli[1], V Brown[2], C Cox[3], F Yang[4], C Borg[5], R Shrimanker[5], M Yavari Ramsheh[1], T C Hardman[6], J R Arron[7], P Bradding[1], D Cowan[8], A H Mansur[9], S J Fowler[10], J Lordan[11], A Menzies-Gow[12], D S Robinson[13], J G Matthews[1], I D Pavord[5], R Chaudhuri[4], L G Heaney[2], M R Barer[1], C E Brightling[1], Medical Research Council: Refractory Asthma Stratification Programme (RASP-UK Consortium)

Affiliations expand

- PMID: 35778780

- DOI: 10.1111/all.15425

Abstract

Background: In T2-mediated severe asthma, biologic therapies such as mepolizumab, are increasingly used to control disease. Current biomarkers can indicate adequate suppression of T2 inflammation, but it is unclear whether they provide information about airway microbial composition. We investigated the relationships between current T2 biomarkers and microbial profiles, characteristics associated with a Proteobacteria^{HIGH} microbial profile and the effects of mepolizumab on airway ecology.

Methods: Microbiota sequencing was performed on sputum samples obtained at stable and exacerbation state from 140 subjects with severe asthma participating in two clinical trials. Inflammatory subgroups were compared on the basis of biomarkers including FeNO and sputum and blood eosinophils. Proteobacteria^{HIGH} subjects were identified by Proteobacteria to Firmicutes ratio ≥0.485. Where paired sputum from stable visits was available we compared microbial composition at baseline and following ≥12 weeks of mepolizumab.

Results: Microbial composition was not related to inflammatory subgroup based on sputum or blood eosinophils. FeNO ≥50 ppb when stable and at exacerbation indicated a group with less dispersed microbial profiles characterised by high alpha-diversity and low Proteobacteria. Proteobacteria^{HIGH} subjects were neutrophilic and had a longer time from asthma diagnosis than Proteobacteria^{LOW} subjects. In those studied, mepolizumab did not alter airway bacterial load or lead to increased Proteobacteria.

Conclusion: High FeNO could indicate a subgroup of severe asthma less likely to benefit from antimicrobial strategies at exacerbation or in the context of poor control. Where FeNO is <50 ppb, biomarkers of microbial composition are required to identify those likely to respond to microbiome-directed strategies. We found no evidence that mepolizumab alters airway microbial composition.

Keywords: asthma; biologics; biomarkers; infection.

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BMC Pulm Med

. 2022 Jul 1;22(1):261.

doi: 10.1186/s12890-022-02038-3.

Associations between comorbidities and annual incidence plus frequency of asthma exacerbation hospitalisation during the past year: data from CARN study

Wenqiao Wang[1], Jiangtao Lin[2], Xin Zhou[3], Changzheng Wang[4], Mao Huang[5], Shaoxi Cai[6], Ping Chen[7], Qichang Lin[8], Jianying Zhou[9], Yuhai Gu[10], Yadong Yuan[11], Dejun Sun[12], Xiaohong Yang[13], Lan Yang[14], Jianmin Huo[15], Zhuochang Chen[16], Ping Jiang[17], Jie Zhang[18], Xianwei Ye[19], Huiguo Liu[20], Huaping Tang[21], Rongyu Liu[22], Chuntao Liu[23], Wei Zhang[24], Chengping Hu[25], Yiqiang Chen[26], Xiaoju Liu[27], Luming Dai[28], Wei Zhou[29], Yijiang Huang[30], Jianying Xu[31]

Affiliations expand

- PMID: 35778740

- DOI: 10.1186/s12890-022-02038-3

Abstract

Purpose: While asthma comorbidities are associated with higher health care utilisation, lower quality of life and poorer asthma control, the impact of asthma comorbidities on hospitalisation for asthma exacerbation (H-AX) remains less recognised. We aim to analyse the impact of asthma comorbidities on H-AX.

Methods: Based on a national survey on asthma control and disease perception (CARN 2015 study), we analysed the impact of comorbidities on annual incidence and frequency of H-AX in China. Information on demographic characteristics, asthma comorbidities and annual incidence and frequency of H-AX were presented in this study.

Results: Among 3875 ambulatory asthma patients, 75.9% (2941/3875) had comorbidities, and 26.4% (1017/3858) experienced H-AX during past year. After adjusting for confounding factors such as demographic data, smoking status and asthma control, COPD [OR = 2.189, 95% CI (1.673, 2.863)] and coronary heart disease [OR = 1.387, 95% CI (1.032, 1.864)] were associated with higher annual incidence, while allergic rhinitis [OR = 0.692, 95% CI (0.588, 0.815)] was associated with lower annual incidence, of H-AX. In terms of frequency, allergic rhinitis [OR = 1.630, 95% CI (1.214, 2.187)], COPD [OR = 1.472, 95% CI (1.021, 2.122)] and anxiety [OR = 2.609, 95% CI (1.051, 6.477)] showed statistically significant correlation with frequent H-AX.

Conclusions: COPD and coronary heart disease were associated with higher annual incidence, while allergic rhinitis was associated with lower annual incidence of H-AX. Allergic rhinitis, COPD and anxiety were associated with frequent H-AX. Comorbidities may have an important role in the risk and frequency of annual hospitalisations due to asthma exacerbation. The goal of asthma control should rely on a multi-disciplinary treatment protocol.

Keywords: Asthma; Comorbidity; Exacerbation; Hospitalisation; Multi-centre cross-sectional study.

- 43 references

SUPPLEMENTARY INFO

Grant supportexpand

Proceed to details

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3

Eur Respir J

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-
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. 2022 Jul 1;2200660.

doi: 10.1183/13993003.00660-2022. Online ahead of print.

Benefits of specialist severe asthma management: demographic and geographic disparities

Charlene Redmond[1], Liam G Heaney[2,3], Rekha Chaudhuri[4], David J Jackson[5,6], Andrew Menzies-Gow[7], Paul Pfeffer[8], John Busby[2], UK Severe Asthma Registry

Affiliations expand

- PMID: 35777771

- DOI: 10.1183/13993003.00660-2022

Abstract

Introduction: The benefits of specialist assessment and management have yet to be evaluated within the biologic era of UK severe asthma treatment, and potential disparities have not been considered.

Methods: In an uncontrolled before-and-after study, we compared asthma symptoms (asthma control questionnaire [ACQ6]), exacerbations, unscheduled secondary care use, lung function (FEV_1) and oral corticosteroid (OCS) dose after one year. We compared outcomes by sex, age (18-34, 35-49, 50-64, 65+ years), ethnicity (Caucasian *versus* Non- Caucasian) and hospital site after adjusting for demographics and variation in biologic therapy use.

Results: 1,140 patients were followed-up for 1,370 person-years from twelve specialist centres. At annual review, ACQ6 score was reduced by a median of 0.7 (IQR:0.0, 1.5), exacerbations by 75% (IQR: 33%, 100%) and unscheduled secondary care by 100% (IQR:67%, 100%). FEV_1 increased by a median of 20 mL (IQR:-200, 340) while OCS dose decreased for 67% of patients. Clinically meaningful improvements occurred across almost all patients, including those not receiving biologic therapy. There was little evidence of differences across demographic groups, although those aged over 65 demonstrated larger reductions in exacerbations (69% *versus* 52%; $p<0.001$) and unscheduled care use (77% *versus* 50%; $p<0.001$) compared to patients aged under 34 years. There were more than 2-fold differences between the best and worst performing centres across all study outcomes.

Conclusions: Specialist assessment and management is associated with substantially improved patient outcomes which are broadly consistent across demographic groups, and are not restricted to those receiving biologic therapy. Significant variation exists between hospitals which requires further investigation.

Eur Respir J

. 2022 Jul 1;2103205.

doi: 10.1183/13993003.03205-2021. Online ahead of print.

An observational study to determine the relationship between cough frequency and markers of inflammation in severe asthma

Joshua Holmes[1], Lorcan Pa McGarvey[1], Surinder S Birring[2], Hannah Fletcher[2], Liam G Heaney[3]

Affiliations expand

- PMID: 35777770

- DOI: 10.1183/13993003.03205-2021

Abstract

Rationale and objective: The relationship between objectively measured cough and type-2 biomarkers and other measures of asthma control and severity is poorly understood. The objective of this study was to assess the relationship between objective and subjective cough measurement tools and clinical biomarkers of asthma.

Methods: Patients with severe asthma and mild/moderate asthma completed validated asthma and cough-related measurement tools (including ambulatory cough monitoring) and measurement of spirometry and T2-biomarkers (fractional exhaled nitric oxide measurement (FeNO) and peripheral blood eosinophil count (PBE)). Patients were classified according to T2-status based on T2-low (FeNO<20ppb AND PBE<150 cells·µl^{-1}), T2-intermediate (FeNO≥20ppb OR PBE≥150 cells·µl^{-1}) or T2-high (FeNO≥20ppb AND PBE≥150 cells·µl^{-1}).

Results: In total, 61 patients completed the study measurements (42 severe asthma, 19 mild/moderate asthma). Patients with severe asthma had higher rates of cough than those with

mild/moderate asthma in terms of total 24-hour cough counts (geometric mean 170·3 (sd 2·7) *versus* 60·8 (sd 4·1), p=0·002) and cough frequency (geometric mean, 7·1 c·h^{-1} (sd 2·7) *versus* 2·5 c·h^{-1} (sd 4·1), p=0·002). T2-low patients with severe asthma had significantly lower 24-hour cough frequency compared to T2-intermediate and T2-high patients.

Conclusions: In patients with low biomarkers of T2 inflammation, cough frequency measurements were not elevated, suggesting that the mechanism for cough in asthma is underlying T2-eosinophilic inflammation and the logical first step for treating cough in asthma may be to achieve adequate suppression of T2 inflammation with currently available therapies.

Review

Nat Rev Dis Primers

. 2022 Jun 30;8(1):45.

doi: 10.1038/s41572-022-00370-w.

Cough hypersensitivity and chronic cough

Kian Fan Chung[1,2], Lorcan McGarvey[3], Woo-Jung Song[4], Anne B Chang[5,6], Kefang Lai[7], Brendan J Canning[8], Surinder S Birring[9], Jaclyn A Smith[10], Stuart B Mazzone[11]

Affiliations expand

- PMID: 35773287

- DOI: 10.1038/s41572-022-00370-w

Abstract

Chronic cough is globally prevalent across all age groups. This disorder is challenging to treat because many pulmonary and extrapulmonary conditions can present with chronic cough, and cough can also be present without any identifiable underlying cause or be refractory to therapies that improve associated conditions. Most patients with chronic cough have cough hypersensitivity, which is characterized by increased neural responsivity to a range of stimuli that affect the airways and lungs, and other tissues innervated by common nerve supplies. Cough hypersensitivity presents as excessive coughing often in response to relatively innocuous stimuli, causing significant psychophysical morbidity and affecting patients' quality of life. Understanding of the mechanisms that contribute to cough hypersensitivity and excessive coughing in different patient populations and across the lifespan is advancing and has contributed to the development of new therapies for chronic cough in adults. Owing to differences in the pathology, the organs involved and individual patient factors, treatment of chronic cough is progressing towards a personalized approach, and, in the future, novel ways to endotype patients with cough may prove valuable in management.

- 255 references

SUPPLEMENTARY INFO

Publication typesexpand

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BMJ Open

. 2022 Jun 30;12(6):e059122.

doi: 10.1136/bmjopen-2021-059122.

Impact of COPD and asthma on in-hospital mortality and management of patients with heart failure in England and Wales: an observational analysis

Claudia Gulea[1,2], Rosita Zakeri[3], Constantinos Kallis[4,2], Jennifer K Quint[4,2]

Affiliations expand

- PMID: 35772828

- DOI: 10.1136/bmjopen-2021-059122

Free article

Abstract

Objective: To evaluate the association between having concomitant chronic obstructive pulmonary disease (COPD) or asthma, and in-patient mortality and post-discharge management among patients hospitalised for acute heart failure (HF).

Setting: Data were obtained from patients enrolled in the National Heart Failure Audit.

Participants: 217 329 patients hospitalised for HF in England-Wales between March 2012 and 2018.

Outcomes: In-hospital mortality, referrals to cardiology follow-up and prescriptions for HF medications were compared between patients with comorbid COPD (COPD-HF) or asthma (asthma-HF) versus HF-alone using mixed-effects logistic regression.

Results: Patients with COPD-HF were more likely to die during hospitalisation, and those with asthma-HF had a reduced likelihood of death, compared with patients who had HF-alone ((adjusted)OR_{adj}, 95% CI: 1.10, 1.06 to 1.14 and OR_{adj}, 95% CI: 0.84, 0.79 to 0.88). In patients who survived to discharge, referral to HF follow-up services differed between groups: patients with COPD-HF had reduced odds of cardiology follow-up (OR_{adj}, 95% CI 0.79, 0.77 to 0.81), while cardiology referral odds for asthma-HF were similar to HF-alone. Overall, proportions of HF medication prescriptions at discharge were low for both COPD-HF and asthma-HF groups, particularly prescriptions for beta-blockers.

Conclusions: In this nationwide analysis, we showed that COPD and asthma significantly impact the clinical course in patients hospitalised for HF. COPD is associated with higher in-patient mortality and lower cardiology referral odds, while COPD and asthma are both associated with lower use of prognostic HF therapies on discharge. These data highlight therapeutic gaps and a need for better integration of cardiopulmonary services to improve healthcare provision for patients with HF and coexisting respiratory disease.

Keywords: epidemiology; heart failure; respiratory medicine (see Thoracic Medicine).

Conflict of interest statement

Competing interests: None declared.

J Allergy Clin Immunol

. 2022 Jun 27;S0091-6749(22)00846-6.

doi: 10.1016/j.jaci.2022.05.024. Online ahead of print.

Comparative efficacy of mepolizumab, benralizumab, and dupilumab in eosinophilic asthma: A Bayesian network meta-analysis

Ayobami Akenroye[1], Grace Lassiter[2], John W Jackson[3], Corinne Keet[4], Jodi Segal[5], G Caleb Alexander[5], Hwanhee Hong[6]

Affiliations expand

- PMID: 35772597

- DOI: 10.1016/j.jaci.2022.05.024

Abstract

Background: The comparative safety and efficacy of the biologics currently approved for asthma is unclear.

Objective: To compare the safety and efficacy of mepolizumab, benralizumab, and dupilumab in individuals with severe eosinophilic asthma.

Methods: Systematic review of peer-reviewed literature from 2000 through 2021, and Bayesian network meta-analyses of exacerbation rates, prebronchodilator FEV1, the Asthma Control Questionnaire (ACQ) and serious adverse events (SAE) in individuals with eosinophilic asthma.

Results: Eight randomized clinical trials (n=6,461) were identified. In individuals with ≥300 eosinophils per microliter (eosin/mcl), in reducing exacerbation rates in comparison to placebo: dupilumab (risk ratio [RR] 0.32; 95% credible interval [CI], 0.23-0.45), mepolizumab (RR, 0.37; 95%CI, 0.30-0.45), and benralizumab (RR, 0.49; 95%CI, 0.43-0.55). In improving FEV1: dupilumab (mean difference in milliliters [MD] 230; [CI], 160-300), benralizumab (MD 150; 95%CI, 100-200), and mepolizumab (MD 150; 95%CI, 66-220); and in reducing ACQ: mepolizumab (MD -0.63; [CI], -0.81 to -0.45), dupilumab (MD -0.48; 95%CI, -0.83 to -0.14), and benralizumab (MD -0.32; 95%CI, -0.43 to -0.21). In individuals with eosinophil counts of 150-299 eosin/mcl, benralizumab (RR, 0.62; 95%CI, 0.52-0.73) and dupilumab (RR, 0.60; 95%CI, 0.38-0.95) were associated with lower exacerbation rates; and only benralizumab (MD 81; 95% CI, 8-150) significantly improved FEV1. These differences were minimal in comparison to clinically important thresholds. For SAE in the overall population, mepolizumab (odds ratio, 0.67; 95% CI, 0.48-0.92) and benralizumab (0.74; 95% CI, 0.59-0.93) were associated with lower odds of a SAE, while dupilumab was not different from placebo (1.0; 95% CI, 0.74-1.4).

Conclusions: There are minimal differences in the efficacy and safety of mepolizumab, benralizumab, and dupilumab in eosinophilic asthma.

Clinical implication: In individuals with eosinophilic asthma, mepolizumab, benralizumab, and dupilumab are similar in their effect on exacerbations, FEV1, or ACQ.

Keywords: Bayesian; asthma; benralizumab; comparative effectiveness; dupilumab; eosinophilic; mepolizumab; monoclonal antibody; network meta-analysis.

Editorial

Respirology

. 2022 Jun 28.

doi: 10.1111/resp.14319. Online ahead of print.

Novel insights into the biological pathways involved in severe asthma

Javier Perez-Garcia[1], Maria Pino-Yanes[1,2,3]

Affiliations expand

- PMID: 35764405

- DOI: 10.1111/resp.14319

No abstract available

Keywords: airway markers; asthma; genetics; molecular biology.

- 10 references

SUPPLEMENTARY INFO

Publication types, Grant supportexpand

FULL TEXT LINKS

WILEY Full Text Article

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PLoS One

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. 2022 Jun 28;17(6):e0270412.

doi: 10.1371/journal.pone.0270412. eCollection 2022.

Impact of acute temperature and air pollution exposures on adult lung function: A panel study of asthmatics

Richard Evoy[1], Laurel Kincl[1], Diana Rohlman[1,2], Lisa M Bramer[3], Holly M Dixon[4], Perry Hystad[1], Harold Bae[1], Michael Barton[4], Aaron Phillips[5], Rachel L Miller[6], Katrina M Waters[2,3,5], Julie B Herbstman[7], Kim A Anderson[2,4]

Affiliations expand

- PMID: 35763502

- PMCID: PMC9239441

- DOI: 10.1371/journal.pone.0270412

Free PMC article

Abstract

Background: Individuals with respiratory conditions, such as asthma, are particularly susceptible to adverse health effects associated with higher levels of ambient air pollution and temperature. This study evaluates whether hourly levels of fine particulate matter (PM2.5) and dry bulb globe temperature (DBGT) are associated with the lung function of adult participants with asthma.

Methods and findings: Global positioning system (GPS) location, respiratory function (measured as forced expiratory volume at 1 second (FEV1)), and self-reports of asthma medication usage and symptoms were collected as part of the Exposure, Location, and Lung Function (ELF) study. Hourly ambient PM2.5 and DBGT exposures were estimated by integrating air quality and temperature public records with time-activity patterns using GPS coordinates for each participant (n = 35). The relationships between acute PM2.5, DBGT, rescue bronchodilator use, and lung function collected in one week periods and over two seasons (summer/winter) were analyzed by multivariate regression, using different exposure time frames. In separate models, increasing levels in PM2.5, but not DBGT, were associated with rescue bronchodilator use. Conversely DBGT, but not PM2.5, had a significant association with FEV1. When DBGT and PM2.5 exposures were placed in the same model, the strongest association between cumulative PM2.5 exposures and the use of rescue bronchodilator was identified at the 0-24 hours (OR = 1.030; 95% CI = 1.012-1.049; p-value = 0.001) and 0-48 hours (OR = 1.030; 95% CI = 1.013-1.057; p-value = 0.001) prior to lung function measure. Conversely, DBGT exposure at 0 hours (β = 3.257; SE = 0.879; p-value>0.001) and 0-6 hours (β = 2.885; SE = 0.903; p-value = 0.001) hours before a reading were associated with FEV1. No significant interactions between DBGT and PM2.5 were observed for rescue bronchodilator use or FEV1.

Conclusions: Short-term increases in PM2.5 were associated with increased rescue bronchodilator use, while DBGT was associated with higher lung function (i.e. FEV1). Further studies are needed to continue to elucidate the mechanisms of acute exposure to PM2.5 and DBGT on lung function in asthmatics.

Conflict of interest statement

I have read the journal's policy and the authors of this manuscript have the following competing interests: KAA and DR disclose a financial interest in MyExposome, Inc., which is marketing products related to the research being reported. The terms of this arrangement have been reviewed and approved by Oregon State University in accordance with its policy on research conflicts of interest. The authors have no other competing interests to disclose.

- 47 references

SUPPLEMENTARY INFO

MeSH terms, Substances, Grant supportexpand

FULL TEXT LINKS

Editorial

Ann Allergy Asthma Immunol

. 2022 Jul;129(1):1-2.

doi: 10.1016/j.anai.2022.04.006.

Vaccination: Just do it!

Mariana Castells[1], Matthew Greenhawt[2]

Affiliations expand

- PMID: 35717128

- PMCID: PMC9197789

- DOI: 10.1016/j.anai.2022.04.006

Free PMC article

No abstract available

- 6 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

ELSEVIER FULL-TEXT ARTICLE

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Review

Eur Respir Rev

. 2022 Jun 14;31(164):220039.

doi: 10.1183/16000617.0039-2022. Print 2022 Jun 30.

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

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

Affiliations expand

- PMID: 35705210

- DOI: 10.1183/16000617.0039-2022

Free article

Abstract

Background: Conflicting literature exists regarding the risk factors for exacerbations among pregnant women with asthma. This systematic review and meta-analysis aimed to determine risk factors for asthma exacerbations during pregnancy.

Methods: Electronic databases were searched for the following terms: (asthma or wheeze) and (pregnan* or perinat* or obstet*) and (exacerb* or flare up or morbidit* or attack*).All studies published between 2000 and 24 August 2021 were considered for inclusion if they reported at least one potential risk factor of asthma exacerbations in pregnant women with asthma. Of the 3337 references considered, 35 publications involving 429 583 pregnant women with asthma were included. Meta-analyses were conducted to determine mean difference in risk factor between exacerbation groups, or the relative risks of exacerbation with certain risk factors. Good study quality was found through the Newcastle-Ottawa Scale (median score 8, interquartile range 7-9).

Results: Increased maternal age (mean difference 0.62, 95% CI 0.11-1.13), obesity (relative risk 1.25, 95% CI 1.15-1.37), smoking (relative risk 1.35, 95% CI 1.04-1.75), black ethnicity (relative risk 1.62, 95% CI 1.52-1.73), multiparity (relative risk 1.31, 95% CI 1.01-1.68), depression/anxiety (relative risk 1.42, 95% CI 1.27-1.59), moderate-severe asthma (relative risk 3.44, 95% CI 2.03-5.83, *versus* mild) and severe asthma (relative risk 2.70, 95% CI 1.85-3.95, *versus* mild-moderate) were associated with an increased risk of asthma exacerbations during pregnancy.

Conclusions: Future interventions aimed at reducing exacerbations in pregnancy could address the modifiable factors, such as smoking and depression/anxiety, and introduce more regular monitoring for those with nonmodifiable risk factors such as obesity and more severe asthma.

Conflict of interest statement

Conflict of interest: M.P. Bokern reports support for the present manuscript from Groningen Research Institute of Pharmacy, PharmacoTherapy, Epidemiology and Economics, University of Groningen, Groningen, the Netherlands and Department of Non-Communicable Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK. M.P. Bokern reports grants or contracts from GlaxoSmithKline (GSK PhD scholarship at London School of Hygiene and Tropical Medicine), outside the submitted work. V.E. Murphy reports support for the present manuscript from Medical Research Future Fund Investigator Grant (paid to her institution). The remaining authors have nothing to disclose.

Review

Respir Med

. 2022 Jul;198:106880.

doi: 10.1016/j.rmed.2022.106880. Epub 2022 May 13.

A systematic review of blood eosinophils and continued treatment with inhaled corticosteroids in patients with COPD

Dagmar Abelone Dalin[1], Anders Løkke[2], Pernille Kristiansen[3], Charlotte Jensen[4], Kirsten Birkefoss[5], Hanne Rolighed Christensen[6], Nina Skavlan Godtfredsen[7], Ole Hilberg[2], Jeanett Friis Rohde[8], Anja Ussing[9], Charlotte Vermehren[10], Mina Nicole Händel[8]

Affiliations expand

- PMID: 35599064

- DOI: 10.1016/j.rmed.2022.106880

Free article

Abstract

Inhaled corticosteroid (ICS) in patients with chronic obstructive pulmonary disease (COPD) has been debated for 20 years. In our systematic literature review and meta-analysis, we addressed the following: Should patients with COPD and a blood eosinophil count (EOS) of, respectively, a) <

150 cells/µl, b) 150-300 cells/µl, and c) > 300 cells/µl continue treatment with ICS? Protocol registered in PROSPERO (CRD42020178110) and funded by the Danish Health Authority. We searched Medline, Embase, CINAHL and Cochrane Central on 22nd July 2020 for randomized controlled trials (RCT) of ICS treatment in patients with COPD (≥40 years, no current asthma), which analyzed outcomes by EOS count and where >50% of patients used ICS prior. We used the GRADE method. Meta-analyzes for the outcomes were divided into EOS subgroups and analyzed for differences. We identified 11 RCTs with a total of 29,654 patients. A significant difference ($p < 0.00001$) between the three subgroups' reduction of risk of moderate to severe exacerbation was found. Rate ratios for EOS counts: <150 cells/µL was 0.88 (95%CI: 0.83, 0.94); 150-300 cells/µL was 0.80 (95%CI: 0.69, 0.94); >300 cells/µL was 0.57 (95%CI: 0.49, 0.66). Overall, the certainty of the effect estimates was low to very low due to risk of bias, unexplained heterogeneity, few RCTs, and wide confidence intervals. A clear correlation was demonstrated between effect of continued ICS treatment (number of exacerbations, lung function, and quality of life) and increasing EOS count. Our meta-analyses suggested that treatment with ICS seemed beneficial for everyone except patients with EOS count below 150 cells/µl.

Keywords: Blood eosinophils; Chronic obstructive pulmonary disease; Eosinophil; Inhaled corticosteroid.

Pediatr Pulmonol

. 2022 Jul;57(7):1677-1683.

doi: 10.1002/ppul.25953. Epub 2022 Jun 2.

Asthma risk after a pediatric intensive care unit admission for respiratory syncytial virus bronchiolitis

Moria Be'er[1], Shai Bushmitz[1], Michal Cahal[1], Efraim Sadot[1,2], Sivan Yochpaz[3], Omri Besor[1], Israel Amirav[1], Moran Lavie[1]

Affiliations expand

- PMID: 35579122

- DOI: 10.1002/ppul.25953

Abstract

Background: Admission to a pediatric intensive care unit (PICU) has been associated with respiratory consequences in children with asthma and carries major implications for management control. Whereas respiratory syncytial virus (RSV) bronchiolitis has been associated with increasing intensity of wheezing, the relationship between RSV-bronchiolitis PICU admission and future asthma is unclear. This retrospective case-control study evaluated whether hospitalization in the PICU due to RSV bronchiolitis is more likely to be associated with future asthma in early life compared with hospitalization in a general pediatric ward.

Methods: Children hospitalized due to RSV bronchiolitis between 2007 and 2019 in the PICU (study group) were compared to those hospitalized in a general pediatric ward (controls). Asthma prevalence was assessed by a follow-up questionnaire based on The International Study of Asthma and Allergies in Childhood questionnaire.

Results: Sixty-three PICU patients and 66 controls were included. The PICU patients presented with more severe disease during RSV hospitalization. At follow-up, significantly more PICU patients aged 3-6 years had physician-diagnosed asthma, respiratory symptoms during the previous 12 months, and underwent respiratory treatment since hospital discharge compared to controls (14 [60.9%] vs. 4 [18.2%] patients; 15 [65.2%] vs. 6 [27.3%]; and 16 [69.6%] vs. 8 [36.4%]; respectively). These differences were no longer observed after 6 years of age.

Conclusions: Children admitted to the PICU for RSV bronchiolitis are at higher risk for asthma in subsequent pre-school years and will require close respiratory follow-up than those admitted to general pediatric wards. Admission venue should be queried when asthma is suspected.

Keywords: asthma; intensive care unit; respiratory syncytial virus.

- 17 references

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

Eur J Pediatr

. 2022 Jul;181(7):2705-2713.

doi: 10.1007/s00431-022-04478-9. Epub 2022 Apr 25.

Sex-differences in incidence of hospitalizations and in hospital mortality of community-acquired pneumonia among children in Spain: a population-based study

Javier de-Miguel-Díez[1], Ana López-de-Andrés[2], Valentín Hernández-Barrera[3], José M de-Miguel-Yanes[4], David Carabantes-Alarcón[5], Zichen Ji[1], Jose J Zamorano-Leon[5], Rodrigo Jiménez-García[5]

Affiliations expand

- PMID: 35469030

- PMCID: PMC9192385

- DOI: 10.1007/s00431-022-04478-9

Abstract

The aim of this study is to examine trends from 2016 to 2019 in the incidence of hospitalizations and in-hospital mortality (IHM) of subjects < 18 years with community-acquired pneumonia (CAP), assessing possible sex differences. We used Spanish national hospital discharge data to select all patients < 18 years with CAP. We identified 43,511 children (53% boys) hospitalized with CAP. The incidence of CAP was significantly higher in boys than in girls, with an age-adjusted incidence rate ratio of 1.05 (95%CI 1.03-1.07) for boys compared to girls, and rose from 126 per 100,000 children in 2016 to 131 in 2019 ($p < 0.0001$). There were no sex differences in isolated pathogens, comorbidities, length of hospital stay, or IHM. Variables independently associated with IHM were age 10 to 17 years, congenital heart disease, neurological diseases, and use of invasive mechanical ventilation. Asthma was a protective factor for IHM among girls.

Conclusion: The incidence of hospital admissions for CAP was higher among boys than among girls and rose significantly from 2016 to 2019. There were no sex differences in hospital outcomes. Age 10 to 17 years, congenital heart disease, neurological diseases, and use of mechanical ventilation were risk factors for IHM in both sexes, while asthma was a protective factor among girls. No differences were found in IHM over time.

What is known: • Community-acquired pneumonia is one of the most common reasons for hospitalizations among children. • There are few studies that allow to know the evolution of community-acquired pneumonia in children.

What is new: • Incidence of hospital admissions for community-acquired pneumonia was higher in boys than girls and it rose significantly from 2016 to 2019. • Age 10 to 17 years, congenital heart disease, neurological diseases and use of mechanical ventilation were risk factors for in-hospital mortality in both sexes.

Keywords: Children; Community-acquired pneumonia; Hospital admissions; In-hospital mortality; Incidence; Sex differences.

Conflict of interest statement

The authors declare no competing interests.

- 46 references
- 1 figure

Pediatr Pulmonol

. 2022 Jul;57(7):1782-1788.

doi: 10.1002/ppul.25939. Epub 2022 May 5.

DNA sequencing analysis of cystic fibrosis transmembrane conductance regulator gene identifies cystic fibrosis–associated variants in the Severe Asthma Research Program

Manuel E Izquierdo[1], Chad R Marion[2], Wendy C Moore[3], Karen S Raraigh[4], Jennifer L Taylor-Cousar[5], Gary R Cutting[6], E Ampleford[7], Gregory A Hawkins[8], Joe Zein[9], M Castro[10], Loren C Denlinger[11], Serpil C Erzurum[12], John V Fahy[13], Elliot Israel[14], Nizar N Jarjour[15], David Mauger[16], Bruce D Levy[14], Sally E Wenzel[17], Prescott Woodruff[18], Eugene R Bleecker[19], Deborah A Meyers[20], Victor E Ortega[21]

Affiliations expand

- PMID: 35451201

- DOI: 10.1002/ppul.25939

Abstract

Background: Heterozygote carriers of potentially pathogenic variants in the cystic fibrosis transmembrane conductance regulator (CFTR) gene have increased asthma risk. However, the frequency and impact of CFTR variation among individuals with asthma is unknown.

Objective: To determine whether potentially pathogenic CFTR variants associate with disease severity and whether individuals with two potentially pathogenic variants exist in a severe asthma-enriched cohort.

Methods: We analyzed sequencing data spanning a 190.5Kb region of CFTR in participants from the Severe Asthma Research Program (SARP1-3). Potentially pathogenic, rare CFTR variants (frequency < 0.05) were classified as CF-causing or of varying clinical consequences (VVCC) (CFTR2. org). Regression-based models tested for association between CFTR genotypes (0-2 potentially pathogenic variants) and severity outcomes.

Results: Of 1401 participants, 9.5% (134) had one potentially pathogenic variant, occurring more frequently in non-Hispanic white (NHW, 10.1% [84 of 831]) compared to African American individuals (AA, 5.2% [22 of 426]). We found ≥2 potentially pathogenic CFTR variants in 1.4% (19); 0.5% (4) of NHW and 2.8% (12) of AA. Potentially pathogenic CFTR variant genotypes (≥1 or ≥2 variants) were not cumulatively associated with lung function or exacerbations. In NHW, we found three F508del compound heterozygotes with F508del and a VVCC (two 5 T; TG12[c.1210-11 T > G] and one Arg1070Trp) and a homozygote for the VVCC, 5 T; TG12.

Conclusions: We found potentially pathogenic CFTR variants within a severe asthma-enriched cohort, including three compound heterozygote genotypes variably associated with CF in NHW individuals. These findings provide the rationale for CFTR sequencing and phenotyping of CF-related traits in individuals with severe asthma.

Keywords: Asthma; CF-Asthma Overlap; CFTR; cystic fibrosis; heterozygote carriers.

- 6 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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WILEY Full Text Article

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Allergy

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. 2022 Jul;77(7):2250-2253.

doi: 10.1111/all.15313. Epub 2022 May 5.

Asthma endotypes in elite athletes: A cross-sectional study of European athletes participating in the Olympic Games

Søren Malte Rasmussen[1], Erik Søren Halvard Hansen[1,2], Trine Stensrud[3], Katja Radon[4], Bernd Wolfarth[5], Marcin Kurowski[6], Jean Bousquet[7], Sergio Bonini[8], Matteo Bonini[9,10], Luis Delgado[11,12], André Moreira[13,14,15,16], Franchek Drobnic[17], Nikolaos G Papadopoulos[18], Sofia Vakali[18], Christina Gratziou[18], Leo Pekka Malmberg[19], Tari Haahtela[19], Vibeke Backer[1,20]

Affiliations expand

- PMID: 35426975

- DOI: 10.1111/all.15313

No abstract available

- 5 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

WILEY Full Text Article

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Ann Allergy Asthma Immunol

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-

. 2022 Jul;129(1):113-115.

doi: 10.1016/j.anai.2022.04.001. Epub 2022 Apr 6.

Effect of daily tiotropium on allergen–induced early asthmatic responses and airway inflammation

Kayla J Cropper[1], Beth E Davis[2], Donald W Cockcroft[3]

Affiliations expand

- PMID: 35395397

- DOI: 10.1016/j.anai.2022.04.001

No abstract available

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

FULL TEXT LINKS

Ann Am Thorac Soc

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doi: 10.1513/AnnalsATS.202105-539OC.

Air Quality Index and Emergency Department Visits and Hospitalizations for Childhood Asthma

Franziska Rosser[1], Yueh-Ying Han[1], Scott D Rothenberger[2], Erick Forno[1], Christina Mair[3], Juan C Celedón[1]

Affiliations expand

- PMID: 35394903

- DOI: 10.1513/AnnalsATS.202105-539OC

Abstract

Rationale: Outdoor air pollution causes emergency department visits and hospitalizations for childhood asthma. In the United States, the Air Quality Index (AQI) alerts the public to air quality and provides behavioral recommendations to reduce exposure and harm, yet little is known about the relationship between the AQI and childhood asthma exacerbations. **Objectives:** To test for association between the AQI and childhood asthma exacerbations resulting in emergency department visits and hospitalizations. **Methods:** This was a retrospective time-stratified case-crossover study, conducted using medical records data from 2010 through 2018 for children aged 6-17 years with a primary diagnosis of an asthma exacerbation (defined as an emergency department visit or hospitalization for asthma) at UPMC Children's Hospital of Pittsburgh. Daily AQI data was obtained for Allegheny County, Pennsylvania from the Environmental Protection Agency. Conditional logistic regression was used for analyses of the AQI (as both a continuous and categorical variable) and asthma exacerbations. Stratified analyses were conducted to explore modification of the AQI effects on asthma exacerbations by race and other covariates. **Results:** There were 6,573 events. Particulate matter <2.5 μm ($PM_{2.5}$) was the primary pollutant responsible for the AQI, followed by ozone (62% and 29% of days with events, respectively). The overall AQI was associated with asthma exacerbations (e.g., as continuous, per 10-unit increase, Lag Day 2: odds ratio [OR], 1.014; 95% confidence interval [CI], 1.003-1.025; Lag Day 3: OR, 1.012; 95% CI, 1.001-1.023). By pollutant-specific AQI, the association was strongest for $PM_{2.5}$. In stratified analyses, the AQI was associated with exacerbations in Black and younger children (6-11 yr) on Lag Day 4. **Conclusions:** The AQI is associated with asthma exacerbations among children in Allegheny County. This is driven primarily by $PM_{2.5}$, with Black and younger children particularly affected. Healthcare providers should discuss the AQI in asthma management.

Keywords: air pollution; air quality index; asthma exacerbations; childhood asthma; emergency department visits.

Lancet Respir Med

. 2022 Jul;10(7):650-660.

doi: 10.1016/S2213-2600(21)00537-3. Epub 2022 Mar 29.

Evaluation of the oral corticosteroid-sparing effect of tezepelumab in adults with oral corticosteroid-dependent asthma (SOURCE): a randomised, placebo-controlled, phase 3 study

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Collaborators, Affiliations expand

- PMID: 35364018

- DOI: 10.1016/S2213-2600(21)00537-3

Erratum in

- Correction to Lancet Respir Med 2022; 10: 650-60.
  [No authors listed]Lancet Respir Med. 2022 Jul;10(7):e72. doi: 10.1016/S2213-2600(22)00128-X. Epub 2022 Apr 5.PMID: 35395206 No abstract available.

Abstract

Background: Tezepelumab is a human monoclonal antibody that blocks the activity of thymic stromal lymphopoietin. SOURCE evaluated the oral corticosteroid-sparing effect of tezepelumab in adults with oral corticosteroid-dependent asthma.

Methods: We conducted this phase 3, multicentre, randomised, double-blind, placebo-controlled study across 60 sites in seven countries. Participants aged 18-80 years with physician-diagnosed asthma, who had been receiving medium-dose or high-dose inhaled corticosteroids and had at least one asthma exacerbation in the 12 months before screening were eligible. Patients who were receiving medium-dose inhaled corticosteroids must have had their dose increased to a high dose for at least 3 months before screening. After an oral corticosteroid optimisation phase of up to 8 weeks, participants were randomly assigned according to a computer-generated fixed block randomisation sequence to receive tezepelumab 210 mg or placebo subcutaneously every 4 weeks during a 48 week treatment period (4 week induction phase, 36 week oral corticosteroid reduction phase, and 8 week maintenance phase). Randomisation was stratified by region. Participants, investigators, and site staff were masked to treatment assignment. The primary endpoint was the categorised percentage reduction from baseline in daily oral corticosteroid dose at week 48 without the loss of asthma control. Efficacy and safety endpoints were assessed in all participants who received at least one dose of study drug. This study is registered with ClinicalTrials.gov, NCT03406078.

Findings: Between March 5, 2018, and Sept 27, 2019, 150 participants were randomly assigned to receive tezepelumab 210 mg (n=74) or placebo (n=76). The cumulative odds of achieving a category of greater percentage reduction in an oral corticosteroid dose for daily maintenance at week 48 were similar with tezepelumab or placebo in the overall population (odds ratio [OR] 1·28 [95% CI 0·69-2·35], p=0·43; the primary endpoint was not met). The cumulative odds were higher with tezepelumab than with placebo in participants with baseline blood eosinophil counts of at least 150 cells per μL (2·58 [1·16-5·75]), but not in participants with counts below 150 cells per μL (0·40 [0·14-1·13]). Tezepelumab was well tolerated, with no safety concerns identified. 53 (72%) of 74 tezepelumab-assigned participants and 65 (86%) of 76 placebo-assigned participants reported an adverse event. Serious adverse events were reported in 12 (16%) participants in the tezepelumab group and 16 (21%) participants in the placebo group.

Interpretation: We did not observe a significant improvement in oral corticosteroid dose reduction with tezepelumab versus placebo in the overall population of this oral corticosteroid-sparing study, although an improvement was observed in participants with baseline blood eosinophil counts of at least 150 cells per μL.

Funding: AstraZeneca and Amgen.

Conflict of interest statement

Declaration of interests MEW is an employee of US National Jewish Health and has received consultancy fees from AstraZeneca, Equillium, Genentech, GlaxoSmithKline, Novartis, Regeneron, resTORbio, Sanofi, and Teva. AM-G has attended advisory boards for AstraZeneca, GlaxoSmithKline, Novartis, Sanofi, and Teva; has received speaker fees from AstraZeneca, Novartis, Roche, and Teva; participated in research with AstraZeneca, for which his institution has been remunerated; has attended international conferences with Teva; and has consultancy agreements with AstraZeneca, Sanofi, and Vectura. CEB has received grants and consultancy fees from AstraZeneca. PK has received personal fees for lectures from Adamed, Alvogen, AstraZeneca, Berlin-Chemie, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, HAL Allergy, LEK-AM, Menarini Group, Mylan, Novartis, Polpharma, Sanofi, and Teva. SK has received fees for lectures and advisory board meetings from AstraZeneca, GlaxoSmithKline, Novartis, Roche, Sanofi Aventis, and Teva. TW has received fees for lectures and advisory board meetings from

AstraZeneca, Berlin-Chemie, GlaxoSmithKline, MSD, Novartis, Roche, and Sanofi Aventis. JMG, KS, ÅH, GA, HL, TS, and GC are employees of AstraZeneca. PK is an employee of Amgen.

SUPPLEMENTARY INFO

Associated dataexpand

FULL TEXT LINKS

Lancet Respir Med

. 2022 Jul;10(7):661-668.

doi: 10.1016/S2213-2600(21)00536-1. Epub 2022 Mar 2.

The role of small airway dysfunction in asthma control and exacerbations: a longitudinal, observational analysis using data from the ATLANTIS study

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Collaborators, Affiliations expand

- PMID: 35247313

- DOI: 10.1016/S2213-2600(21)00536-1

Abstract

Background: Although small airway disease is a feature of asthma, its association with relevant asthma outcomes remains unclear. The ATLANTIS study was designed to identify the combination of physiological and imaging variables that best measure the presence and extent of small airway disease in asthma, both cross-sectionally and longitudinally. In this longitudinal analysis, we evaluated which small airway parameters studied were most strongly associated with asthma control, exacerbations, and quality of life.

Methods: In this observational cohort study, participants with mild, moderate, or severe stable asthma were recruited between June 30, 2014, and March 3, 2017, via medical databases and advertisements in nine countries worldwide. Eligible participants were aged 18-65 years with a clinical asthma diagnosis for at least 6 months. Participants were followed up for 1 year, with visits at baseline, 6 months, and 12 months. Physiological tests included spirometry, lung volumes, impulse oscillometry, multiple breath nitrogen washout (MBNW), and percentage decrease in forced vital capacity during methacholine challenge. CT densitometry was performed to evaluate small airway disease. We examined the associations between these measurements and asthma exacerbations, asthma control, and quality of life using univariate and multivariate analyses. A composite ordinal score comprising percent predicted R5-20 (resistance of small-to-mid-sized airways), AX (area of reactance), and X5 (reactance of more central, conducting small airways at 5 Hz) was constructed.

Findings: 773 participants (median age 46 years [IQR 34-54]; 450 [58%] female) were included in this longitudinal study. Univariate analyses showed that components of impulse oscillometry, lung volumes, MBNW, and forced expiratory flow at 25-75% of FVC were significantly correlated with asthma control and exacerbations (Spearman correlations 0·20-0·25, $p<0·0001$ after Bonferroni correction). As a composite of impulse oscillometry, the ordinal score independently predicted asthma control and exacerbations in a multivariate analysis with known exacerbation predictors. CT parameters were not significantly correlated with asthma control, exacerbation, or quality of life.

Interpretation: Small airway disease, as measured by physiological tests, is longitudinally associated with clinically important asthma outcomes, such as asthma control and exacerbations.

Funding: Chiesi Farmaceutici.

Conflict of interest statement

Declaration of interests MK reports grants paid to their institution for their research from the National Institutes of Health, American Lung Association, Chiesi Farmaceutici (for support of this study), AstraZeneca and Sanofi-Regeneron; personal fees for consultancies from Chiesi Farmaceutici, Genentech (Roche), GSK, Sanofi Regeneron, and AstraZeneca; speaker fees from Chiesi Farmaceutici; personal fees from participation in a data safety and monitoring board for AstraZeneca and ALung; and leadership in the American Thoracic Society. MVdB receives grants paid to their institution from Chiesi Farmaceutici (for this study), Sanofi, Genentech, GSK, and Roche. LMF reports personal fees for consultancies from Chiesi Farmaceutici; speaker fees from participation in advisory boards for Chiesi Farmaceutici, AstraZeneca, GSK, Alfasigma, Novartis, and Verona Pharma; travel expense reimbursement from Chiesi Farmaceutici, Novartis, and Menarini; and personal fees from participation in a data safety and monitoring board for Novartis.

TVdM reports part-time employment with GSK and personal fees for consultancies from Chiesi Farmaceutici. GN reports being employed by Chiesi Farmaceutici. AP reports funding by Chiesi Farmaceutici (for this and other studies), AstraZeneca, GSK, Boehringer Ingelheim, Pfizer, Teva, and Sanofi paid to their institution; personal fees for consulting from Chiesi Farmaceutici, AstraZeneca, GSK, Novartis, Sanofi, Iqvia, Avillion, Elpen Pharmaceutic, and ALS; personal fees for lectures and presentations from Chiesi Farmaceutici, AstraZeneca, GSK, Boehringer Ingelheim, Menarini, Novartis, Zambon, Mundipharma, Teva, Sanofi, Edmond Pharma, Iqvia, MSD, Avillion, Elpen Pharmaceutic, ALS. KFR reports support from Chiesi Farmaceutici paid to their institution for this study; speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi Farmaceutici, Novartis, Sanofi/Regeneron, GlaxoSmithKline, Berlin Chemie, and Roche Pharma; personal fees from participation in a data safety and monitoring board for AstraZeneca, Boehringer Ingelheim, and Sanofi/Regeneron; and a leadership or fiduciary role for the German Center for Lung Research, the German Chest Society, and the American Thoracic Society. DS reports personal fees for consulting from Aerogen, AstraZeneca, Boehringer Ingelheim, Chiesi Farmaceutici, Cipla, CSL Behring, Epiendo, Genentech, GlaxoSmithKline, Glenmark, Gossamerbio, Kinaset, Menarini, Novartis, Pulmatrix, Sanofi, Teva, Theravance, and Verona. CB reports support paid to their institution from Chiesi Farmaceutici for this study; grants paid to their institution from GSK, AstraZeneca, Boehringer Ingelheim, Novartis, Chiesi Farmaceutici, Sanofi, Genetech, Merck, Mologic, 4DPharma, and Gossamer; and personal fees for consulting from GSK, AstraZeneca, Boehringer Ingelheim, Novartis, Chiesi Farmaceutici, Sanofi, Genentech, Merck, Mologic, 4DPharma, Gossamer, TEVA, Regeneron, Roche, and CSL Behring. SS reports funding paid to their institution from Chiesi Farmaceutici for support of this study; personal fees from GSK, Novartis, ERT Medical, AstraZeneca, Knopp Biotech, Owlstone Medical, Mundipharma, CSL Behring, and Boehringer Ingelheim; and personal fees for lectures from Chiesi Farmaceutici. All other authors declare no competing interests.

Trends Pharmacol Sci

. 2022 Jul;43(7):539-541.

doi: 10.1016/j.tips.2022.02.009. Epub 2022 Mar 2.

Chemokine receptor CCR1: new target for asthma therapy

Peter J Barnes[1]

Affiliations expand

- PMID: 35246315

- DOI: 10.1016/j.tips.2022.02.009

Abstract

A recent study shows that chemokine receptor 1 (CCR1) plays a role in eosinophilic inflammation and that its ligand CCL15 is increased in asthmatic eosinophils (Du et al.). A companion study reports that N-truncated forms of CCL15 generated by tissue proteases induce biased CCR1 signaling (Shao et al.). These insights may provide the basis for the generation of more effective CCR antagonists as an oral therapy for asthma.

Keywords: CCR1; asthma; biased agonist; chemokine; chemokine receptor; eosinophil.

Thorax

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. 2022 Jul;77(7):641-642.

doi: 10.1136/thoraxjnl-2021-218296. Epub 2022 Jan 7.

Does impaired respiratory function lead to sudden cardiac death?

Rebecca F D'Cruz[1 2 3], Georgios Kaltsakas[4 2 3]

Affiliations expand

- PMID: 34996850

- DOI: 10.1136/thoraxjnl-2021-218296

No abstract available

Keywords: COPD; Lung function; Sudden cardiac death; asthma; clinical epidemiology; respiratory physiology.

Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

MeSH termsexpand

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BMJ Full Text

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Eur Respir J

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. 2022 Jun 30;59(6):2101733.

doi: 10.1183/13993003.01733-2021. Print 2022 Jun.

Urinary metabotype of severe asthma evidences decreased carnitine metabolism independent of oral corticosteroid treatment in the U-BIOPRED study

Stacey N Reinke[1,2,3], Shama Naz[1,3], Romanas Chaleckis[1,4], Hector Gallart-Ayala[1], Johan Kolmert[1,5], Nazanin Z Kermani[6], Angelica Tiotiu[6,7], David I Broadhurst[2], Anders Lundqvist[8], Henric Olsson[9], Marika Ström[10,11], Åsa M Wheelock[10,11], Cristina Gómez[1,5], Magnus Ericsson[12], Ana R Sousa[13], John H Riley[13], Stewart Bates[13], James Scholfield[14], Matthew Loza[15], Frédéric Baribaud[15], Per S Bakke[16], Massimo Caruso[17], Pascal Chanez[18], Stephen J Fowler[19], Thomas Geiser[20], Peter Howarth[14], Ildikó Horváth[21], Norbert Krug[22], Paolo Montuschi[23], Annelie Behndig[24], Florian Singer[25], Jacek Musial[26], Dominick E Shaw[27], Barbro Dahlén[11], Sile Hu[28], Jessica Lasky-Su[29], Peter J Sterk[30], Kian Fan Chung[6], Ratko Djukanovic[14], Sven-Erik Dahlén[5,11], Ian M Adcock[6], Craig E Wheelock[3,14,11], U-BIOPRED Study Group

Affiliations expand

- PMID: 34824054

- PMCID: PMC9245194

- DOI: 10.1183/13993003.01733-2021

Free PMC article

Abstract

Introduction: Asthma is a heterogeneous disease with poorly defined phenotypes. Patients with severe asthma often receive multiple treatments including oral corticosteroids (OCS). Treatment may modify the observed metabotype, rendering it challenging to investigate underlying disease mechanisms. Here, we aimed to identify dysregulated metabolic processes in relation to asthma severity and medication.

Methods: Baseline urine was collected prospectively from healthy participants (n=100), patients with mild-to-moderate asthma (n=87) and patients with severe asthma (n=418) in the cross-sectional U-BIOPRED cohort; 12-18-month longitudinal samples were collected from patients with severe asthma (n=305). Metabolomics data were acquired using high-resolution mass spectrometry and analysed using univariate and multivariate methods.

Results: A total of 90 metabolites were identified, with 40 significantly altered ($p<0.05$, false discovery rate <0.05) in severe asthma and 23 by OCS use. Multivariate modelling showed that observed metabotypes in healthy participants and patients with mild-to-moderate asthma differed significantly from those in patients with severe asthma ($p=2.6\times10^{-20}$), OCS-treated asthmatic patients differed significantly from non-treated patients ($p=9.5\times10^{-4}$), and longitudinal metabotypes demonstrated temporal stability. Carnitine levels evidenced the strongest OCS-independent decrease in severe asthma. Reduced carnitine levels were associated with mitochondrial dysfunction *via* decreases in pathway enrichment scores of fatty acid metabolism and reduced expression of the carnitine transporter SLC22A5 in sputum and bronchial brushings.

Conclusions: This is the first large-scale study to delineate disease- and OCS-associated metabolic differences in asthma. The widespread associations with different therapies upon the observed metabotypes demonstrate the need to evaluate potential modulating effects on a treatment- and metabolite-specific basis. Altered carnitine metabolism is a potentially actionable therapeutic target that is independent of OCS treatment, highlighting the role of mitochondrial dysfunction in severe asthma.

Conflict of interest statement

Conflict of interest: S.N. Reinke reports grants from Canadian Institutes of Health Research, during the conduct of the study. Conflict of interest: S. Naz has nothing to disclose. Conflict of interest: R. Chaleckis has nothing to disclose. Conflict of interest: H. Gallart-Ayala has nothing to disclose. Conflict of interest: J. Kolmert reports personal fees for consultancy from Gesynta Pharma AB, outside the submitted work. Conflict of interest: N.Z. Kermani has nothing to disclose. Conflict of interest: A. Tiotiu has nothing to disclose. Conflict of interest: D.I. Broadhurst has nothing to disclose. Conflict of interest: A. Lundqvist has nothing to disclose. Conflict of interest: H. Olsson is an employee and shareholder of AstraZeneca. Conflict of interest: M. Ström has nothing to disclose. Conflict of interest: Å.M. Wheelock has nothing to disclose. Conflict of interest: C. Gómez has nothing to disclose. Conflict of interest: M. Ericsson has nothing to disclose. Conflict of interest: A.R. Sousa has nothing to disclose. Conflict of interest: J.H. Riley works for and own shares in GlaxoSmithKline. Conflict of interest: S. Bates is an employee of Johnson & Johnson and has previously worked for and holds stock in GlaxoSmithKline. Conflict of interest: J. Scholfield reports grants from Innovative Medicines Initiative, during the conduct of the study; and is director and employee of TopMD Precision Medicine Ltd. Conflict of interest: M. Loza is an employee of and owns stock in Johnson & Johnson. Conflict of interest: F. Baribaud is a shareholder of Johnson & Johnson and a current employee of Bristol Myers Squibb. Conflict of interest: P.S. Bakke reports personal fees for advisory board work and lectures from AstraZeneca, and personal fees for lectures from Novartis and Boehringer Ingelheim, outside the submitted work. Conflict of interest: M. Caruso has nothing to disclose. Conflict of interest: P. Chanez reports grants and personal fees from AstraZeneca, ALK, Boehringer Ingelheim, Chiesi, Sanofi-Aventis, Novartis and GlaxoSmithKline, outside the submitted work. Conflict of interest: S.J. Fowler reports personal fees from AstraZeneca, Novartis, TEVA and Chiesi, outside the submitted work. Conflict of interest: T. Geiser has nothing to disclose. Conflict of interest: P. Howarth has nothing to disclose. Conflict of interest: I. Horvath has nothing to disclose. Conflict of interest: N. Krug has nothing to disclose. Conflict of interest: P. Montuschi has nothing to disclose. Conflict of interest: A. Behndig has nothing to disclose. Conflict of interest: F. Singer reports personal fees from Vertex Pharmaceuticals (CH) and Novartis, outside the submitted work. Conflict of interest: J. Musial has nothing to disclose. Conflict of interest: D.E. Shaw has nothing to disclose. Conflict of interest: B. Dahlén reports personal fees for advisory board work and lectures from AstraZeneca, TEVA and

Sanofi, and grants from Novartis and GlaxoSmithKline, outside the submitted work. Conflict of interest: S. Hu has nothing to disclose. Conflict of interest: J. Lasky-Su has nothing to disclose. Conflict of interest: P.J. Sterk reports a public private grant from the Innovative Medicines Initiative (IMI) covered by the EU and EFPIA, during the conduct of the study. Conflict of interest: K.F. Chung has received honoraria for participating in advisory board meetings of GlaxoSmithKline, AstraZeneca, Roche, Novartis, Merck, Nocion and Shionogi regarding treatments for asthma, COPD and chronic cough and has also been remunerated for speaking engagements. Conflict of interest: R. Djukanovic reports receiving fees for lectures at symposia organised by Novartis, AstraZeneca and TEVA, consultation for TEVA and Novartis as member of advisory boards, and participation in a scientific discussion about asthma organised by GlaxoSmithKline; and is a co-founder and current consultant, and has shares in Synairgen, a University of Southampton spin out company. Conflict of interest: S-E. Dahlén reports personal fees for consultancy from AstraZeneca, Cayman Chemical, GlaxoSmithKline, Novartis, Merck, Regeneron, Sanofi and TEVA, outside the submitted work. Conflict of interest: I.M. Adcock has nothing to disclose. Conflict of interest: C.E. Wheelock has nothing to disclose.

Clinical Trial

J Asthma

. 2022 Jul;59(7):1420-1432.

doi: 10.1080/02770903.2021.1938603. Epub 2021 Aug 1.

A randomized controlled trial of glycopyrrolate administered by metered dose inhaler in patients with

uncontrolled asthma despite ICS/LABA treatment

Edward Kerwin[1], Paul Dorinsky[2], Mehul Patel[3], Kimberly Rossman[4], Colin Reisner[4], Andrea Maes[5], Patrick Darken[6], Dianne Griffis[2], Harald Fjällbrant[7]

Affiliations expand

- PMID: 34338132

- DOI: 10.1080/02770903.2021.1938603

Abstract

Objective: To evaluate the efficacy and safety of three doses of glycopyrrolate metered dose inhaler (GP MDI) in patients with uncontrolled asthma despite treatment with inhaled corticosteroid/long-acting β_2-agonists (ICS/LABA) with or without tiotropium, to characterize the benefit of triple therapy.

Method: This phase II/III, double-blind study randomized patients to 24 weeks' treatment with twice-daily GP MDI 36 µg, 18 µg, 9 µg, or placebo MDI (all delivered *via* Aerosphere inhalers), or once-daily open-label tiotropium 2.5 µg. Patients continued their own ICS/LABA regimen throughout the study. The primary endpoint was change from baseline in forced expiratory volume in 1 s (FEV_1) area under the curve from 0 - 4 h (AUC_{0-4}) at Week 24. Secondary endpoints included patient questionnaires to measure asthma control or symptoms. Safety was also assessed.

Results: The primary analysis (modified intent-to-treat) population included 1066 patients. The primary study endpoint was not met (changes from baseline in FEV_1 AUC_{0-4} at Week 24 were 294 mL, 284 mL, 308 mL, 240 mL, and 347 mL for GP MDI 36 µg, GP MDI 18 µg, GP MDI 9 µg, placebo, and open-label tiotropium, respectively). There were no significant differences between treatment and placebo in secondary endpoints at Week 24. *Post-hoc* analyses using post-bronchodilator FEV_1 as the baseline measurement, or averaging values across multiple baseline visits, showed a dose-related response to GP MDI. The incidence of adverse events was low and similar across treatments.

Conclusion: Although this study did not meet its primary endpoint, *post hoc* analyses identified a dose-related response to GP MDI when alternative definitions of baseline FEV_1 were used in the analyses.

J Asthma

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doi: 10.1080/02770903.2021.1934696. Epub 2021 Jun 5.

Children with under-diagnosed asthma presenting to a pediatric emergency department

Kathryn H Pade[1], Lindsey R Thompson[2], Bahareh Ravandi[3], Todd P Chang[3], Frances Barry[2], Jill S Halterman[4], Peter G Szilagyi[2], Sande O Okelo[2]

Affiliations expand

- PMID: 34034597

- DOI: 10.1080/02770903.2021.1934696

Abstract

Background: Undiagnosed asthma in children presenting to the emergency department (ED) for respiratory illnesses might be associated with subsequent asthma morbidity and repeat ED visits.

Objective: To examine the prevalence of undiagnosed asthma among children presenting for ED care, and explore associations with sociodemographic and clinical characteristics.

Methods: We surveyed parents of children ages 2-17 years seeking ED care for respiratory symptoms (including asthma) regarding sociodemographic characteristics, asthma symptoms, prior asthma care and morbidity, and prior asthma diagnosis. Undiagnosed asthma was defined as a positive screening for asthma and no prior diagnosis. We compared sociodemographic and clinical

factors of those with diagnosed versus undiagnosed asthma using chi-square, t-tests and multivariable logistic regression model.

Results: Of 362 children, 36% had undiagnosed asthma. Undiagnosed children were younger, had younger parents, and had parents less likely to speak English versus diagnosed children (all $p < 0.05$). Among undiagnosed children, 42% had moderate or severe asthma and 66% reported ≥1 exacerbation in the prior 12 months. Parent-reported controller medication use was higher among diagnosed versus undiagnosed children (60% vs. 21%, p=.001). In a multivariable logistic regression (adjusting for insurance, education, income and preferred language), no controller usage (aOR 4.26), no asthma exacerbations in the prior year (aOR 2.41) and younger age (aOR 0.76) were significantly associated with undiagnosed asthma.

Conclusion: Children presenting to the ED with undiagnosed asthma commonly experience significant prior asthma morbidity. Strategies to improve asthma diagnosis and messaging to their parents may reduce future morbidity.

Clinical Trial

J Asthma

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. 2022 Jul;59(7):1410-1419.

doi: 10.1080/02770903.2021.1928184. Epub 2021 May 24.

Efficacy and safety of inhaled extrafine beclomethasone dipropionate in adults

with asthma: a randomized, parallel-group, dose-ranging study (BEAM)

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Affiliations expand

- PMID: 34030555

- DOI: 10.1080/02770903.2021.1928184

Abstract

Introduction: This manuscript describes a Phase II, dose-ranging, randomized, double-blind, placebo- and active-controlled, parallel-group study conducted to identify the appropriate dose of beclomethasone dipropionate (BDP) to be used in a single-inhaler extrafine formulation triple combination of BDP, formoterol fumarate and glycopyrronium.**Methods:** Patients aged 18-75 years with poorly-controlled asthma, receiving low/medium-dose inhaled corticosteroid (ICS), and who had forced expiratory volume in the 1st second (FEV_1) 50-85% predicted, were randomized to inhale BDP 50, 200 or 400 µg twice daily (BID; total daily doses of 100, 400 and 800 µg), placebo, or the active comparator QVAR® 160 µg BID, all via pressurized metered-dose inhalers for 8 weeks. The primary objective was to evaluate superiority of BDP over placebo for change from baseline in pre-dose morning FEV_1 at Week 8. ClinicalTrials.gov: NCT03084718.**Results:** Of 610 patients randomized, 559 (91.6%) completed the study. For pre-dose morning FEV_1 at Week 8, BDP 200 µg BID was superior to placebo, with a statistically significant difference of 113 ml (95% CI 18, 209); differences vs placebo for BDP 50 and 400 µg BID were not significant (44 [-52, 140] and 93 [-3, 188] ml, respectively). Secondary efficacy endpoint results supported the primary endpoint in identifying BDP 200 µg BID as the appropriate dose. Adverse events were experienced by 23.5, 25.0 and 30.6% patients with BDP 50, 200 and 400 µg BID, 34.7% with placebo, and 30.6% with the active comparator.**Conclusion:** In this dose-ranging study, BDP 200 µg BID offered the optimal balance of efficacy and safety in patients with asthma poorly controlled on low/medium-dose ICS.Supplemental data for this article is available online at at www.tandfonline.com/ijas .

Keywords: Lung function; asthma control; inhaled corticosteroid; spirometry; symptoms.

J Asthma

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Effects of short-term exposure to particulate matter on emergency department admission and hospitalization for asthma exacerbations in Brescia district

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Affiliations expand

- PMID: 33980121

- DOI: 10.1080/02770903.2021.1929310

Abstract

Background: Rising pollution plays a crucial role in worsening several respiratory diseases. Particulate Matter (PM)-induced asthma exacerbations are one of the most dangerous events.

Objectives: To assess the correlation between progressive particulate matter short-term exposure and asthma exacerbations, we investigated the role of PM levels on Emergency Department (ED) admissions and hospitalizations for these events in Brescia, an important industrial city located in northern Italy with high yearly levels of air pollution.

Methods: We analyzed 1050 clinical records of ED admissions for suspected asthma exacerbation, starting from January 2014 to December 2017. Daily PM levels were collected from the Environmental Protection Regional Agency. We performed a time-series analysis using a Poisson

regression model with single and multiple day-lag. Results were expressed as Relative Risk (RR) and Excess of Relative Risk (ERR) of severe asthma exacerbation over a 10 µg/m^3 increase in PM10 and PM2.5 concentration.

Results: We selected and focused our analysis on 543 admissions for indisputable asthma exacerbation in ED and hospital. The time-series study showed an increase of the RR (CI95%) for asthma exacerbation-related ED admissions of 1.24 with an ERR of 24.2% for PM2.5 at lag0-1 ($p < 0.05$). We also estimated for PM2.5 a RR (CI95%) of 1.12 with an ERR of 12.5% at lag0-5 ($p \leq 0.05$). Again, for PM2.5, an increase of the RR (CI95%) for asthma exacerbation-related hospitalizations of 1.31 with an ERR of 30.7% at lag0-1 ($p < 0.05$) has been documented. These findings were confirmed and even reinforced considering only the population living in the city.

Conclusions: Short-term PM exposure, especially for PM2.5, plays a critical role in inducing asthma exacerbation events leading to ED admission or hospitalization.

Keywords: PM10; PM2.5; Particulate matter; airborne pollutants; asthma; asthma exacerbation; emergency department; hospitalization.

J Asthma

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Glucocorticoid-induced myopathy in people with asthma: a systematic review

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Affiliations expand

- PMID: 33951991

- DOI: 10.1080/02770903.2021.1926488

Abstract

Objectives: To review the current literature on the evidence and the underlying characteristics of glucocorticoids (type, dosage, and duration) associated with myopathy in asthma.

Data sources: Four electronic databases were searched to October 19, 2020.

Study selection: Inclusion criteria: adults or adolescents with asthma, taking systemic glucocorticoids, and measures of muscle impairments.

Results: Nine studies met the eligibility criteria. The methodologic quality of most studies was fair or good. Two studies reported significantly lower inspiratory muscle function in outpatients taking daily oral glucocorticoids (≥10 mg), but one study reported no such difference. No differences was found in limb muscle strength in one study. Only 11-36% patients with acute exacerbation taking glucocorticoids intravenously suffered from limb muscle weakness during/after critical care admissions. Two studies reported significant associations between *dosage* of oral glucocorticoid use and inspiratory and limb muscle function, whereas seven studies did not find any significant correlations among the characteristics of systemic glucocorticoids and myopathy. Two studies comparing people with non-glucocorticoid dependent asthma taking inhaled glucocorticoid and healthy people did not find any significant differences in their inspiratory muscle strength and endurance.

Conclusions: There were limited studies and inconsistent results on glucocorticoid-induced myopathy in people with asthma, and its association with the characteristics of glucocorticoids use. We recommended future studies should use a commonly accepted operational definition of myopathy, utilize a cohort study design, measure the cumulative dosage of glucocorticoids, and integrate possible confounding factors in the analysis.

Keywords: Corticosteroid; muscle atrophy; muscle weakness; musculoskeletal; steroid.

- Cited by 1 article

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Case Reports

Eur J Hosp Pharm

. 2022 Jul;29(4):235-236.

doi: 10.1136/ejhpharm-2020-002660. Epub 2021 Apr 21.

Administration of benralizumab in a patient with severe asthma admitted to the intensive care unit with COVID-19 pneumonia: case report

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Affiliations expand

- PMID: 33883206

- DOI: 10.1136/ejhpharm-2020-002660

Abstract

A patient with severe asthma on benralizumab therapy was admitted to the intensive care unit (ICU) for a coronavirus disease 2019 (COVID-19) infection. At the end of the 8 week benralizumab dosing interval, discussion arose as to whether benralizumab should be administered or if treatment should be discontinued, due to the lack of experience with benralizumab in this situation. Severe broncho-obstruction developed, and the next injection of benralizumab was administered during ICU admission without detrimental symptoms. With this case report, we would like to share our experience with the safe administration of benralizumab during COVID-19 pneumonia, guiding doctors in future decision making.

Keywords: COVID-19; case reports; critical care; pulmonary medicine; safety.

Conflict of interest statement

Competing interests: Conflicts of interest/competing interests: Mr Kroes reports grants from AstraZeneca, outside the submitted work. Dr Zielhuis reports grants from AstraZeneca, personal fees from Novartis, personal fees from GSK, personal fees from Sanofi, personal fees from Lilly, personal fees from MSD, outside the submitted work. Ms Bethlehem has nothing to disclose. Dr Ten Brinke reports grants, personal fees and others from GSK, grants, personal fees and others from TEVA, grants, personal fees and others from AstraZeneca, others from Sanofi, others from Boehringer Ingelheim, outside the submitted work. Dr Van Roon has nothing to disclose.

Multiparametric Analysis of Factors Associated With Eosinophilic Chronic Rhinosinusitis With Nasal Polyps

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Affiliations expand

- PMID: 33023335

- DOI: 10.1177/0145561320960357

Free article

Abstract

Introduction: Previous studies have reported a diverse range of threshold values for blood eosinophilia. In addition, a single predictive biomarker for eosinophilic chronic rhinosinusitis (CRS) with nasal polyps (ECRSwNP) has not yet been identified.

Objectives: The aim of this study is to compare the clinical characteristics of ECRSwNP and non-ECRSwNP to evaluate the preoperative risk of tissue eosinophilia of chronic rhinosinusitis with nasal polyps (CRSwNP) through a multiparametric statistical analysis.

Methods: One hundred ten patients with evidence of chronic polypoid rhinosinusitis were included in this study and clinical records were retrospectively reviewed. Eosinophilic CRSwNP was diagnosed based on the presence of at least 10 eosinophils per high-power field. The demographic and clinical features of ECRSwNP and non-ECRSwNP are described. The values of blood eosinophilia as predictors of tissue eosinophilia have been identified using receiver operating characteristic curves. As the predictive value of the identified cutoff through regression analysis was low, we evaluated whether other risk factors could be statistically associated with ECRSwNP, and from this, a new predictive model was proposed for the identification of eosinophilic nasal polyps before surgery.

Results: We found that the best method for predicting ECRSwNP is based on a model having asthma, blood eosinophil percentage, posterior ethmoid value in Lund-Mackay score, and modified Lund-Kennedy score as explanatory variables.

Conclusions: This study provides new data for a better understanding of the polypoid CRS endotypes, and the proposed model allows the endotype to be identified preoperatively.

Keywords: nasal polyps; paranasal sinus diseases; paranasal sinuses; quality of life; sinusitis.

RHINITIS

BMC Pulm Med

. 2022 Jul 1;22(1):261.

doi: 10.1186/s12890-022-02038-3.

Associations between comorbidities and annual incidence plus frequency of asthma exacerbation hospitalisation during the past year: data from CARN study

Wenqiao Wang [1], Jiangtao Lin [2], Xin Zhou [3], Changzheng Wang [4], Mao Huang [5], Shaoxi Cai [6], Ping Chen [7], Qichang Lin [8], Jianying Zhou [9], Yuhai Gu [10], Yadong Yuan [11], Dejun Sun [12], Xiaohong Yang [13], Lan Yang [14], Jianmin Huo [15], Zhuochang Chen [16], Ping Jiang [17], Jie Zhang [18], Xianwei Ye [19], Huiguo Liu [20], Huaping Tang [21], Rongyu Liu [22], Chuntao Liu [23], Wei Zhang [24], Chengping Hu [25], Yiqiang Chen [26], Xiaoju Liu [27], Luming Dai [28], Wei Zhou [29], Yijiang Huang [30], Jianying Xu [31]

Affiliations expand

- PMID: 35778740

- DOI: 10.1186/s12890-022-02038-3

Abstract

Purpose: While asthma comorbidities are associated with higher health care utilisation, lower quality of life and poorer asthma control, the impact of asthma comorbidities on hospitalisation for asthma exacerbation (H-AX) remains less recognised. We aim to analyse the impact of asthma comorbidities on H-AX.

Methods: Based on a national survey on asthma control and disease perception (CARN 2015 study), we analysed the impact of comorbidities on annual incidence and frequency of H-AX in China. Information on demographic characteristics, asthma comorbidities and annual incidence and frequency of H-AX were presented in this study.

Results: Among 3875 ambulatory asthma patients, 75.9% (2941/3875) had comorbidities, and 26.4% (1017/3858) experienced H-AX during past year. After adjusting for confounding factors such as demographic data, smoking status and asthma control, COPD [OR = 2.189, 95% CI (1.673, 2.863)] and coronary heart disease [OR = 1.387, 95% CI (1.032, 1.864)] were associated with higher annual incidence, while allergic rhinitis [OR = 0.692, 95% CI (0.588, 0.815)] was associated with lower annual incidence, of H-AX. In terms of frequency, allergic rhinitis [OR = 1.630, 95% CI (1.214, 2.187)], COPD [OR = 1.472, 95% CI (1.021, 2.122)] and anxiety [OR = 2.609, 95% CI (1.051, 6.477)] showed statistically significant correlation with frequent H-AX.

Conclusions: COPD and coronary heart disease were associated with higher annual incidence, while allergic rhinitis was associated with lower annual incidence of H-AX. Allergic rhinitis, COPD and anxiety were associated with frequent H-AX. Comorbidities may have an important role in the risk and frequency of annual hospitalisations due to asthma exacerbation. The goal of asthma control should rely on a multi-disciplinary treatment protocol.

Keywords: Asthma; Comorbidity; Exacerbation; Hospitalisation; Multi-centre cross-sectional study.

- 43 references

SUPPLEMENTARY INFO

Grant supportexpand

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Am J Otolaryngol

. Jul-Aug 2022;43(4):103509.

doi: 10.1016/j.amjoto.2022.103509. Epub 2022 May 21.

A prospective study on the difference of clinical outcomes between elderly and adult patients with allergic rhinitis

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Affiliations expand

- PMID: 35636087

- DOI: 10.1016/j.amjoto.2022.103509

Abstract

Objective: The guiding significance of existing guidelines for the diagnosis, treatment and health management of AR in elderly patients is unclear. The aim of this study is to analyze the clinical characteristics and therapeutic effects of elderly and adult AR patients by prospective study.

Methods: A total of 131 AR patients were recruited and divided into elderly group and adult group according to age. After receiving the same pharmacological treatment for 4 weeks, the differences of the two groups in clinical scores including TNSS-4, RQLQ and VAS were compared.

Results: After 4 weeks treatment, all clinical scores in the adult group were improved compared with the baseline levels, while in the elderly group, only the TNSS-4 score was significantly reduced, and the RQLQ and VAS scores were not significantly improved. The changes of TNSS-4, RQLQ, and VAS scores in the elderly group were significantly inferior to those in the adult group (LS mean differences were 1.60, 8.80, and 11.10, respectively; $P < 0.001$).

Conclusion: We confirmed that elderly and adult AR patients had different clinical characteristics and outcomes, and the degree of improvement in the adult group was significantly better than that in the elderly group. Therefore, it is urgent for us to establish a clinical guideline suitable for the elderly AR population to give more scientific and reasonable recommendations for diagnosis and treatment.

Keywords: Allergic rhinitis; Drug treatment; Quality of life; Symptoms; The elderly.

Randomized Controlled Trial

Eur J Drug Metab Pharmacokinet

. 2022 Jul;47(4):509-521.

doi: 10.1007/s13318-022-00769-6. Epub 2022 Apr 16.

Safety, Tolerability, and Pharmacokinetic Study of 101BHG-D01 Nasal Spray, a Novel Long-Acting and Selective Cholinergic M Receptor

Antagonist, in Healthy Chinese Volunteers: A Randomized, Double-Blind, Placebo-Controlled, Single-Dose Escalation, First-In-Human Study

Nan-Nan Chu[#1], Kai Huang[#1], Lin-Ling Que[1], Ying Ding[1], Xiang-Hong Gu[1], Lin Zhang[1], Jia-Kun Wang[1], Xiao-Ping Chen[2], Zhan-Guo Sun[2], Qing He[3]

Affiliations expand

- PMID: 35429285

- DOI: 10.1007/s13318-022-00769-6

Abstract

Background and objective: 101BHG-D01 nasal spray is the first novel long-acting cholinergic M receptor antagonist under development to treat rhinorrhea in rhinitis. This first-in-human study aimed to evaluate the safety, tolerability, and pharmacokinetics of 101BHG-D01 nasal spray following single intranasal doses in healthy Chinese subjects.

Methods: A randomized, double-blind, placebo-controlled, single-dose escalation study was conducted in healthy Chinese volunteers after intranasal doses of 101BHG-D01 nasal spray or placebo ranging from 40 μg to 960 μg (total of six doses). Blood samples were collected at scheduled time points, and plasma concentrations were determined using a validated high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) method. A non-compartmental method was used to calculate the main pharmacokinetic parameters, including the area under the plasma concentration-time curve from time zero to the time of the last measurable concentration (AUC_{0-t}), the area under the plasma concentration-time curve from time zero to infinity ($AUC_{0-\infty}$), the maximum plasma concentration (C_{max}), the time to maximum plasma concentration (T_{max}), and the elimination half-life ($t_{1/2}$). Safety was evaluated by monitoring adverse events, laboratory assays, vital signs, physical examinations, 12-lead electrocardiograms (ECGs), anterior rhinoscopy, ophthalmic examination, and ambulatory ECG monitoring.

Results: Following single intranasal dosing, 101BHG-D01 was rapidly absorbed with a median T_{max} of 0.34-0.50 h and eliminated slowly with a mean $t_{1/2}$ ranging from 4.29 to 46.76 h for different dose groups. The C_{max} and AUC of 101BHG-D01 increased linearly across the examined dose range of 40-960 μg. 101BHG-D01 nasal spray was well tolerated, all AEs were mild, and no serious adverse events occurred during the study.

Conclusions: 101BHG-D01 nasal spray was safe and well tolerated in healthy Chinese subjects when administered intranasally in single escalating doses. The mean C_{max} and AUC increased proportionally to the studied dose. The pharmacokinetic, safety, and tolerability profiles of 101BHG-D01 nasal spray indicate that it is a good candidate for further development as a treatment for rhinorrhea in rhinitis.

- 11 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Indian J Pediatr

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. 2022 Jul;89(7):673-681.

doi: 10.1007/s12098-021-04052-5. Epub 2022 Mar 4.

Allergic Rhinitis and House Dust Mite Sensitization Determine Persistence of Asthma in Children

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Affiliations expand

- PMID: 35244877

- PMCID: PMC9205813

- DOI: 10.1007/s12098-021-04052-5

Free PMC article

Abstract

Objective: To specify clinical and immunological parameters of the mechanisms, which may lead to development of persistent asthma, or regression of the disease symptoms.

Methods: Eighty children with childhood asthma, diagnosed in the past by using the modified Asthma Predicted Index (mAPI), were divided into two groups: remission group and persistent group. There were 3 study visits (baseline, at 6 mo, and at 12 mo). Clinical remission of asthma was defined as the absence of asthma symptoms for at least 12 mo without treatment. The patients could switch from one group to another during the 12 mo of follow-up. Clinical, inflammatory, and immunoregulatory predictors of asthma remission/persistence were analyzed.

Results: The presence of mAPI criteria as well as house dust mite (HDM) allergy and allergic rhinitis at 7-10 y, were associated with a reduced prevalence of asthma remission. The increased eosinophil blood count in mAPI criteria was associated with a lower expression of CD25 positive cells. HDM allergy was associated with a higher fractional exhaled nitric oxide (FeNO) level ($p = 0.0061$) and higher expression of CD25CD71 ($p = 0.0232$). Allergic rhinitis was associated with a higher expression of PPAR ($p = 0.0493$) and CD25CD71 ($p = 0.0198$), and lower expression of glycoprotein A repetitions predominant (GARP).

Conclusions: Persistence of childhood asthma was largely determined by the presence of allergic rhinitis and sensitization to HDM. Additionally, API criteria but not immunoregulation processes, were related to asthma persistence.

Keywords: Allergic rhinitis; Asthma persistence; Children; House dust mite sensitization.

Conflict of interest statement

None.

- 29 references
- 1 figure

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

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Allergy

. 2022 Jul;77(7):2163-2174.

doi: 10.1111/all.15223. Epub 2022 Jan 25.

The prevalence of non-allergic rhinitis phenotypes in the general population: A cross-sectional study

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Affiliations expand

- PMID: 35038765

- DOI: 10.1111/all.15223

Abstract

Background: Non-allergic rhinitis (NAR) can be subdivided into several phenotypes: rhinorrhea of the elderly, rhinitis medicamentosa, smokers', occupational, hormonal, drug-induced, gustatory, and idiopathic rhinitis. There are two pathophysiological endotypes of

NAR: inflammatory and neurogenic. Phenotypes may serve as an indicator of an underlying endotype and, therefore, help to guide the treatment. The prevalence of each phenotype in the general population is currently unknown.

Methodology/principal: Cross-sectional questionnaire-based study in the general population of the Netherlands.

Results: The prevalence of chronic rhinitis in the general population was 40% (N = 558, of those, 65% had NAR and 28% AR, in 7% allergy status is unknown). Individuals with NAR (N = 363) had significantly more complaints in October-February. Those with AR (N = 159) had significantly more complaints in April-August. The most common NAR phenotypes were idiopathic (39%) and rhinitis medicamentosa (14%), followed by occupational (8%), smokers' (6%), hormonal (4%), gustatory (4%), and rhinorrhea of the elderly (4%). The least prevalent phenotype was drug induced (1%). Nineteen percent of the NAR group could not be classified into any of the phenotypes.

Conclusions: This is the first study to describe the prevalences of NAR phenotypes in the general population. AR and NAR have a distinct seasonality pattern with NAR being more prevalent in autumn/winter and AR in spring/summer. Our data on the prevalence of phenotypes may help clinicians to anticipate the type of patients at their clinic and help guide a tailored treatment approach. The high prevalence of rhinitis medicamentosa is alarming, since this is a potentially preventable phenotype.

Keywords: endotype; epidemiology; non-allergic rhinitis; phenotype; prevalence.

- 52 references

SUPPLEMENTARY INFO

MeSH termsexpand

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Randomized Controlled Trial

Allergy

. 2022 Jul;77(7):2211-2221.

doi: 10.1111/all.15222. Epub 2022 Feb 1.

Dupilumab improves health related quality of life: Results from the phase 3 SINUS studies

Stella E Lee[1], Claire Hopkins[2], Joaquim Mullol[3], Jérôme Msihid[4], Isabelle Guillemin[5], Nikhil Amin[6], Leda P Mannent[4], Yongtao Li[7], Shahid Siddiqui[6], Chien-Chia Chuang[8], Siddhesh Kamat[6], Asif H Khan[4]

Affiliations expand

- PMID: 35034364

- DOI: 10.1111/all.15222

Abstract

Background: Chronic rhinosinusitis with nasal polyps (CRSwNP) is a predominantly type 2-mediated inflammatory disease with high symptom burden and reduced health-related quality of life (HRQoL). This report aimed to comprehensively understand the effects of dupilumab on domains of HRQoL, their individual elements, and health status in patients with severe CRSwNP from phase 3 SINUS-24 (NCT02912468) and SINUS-52 (NCT02898454) trials.

Methods: Patients were randomized to dupilumab (n = 438) or placebo (n = 286) for 24 weeks (SINUS-24), or 52 weeks (SINUS-52). Disease-specific HRQoL using 22-item sino-nasal outcome test (SNOT-22), and health status using EuroQoL-visual analog scale (EQ-VAS) was evaluated in the pooled intention-to-treat (ITT) population (Week 24), SINUS-52 ITT (Week 52) and in the subgroups with/without asthma; non-steroidal anti-inflammatory drug-exacerbated respiratory disease (NSAID-ERD); and prior sinus surgery.

Results: At baseline, patients had poor disease-specific HRQoL and general health status and identified "Decreased sense of smell/taste" and "Nasal blockage" as the most important symptoms. Dupilumab significantly improved SNOT-22 total, domain (Nasal, Sleep, Function, Emotion, and Ear/facial), and 22-item scores, and EQ-VAS, at Week 24 vs placebo (all $p < .0001$), with continued improvements to Week 52 in SINUS-52. Improvements occurred irrespective of comorbid asthma, NSAID-ERD, or prior surgery. A significantly greater proportion of dupilumab-treated patients exceeded clinically meaningful thresholds for SNOT-22 total score and EQ-VAS vs placebo (all subgroups $p < .05$ except patients without surgery at Week 24).

Conclusions: Dupilumab treatment led to significant clinically meaningful improvements across all aspects of disease-specific HRQoL, and general health status in patients with severe CRSwNP.

Keywords: CRSwNP; HRQoL; SNOT-22; comorbidities; dupilumab.

- 35 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated data, Grant supportexpand

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7

Allergy

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. 2022 Jul;77(7):2147-2162.

doi: 10.1111/all.15199. Epub 2022 Jan 15.

Development and validation of combined symptom–medication scores for allergic rhinitis

Bernardo Sousa-Pinto[1,2], Luís Filipe Azevedo[1,2], Marek Jutel[3,4], Ioana Agache[5], G Walter Canonica[6,7], Wienczyslawa Czarlewski[8,9], Nikolaos G Papadopoulos[10], Karl-Christian Bergmann[11,12], Philippe Devillier[13], Daniel Laune[14], Ludger Klimek[15,16], Aram Anto[9], Josep M Anto[17,18,19,20], Patrik Eklund[21], Rute Almeida[1,2], Anna Bedbrook[22], Sinthia Bosnic-Anticevich[23,24], Helen A Brough[25], Luisa Brussino[26], Victoria Cardona[27], Thomas Casale[25], Lorenzo Cecchi[28], Denis Charpin[29], Tomás Chivato[30], Elisio M Costa[31], Alvaro A Cruz[32], Stephanie Dramburg[33], Stephen R Durham[34], Giulia De Feo[35], Roy Gerth van Wijk[36], Wystke J Fokkens[37], Bilun Gemicioglu[38], Tari Haahtela[39], Maddalena Illario[40], Juan Carlos Ivancevich[41], Violeta Kvedariene[42,43], Piotr Kuna[44], Désirée E Larenas-Linnemann[45], Michael Makris[46], Eve Mathieu-Dupas[14], Erik Melén[47,48], Mario Morais-Almeida[49], Ralph Mösges[50], Joaquim Mullol[51,52], Kari C Nadeau[53], Nhân Pham-Thi[54], Robyn O'Hehir[55], Frederico S Regateiro[56,57,58], Sietze Reitsma[59], Boleslaw Samolinski[60], Aziz Sheikh[61], Cristiana Stellato[35], Ana Todo-Bom[62], Peter Valentin Tomazic[63], Sanna Toppila-Salmi[64], Antonio Valero[65], Arunas Valiulis[66,67], Maria Teresa Ventura[68], Dana Wallace[69], Susan Waserman[70], Arzu Yorgancioglu[71], Govert De Vries[72], Michiel van Eerd[72], Petra Zieglmayer[73,74], Torsten Zuberbier[11,12], Oliver Pfaar[75], João Almeida Fonseca[76,77,78], Jean Bousquet[11,12,22,79]

Affiliations expand

- PMID: 34932829

- DOI: 10.1111/all.15199

Abstract

Background: Validated combined symptom-medication scores (CSMSs) are needed to investigate the effects of allergic rhinitis treatments. This study aimed to use real-life data from the MASK-air® app to generate and validate hypothesis- and data-driven CSMSs.

Methods: We used MASK-air® data to assess the concurrent validity, test-retest reliability and responsiveness of one hypothesis-driven CSMS (modified CSMS: mCSMS), one mixed hypothesis- and data-driven score (mixed score), and several data-driven CSMSs. The latter were generated with MASK-air® data following cluster analysis and regression models or factor analysis. These CSMSs were compared with scales measuring (i) the impact of rhinitis on work productivity (visual analogue scale [VAS] of work of MASK-air® , and Work Productivity and Activity Impairment: Allergy Specific [WPAI-AS]), (ii) quality-of-life (EQ-5D

VAS) and (iii) control of allergic diseases (Control of Allergic Rhinitis and Asthma Test [CARAT]).

Results: We assessed 317,176 days of MASK-air® use from 17,780 users aged 16-90 years, in 25 countries. The mCSMS and the factor analyses-based CSMSs displayed poorer validity and responsiveness compared to the remaining CSMSs. The latter displayed moderate-to-strong correlations with the tested comparators, high test-retest reliability and moderate-to-large responsiveness. Among data-driven CSMSs, a better performance was observed for cluster analyses-based CSMSs. High accuracy (capacity of discriminating different levels of rhinitis control) was observed for the latter (AUC-ROC = 0.904) and for the mixed CSMS (AUC-ROC = 0.820).

Conclusion: The mixed CSMS and the cluster-based CSMSs presented medium-high validity, reliability and accuracy, rendering them as candidates for primary endpoints in future rhinitis trials.

Keywords: medication score; quality-of-life; rhinitis; symptom score; work.

Int Forum Allergy Rhinol

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. 2022 Jul;12(7):917-934.

doi: 10.1002/alr.22938. Epub 2022 Jan 5.

Taste receptors in chronic rhinosinusitus, what is the evidence? A systematic review

Jonathan H Chen[1], Christopher I Song[2], Nanki Hura[3,4], Anirudh Saraswathula[2], Stella M Seal[3], Andrew P Lane[2], Nicholas R Rowan[2]

Affiliations expand

- PMID: 34913601

- PMCID: PMC9200906

- DOI: 10.1002/alr.22938

Free PMC article

Abstract

Background: Bitter and sweet taste receptors (T2Rs and T1Rs), respectively, are involved in the innate immune response of the sinonasal cavity and associated with chronic rhinosinusitis (CRS). Growing evidence suggests extraoral TRs as relevant biomarkers, but the current understanding is incomplete. This systematic review synthesizes current evidence of extraoral taste receptors in CRS.

Methods: PubMed, Embase, Cochrane, Web of Science, and Scopus were reviewed in accordance with Preferred Reporting Items for Systemic Reviews and Meta-Analyses guidelines and included studies of genotypic and phenotypic T2R/T1R status in CRS patients.

Results: Twenty-two studies with 3845 patients were included. Seventeen studies evaluated genotype and 10 evaluated taste phenotypes. Four of 6 studies examining the haplotype distribution of the T2R, TAS2R38, demonstrated increased AVI/AVI haplotype ("nontaster") frequency in CRS. Meanwhile, 2 studies demonstrated decreased bitter sensitivity in CRS with nasal polyposis (CRSwNP), whereas 3 other studies reported decreased bitter sensitivity only in CRS without nasal polyposis (CRSsNP). Findings regarding sweet sensitivity were mixed. Three studies with cystic fibrosis patients (n =

1393) were included. Studies investigating the association between clinical outcomes and TAS2R38 alleles were limited, but the nonfunctional combination of AVI/AVI was associated with increased utilization of sinus surgery and, in CRSsNP patients, with poorer improvement of symptoms postoperatively.

Conclusion: Both genotypic and phenotypic assessments of T2Rs suggest a potential association with CRS, particularly CRSsNP. However, limited evidence and mixed conclusions cloud the role of T2Rs in CRS. Future investigations should aim to increase diverse populations, broaden institutional diversity, examine T1Rs, and utilize uniform assessments.

Keywords: G-protein-coupled; biomarkers; genotype; haplotype; immunity; innate; phenotype; quinine; receptors; taste.

Conflict of interest statement

Potential conflict of interest: None disclosed.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

FULL TEXT LINKS

1

Eur Heart J

. 2022 Jun 25;ehac322.

doi: 10.1093/eurheartj/ehac322. Online ahead of print.

Polygenic risk score for ACE-inhibitor-associated cough based on the discovery of new genetic loci

Jonas Ghouse[1,2], Vinicius Tragante[3], Ayesha Muhammad[4], Gustav Ahlberg[1,2], Morten W Skov[1,2], Dan M Roden[4,5], Ingileif Jonsdottir[3,6,7], Laura Andreasen[1,2], Pia Rengtved Lundegaard[1,2], Linea C Trudsø[1,2], Karina Banasik[8], Søren Brunak[8], Sisse R Ostrowski[9,10], eMERGE consortium; Christian Torp-Pedersen[11,10], Ole V Pedersen[12,10], Erik Sørensen[9,10], Lars Køber[13,10], Kasper Iversen[14,10], Unnur Thorsteinsdottir[3,6], Gudmundur Thorgeirsson[3,15], Henrik Ullum[16], Daniel F Gudbjartsson[3,17], Jonathan D Mosley[5], Hilma Holm[3], Kari Stefansson[3,6], Henning Bundgaard[13,10], Morten Salling Olesen[1,2]

Affiliations expand

- PMID: 35751511

- DOI: 10.1093/eurheartj/ehac322

Abstract

Aims: To search for sequence variants associated with ACEi discontinuation and to test their association with ACEi-associated adverse drug reactions (ADRs).

Methods and results: A genome-wide association study (GWAS) on ACEi discontinuation was conducted, including 33 959 ACEi-discontinuers and 44 041 controls. Cases were defined as persons who switched from an ACEi treatment to an angiotensin receptor blocker. Controls were defined as persons who continued ACEi treatment for at least 1 year. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were computed for ACEi discontinuation risk by mixed model regression analysis. Summary statistics from the individual cohorts were meta-analyzed with a fixed-effects model. To test for association with specific ACEi-associated ADRs, any genome-wide significant ($P < 5 \times 10\text{-}8$) ACEi discontinuation variants was tested for association with ACEi-associated cough and angioedema. A polygenetic risk score (PRS) based on ACEi discontinuation GWAS data was constructed and tested for association with ACEi-associated cough and angioedema in two population-based samples. In total, seven genetic genome-wide loci were identified, of which six were previously unreported. The strongest association with ACEi discontinuation was at 20q13.3 (NTSR1; OR: 1.21; 95% CI: 1.17-1.24; $P = 2.1 \times 10\text{-}34$). Five of seven lead variants were associated with ACEi-associated cough, whereas none were associated with ACEi-associated angioedema. The ACEi discontinuation PRS was associated with ACEi-associated cough in a dose-response manner but not with ACEi-associated angioedema. ACEi discontinuation was genetically correlated with important causes for cough, including gastro-esophageal reflux disease, allergic rhinitis, hay fever, and asthma, which indicates partly shared genetic underpinning between these traits.

Conclusion: This study showed the advantage of using prescription patterns to discover genetic links with ADRs. In total, seven genetic loci that associated with ACEi discontinuation were identified. There was evidence of a strong association between our

ADR phenotype and ACEi-associated cough. Taken together, these findings increase insight into the pathophysiological processes that underlie ACEi-associated ADRs.

Keywords: ACE inhibitors; ACE-inhibitor associated cough; ADR; Adverse drug reaction; Drug discontinuation; GWAS; Genome-wide association study.

J Allergy Clin Immunol Pract

. 2022 Jun 21;S2213-2198(22)00591-8.

doi: 10.1016/j.jaip.2022.06.006. Online ahead of print.

The Environmental Microbiome, Allergic Disease and Asthma

Michael S Kelly[1], Supinda Bunyavanich[2], Wanda Phipatanakul[3], Peggy S Lai[4]

Affiliations expand

- PMID: 35750322

- DOI: 10.1016/j.jaip.2022.06.006

Abstract

The environmental microbiome represents the entirety of the microbes and their metabolites that we encounter in our environments. A growing body of evidence supports the role of the environmental microbiome in risk for and severity of allergic diseases and

asthma. The environmental microbiome represents a ubiquitous, lifelong exposure to non-self antigens. During the critical window between birth and one year of life, interactions between our early immune system and the environmental microbiome have two consequences: our individual microbiome is populated by environmental microbes, and our immune system is trained regarding which antigens to tolerate. During this time, a diversity of exposures appears largely protective, dramatically decreasing the risk of developing allergic diseases and asthma. As we grow older, our interactions with the environmental microbiome change. While it continues to exert influence over the composition of the human microbiome, the environmental microbiome becomes increasingly a source for antigenic stimulation and infection. The same microbial exposure protective against disease development may exacerbate disease severity. While much has been learned about the importance of the environmental microbiome in allergic disease, much more remains to be understood about these complicated interactions between our environment, our microbiome, our immune system and disease.

Keywords: Food allergy (FA); allergic rhinitis (AR); asthma; atopic dermatitis (AD); built environment; environment; exposure; metagenomics; microbiome; microbiota.

Allergy Asthma Clin Immunol

. 2022 Jun 20;18(1):56.

doi: 10.1186/s13223-022-00686-y.

Intranasal budesonide for rhinitis during a high airborne pollution period: a randomized controlled trial

Yuan Zhang[1 2 3], Chunguang Shan[4], Weiwei Liu[5], Yaozhong Han[6], Guanggang Shi[7], Yongjian Ma[8], Kerstin Wagner[9], Xiaoyan Tian[10], Lili Zhang[10], Allan Joseph Larona[11], Steven Sacavage[9], Kathleen Franklin[9], Chengshuo Wang[12 13 14], Luo Zhang[15 16 17]

Affiliations expand

- PMID: 35725523

- PMCID: PMC9207822

- DOI: 10.1186/s13223-022-00686-y

Free PMC article

Abstract

Background: Air pollution may induce or reinforce nasal inflammation regardless of allergy status. There is limited direct clinical evidence informing the treatment of airborne pollution-related rhinitis.

Objective: To assess the effectiveness of intranasal budesonide in adults with self-reported rhinitis symptoms triggered/worsened by airborne pollution.

Methods: Adults in northern China with self-reported rhinitis symptoms triggered or worsened by airborne pollution were randomized to budesonide 256 μg/day or placebo for 10 days in pollution season (October 2019 to February 2020). The primary endpoint was the mean change from baseline in 24-h reflective total nasal symptom score (rTNSS) averaged over 10 days. The secondary endpoints were subject-assessed Global Impression of Change (SGIC), mean change from baseline in individual nasal symptom severity, and mean change from baseline in individual non-nasal symptoms of cough and postnasal drip severity. One-sided $P < 0.0125$ was considered statistically significant.

Results: After an interruption by COVID-19, an interim analysis showed that the study could be ended for efficacy with n = 206 participants (103/group) since the primary efficacy endpoint demonstrated significant results. The final efficacy results showed that the 10-day-averaged rTNSS change in the budesonide group was greater than with placebo (- 2.20 vs - 1.72, P = 0.0107). Budesonide also significantly improved 10-day-averaged itching/sneezing change (- 0.75 vs - 0.51, P = 0.0009). Results for SGIC and all other individual symptoms did not show significant differences between the two groups.

Conclusions: Intranasal budesonide 256 μg once daily improved the total nasal symptoms and itching/sneezing over 10 days in adults with rhinitis triggered/worsened by airborne pollution.

Keywords: Air quality index; Airborne pollution; Budesonide; Intranasal corticosteroid; Intranasal spray; Non-allergic rhinitis; Perennial allergic rhinitis; Pollution; Rhinitis; Seasonal allergic rhinitis.

Conflict of interest statement

YZ, CS, WL, YH, GS, YM, CW, and LZ are investigators for the clinical trial. KW, XT, LiliZ, AJL, SS, and KF are employees of the Johnson & Johnson Family of Consumer Companies.

- 31 references
- 4 figures

Allergy

. 2022 Jun 18.

doi: 10.1111/all.15415. Online ahead of print.

Intranasal antihistamine and corticosteroid to treat in allergic rhinitis: A systematic review and meta-analysis

Minji Kim[#1], Gwanghui Ryu[#2], Sung-Yoon Kang[3], Mi-Ae Kim[4], Song-I Yang[5], Il Hwan Lee[6], Gil-Soon Choi[7], Hyun-Jung Kim[8], Sang Min Lee[3], Dong-Kyu Kim[6], Jeong Hee Choi[9], Hyeon-Jong Yang[10], Soo

Whan Kim[11], Work Group for Rhinitis, the Korean Academy of Asthma, Allergy and Clinical Immunology

Affiliations expand

- PMID: 35716356

- DOI: 10.1111/all.15415

No abstract available

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

Expert Rev Clin Immunol

. 2022 Jun 19;1-12.

doi: 10.1080/1744666X.2022.2089654. Online ahead of print.

Comorbid allergic rhinitis and asthma: important clinical considerations

E Nappi[1,2], G Paoletti[1,2], L Malvezzi[1,3], S Ferri[2], F Racca[2], M R Messina[1,2], F Puggioni[1,2], E Heffler[1,2], G W Canonica[1,2]

Affiliations expand

- PMID: 35695326

- DOI: 10.1080/1744666X.2022.2089654

Abstract

Introduction: The numerous links between allergic rhinitis and asthma have been extensively explored in the last two decades, gaining great concern within the scientific community. These two conditions frequently coexist in the same patient and share numerous pathogenetic and pathophysiological mechanisms.

Areas covered: We reviewed major pathophysiological, epidemiological, and clinical links between allergic rhinitis and asthma. We also provided a comprehensive discussion of allergic rhinitis treatment according to current guidelines, with a particular focus on the relevance of allergic rhinitis therapies in patients with comorbid asthma.

Expert opinion: We believe that there are several unmet needs for our patients, however, there are promising advances forecasted for the future. Although allergic rhinitis is a recognized risk factor for asthma, a proper asthma detection and prevention plan in allergic rhinitis patients is not available. Allergen immunotherapy (AIT) represents a promising preventive strategy and may deserve an earlier positioning in allergic rhinitis management. A multidisciplinary approach should characterize the journey of patients with respiratory allergies, with an adequate referral to specialized Allergy/Asthma centers. Molecular Allergy Diagnosis may provide support for optimal AIT use. Finally, a possible evolution of biological treatment can be envisaged, mainly if biosimilars decrease such therapies' costs.

Keywords: United airway disease; allergen immunotherapy; allergic rhinitis; allergic rhinitis treatment; asthma; asthma comorbidities; respiratory allergies.

Pediatr Pulmonol

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. 2022 Jul 1.

doi: 10.1002/ppul.26048. Online ahead of print.

A child with chronic cough and eosinophilia secondary to Strongyloides stercoralis infection

Guy Hazan [1], Rachel C Orscheln [2], Lila Kertz [1], Katherine Rivera-Spoljaric [1]

Affiliations expand

- PMID: 35778783

- DOI: 10.1002/ppul.26048

Abstract

we presented the case of a 3-year-old, Caucasian female, with history of severe persistent asthma, who presented with chronic cough. Symptoms were present since 18 months of age but worsened in the 5 months prior to presentation. Cough was initially described as dry but became productive and was accompanied by wheezing along with nasal congestion. This article is protected by copyright. All rights reserved.

2

Nat Rev Dis Primers

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. 2022 Jun 30;8(1):46.

doi: 10.1038/s41572-022-00379-1.

Cough hypersensitivity and chronic cough

No authors listed

- PMID: 35773452

- DOI: 10.1038/s41572-022-00379-1

No abstract available

Proceed to details

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3

Review

Nat Rev Dis Primers

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. 2022 Jun 30;8(1):45.

doi: 10.1038/s41572-022-00370-w.

Cough hypersensitivity and chronic cough

Kian Fan Chung [1,2], Lorcan McGarvey [3], Woo-Jung Song [4], Anne B Chang [5,6], Kefang Lai [7], Brendan J Canning [8], Surinder S Birring [9], Jaclyn A Smith [10], Stuart B Mazzone [11]

Affiliations expand

- PMID: 35773287

- DOI: 10.1038/s41572-022-00370-w

Abstract

Chronic cough is globally prevalent across all age groups. This disorder is challenging to treat because many pulmonary and extrapulmonary conditions can present with chronic cough, and cough can also be present without any identifiable underlying cause or be refractory to therapies that improve associated conditions. Most patients with chronic cough have cough hypersensitivity, which is characterized by increased neural responsivity to a range of stimuli that affect the airways and lungs, and other tissues innervated by common nerve supplies. Cough hypersensitivity presents as excessive coughing often in response to relatively innocuous stimuli, causing significant psychophysical morbidity and affecting patients' quality of life. Understanding of the mechanisms that contribute to cough hypersensitivity and excessive coughing in different patient populations and across the lifespan is advancing and has contributed to the development of new therapies for chronic cough in adults. Owing to differences in the pathology, the organs involved and individual patient factors, treatment of chronic cough is progressing towards a personalized approach, and, in the future, novel ways to endotype patients with cough may prove valuable in management.

- 255 references

SUPPLEMENTARY INFO

Publication typesexpand

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4

Review

Aging Clin Exp Res

. 2022 Jul;34(7):1529-1550.

doi: 10.1007/s40520-022-02154-4. Epub 2022 Jun 6.

Chronic cough in adults: recommendations from an Italian intersociety consensus

Antonio De Vincentis [1], Fabio Baldi [2], Massimo Calderazzo [3], Umberto Caliceti [4], Gabriella Guarnieri [5], Francesco Lombardi [6], Francesco Paolo Lombardo [7], Stefania Maggi [8], Graziano Onder [9], Adriano Vaghi [10], Alessandro Zanasi [11], Raffaele Antonelli Incalzi [12], Associazione Italiana Pneumologi Ospedalieri (AIPO), Associazione Italiana Studio Tosse (AIST), Consiglio Nazionale delle Ricerche (CNR), Istituto Superiore Sanità (ISS), Società Italiana di Allergologia, Asma ed Immunologia Clinica (SIAAIC), Società Italiana di Geriatria e Gerontologia (SIGG), Società Italiana di Medicina Generale e delle Cure Primarie (SIMG), Società Italiana di Pneumologia (SIP)

Affiliations expand

- PMID: 35666453

- DOI: 10.1007/s40520-022-02154-4

Abstract

Background: Chronic cough (CC) is a burdensome health problem in adult and older people, with a major impact on quality of life. Its management is often troublesome, and many guidelines have been released. Notwithstanding, a proportion of cases still do not reach a definite diagnosis and resolutive treatment. A coordinated approach between different specialists would be highly recommended, but its implementation in clinical practice suffers from the lack of shared protocols and poor awareness of the problem. The present consensus document has been implemented to address these issues.

Aims: To develop evidence-based recommendations for the management of adults with CC.

Methods: A 12-member expert task force of general practitioners, geriatricians, pneumologists, allergologists, otorhynolaringologists and gastroenterologists was established to develop evidence-based recommendations for the diagnostic and therapeutic approach to subjects with CC. A modified Delphi approach was used to achieve consensus, and the US Preventive Services Task Force system was used to rate the strength of recommendations and the quality of evidence.

Results: A total of 56 recommendations were proposed, covering 28 topics and concerning definitions and epidemiology, pathogenesis and etiology, diagnostic and therapeutic approach along with the consideration of specific care settings.

Conclusion: These recommendations should ease the management of subjects with CC by coordinating the expertise of different specialists. By providing a convenient list of topics of interest, they might assist in identifying unmet needs and research priorities.

Keywords: Adult cough hypersensitivity syndrome; Chronic cough; Multidisciplinary care team; Refractory chronic cough; Unexplained chronic cough.

- 91 references

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

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5

Respir Med

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. 2022 Jul;198:106865.

doi: 10.1016/j.rmed.2022.106865. Epub 2022 May 7.

Depressive and anxiety symptoms in patients with COPD: A network analysis

Abebaw M Yohannes [1], Martino Belvederi Murri [2], Nicola A Hanania [3], Elizabeth A Regan [4], Anand Iyer [5], Surya P Bhatt [6], Victor Kim [7], Gregory L Kinney [8], Robert A Wise [9], Michelle N Eakin [9], Karin F Hoth [10], COPDGene Investigators

Affiliations expand

- PMID: 35576775

- DOI: 10.1016/j.rmed.2022.106865

Abstract

Background: Individuals with Chronic Obstructive Pulmonary Disease (COPD) often develop anxiety and depression, which worsen illness management and prognosis. Physical and psychological symptoms, contextual and illness-related factors display complex reciprocal interactions, which give rise to heterogeneous presentations. Examining the patterns of association between specific physical and psychological symptoms in patients with COPD may help to focus on the precision of the patient-centred care.

Research question: We used network analyses to examine the links between symptoms of COPD, depression and anxiety.

Methods: Data from 1587 individuals with COPD from the COPDGene study were included. We estimated a Bayesian Gaussian Graphical Model to highlight the unique associations between symptoms of COPD (assessed with the COPD Assessment Test), depression and anxiety (assessed with the Hospital Anxiety and Depression Scale (HADS), while examining the role of sociodemographic characteristics, lung function tests, and health status.

Results: Unique Variable Analysis reduced 14 HADS items to Tension/worry (chronic anxiety), Fear/panic (acute anxiety), Restlessness, Anhedonia, Sadness and Slowing. In network analyses, chest-tightness was related to acute anxiety, while cough and weakness were connected with core depressive symptoms (sadness and lack of pleasure). Chronic anxiety was linked with acute anxiety and depressive symptoms. Findings were confirmed accounting for the role of confounders, including lung function, sex, ethnicity and lifestyle factors. A simulation based on our model yielded distinct predictions about anxiety and depression in two participants with similar COPD severity, but different symptom profiles.

Conclusion: Network analyses highlighted specific associations between symptoms of COPD, depression and anxiety. Accounting for symptom-level interactions may help to promote personalized treatment approaches.

Keywords: Anxiety; COPD; Depression; Dyspnoea; Network analysis; Panic; Worries.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

FULL TEXT LINKS

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6

Review

Eur Respir Rev

. 2022 May 4;31(164):210196.

doi: 10.1183/16000617.0196-2021. Print 2022 Jun 30.

The impact of long-acting muscarinic antagonists on mucus hypersecretion and cough in chronic obstructive pulmonary disease: a systematic review

Luigino Calzetta [1], Beatrice Ludovica Ritondo [2], Maria Cristina Zappa [3], Gian Marco Manzetti [2], Andrea Perduno [2], Janis Shute [4], Paola Rogliani [2]

Affiliations expand

- PMID: 35508331

- DOI: 10.1183/16000617.0196-2021

Free article

Abstract

Patients suffering from chronic obstructive pulmonary disease (COPD) clinically manifest airway mucus hypersecretion as sputum expectoration and cough. Evidence accumulated in the past decade has shown that the cholinergic system not only regulates airway smooth muscle contraction but also the activity of inflammatory and airway epithelial cells, including goblet cells, and submucosal gland activity. Long-acting muscarinic antagonists (LAMAs) with the most favourable M_3/M_2 muscarinic acetylcholine (ACh) receptors residency properties are not only excellent bronchodilators but potentially also mucus-modifying agents, able to positively impact on mucus hypersecretion and cough. The aim of this systematic review was to investigate the impact of LAMAs on mucus hypersecretion and cough in COPD patients. The evidence confirmed that LAMAs, mainly tiotropium and aclidinium, improved sputum production and cough in moderate to severe COPD. Thus, LAMAs not only antagonise the ACh-induced bronchoconstriction of the airways but also appear to limit the production of mucus secreted in response to ACh by airway goblet cells and/or submucosal glands. Further clinical studies are necessary to evaluate the impact of LAMAs exclusively on sputum symptoms and cough as primary end-points and to investigate whether LAMAs have a modulatory action on the rheological properties of mucus.

Conflict of interest statement

Conflict of interest: L. Calzetta reports grants and personal fees from Boehringer Ingelheim, grants and personal fees from Novartis, non-financial support from AstraZeneca, grants from Chiesi Farmaceutici, grants from Almirall, personal fees from ABC Farmaceutici, personal fees from Edmond Pharma, grants and personal fees from Zambon, personal fees from Verona Pharma, and personal fees from Ockham Biotech. Conflict of interest: B.L. Ritondo declares no conflict of interest. Conflict of interest: M.C. Zappa declares no conflict of interest. Conflict of interest: G.M. Manzetti. declares no conflict of interest. Conflict of interest: A. Perduno declares no conflict of interest. Conflict of interest: J. Shute is the Scientific Director of Ockham

Biotech Ltd. Conflict of interest: P. Rogliani reports grants and personal fees from Boehringer Ingelheim, grants and personal fees from Novartis, personal fees from AstraZeneca, grants and personal fees from Chiesi Farmaceutici, grants and personal fees from Almirall, grants from Zambon, personal fees from Biofutura, personal fees from GlaxoSmithKline, personal fees from Menarini, and personal fees from Mundipharma.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

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7

Review

Expert Opin Ther Pat

. 2022 Jul;32(7):769-790.

doi: 10.1080/13543776.2022.2069010. Epub 2022 May 11.

P2X receptor antagonists and their potential as therapeutics: a patent review (2010-2021)

Chianna Dane [1], Leanne Stokes [2], William T Jorgensen [1]

Affiliations expand

- PMID: 35443137

- DOI: 10.1080/13543776.2022.2069010

Abstract

Introduction: Purinergic receptors play a critical role in neurotransmission, and modulation of complex physiological functions and thus have implications in numerous disease states. The past decade has seen substantial progress in the design of novel chemical compounds that act on the P2X class of receptors and warrants an updated review of this field.

Areas covered: This review provides a summary of the patent literature describing the discovery and clinical uses of P2X receptor antagonists published between 2010 and September 2021. The reader will gain information on structural claims, representative structures, and biological data of recently reported P2X antagonists.

Expert opinion: Despite continual advancement in both crystallography and chemical biology strengthening our understanding of purinergic signalling, there remains an absence of clinically approved chemotypes. A testament to both the therapeutic potential and academic perseverance in purinergic research is the multitude of research initiatives that maintain active P2X receptor programs that have spanned decades. Very recently, the FDA declined Merck Pharmaceuticals application for Gefapixant, a P2X3 selective inhibitor as a treatment for chronic cough, requesting additional data. This unfortunate setback will ultimately be insignificant considering the long history of P2X investigation and the preclinical and clinical development that will undoubtedly occur over the next decade.

Keywords: Drug discovery; P2X antagonists; inhibitors; purinergic; therapeutic applications.

Eur Respir J

. 2022 Jun 30;59(6):2101733.

doi: 10.1183/13993003.01733-2021. Print 2022 Jun.

Urinary metabotype of severe asthma evidences decreased carnitine metabolism independent of oral corticosteroid treatment in the U-BIOPRED study

Stacey N Reinke [1 2 3], Shama Naz [1 3], Romanas Chaleckis [1 4], Hector Gallart-Ayala [1], Johan Kolmert [1 5], Nazanin Z Kermani [6], Angelica Tiotiu [6 7], David I Broadhurst [2], Anders Lundqvist [8], Henric Olsson [9], Marika Ström [10 11], Åsa M Wheelock [10 11], Cristina Gómez [1 5], Magnus Ericsson [12], Ana R Sousa [13], John H Riley [13], Stewart Bates [13], James Scholfield [14], Matthew Loza [15], Frédéric Baribaud [15], Per S Bakke [16], Massimo Caruso [17], Pascal Chanez [18], Stephen J Fowler [19], Thomas Geiser [20], Peter Howarth [14], Ildikó Horváth [21], Norbert Krug [22], Paolo Montuschi [23], Annelie Behndig [24], Florian Singer [25], Jacek Musial [26], Dominick E Shaw [27], Barbro Dahlén [11], Sile Hu [28], Jessica Lasky-Su [29], Peter J Sterk [30], Kian Fan Chung [6], Ratko Djukanovic [14], Sven-Erik Dahlén [5 11], Ian M Adcock [6], Craig E Wheelock [31 4 11], U-BIOPRED Study Group

Affiliations expand

- PMID: 34824054

- PMCID: PMC9245194

- DOI: 10.1183/13993003.01733-2021

Free PMC article

Abstract

Introduction: Asthma is a heterogeneous disease with poorly defined phenotypes. Patients with severe asthma often receive multiple treatments including oral corticosteroids (OCS). Treatment may modify the observed metabotype, rendering it challenging to investigate underlying disease mechanisms. Here, we aimed to identify dysregulated metabolic processes in relation to asthma severity and medication.

Methods: Baseline urine was collected prospectively from healthy participants (n=100), patients with mild-to-moderate asthma (n=87) and patients with severe asthma (n=418) in the cross-sectional U-BIOPRED cohort; 12-18-month longitudinal samples were collected from patients with severe asthma (n=305). Metabolomics data were acquired using high-resolution mass spectrometry and analysed using univariate and multivariate methods.

Results: A total of 90 metabolites were identified, with 40 significantly altered ($p<0.05$, false discovery rate <0.05) in severe asthma and 23 by OCS use. Multivariate modelling showed that observed metabotypes in healthy participants and patients with mild-to-moderate asthma differed significantly from those in patients with severe asthma ($p=2.6\times10^{-20}$), OCS-treated asthmatic patients differed significantly from non-treated patients ($p=9.5\times10^{-4}$), and longitudinal metabotypes demonstrated temporal stability. Carnitine levels evidenced the strongest OCS-independent decrease in severe asthma. Reduced carnitine levels were associated with mitochondrial dysfunction *via* decreases in pathway enrichment scores of fatty acid metabolism and reduced expression of the carnitine transporter SLC22A5 in sputum and bronchial brushings.

Conclusions: This is the first large-scale study to delineate disease- and OCS-associated metabolic differences in asthma. The widespread associations with different therapies upon the observed metabotypes demonstrate the need to

evaluate potential modulating effects on a treatment- and metabolite-specific basis. Altered carnitine metabolism is a potentially actionable therapeutic target that is independent of OCS treatment, highlighting the role of mitochondrial dysfunction in severe asthma.

Conflict of interest statement

Conflict of interest: S.N. Reinke reports grants from Canadian Institutes of Health Research, during the conduct of the study. Conflict of interest: S. Naz has nothing to disclose. Conflict of interest: R. Chaleckis has nothing to disclose. Conflict of interest: H. Gallart-Ayala has nothing to disclose. Conflict of interest: J. Kolmert reports personal fees for consultancy from Gesynta Pharma AB, outside the submitted work. Conflict of interest: N.Z. Kermani has nothing to disclose. Conflict of interest: A. Tiotiu has nothing to disclose. Conflict of interest: D.I. Broadhurst has nothing to disclose. Conflict of interest: A. Lundqvist has nothing to disclose. Conflict of interest: H. Olsson is an employee and shareholder of AstraZeneca. Conflict of interest: M. Ström has nothing to disclose. Conflict of interest: Å.M. Wheelock has nothing to disclose. Conflict of interest: C. Gómez has nothing to disclose. Conflict of interest: M. Ericsson has nothing to disclose. Conflict of interest: A.R. Sousa has nothing to disclose. Conflict of interest: J.H. Riley works for and own shares in GlaxoSmithKline. Conflict of interest: S. Bates is an employee of Johnson & Johnson and has previously worked for and holds stock in GlaxoSmithKline. Conflict of interest: J. Scholfield reports grants from Innovative Medicines Initiative, during the conduct of the study; and is director and employee of TopMD Precision Medicine Ltd. Conflict of interest: M. Loza is an employee of and owns stock in Johnson & Johnson. Conflict of interest: F. Baribaud is a shareholder of Johnson & Johnson and a current employee of Bristol Myers Squibb. Conflict of interest: P.S. Bakke reports personal fees for advisory board work and lectures from AstraZeneca, and personal fees for lectures from Novartis and Boehringer Ingelheim, outside the submitted work. Conflict of interest: M. Caruso has nothing to disclose. Conflict of interest: P. Chanez reports grants and personal fees from AstraZeneca, ALK, Boehringer Ingelheim, Chiesi, Sanofi-Aventis, Novartis and GlaxoSmithKline, outside the submitted work. Conflict of interest: S.J. Fowler reports personal fees from AstraZeneca, Novartis, TEVA and Chiesi, outside the submitted work. Conflict of interest: T. Geiser has nothing to disclose.

Conflict of interest: P. Howarth has nothing to disclose. Conflict of interest: I. Horvath has nothing to disclose. Conflict of interest: N. Krug has nothing to disclose. Conflict of interest: P. Montuschi has nothing to disclose. Conflict of interest: A. Behndig has nothing to disclose. Conflict of interest: F. Singer reports personal fees from Vertex Pharmaceuticals (CH) and Novartis, outside the submitted work. Conflict of interest: J. Musial has nothing to disclose. Conflict of interest: D.E. Shaw has nothing to disclose. Conflict of interest: B. Dahlén reports personal fees for advisory board work and lectures from AstraZeneca, TEVA and Sanofi, and grants from Novartis and GlaxoSmithKline, outside the submitted work. Conflict of interest: S. Hu has nothing to disclose. Conflict of interest: J. Lasky-Su has nothing to disclose. Conflict of interest: P.J. Sterk reports a public private grant from the Innovative Medicines Initiative (IMI) covered by the EU and EFPIA, during the conduct of the study. Conflict of interest: K.F. Chung has received honoraria for participating in advisory board meetings of GlaxoSmithKline, AstraZeneca, Roche, Novartis, Merck, Nocion and Shionogi regarding treatments for asthma, COPD and chronic cough and has also been remunerated for speaking engagements. Conflict of interest: R. Djukanovic reports receiving fees for lectures at symposia organised by Novartis, AstraZeneca and TEVA, consultation for TEVA and Novartis as member of advisory boards, and participation in a scientific discussion about asthma organised by GlaxoSmithKline; and is a co-founder and current consultant, and has shares in Synairgen, a University of Southampton spin out company. Conflict of interest: S-E. Dahlén reports personal fees for consultancy from AstraZeneca, Cayman Chemical, GlaxoSmithKline, Novartis, Merck, Regeneron, Sanofi and TEVA, outside the submitted work. Conflict of interest: I.M. Adcock has nothing to disclose. Conflict of interest: C.E. Wheelock has nothing to disclose.

- 55 references
- 6 figures