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COPD

1
Sci Rep

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. 2022 Oct 15;12(1):17313.

doi: 10.1038/s41598-022-20176-w.

Identifying pre-existing conditions and multimorbidity patterns associated with in-hospital mortality in patients with COVID-19

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Affiliations expand

- PMID: 36243878

- DOI: 10.1038/s41598-022-20176-w

Abstract

We investigated the association between a wide range of comorbidities and COVID-19 in-hospital mortality and assessed the influence of multi morbidity on the risk of COVID-19-related death using a large, regional cohort of 6036 hospitalized patients. This retrospective cohort study was conducted using Patient Administration System Admissions and Discharges data. The International Classification of Diseases 10th edition (ICD-10) diagnosis codes were used to identify common comorbidities and the outcome measure. Individuals with lymphoma (odds ratio [OR], 2.78;95% CI,1.64-4.74), metastatic cancer (OR, 2.17; 95% CI,1.25-3.77), solid tumour without metastasis (OR, 1.67; 95% CI,1.16-2.41), liver disease (OR: 2.50, 95% CI,1.53-4.07), congestive heart failure (OR, 1.69; 95% CI,1.32-2.15), chronic obstructive pulmonary disease (OR, 1.43; 95% CI,1.18-1.72), obesity (OR, 5.28; 95% CI,2.92-9.52), renal disease (OR, 1.81; 95% CI,1.51-2.19), and dementia (OR, 1.44; 95% CI,1.17-1.76) were at increased risk of COVID-19 mortality. Asthma was associated with a lower risk of death compared to non-asthma controls (OR, 0.60; 95% CI,0.42-0.86). Individuals with two (OR, 1.79; 95% CI, 1.47-2.20; P < 0.001), and three or more comorbidities (OR, 1.80; 95% CI, 1.43-2.27; P < 0.001) were at increasingly higher risk of death when compared to those with no underlying conditions. Furthermore, multi morbidity patterns were analysed by identifying clusters of conditions in hospitalised COVID-19 patients using k-mode clustering, an unsupervised machine learning technique. Six patient clusters were identified, with recognisable co-occurrences of COVID-19 with different combinations of diseases, namely, cardiovascular (100%) and renal (15.6%) diseases in patient Cluster 1; mental and neurological disorders (100%) with metabolic and endocrine diseases (19.3%) in patient Cluster 2; respiratory (100%) and cardiovascular (15.0%) diseases in patient Cluster 3, cancer (5.9%) with genitourinary (9.0%) as well as metabolic and endocrine diseases (9.6%) in patient Cluster 4; metabolic and endocrine diseases (100%) and cardiovascular diseases (69.1%) in patient Cluster 5; mental and neurological disorders (100%) with cardiovascular diseases (100%) in patient Cluster 6. The highest mortality of 29.4% was reported in Cluster 6.

- 72 references

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. 2022 Oct 15.

doi: 10.1007/s43678-022-00373-2. Online ahead of print.

Association between antibiotics and rehospitalization in patients with acute exacerbations of chronic obstructive pulmonary disease discharged from the emergency department

Bo Zheng[1,2], Monica Taljaard[3,4], Shawn D Aaron[4,5], Krishan Yadav[4,6], Brian H Rowe[7,8], Chrystal Chan[9], Ian G Stiell[3,4,6]

Affiliations expand

- PMID: 36242731

- DOI: 10.1007/s43678-022-00373-2

Abstract

in English, French

Background: Patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD) are frequently discharged from the emergency department (ED) and treated with antibiotics. The role of antibiotics in the outpatient management of AECOPD is controversial and has never been studied in the ED setting.

Methods: We conducted a secondary analysis of prospectively collected data from the validation study of the Ottawa COPD Risk Scale. We included adult patients with AECOPD who were discharged from six tertiary care EDs in Canada over a two-year period and assessed rates of rehospitalization within 14 days of ED discharge. To examine the association between antibiotic treatment and rehospitalization, we performed multivariable logistic regression and propensity score-matched analyses.

Results: A total of 774 patients were included in the analysis. The mean age was 69.4 years, 388 patients (50.1%) were female, and 451 patients (58.3%) were discharged with antibiotics. Twenty-nine (6.4%) and 36 (11.1%) patients returned to hospital with admission in the antibiotic and no antibiotic groups, respectively (unadjusted OR 0.55; 95% CI 0.33-0.92); adjustment for prespecified baseline characteristics using logistic regression yielded

OR 0.65; 95% CI 0.38-1.08. In the propensity score-matched analysis comprising of 197 matched pairs, 15 (7.6%) and 19 patients (9.6%) in the antibiotic and no antibiotic groups returned with admission, respectively (OR 0.69; 95% CI 0.29-1.62).

Conclusion: For patients with AECOPD discharged from the ED, we did not find an association between outpatient treatment with antibiotics and lower rates of rehospitalization after accounting for differences in baseline patient characteristics. However, the small sample size and low observed rate of the primary outcome created substantial risk of Type II error. Until further evidence is available, clinicians should continue prescribing antibiotics for patients with AECOPD based on clinical judgement and current practice guidelines.

Keywords: Antibiotics; COPD; Emergency department; Exacerbation.

- 23 references

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BMJ Support Palliat Care

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. 2022 Oct 13;spcare-2022-003905.

doi: 10.1136/spcare-2022-003905. Online ahead of print.

Non-invasive advanced respiratory support in end-of-life care and symptom management: systematic review

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Affiliations expand

- PMID: 36229167

- DOI: 10.1136/spcare-2022-003905

Abstract

Objectives: To narrate the canon of knowledge around symptom control at end of life for patients using, or having recently used, non-invasive advanced respiratory support (NARS) at end of life for respiratory failure.

Methods: A systematic review forming a narrative synthesis from a wide range of sample papers from Medline, Embase, CINAHL, Emcare, Cochrane and OpenGrey databases. A secondary search of grey literature was also performed with hand searching reference lists and author citations. The review was undertaken using the ENTREQ checklist for quality.

Results: In total, 22 studies were included in the synthesis and four themes were generated: NARS as a buoy (NARS can represent hope and relief from the symptoms of respiratory failure), NARS as an anchor (NARS brings significant treatment burden), Impact on Staff (uncertainty over the balance of benefit and burden as well as complex patient care drives distress among staff providing care) and the Process of Withdrawal (withdrawal of therapy felt to be futile exists as discrete event in patient care but is otherwise poorly defined).

Conclusion: NARS represents a complex interplay of hope, symptom control, unnaturally prolonged death and treatment burden. The literature captures the breadth of these issues, but further, detailed, research is required in almost every aspect of practice around end-of-life care and NARS-especially how to manage symptoms at the end of life.

Keywords: COVID-19; chronic obstructive pulmonary disease; dyspnoea; end of life care; respiratory conditions.

Conflict of interest statement

Competing interests: None declared.

Review

Postgrad Med

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Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommendations: strengths and concerns for future needs

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Affiliations expand

- PMID: 36226501

- DOI: 10.1080/00325481.2022.2135893

Abstract

Chronic Obstructive Pulmonary Disease (COPD) is already the third leading cause of death worldwide and simultaneously a major cause of morbidity and mortality. Global initiative for Chronic Obstructive Lung Disease (also known as GOLD) committee, has been created in 1997 to increase the awareness regarding the burden of COPD. GOLD recommendations have been contributing to diagnosis, management and therapy of COPD since 2001.

Through these years, by reviewing published articles, GOLD aimed to provide state-of-the-art information not only for pulmonologists, but also for non-respiratory physicians, and to encourage research on COPD. From 2011, GOLD annual reports have changed the way of COPD evaluation from based entirely on spirometric parameters to more clinical indices, such as the assessment of symptoms and dyspnea alongside with exacerbations. Moreover, according to recent developments in pathophysiology of COPD, there is a trend in identifying new pre-clinical stages, contributing to prevention and early COPD treatment. In the field of therapeutic algorithms, changes turn to a more personalized approach. However, it is not clear in what extent this personalized disease management would be feasible and the real challenge for current recommendations is to include more patient characteristics such as co-morbidities and multidimensional scores in disease evaluation.

Keywords: COPD; GOLD; co-morbidities; personalized medicine.

J Cardiopulm Rehabil Prev

. 2022 Oct 10.

doi: 10.1097/HCR.0000000000000726. Online ahead of print.

Chronic Obstructive Pulmonary Disease Patients With High Peripheral Blood Eosinophil Counts Have Better

Predicted Improvement in 6MWD After Rehabilitation: A PRELIMINARY STUDY

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Affiliations expand

- PMID: 36223406

- DOI: 10.1097/HCR.0000000000000726

Abstract

Purpose: The objective of this investigation was to determine whether chronic obstructive pulmonary disease (COPD) patients with high blood eosinophil (EOS) counts had better improvement in 6-min walk test (6MWT) after pulmonary rehabilitation (PR).

Methods: Fifty COPD patients were randomly assigned to either the rehabilitation group (RG) or the control group (CG). Patients in the RG (8 wk PR + routine medication) and the CG (routine medication) were followed for 32 wk. According to the blood EOS level, the RG was divided into an EOS ≥ 200 cells/μL group and EOS < 200 cells/μL group. The 6MWT distance, Borg Scale, and COPD Assessment Test (CAT) were evaluated before intervention and 8 wk and 32 wk later.

Results: After the 8-wk intervention, 37 patients (19 RG/18 CG) completed the study. At 8-wk and 32-wk follow-up from baseline, a statistically significant difference was found between these two groups in the 6MWT, Borg Scale, and CAT. Compared with baseline, the 6MWT in the RG increased 49.1 ± 40.2 m (95% CI, 29.7-68.5, P < .001) at 8 wk and 60.8 ± 42.1 m (95% CI, 40.5-81.6, P < .001) at 32 wk. In addition, the improvement of 6MWT in the EOS ≥ 200 cells/μL RG group was higher than that in the EOS < 200 cells/μL group (40.1 ± 17.6 m, 95% CI, 36.8-43.4; P = .036) at 32-wk follow-up from baseline.

Conclusion: An 8-wk PR can improve the exercise capacity of COPD patients, and the benefits persistent for 24 wk. The improvement in the 6MWT was more significant in COPD patients with a high blood EOS count.

Conflict of interest statement

The authors declare no conflicts of interest.

- 41 references

FULL TEXT LINKS

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Adv Ther

.

. 2022 Oct 11.

doi: 10.1007/s12325-022-02331-x. Online ahead of print.

The Prescribing Practice for COPD: Relationship to Circadian Rhythm, Disease Severity, and Clinical Phenotype in the STORICO Observational Study

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Affiliations expand

- PMID: 36219388

- DOI: 10.1007/s12325-022-02331-x

Abstract

Introduction: While selected clinical and laboratory findings are taken into account to find the best therapeutic strategies for chronic obstructive pulmonary disease (COPD), it is unknown whether the circadian rhythm of respiratory symptoms, a distinctive feature of COPD, affects the prescription pattern of pharmacological therapy. The main aim of this study was to verify whether the circadian rhythm of symptoms correlates with bronchodilating therapy prescribed to COPD patients as per clinical practice. A secondary objective was to assess the relationship between Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage and circadian rhythm of symptoms and health status.

Methods: Five hundred sixty-six COPD patients were enrolled in the Italian multicenter STORICO study. Patients underwent a multidimensional assessment, and correlates of prescribed therapy were assessed through a multivariate multilevel model.

Results: As expected, patients in GOLD D stage were more likely to receive triple inhaled therapy than GOLD A-C patients, but the circadian rhythm of symptoms, assessed by the nighttime, morning, and daytime symptoms of the COPD questionnaire, was unrelated to the prescription pattern. The multivariate model showed that emphysematous (EM) patients had a 50% increased risk compared with patients affected by chronic bronchitis (CB) of being prescribed long-acting β2-agonists (LABA)/long-acting muscarinic antagonist (LAMA) fixed-dose combination (FDC) instead of triple therapy [relative risk (RR) $_{\text{EM versus CB}}$ 1.50, 95% CI 1.11, 2.03]. Symptoms, mainly in the early morning and daytime, were highly prevalent, even in GOLD B stage (76%).

Conclusion: Even if we cannot infer about causality of the symptoms-therapy relationship, based on the structured recording of circadian symptoms clearly shows that symptoms are poorly controlled as the circadian rhythm of symptoms does not correlate with the prescription pattern, and many patients are symptomatic both at daytime and by nighttime. Thus, therapy should be better tailored to the individual needs, with special attention to control nocturnal symptoms.

Trial registration: ClinicalTrials.gov identifier, NCT03105999.

Keywords: COPD; Circadian rhythm; Clinical phenotype; Observational; Prescribed therapies; Real-world.

- 15 references

SUPPLEMENTARY INFO

Associated dataexpand

FULL TEXT LINKS

Sci Total Environ

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doi: 10.1016/j.scitotenv.2022.156969. Epub 2022 Jun 25.

Climate-mediated air pollution associated with COPD severity

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Affiliations expand

- PMID: 35760178

- DOI: 10.1016/j.scitotenv.2022.156969

Abstract

Air pollution has been reported to be associated with chronic obstructive pulmonary disease (COPD). Our study aim was to examine the mediating effects of air pollution on climate-associated health outcomes of COPD patients. A cross-sectional study of 117 COPD patients was conducted in a hospital in Taiwan. We measured the lung function, 6-min walking distance, oxygen desaturation, white blood cell count, and percent emphysema (low attenuation area, LAA) and linked these to 0-1-, 0-3-, and 0-5-year lags of individual-level exposure to relative humidity (RH), temperature, and air pollution. Linear regression models were conducted to examine associations of temperature, RH, and air pollution with severity of health outcomes. A mediation analysis was conducted to examine

the mediating effects of air pollution on the associations of RH and temperature with health outcomes. We observed that a 1 % increase in the RH was associated with increases in forced expiratory volume in 1 s (FEV_1), eosinophils, and lymphocytes, and a decrease in the total-lobe LAA. A 1 °C increase in temperature was associated with decreases in oxygen desaturation, and right-, left-, and upper-lobe LAA values. Also, a 1 μg/m^3 increase in $PM_{2.5}$ was associated with a decrease in the FEV_1 and an increase in oxygen desaturation. A 1 μg/m^3 increases in PM_{10} and $PM_{2.5}$ was associated with increases in the total-, right-, left, upper-, and lower-lobe ($PM_{2.5}$ only) LAA. A one part per billion increase in NO_2 was associated with a decrease in the FEV_1 and an increase in the upper-lobe LAA. Next, we found that NO_2 fully mediated the association between RH and FEV_1. We found $PM_{2.5}$ fully mediated associations of temperature with oxygen saturation and total-, right-, left-, and upper-lobe LAA. In conclusion, climate-mediated air pollution increased the risk of decreasing FEV_1 and oxygen saturation and increasing emphysema severity among COPD patients. Climate change-related air pollution is an important public health issue, especially with regards to respiratory disease.

Keywords: Air pollution; Climate change; Lung function; Oxygen desaturation; Relative humidity.

Conflict of interest statement

Declaration of competing interest The authors declare that they have no conflicts of interest.

. 2022 Oct 15;206(8):1044-1047.

doi: 10.1164/rccm.202112-2807LE.

Care Fragmentation Is Associated with Increased Chronic Obstructive Pulmonary Disease Exacerbations in a U.S. Urban Care Setting

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Affiliations expand

- PMID: 35731975

- DOI: 10.1164/rccm.202112-2807LE

No abstract available

SUPPLEMENTARY INFO

Publication types, Grant supportexpand

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ASTHMA

1
Pulm Pharmacol Ther

. 2022 Oct 12;102171.

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Comparative clinical pharmacology of mometasone furoate, fluticasone propionate and fluticasone furoate

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Affiliations expand

- PMID: 36243386

- DOI: 10.1016/j.pupt.2022.102171

Abstract

Aims: To investigate the pharmacokinetics and effects on the hypothalamic-pituitary-adrenal (HPA) axis of mometasone furoate (MF), fluticasone propionate (FP) and fluticasone furoate (FF).

Methods: Study 1: Fourteen healthy participants received inhaled and intravenous MF (inhaled dose via Twisthaler) and FP (inhaled dose via Diskus), both given at 400 µg, using a randomised, single-dose, four-way crossover design. Study 2: Twenty-seven participants with mild to moderate asthma, who discontinued their corticosteroid medication for 5 days to obtain a baseline 24 h serum cortisol, received inhaled MF Twisthaler and FP Diskus, both given at 400 µg twice daily (BID), using a randomised, 14-day repeat dose, two-way crossover design. Study 3: Forty-four healthy participants were randomised to a double-blind, placebo-controlled, five-period crossover study where the following treatments were administered via the inhaled route for 7 days: FP Diskus (250, 500, 1000 µg BID), FF Diskus (100, 200, 400, 800, 1600 µg once daily [QD]) or placebo Diskus. In each study, 24-h serial blood samples were collected and assayed to assess concentrations of MF, 6β-hydroxy mometasone, mometasone, FP, FF and cortisol. Pharmacokinetic and serum cortisol parameters were estimated as geometric means and 95% confidence intervals (CI).

Results: Study 1: For intravenous MF and FP, respectively: absolute bioavailability was 11.4% (95% CI: 7.5, 17.6) and 7.8% (6.3, 9.6); plasma clearance was 47 L/h (41, 52) and 60 L/h (52, 69); half-life was 7.4 h (6.9, 8.0) and 7.2 h (6.5, 8.0); and volume of distribution was 499 L (439, 567) and 623 L (557, 698). Inhalation of single dose MF or FP did not significantly affect serum cortisol (<10% reduction from baseline), whereas intravenous administration of MF or FP each changed serum cortisol by approximately -50% from baseline. Study 2: For MF and FP, respectively: area under the curve up to the last measurable concentration on Day 1 was 421 pg. h/mL (270, 659) and 248 pg.h/mL (154, 400), and on Day 14 was 1092 pg.h/mL (939, 1269) and 591 pg.h/mL (501, 696); absolute

bioavailability was 12.8% (11.2, 14.2) and 8.9% (7.7, 10.2). On Day 14, 24-h serum cortisol change from baseline was -35% (-44%, -26%) and -18% (-28%, -5%) for MF and FP, respectively; the reduction was significantly greater for MF than FP (ratio for geometric adjusted mean serum cortisol concentration: 1.28 [1.04, 1.56]). Low plasma concentrations of 6β-hydroxy mometasone were detected after intravenous dosing (Study 1) and after multiple inhaled dosing (Study 2); mometasone was not detected in any samples. Study 3: Inhaled FP and FF had similar systemic bioavailability estimates (12.0% [11.0, 13.2] and 15.0% [12.0, 17.3], respectively), but a differential effect on the HPA axis which was in agreement with the known 1.7-fold higher glucocorticoid receptor-binding affinity of FF versus FP. However, for FP 250 µg BID and FF 100, 200 and 400 µg QD, reduction in serum cortisol was not significantly different from placebo. For higher doses, FP 500 and 1000 µg BID, and FF 800 and 1600 µg QD, changes in serum cortisol concentration relative to placebo were -30%, -70%, -41% and -90%, respectively. Repeat inhaled dosing of FP 1000 µg/day (within the therapeutic dose range) resulted in comparable cortisol suppression to MF in the therapeutic range (30% reduction); whereas for FF this occurred at more than 3-fold above the therapeutic dose range (644 µg/day).

Conclusions: Single inhaled and intravenous doses of MF and FP (400 µg) resulted in similar bioavailability and reductions in serum cortisol. Repeat dosing of inhaled MF and FP in the therapeutic range (800 µg/day) resulted in greater systemic exposure for MF, and a 35% reduction in serum cortisol that was 2-fold greater than for FP. The higher glucocorticoid receptor-binding affinity and bioavailability, lower clearance and the presence of active metabolites may contribute to the greater systemic exposure and effect on cortisol for MF. Repeat dosing of inhaled FP and FF resulted in similar systemic bioavailability but differed in terms of the dose required for comparable cortisol suppression to MF in the therapeutic range. Unlike FP and FF, MF has active metabolites that may contribute to its systemic effects, while device/formulation performance differences also exist between MF-containing products.

Keywords: Bioavailability; Cortisol suppression; Fluticasone furoate; Fluticasone propionate; Mometasone furoate; Pharmacokinetics.

Conflict of interest statement

Declaration of competing interest PDY, AD, RM and ARS are employees of and own stocks/shares in GSK.

2

Sci Total Environ

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Association between cold weather, influenza infection, and asthma exacerbation in adults in Hong Kong

Xi Xiong[1], Yuchen Wei[2], Holly Ching Yu Lam[3], Carlos King Ho Wong[4], Steven Yuk Fai Lau[5], Shi Zhao[6], Jinjun Ran[7], Conglu Li[5], Xiaoting Jiang[5], Qianying Yue[5], Wei Cheng[8], Huwen Wang[5], Yawen Wang[5], Ka Chun Chong[9]

Affiliations expand

- PMID: 36240934

- DOI: 10.1016/j.scitotenv.2022.159362

Abstract

Despite a conspicuous exacerbation of asthma among patients hospitalized due to influenza infection, no study has been attempted previously to elucidate the relationship between environmental factors, influenza activity, and asthma simultaneously in adults. In this study, we examined this relationship in adults using population-based hospitalization records over 22 years. Daily numbers of hospitalizations due to asthma in adults of 41 public hospitals in Hong Kong during 1998-2019 were obtained. The data were matched with meteorological records and air pollutant concentrations. We used type-specific and all-type influenza-like illness plus (ILI+) rates as proxies for seasonal influenza activity. Quasi-Poisson generalized additive models together with distributed-lag non-linear models were used to examine the association. A total of 212,075 hospitalization episodes due to asthma were reported. The cumulative adjusted relative risk (ARR) of asthma hospitalizations reached 1.15 (95 % confidence interval [CI], 1.12-1.18) when the ILI+ total rate increased from zero to 20.01 per 1000 consultations. Compared with the median temperature, a significantly increased risk of asthma hospitalization (cumulative ARR = 1.10, 95 % CI, 1.05-1.15) was observed at the fifth percentile of temperature (i.e., 14.6 °C).

Of the air pollutants, oxidant gas was significantly associated with asthma, but only at its extreme level of concentrations. In conclusion, cold conditions and influenza activities are risk factors to asthma exacerbation in adult population. Influenza-related asthma exacerbation that appeared to be more common in the warm and hot season, is likely to be attributable to influenza A/H3N2. The heavy influence of both determinants on asthma activity implies that climate change may complicate the asthma burden.

Keywords: Influenza; Pollution; Statistical model; Temperature; Weather.

Int J STD AIDS

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The use of dupilumab in patients with HIV

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Affiliations expand

- PMID: 36240731

- DOI: 10.1177/09564624221129406

Abstract

Background: The goal of this study was to complete the first Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) based systematic review of dupilumab use in patients living with human immunodeficiency virus (HIV).

Methods: A systematic literature review was performed using PubMed, Google Scholar, Ovid MEDLINE, and Science Direct databases as well as an internal review using University of Virginia's electronic medical record system. All reports of dupilumab use in patients with confirmed HIV were included.

Results: 14 published cases comprising 23 patients were identified and included in the review. Additionally, four unpublished cases from our own institution were included for a final cohort of 27 patients. A total of 25 patients (96%) were observed to have a clinical response, defined as improvement or complete resolution of their cutaneous or asthmatic symptoms. In 100% of patients, viral load improved or did not change, and in 80% of patients, CD4 counts remained stable. Side effects occurred in 48% of patients but were self-limited.

Discussion and conclusions: All reported cases indicate that dupilumab is safe in patients with HIV with stable CD4 counts and low viral loads. Most patients had significant improvement within 2 months of treatment with mild side effects.

Keywords: General dermatology; HIV; TH2 phenotype; asthma; atopic dermatitis; dupilumab; human immunodeficiency virus; medical dermatology; prurigo nodularis.

Review

Lung

. 2022 Oct 14.

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Impact of Biologic Therapy on the Small Airways Asthma Phenotype

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Affiliations expand

- PMID: 36239786

- DOI: 10.1007/s00408-022-00579-2

Abstract

The small airways dysfunction (SAD) asthma phenotype is characterised by narrowing of airways < 2 mm in diameter between generations 8 and 23 of the bronchial tree. Recently, this has become particularly relevant as measurements of small airways using airway oscillometry for example, are strong determinants of asthma control and exacerbations in moderate-to-severe asthma. The small airways can be assessed using spirometry as forced expiratory flow rate between 25 and 75% of forced vital capacity (FEF_{25-75}) and has been deemed more accurate in detecting small airways dysfunction than forced expiratory volume in 1 s (FEV_1). Oscillometry as the heterogeneity in resistance between 5 and 20 Hz (R5-R20), low frequency reactance at 5 Hz (X5) or area under the reactance curve between 5 Hz and the resonant frequency can also be used to assess the small airways. The small airways can also be assessed using the multiple breath nitrogen washout (MBNW) test giving rise to values including functional residual capacity, lung clearance index and ventilation distribution heterogeneity in the conducting (Scond) and the acinar (Sacin) airways. The ATLANTIS group showed that the prevalence of small airways disease in asthma defined on FEF_{25-75}, oscillometry and MBNW all increased with progressive GINA asthma disease stages. As opposed to topical inhaler therapy that might not adequately penetrate the small airways, it is perhaps more intuitive that systemic anti-inflammatory therapy with biologics targeting downstream cytokines and upstream epithelial anti-alarmins may offer a promising solution to SAD. Here we therefore aim to appraise the available evidence for the effect of anti-IgE, anti-IL5 (Rα), anti-IL4Rα, anti-TSLP and anti-IL33 biologics on small airways disease in patients with severe asthma.

Keywords: Benralizumab; Dupilumab; FEF25–75; Itepekimab; Mepolizumab; Multiple breath nitrogen washout; Omalizumab; Oscillometry; Reslizumab; Severe asthma; Small airways; Tezepelumab.

- 53 references

J Asthma

. 2022 Oct 14;1-11.

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The Relationship Between General and Abdominal Obesity, Nutrition and Respiratory Functions in Adult Asthmatics

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Affiliations expand

- PMID: 36239386

- DOI: 10.1080/02770903.2022.2137038

Abstract

Objective: Although obesity is known to have adverse effects on asthma, it is not fully known whether general or abdominal obesity affects asthma symptoms more. In this study, the effects of diet and general/abdominal obesity on respiratory functions were evaluated.**Methods:** A total of 204 adult asthmatic individuals participated in the study. Anthropometric measurements, respiratory functions, asthma control test (ACT) scores, and 24-hour food consumption were recorded. The results were compared according to

body mass index (BMI), waist circumference (WC), and waist-hip ratio (WHR) classification.**Results:** FEV_1, FVC, MEF_{25-75}, MEF_{50}, and MEF_{25} decreased with the increase in BMI, WC, and WHR. FEV_1 showed a negative linear relationship with BMI, WC and WHR and these results were more significant in WC and WHR than BMI. Similarly, the ACT score also showed a negative correlation with BMI (r = -0.372; p = 0.023), WC (r = -0.402; p = 0.001) and WHR (r = -0.387; p = 0.011), and the results were more significant in WC and WHR than BMI. Individuals whose WC (OR: 2.170 CI (1.325-3.182)) and WHR (OR: 2.119 CI (1.246-3.338)) were at risk had higher odds of uncontrolled asthma than those with normal WC and WHR. Each 100-kcal increase in total energy consumption increased the odds of uncontrolled asthma (OR: 1.125 CI (1.086-2.217)) ($p < 0.05$).**Conclusions:** The effects of WC and WHR, which are indicators of abdominal obesity, on respiratory functions and ACT score were found to be higher than BMI. Obese individuals should be referred to diet clinics to improve their asthma symptoms.

Keywords: Asthma; central obesity; general obesity; nutrition.

Review

J Adv Nurs

. 2022 Oct 14.

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Youths with asthma and their experiences of self-management education: A systematic review of qualitative evidence

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Affiliations expand

- PMID: 36239214

- DOI: 10.1111/jan.15459

Abstract

Aims: To identify and synthesize the available evidence of youths with asthma and their experience of self-management education.

Design: Systematic literature review of qualitative studies with meta-synthesis of findings.

Data sources: We searched five databases, CINAHL Complete, Embase, MEDLINE (EBSCO) PsycINFO, ASSIA and the Global Index Medicus (formerly the WHOLIS). Initial search in September 2019 and updated in July 2020 and July 2022.

Review methods: The systematic review was conducted in accordance with the JBI methodology for systematic reviews of qualitative evidence. Qualitative data were extracted, meta-summarized and then meta-synthesized.

Results: Eighteen studies were identified for inclusion in this review and three themes were identified: The theory and practice gap, contemporary health-seeking preferences and the psychosocial impacts of living with asthma.

Conclusion: The needs of youths with asthma are specific and must be measurable against the change in asthma outcomes for this group. They have unmet self-management educational needs that stakeholders, involved in their care and support, should address. Education and practice policy should focus on youth-centric approaches. Through meaningful engagement with youths, stakeholders can identify their support needs, requirements and preferences to successfully underpin the theory and practice of self-management education.

Impact: This review synthesized evidence of youths with asthma and their experiences of self-management education, highlighting their specific self-management information needs. The findings highlight several implications for healthcare professionals in education, practice and research. This age profile is under-explored and further research into this population would work towards filling the theory and practice gap and highlighting the identified psychosocial issues faced by this group.

Keywords: asthma; education; nurse; qualitative research; self-management; systematic literature review; youth; adolescents.

- 44 references

SUPPLEMENTARY INFO

Publication typesexpand

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Allergy

. 2022 Oct 14.

doi: 10.1111/all.15553. Online ahead of print.

Specific IgE against the house dust mite allergens Der p 5, 20 and 21 influences the phenotype and severity of atopic diseases

Theresa Walsemann[1], Marisa Böttger[1], Stephan Traidl[2], Christian Schwager[1], Askin Gülsen[3], Sina Freimooser[2], Lennart Matthias Rösner[2,4], Thomas Werfel[2,4], Uta Jappe[1,3]

Affiliations expand

- PMID: 36239002

- DOI: 10.1111/all.15553

Abstract

Background: House dust mites (HDM) are among the most important sources for airborne allergens with high relevance for atopic diseases. Routine tests contain only 4 of 32

registered allergens of Dermatophagoides pteronyssinus. Clinical relevance and pathomechanistic properties of many allergens are not well understood.

Objective: The association of several HDM allergens with allergic rhinitis, allergic asthma and atopic dermatitis was investigated to identify allergens with biomarker potential and to transfer them into diagnostics.

Methods: Eight out of nine D. pteronyssinus allergens (nDer p 1, rDer p 2, rDer p 5, rDer p 7, rDer p 10, rDer p 13, rDer p 20, rDer p 21, rDer p 23) were recombinantly expressed and purified. Sensitization patterns of 384 HDM-allergic individuals exhibiting different clinical phenotypes were analyzed with a serum-saving multiplex-array.

Results: Sensitization to more than three mite allergens (sensitization count) was associated with allergic asthma and/or atopic dermatitis. Reactions to Der p 5 and Der p 21 were more frequent in allergic asthma compared to allergic rhinitis. Atopic dermatitis patients were more often sensitized to Der p 5, Der p 20 and Der p 21 among others. Der p 20-IgE >80 kU/l were associated with severe atopic dermatitis in 75% of patients.

Conclusion: This study demonstrates the clinical importance of the sensitization count and of certain allergens (Der p 5, Der p 20 and Der p 21) not available for routine diagnostics yet. Implementing them as well as the sensitization count in diagnostic measures will improve diagnosis and risk assessment of HDM-allergic patients.

Keywords: Allergens and epitopes; allergy diagnosis; asthma; atopic dermatitis; biomarkers.

Editorial

Clin Exp Allergy

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doi: 10.1111/cea.14242. Online ahead of print.

Anti-interleukin-4 or -13 agents for treating asthma

Anne Pacita Rosillo Boulton[1], Yitong Shen[1]

Affiliations expand

- PMID: 36229954

- DOI: 10.1111/cea.14242

No abstract available

- 9 references

SUPPLEMENTARY INFO

Publication typesexpand

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9

Syst Rev

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. 2022 Oct 13;11(1):216.

doi: 10.1186/s13643-022-02078-0.

Computational phenotyping of obstructive airway diseases: protocol for a systematic review

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Affiliations expand

- PMID: 36229872

- DOI: 10.1186/s13643-022-02078-0

Abstract

Background: Over the last decade, computational sciences have contributed immensely to characterization of phenotypes of airway diseases, but it is difficult to compare derived phenotypes across studies, perhaps as a result of the different decisions that fed into these phenotyping exercises. We aim to perform a systematic review of studies using computational approaches to phenotype obstructive airway diseases in children and adults.

Methods and analysis: We will search PubMed, Embase, Scopus, Web of Science, and Google Scholar for papers published between 2010 and 2020. Conferences proceedings, reference list of included papers, and experts will form additional sources of literature. We will include observational epidemiological studies that used a computational approach to derive phenotypes of chronic airway diseases, whether in a general population or in a clinical setting. Two reviewers will independently screen the retrieved studies for eligibility, extract relevant data, and perform quality appraisal of included studies. A third reviewer will arbitrate any disagreements in these processes. Quality appraisal of the studies will be undertaken using the Effective Public Health Practice Project quality assessment tool. We will use summary tables to describe the included studies. We will narratively synthesize the generated evidence, providing critical assessment of the populations, variables, and computational approaches used in deriving the phenotypes across studies CONCLUSION: As progress continues to be made in the area of computational phenotyping of chronic obstructive airway diseases, this systematic review, the first on this topic, will provide the state of the art on the field and highlight important perspectives for future works.

Ethics and dissemination: No ethical approval is needed for this work is based only on the published literature and does not involve collection of any primary or human data.

Registration and reporting: SYSTEMATIC REVIEW REGISTRATION: PROSPERO CRD42020164898.

Keywords: Airway disease; Asthma; COPD; Clustering; Computation; Machine learning; Phenotype; Systematic review.

- 28 references

Proceed to details

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Eur Respir J

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. 2022 Oct 13;2200611.

doi: 10.1183/13993003.00611-2022. Online ahead of print.

Clinical outcomes of bronchiectasis in India; Data from the EMBARC/Respiratory Research Network of India registry

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Affiliations expand

- PMID: 36229049

- DOI: 10.1183/13993003.00611-2022

Abstract

Introduction: Identifying risk factors for poor outcomes can help with risk stratification and targeting of treatment. Risk factors for mortality and exacerbations have been identified in bronchiectasis but have been almost exclusively studied in European and North American populations. This study investigated the risk factors for poor outcome in a large population of bronchiectasis patients enrolled in India.

Methods: The EMBARC-India registry is a prospective observational study of adults with CT confirmed bronchiectasis enrolled at 31 sites across India. Baseline characteristics of patients were used to investigate associations with key clinical outcomes: Mortality, severe exacerbations requiring hospital admission, overall exacerbation frequency and FEV_1 decline.

Results: 1018 patients with at least 12 months follow-up data were enrolled in the follow-up study. Frequent exacerbations (3 or more per year) at baseline were associated with an increased risk of mortality (hazard ratio(HR) 3.23 95%CI 1.39-7.50), severe exacerbations (HR 2.71 95%CI 1.92-3.83), future exacerbations (rate ratio(RR) 3.08 95%CI 2.36-4.01) and lung function decline. Co-existing COPD, dyspnoea and current cigarette smoking were similarly associated with a worse outcome across all endpoints studied. Additional predictors of mortality and severe exacerbations were increasing age and cardiovascular co-morbidity. Infection with Gram-negative pathogens (predominantly Klebsiella pneumoniae) was independently associated with increased mortality (HR 3.13 95%CI 1.62-6.06), while *Pseudomonas aeruginosa* infection was associated with severe exacerbations (HR 1.41 95%CI 1.01-1.97) and overall exacerbation rate (RR 1.47 95%CI 1.13-1.91).

Conclusion: This study identifies risk factors for morbidity and mortality among bronchiectasis patients in India. Identification of these risk factors may support treatment approaches optimised to an Asian setting.

Funding: EU/European Federation of Pharmaceutical Industries and Associations Innovative Medicines Initiative inhaled Antibiotics in Bronchiectasis and Cystic Fibrosis Consortium, European Respiratory Society, and Asthma and Lung UK.

Review

Eur Respir J

. 2022 Oct 13;2200606.

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Development of Core Outcome Measures sets for paediatric and adult Severe Asthma (COMSA)

Ekaterina Khaleva[1], Anna Rattu[1], Chris Brightling[2], Andrew Bush[3], Apostolos Bossios[4], Arnaud Bourdin[5], Kian Fan Chung[6], Rekha Chaudhuri[7], Courtney Coleman[8], Sven-Erik Dahlén[4], Ratko Djukanovic[9], Antoine Deschildre[10,11], Louise Fleming[6], Stephen J Fowler[12], Atul Gupta[13], Eckard Hamelmann[14], Simone Hashimoto[15,16], Gunilla Hedlin[17], Gerard H Koppelman[18,19], Erik Melén[20], Clare S Murray[21], Charles Pilette[22], Celeste Porsbjerg[23], Katharine C Pike[24], Franca Rusconi[25], Clare Williams[8], Birgit Ahrens[26], Peter Alter[27], Freja Anckers[28], Maarten van den Berge[19,29], Katharina Blumchen[30], Guy Brusselle[31], Graham W Clarke[32], Danen Cunoosamy[33], Barbro Dahlén[4], Piers Dixey[6,34], Andrew Exley[35], Urs Frey[36], Erol A Gaillard[37], Lisa Giovannini-Chami[38,39], Jonathan Grigg[40], Diana Hartenstein[26], Liam G Heaney[41], Bülent Karadag[42], Susanne Kaul[26], Inger Kull[20], Amelia Licari[43], Anke H Maitland-van der Zee[16,44], Vera Mahler[26], Ann-Marie M Schoos[45,46], Prasad Nagakumar[47,48], Jenny Negus[49], Hanna Nielsen[28,50], James Paton[51], Mariëlle Pijnenburg[52], Valeria Ramiconi[53], Sofia Romagosa Vilarnau[53], Stefania Principe[16,54], Niels Rutjes[55], Sejal Saglani[6], Paul Seddon[56], Florian Singer[57,58], Heribert Staudinger[59], Steve Turner[60,61], Susanne Vijverberg[16,62], Tonya Winders[63,64], Valentyna Yasinska[4], Graham Roberts[65,66], COMSA working group in the 3TR consortium

Affiliations expand

- PMID: 36229046

- DOI: 10.1183/13993003.00606-2022

Abstract

Background: Effectiveness studies with biological therapies for asthma lack standardised outcome measures. The COMSA (Core Outcome Measures sets for paediatric and adult Severe Asthma) working group sought to develop Core Outcome Measures (COM) sets to facilitate better synthesis of data and appraisal of biologics in paediatric and adult asthma clinical studies.

Methods: COMSA utilised a multi-stakeholder consensus process among patients with severe asthma, adult, and paediatric clinicians, pharmaceutical representatives and health regulators from across Europe. Evidence included a systematic review of development, validity, and reliability of selected outcome measures plus a narrative review and a pan-European survey to better understand patients' and carers' views about outcome measures. It was discussed using a modified GRADE Evidence to Decision framework. Anonymous voting was conducted using predefined consensus criteria.

Results: Both adult and paediatric COM sets include forced expiratory volume in 1 s (FEV_1) as z scores, annual frequency of severe exacerbations and maintenance oral corticosteroid use. Additionally, the paediatric COM set includes the Paediatric Asthma Quality of Life Questionnaire, and Asthma Control Test (ACT) or Childhood-ACT while the adult COM includes the Severe Asthma Questionnaire and the Asthma Control Questionnaire-6 (symptoms and rescue medication use reported separately).

Conclusions: This patient-centred collaboration has produced two COM sets for paediatric and adult severe asthma. It is expected that they will inform the methodology of future clinical trials, enhance comparability of efficacy and effectiveness of biological therapies, and help assess their socioeconomic value. COMSA will inform definitions of non-response and response to biological therapy for severe asthma.

Life Sci

. 2022 Oct 10;121056.

doi: 10.1016/j.lfs.2022.121056. Online ahead of print.

The mechanisms underlying montelukast's neuropsychiatric effects – new insights from a combined metabolic and multiomics approach

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Affiliations expand

- PMID: 36228771

- DOI: 10.1016/j.lfs.2022.121056

Abstract

Aims: Montelukast (MTK) is an antagonist of the cysteinyl leukotrienes receptor 1 widely used to manage asthma symptoms among adults and children. However, it has been associated with an increasing number of neuropsychiatric adverse drug reactions (ADRs), particularly among children, including depression, sleep disturbance, and suicidal ideation. The aims of this work were to characterize MTK metabolism in vitro and in vivo and to identify its effects at the metabolome and proteome levels in order to explain its toxicity.

Main methods: An extensive study of montelukast metabolism was carried out using in vitro systems, an embryonic neuron-enriched cell model, and a mouse model. Metabolites were identified by high-resolution mass spectrometry, and a combined mass spectrometry-based metabolomics and proteomics approach was employed to assess the effect of MTK on mice and isolated chicken neurons.

Key findings: Eighteen new MTK metabolites were identified. MTK's ability to react with glutathione was confirmed. The multi-omics approach employed confirmed that montelukast interferes with the glutathione detoxification system in the brain. Moreover, montelukast is also able to dysregulate various neurotransmitter and neurosteroid pathways, particularly those involved in regulation of the hypothalamic-pituitary-adrenal axis, also interfering with mitochondrial function in neuronal cells.

Significance: Results clearly indicate that montelukast therapeutic effects are accompanied by a strong modulation of specific processes in the central nervous system that may explain the observed neuropsychiatric reactions. Moreover, the results also suggest that adverse drug reactions are more likely to occur in children, due to the early maturation stage of their brains.

Keywords: Adverse drug reactions; Drug metabolism; Metabolomics; Montelukast; Montelukast (PubChem CID: 5281040); Neurotoxicity; Proteomics.

Conflict of interest statement

Declaration of competing interest None.

Review

Lung

. 2022 Oct 13.

doi: 10.1007/s00408-022-00575-6. Online ahead of print.

Narrative Review of the Mechanisms and Treatment of Cough in Asthma,

Cough Variant Asthma, and Non-asthmatic Eosinophilic Bronchitis

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Affiliations expand

- PMID: 36227349

- DOI: 10.1007/s00408-022-00575-6

Abstract

Chronic cough is a debilitating condition affecting 10-12% of the general population and is one of the leading causes for referral to secondary care. Many conditions have been associated with chronic cough, including asthma, gastro-esophageal reflux disease and upper airways cough syndrome. Inflammatory airway conditions including cough variant asthma (CVA) and non-asthmatic eosinophilic bronchitis (NAEB) contribute to a significant proportion of presentations with chronic cough, with differing diagnostic criteria and different responses to commonly used asthma therapy for their respective diagnoses. Mechanistic studies in both animal models and humans have identified increased neuronal sensitivity and subsequent central sensitization. These mechanisms include inflammatory-mediated nociceptor sensitization and alterations of afferent nerve terminal excitability, phenotypic changes in the vagal afferent neurons over time, and central neuroplasticity resulting from increased synaptic signalling from peripheral afferents. The aim of this review is to discuss the mechanisms, neurophysiology, and management approaches currently available for patients presenting with chronic cough with underlying asthma, CVA, and NAEB and to shed a light on areas of further research required to elucidate the mechanisms of cough in this patient population.

Keywords: Asthma; Chronic cough; Cough variant asthma; Eosinophils; Nerves; Non-asthmatic eosinophilic bronchitis.

- 94 references

SUPPLEMENTARY INFO

Publication typesexpand

Pediatr Pulmonol

. 2022 Oct 13.

doi: 10.1002/ppul.26205. Online ahead of print.

INHALER TECHNIQUE IN A PEDIATRIC EMERGENCY DEPARTMENT: IMPACT OF AN EDUCATION INTERVENTION AMONG HEALTHCARE PROFESSIONALS

Ana Jové Blanco[1], Javier Toledano Revenga[2], Arístides Rivas García[1], Paula Vazquez López[3], Jorge Lorente Romero[1], Rafael Marañón[1]

Affiliations expand

- PMID: 36226385

- DOI: 10.1002/ppul.26205

Abstract

Background: Inhaler technique (IT) knowledge among healthcare providers is poor. The aim was to improve Pediatric Emergency Department (PED) healthcare providers' IT technique by carrying out an education intervention and sustain it for 6 months.

Methods: open-label, quasi-experimental, prospective and unicentric study. Healthcare professionals working at the PED were enrolled. The study was developed in three phases: baseline evaluation and education intervention (P1) and reevaluation 1 month (P2) and 6 months (P3) after the education intervention. Participants fulfilled an eight-question theoretical test. Practical skills were evaluated by demonstrating IT in all three phases. The education intervention consisted in a verbal explanation of IT followed by a demonstration of IT with metered-dose inhaler using a mannequin.

Results: 84 healthcare providers (medical residents, nurses and nursing assistants) were involved. In the theoretical questionnaire, the mean score at baseline was 4.4/8 (SD 1.7) improving to 6.3/8 (SD 1.2) in P2 and 6.47/8 (SD 1.1) in P3. In the IT evaluation for children <7 years old, the score improved from 5.7/7 (SD1.3) to 6.5/7 in P2 and 6.7/7 in P3 ($p<0.001$). For children >7 years old, the mean score of IT at baseline was 3.1/10 (SD 4), which improved to 7.4/10 (SD3) and 8.2/10 in P2 and P3 respectively ($p<0.001$). Only professional category influenced results at baseline.

Conclusion: Healthcare providers' theoretical knowledge and practical skills on IT are low. The education intervention performed is a useful strategy to ameliorate IT among healthcare providers. This article is protected by copyright. All rights reserved.

Keywords: asthma; emergency service; metered-dose inhalers; nebulizers and vaporizers; quality of healthcare.; teacher training.

Ann Otol Rhinol Laryngol

. 2022 Oct 12;34894221129329.

doi: 10.1177/00034894221129329. Online ahead of print.

Assessing Stakeholder Engagement for Outcomes-Based Research Among Patients With Chronic Rhinosinusitis and Asthma: A Survey-Based Investigation

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Affiliations expand

- PMID: 36226327

- DOI: 10.1177/00034894221129329

Abstract

Background: Despite significant morbidity, there remains a critical need for prospective analyses to investigate the impact of comorbid chronic rhinosinusitis (CRS) with asthma (CRSwA) on patient centered outcomes. The objective of this study was to ascertain critical stakeholder feedback from patients that could inform future study design based on patient preferences, in an effort to optimize patient enrollment.

Methods: A prospective, descriptive study was performed in order to determine the importance of various factors on CRSwA treatment among critical stakeholders. A Likert-scale survey highlighting various aspects of treatment of CRSwA and elucidating patient enthusiasm for clinical enrollment was constructed and prospectively administered to patients with CRSwA. A univariate analysis was instituted to understand the significance of the different trial design preferences.

Results: Survey responses were collected from a total of 17 patients with CRSwA. With Likert scores >4/5, responses indicated significant stakeholder interest in research focused on understanding symptom triggers, including the impact of air quality and allergens. Importantly, the highest mean scores noted were for studies focused on improving (1) overall quality of life (4.8/5) and (2) lung function (4.8/5). Patients appeared least interested in participation in a randomized trial, whereas the greatest support was communicated for a purely observational trial (P = .08).

Conclusion: Patients with CRSwA demonstrate enthusiasm for participation in research that focuses on improving patient centered outcomes-specifically quality of life and lung

function. Stakeholder feedback also indicates a preference for observational study design over randomized control trials.

Keywords: asthma; chronic rhinosinusitis; patient centered outcomes research; stakeholder engagement.

J Allergy Clin Immunol

. 2022 Oct 9;S0091-6749(22)01333-1.

doi: 10.1016/j.jaci.2022.08.029. Online ahead of print.

Effects of combination treatment with tezepelumab and allergen immunotherapy on nasal responses to allergen: a randomized controlled trial

Jonathan Corren[1], David Larson[2], Matthew C Altman[3], R Max Segnitz[4], Pedro C Avila[5], Paul A Greenberger[5], Fuad Baroody[6], Mark H Moss[7], Harold Nelson[8], Allison J Burbank[9], Michelle L Hernandez[9], David Peden[9], Sarbjit Saini[10], Stephen Tilles[11], Iftikhar Hussain[12], Don Whitehouse[13], Tielin Qin[2], Miguel Villarreal[14], Michelle Sever[14], Lisa M Wheatley[15], Gerald T Nepom[16], Srinath Sanda[13], Immune Tolerance Network ITN057AD CATNIP Study Team

Affiliations expand

- PMID: 36223848

- DOI: 10.1016/j.jaci.2022.08.029

Abstract

Background: Thymic stromal lymphopoietin (TSLP) has been shown to play a central role in the initiation and persistence of allergic responses.

Objective: We evaluated whether tezepelumab, a human monoclonal anti-TSLP antibody, improved the efficacy of subcutaneous allergen immunotherapy (SCIT) and promoted the development of tolerance in patients with allergic rhinitis.

Methods: We conducted a double-blind parallel design trial in patients with cat allergy. A total of 121 patients were randomized to receive either intravenous tezepelumab plus subcutaneous cat SCIT, cat SCIT alone, tezepelumab alone, or placebo for 52 weeks followed by 52 weeks of observation. Nasal allergen challenges (NAC), skin testing, and blood and nasal samples were obtained throughout the study.

Results: At week 52, the NAC-induced total nasal symptom scores (TNSS) (calculated as an area-under-the-curve [AUC 0-1 hr] and as a peak score [peak 0-1 hr] during the first hour after nasal allergen challenge) were significantly reduced in patients receiving tezepelumab/SCIT compared with SCIT alone. At week 104, one year after stopping treatment, the primary endpoint TNSS AUC 0-1hr was not significantly different in the tezepelumab/SCIT group compared to SCIT alone, while TNSS peak 0-1 hr was significantly lower in those receiving combination treatment vs. SCIT. Transcriptomic analysis of nasal epithelial samples demonstrated that treatment with the combination of SCIT/tezepelumab, but neither monotherapy, caused persistent downregulation of a gene network related to type 2 inflammation which was associated with improvement in NAC responses.

Conclusions: These results suggest that inhibition of TSLP augments the efficacy of SCIT during therapy and may promote tolerance following a one year course of treatment. (ClinicalTrials.gov Identifier: NCT02237196).

Keywords: Allergy; cytokine; epithelium; inflammation; late phase; lymphocyte; mast cell; rhinitis; thymic stromal lymphopoietin; tolerance; tryptase.

SUPPLEMENTARY INFO

Associated dataexpand

FULL TEXT LINKS

Int Arch Allergy Immunol

. 2022 Oct 12;1-10.

doi: 10.1159/000526803. Online ahead of print.

IL-12 Contributes to the Development of Asthma by Targeting HIF-1α/NLRP3 Pathway through Runx3

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Affiliations expand

- PMID: 36223757

- DOI: 10.1159/000526803

Abstract

Introduction: The aim of the study was to determine the role and mechanism of runt-related transcription factor 3 (Runx3) in the development of asthma.

Methods: An asthma mouse model was constructed and validated by hematoxylin-eosin analysis of lung tissue and noninvasive enhanced pause (Penh) evaluation of airway hyperresponsiveness. Then, the levels of Runx3 and interleukin (IL)-12 in peripheral blood and lung tissue were detected by enzyme-linked immunosorbent assay (ELISA) and immunohistochemistry. By use Runx3+/- mice, the effect of Runx3 downregulation on ovalbumin (OVA)-induced asthma was investigated. After stimulated by different doses of IL-12, the expressions of Runx3, hypoxia inducible factor-1α (HIF-1α), and NOD-like receptor thermal protein domain associated protein 3 (NLRP3) in BEAS-2B cells were tested

through Western blot and immunofluorescence. Subsequently, BEAS-2B cells treated with 20 ng/mL IL-12 were divided into control, Runx3 overexpression negative control, Runx3 overexpression, HIF-1α inhibitor, and Runx3 overexpression + HIF-1α agonist groups. The Western blot, immunofluorescence, and ELISA indicators were tested repeatedly.

Results: The increased number of inflammatory cells and Penh value confirmed the success of the asthma mouse model. IL-12 expression was significantly increased, and Runx3 was reduced in asthma mice compared with wild-type mice. Meanwhile, the level of immunoglobulin E (IgE) in serum, cytokines in bronchoalveolar lavage fluid, and IL-12, HIF-1α, NLRP3 in the lung were significantly elevated in Runx3+/- mice. With the increase of IL-12 concentration, Runx3 protein expression decreased, while HIF-1α and NLRP3 expression increased. Further mechanistic studies suggest that Runx3 ameliorates IL-12-induced BEAS-2B injury by inhibiting HIF-1α/NLRP3 pathway.

Conclusion: These results suggested that IL-12 contributes to the development of asthma by targeting HIF-1α/NLRP3 pathway through Runx3, thus providing a novel strategy for asthma therapy.

Keywords: Asthma; HIF-1α/NLRP3; Inflammation; Interleukin-12; Runx3.

Case Reports

Curr Drug Saf

. 2022 Oct 10.

doi: 10.2174/1574886317666221010092132. Online ahead of print.

Off-label use of oral immunotherapy for rhinoconjunctivitis and asthma due to grass pollen: a safe and effective alternative in patients over 65 years old. A series of case reports

Lucía González-Bravo[1], Jimena Laiseca García[1], Martina Privitera[1], Ana Rosado[1]

Affiliations expand

- PMID: 36221873

- DOI: 10.2174/1574886317666221010092132

Abstract

Introduction: Allergic rhinoconjunctivitis and asthma are the most common IgE-mediated diseases worldwide. Allergen-specific immunotherapy (AIT) is currently the only modifying treatment for these IgE-mediated diseases, in both children and adults. Subcutaneous immunotherapy is widely used, but in patients over 65 years old there may be an increased risk of adverse reactions and a worse response to treatment. Oral immunotherapy (OIT) has been proved to be effective and safe, but currently, in most countries, it has been licensed only for patients up to 65 years old based on its technical datasheet. No studies into the efficacy and safety of this type of immunotherapy in patients older than 65 years old have been published.

Case presentation: We present four patients older than 65 years old with a diagnosis of moderate seasonal rhinoconjunctivitis and moderate-persistent seasonal pollen-induced asthma. Off-label use of oral immunotherapy (OIT) for grass pollen was prescribed, due to the severity of their rhinoconjunctivitis symptoms and worsening of asthma symptoms during the spring. Improvement in the rhinoconjunctivitis and asthma symptoms was reported by all patients since the first spring season and was maintained during the following two years of follow-up. There were no systemic reactions and only two patients initially had self-limiting oral pruritus Conclusion: Oral immunotherapy for pollens appears to be a convenient, effective, and safe option in older patients (>65 years) with comorbidities after a three-year treatment. This is, to the best of our knowledge, the first report of the off-label use of OIT in patients over 65 years old with symptoms of allergic rhinoconjunctivitis and asthma.

Keywords: Oral immunotherapy; asthma; grass pollen; off-label; rhinoconjunctivitis; safety.

Am J Respir Crit Care Med

. 2022 Oct 11.

doi: 10.1164/rccm.202210-1870ED. Online ahead of print.

Interplay Between Immune and Airway Smooth Muscle Cells in Obese Asthma

A E Dixon[1], L G Que[2]

Affiliations expand

- PMID: 36219828

- DOI: 10.1164/rccm.202210-1870ED

No abstract available

Keywords: Lymphocyte; airway reactivity.

Sci Signal

. 2022 Oct 11;15(755):adf2043.

doi: 10.1126/scisignal.adf2043. Epub 2022 Oct 11.

Macrophages present antigens in allergic asthma

Annalisa M VanHook[1]

Affiliations expand

- PMID: 36219684

- DOI: 10.1126/scisignal.adf2043

Abstract

Resident macrophages mediate antigen capture and presentation in allergic airway inflammation in mice.

Share

21

Allergy

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. 2022 Oct 11.

doi: 10.1111/all.15549. Online ahead of print.

IN MEMORIAM : Lawrence M. Lichtenstein (1934-2022)

Gianni Marone[1,2,3,4], Massimo Triggiani[5], Vincenzo Casolaro[6], Cristiana Stellato[6], Amato de Paulis[1,2,3], Stephen T Holgate[7], Cezmi A Akdis[8], Stephen J Galli[9,10]

Affiliations expand

- PMID: 36219503

- DOI: 10.1111/all.15549

No abstract available

. 2022 Oct 11;1-16.

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Impact of exacerbations on lung function, resource utilization, and productivity: results from an observational, prospective study in adults with uncontrolled asthma

Juan Wisnivesky[1,2], Emily Federmann[1], Laurent Eckert[3], Erin West[4], Caroline Amand[3], Driss Kamar[5], Ariel Teper[6], Asif H Khan[3]

Affiliations expand

- PMID: 36218309

- DOI: 10.1080/02770903.2022.2130800

Abstract

Exacerbations have a major impact on the well-being of patients with uncontrolled asthma. This study evaluated lung function, healthcare resource utilization (HCRU), and productivity loss following asthma exacerbations. This single-center, observational, prospective cohort study recruited US patients with an acute asthma exacerbation; a reference group without exacerbations was included for comparison. Lung function (forced expiratory volume in 1 second [FEV_1]), reported as FEV_1 percent predicted (FEV_1pp), was collected at baseline, daily during Month 1, and monthly for Months 2-5. HCRU (outpatient visits to a healthcare practitioner, emergency room [ER] visits, and hospitalizations for asthma), oral corticosteroid (OCS) use, and asthma-related work/school absence were collected monthly for 6 months. Overall, 150 patients were recruited (exacerbation: n = 102; reference: n = 48; mean [SD] age: 42.7 [15.2] and 49.6 [12.4] years; female: 73% and 71%). In both groups, similar trends were observed in FEV_1, with significant improvement from baseline to Week 1 ($p < 0.05$), followed by a continuous decline. FEV_1pp was 7.7% lower at baseline and 8.9% lower at Month 5 in the exacerbation versus reference group. The exacerbation group had significantly higher rates of OCS prescriptions (p = 0.04) and increased work absences (p = 0.001) during follow-up versus reference group. There were no significant differences in other HCRU measures (e.g., outpatient visits, ER visits, and hospitalizations). Although patients with exacerbations had rapid recovery of lung function, this was not maintained

and declined faster than in patients without exacerbations. The results suggest that intensive disease management and monitoring are important in patients with asthma who experience an exacerbation.

Keywords: Airway disease; Asthma exacerbations; Forced expiratory volume; Healthcare resource utilization; Symptom exacerbation.

J Asthma

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. 2022 Oct 11;1-13.

doi: 10.1080/02770903.2022.2134795. Online ahead of print.

Airwave oscillometry and spirometry in children with asthma or wheeze

Shannon Gunawardana[1], Mark Tuazon[2], Lorna Wheatley[2], James Cook[3], Christopher Harris[4], Anne Greenough[1,5]

Affiliations expand

- PMID: 36218195

- DOI: 10.1080/02770903.2022.2134795

Abstract

Objective: Lung function testing is used in diagnosing asthma and assessing asthma control. Spirometry is most commonly used, but younger children can find performing this test challenging. Non-volitional tests such as airwave oscillometry (AOS) may be helpful in that population. We compared the success of spirometry and AOS in assessing bronchodilator responsiveness in children.

Methods: AOS was conducted alongside routine lung function testing. Resistance at 5Hz (R5), the difference between the resistance at 5 and 20Hz (R5-20) and the area under the reactance curve (AX) were assessed. Patients between 5-16 years old attending clinic with wheeze or asthma were assessed. Patients performed AOS, followed by spirometry and were then given 400µg salbutamol; the tests were repeated 15 minutes later.

Results: Lung function testing was performed in 47 children of whom 46 (98%) and 32 (68%) performed acceptable baseline oscillometry and spirometry, respectively ($p < 0.001$). Children unable to perform acceptable spirometry were younger (7.35 range 5.4-10.3 years) than those who could (10.4 range 5.5-16.9 years), $p < 0.001$. The baseline z-scores of AOS R5 correlated with FEV_1 ($r = 0.499$, $p = 0.004$), FEF_{75} ($r = 0.617$, $p < 0.001$) and FEV_1/FVC ($r = 0.618$, $p < 0.001$). There was a positive bronchodilator response assessed by spirometry (change in $FEV_1 \geq 12\%$) in eight children which corresponded to a change in R5 of 36% (range 30-50%) and a change in X5 of 39% (range 15-54%).

Conclusions: Oscillometry is a useful adjunct to spirometry in assessing young asthmatic children's lung function. The degree of airway obstruction, however, might affect the comparability of the results of the two techniques.

Keywords: Resistance at 5Hz (R5); bronchodilator responsiveness; forced expiratory volume in 1 second (FEV1); lung function; pediatrics.

Randomized Controlled Trial

Respir Res

. 2022 Oct 10;23(1):279.

doi: 10.1186/s12931-022-02114-6.

Effects of treatment with montelukast alone, budesonide/formoterol alone and a combination of both in cough variant asthma

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Affiliations expand

- PMID: 36217131

- PMCID: PMC9552469

- DOI: 10.1186/s12931-022-02114-6

Free PMC article

Abstract

Background: Whether cysteinyl-leukotriene receptor antagonists (LTRAs) have a similar antitussive effect to inhaled corticosteroids and long-acting β2-agonist (ICS/LABA), and that LTRA plus ICS/LABA is superior to LTRAs alone or ICS/LABA alone in treating cough variant asthma (CVA) remain unclear. This study aimed to investigate and compare the efficacy of montelukast alone, budesonide/formoterol alone and the combination of both in the treatment of CVA.

Methods: Ninety-nine CVA patients were assigned randomly in a 1:1:1 ratio to receive montelukast (M group: 10 mg, once daily), budesonide/formoterol (BF group: 160/4.5 μg, one puff, twice daily), or montelukast plus budesonide/formoterol (MBF group) for 8 weeks. The primary outcomes were changes in the cough visual analogue scale (VAS) score, daytime cough symptom score (CSS) and night-time CSS, and the secondary outcomes comprised changes in cough reflex sensitivity (CRS), the percentage of sputum

eosinophils (sputum Eos%) and fractional exhaled nitric oxide (FeNO). CRS was presented with the lowest concentration of capsaicin that induced at least 5 coughs (C5). The repeated measure was used in data analysis.

Results: The median cough VAS score (median from 6.0 to 2.0 in the M group, 5.0 to 1.0 in the BF group and 6.0 to 1.0 in the MBF group, all $p < 0.001$), daytime CSS (all $p < 0.01$) and night-time CSS (all $p < 0.001$) decreased significantly in all three groups after treatment for 8 weeks. Meanwhile, the LogC5 and sputum Eos% improved significantly in all three groups after 8 weeks treatment (all $p < 0.05$). No significant differences were found in the changes of the VAS score, daytime and night-time CSSs, LogC5 and sputum Eos% among the three groups from baseline to week 8 (all $p > 0.05$). The BF and MBF groups also showed significant decreases in FeNO after 8 weeks treatment ($p = 0.001$ and $p = 0.008$, respectively), while no significant change was found in the M group ($p = 0.457$). Treatment with MBF for 8 weeks significantly improved the FEV_1/FVC as well as the MMEF% pred and decreased the blood Eos% (all $p < 0.05$).

Conclusions: Montelukast alone, budesonide/formoterol alone and a combination of both were effective in improving cough symptom, decreasing cough reflex sensitivity and alleviating eosinophilic airway inflammation in patients with CVA, and the antitussive effect and anti-eosinophilic airway inflammation were similar. Trial registration ClinicalTrials.gov, number NCT01404013.

Keywords: Budesonide/formoterol; Cough; Cough variant asthma; Eosinophilic airway inflammation; Montelukast.

Conflict of interest statement

All authors reported no conflicts of interest.

- 37 references
- 4 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated dataexpand

FULL TEXT LINKS

Am J Respir Crit Care Med

. 2022 Oct 10.

doi: 10.1164/rccm.202205-0951OC. Online ahead of print.

Mendelian Randomization Analysis Reveals a Complex Genetic Interplay Among Atopic Dermatitis, Asthma, and GERD

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Affiliations expand

- PMID: 36214830

- DOI: 10.1164/rccm.202205-0951OC

Abstract

Rationale: Gastroesophageal reflux disease (GERD) is commonly associated with atopic disorders, but cause-effect relationships remain unclear.

Objectives: We applied Mendelian randomization (MR) analysis to explore whether GERD is causally related to atopic disorders of the lung (asthma) and/or skin (atopic dermatitis).

Methods: We conducted two-sample bidirectional MR to infer the magnitude and direction of causality between asthma and GERD, using summary statistics from the largest genome-wide association studies (GWAS) conducted on asthma (Ncases=56,167) and GERD (Ncases=71,522). Additionally, we generated instrumental variables (IVs) for atopic dermatitis (AD) from the latest population-level GWAS meta-analysis (Ncases=22,474) and

assessed their fidelity and confidence of predicting the likely causal pathway(s) leading to asthma and/or GERD.

Measurements and main results: Applying three different methods, each method found similar magnitude of causal estimates that were directionally consistent across the sensitivity analyses. Using an inverse-variance weighted method, the largest effect size was detected for asthma predisposition to AD (odds ratio [OR], 1.46; 95% confidence interval [CI], 1.34-1.59), followed by AD to asthma (OR, 1.34; CI, 1.24-1.45). A significant association was detected for genetically determined asthma on risk of GERD (OR, 1.06; CI, 1.03-1.09), but not genetically determined AD on GERD. In contrast, GERD equally increased risks of asthma (OR, 1.21; CI, 1.09-1.35) and AD (OR, 1.21; CI, 1.07-1.37).

Conclusions: This study uncovers previously unrecognized causal pathways that have clinical implications in European-ancestry populations: 1) asthma is a causal risk for AD; and 2) the predisposition to AD, including asthma, can arise from specific pathogenic mechanisms manifested by GERD.

Keywords: Human genetics, epidemiological approach, causal pathways, risk factors.

Allergy

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. 2022 Oct 10.

doi: 10.1111/all.15548. Online ahead of print.

Sex hormones and asthma: the role of estrogen in asthma development and severity

Urszula Radzikowska[1], Korneliusz Golebski[2]

Affiliations expand

- PMID: 36214616

- DOI: 10.1111/all.15548

No abstract available

Keywords: asthma; estrogen; immune mechanisms; menopause; testosterone.

J Asthma

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. 2022 Oct 10;1-13.

doi: 10.1080/02770903.2022.2132959. Online ahead of print.

Association between asthma and work absence in working adults in the United States

Louis Jacob, Md-PhD[1,2,3], Jae Il Shin, Md-PhD[4], Guillermo F López-Sánchez[5], Josep Maria Haro, Md-PhD[1,2], Ai Koyanagi, Md-PhD[1,2,6], Karel Kostev[7], Laurie Butler[8], Yvonne Barnett[8], Hans Oh[9], Lee Smith[10]

Affiliations expand

- PMID: 36214492

- DOI: 10.1080/02770903.2022.2132959

Abstract

The present study aimed to investigate the association between asthma and work absence in a large sample of US working adults, while controlling for several sociodemographic and health characteristics. This study used data from the 2019 Health and Functional Capacity Survey of the RAND American Life Panel (ALP). Work absence corresponded to the number of days of absence from work for health-related reasons in the past 12 months. Current asthma was self-reported and was included in the analyses as a dichotomous variable. Control variables included sex, age, ethnicity, marital status, education, occupation, annual family income, health insurance, and number of chronic physical or psychiatric conditions. Finally, the association between asthma and work absence was analyzed using logistic regression models. This study included 1,323 adults aged 22-65 years (53.1% males; mean [SD] age 43.1 [11.7] years). Individuals with asthma were more likely to report at least one (81.5% versus 56.8%, p-value <0.001) or three days of absence (56.9% versus 31.3%, p-value =0.003) from work in the past 12 months than those without asthma. These findings were corroborated in the regression analyses, as asthma was positively and significantly associated with work absence after adjusting for all control variables (at least one day of absence: OR =3.24, 95% CI =1.44-7.29; at least three days of absence: OR =2.61, 95% CI =1.26-5.40). This US study of working adults showed that asthma was a risk factor for work absence. Further research is warranted to better understand the factors predisposing to work absence in the asthma population.

Keywords: Asthma; Cross-Sectional Study; Epidemiology; United States; Work Absence.

J Asthma

. 2022 Oct 10;1-18.

doi: 10.1080/02770903.2022.2134794. Online ahead of print.

The impact of obesity and uncontrolled asthma during pregnancy on metabolic and inflammatory pathways

Sreeparna Bhaumik[1], Jack Lockett[1,2], Zarqa Saif[1], Andrew Lai[3], Carlos Salomon[3], Jon Whitehead[4], Vicki L Clifton[1]

Affiliations expand

- PMID: 36214455

- DOI: 10.1080/02770903.2022.2134794

Abstract

Asthma and obesity are both inflammatory complications of pregnancy and when combined contribute to an increased risk of uncontrolled asthma during pregnancy and poor perinatal outcomes. Our previous work has identified the presence of maternal asthma is associated with a proinflammatory milieu in the placenta and reduced fetal growth. The current study was designed to determine the relationships between immunomodulatory metabolic pathways and inflammation and establish whether these pathways are associated with uncontrolled asthma in obese pregnant women.Fifty-three obese (BMI >30) pregnant women were recruited prospectively. Participants were classified as having no asthma, controlled asthma, and uncontrolled asthma based on a doctor diagnosis and assessment using the Asthma Control Questionnaire (ACQ). Circulating

plasma concentrations of metabolic hormones leptin, adiponectin, insulin, glucose, and extracellular vesicle (EVs) associated cytokines were measured at 18- and 36-weeks gestation.Concentrations of metabolic and inflammatory markers among obese participants with or without asthma were not significantly different throughout gestation. However total adiponectin concentrations increased as gestation progressed in obese, non-asthmatic women but did not increase in women with asthma. Plasma adiponectin and leptin levels in women with uncontrolled asthma were positively correlated with EV inflammatory markers including GM-CSF, IL-6, TNFα and IFNγ protein.This study demonstrated that most metabolic markers remain unchanged with the presence and severity of asthma in obese pregnant women. However, differences in the associations between metabolic and inflammatory pathways were observed in women with asthma and may be one of the mechanisms contributing to uncontrolled asthma in obese pregnant women.

Keywords: cytokines; inflammation; obesity; pregnancy; uncontrolled asthma.

Review

Eur Ann Allergy Clin Immunol

. 2022 Oct 10.

doi: 10.23822/EurAnnACI.1764-1489.271. Online ahead of print.

From triggers to asthma: a narrative review on epithelium dysfunction

L Cecchi[1,2], A Vaghi[3], F Bini[3], M Martini[4,5], A Musarra[6], M B Bilò[4,7]

Affiliations expand

- PMID: 36214074

- DOI: 10.23822/EurAnnACI.1764-1489.271

Free article

Abstract

It is currently recognized that the airway epithelium plays a pivotal role in orchestrating inflammatory, immune, and regenerative responses to allergens, viruses and environmental pollutants that contribute to asthma pathogenesis. The impact of pollen on respiratory epithelium is multifaceted and goes beyond the direct barrier damage driven by the best-known Type-2 response. After pollen-driven activation, airway epithelial cells play an active role in triggering several pathways. In particular, the release of epithelial cytokines (or alarmins) activates both innate and adaptive immunity, with downstream effects implicated to the pathogenesis of asthma. Pollutants also have a pleiotropic effect on respiratory epithelium. Diesel exhaust particles can directly damage the respiratory epithelium with consequent barrier dysfunction, increased permeability, and local inflammation, but they can also activate Th2 responses. Innate immune responses also are triggered by pollutants through release of epithelial cytokines and redox-sensitive pathways that generate mechanical and immunologic changes in the respiratory epithelium. In addition to the typical Type-1 immune response, respiratory virus infections stimulate type-2 innate lymphoid cells in the airway epithelium to release epithelial cytokines. Finally, the action of epithelial triggers on airway smooth muscle is the central element in the induction of remodeling and hyperreactivity of the airways in asthma. This article reviews the pathophysiology and functions of the airway epithelium and the role of epithelial damage by different triggers in the development, persistence, and exacerbations of asthma.

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J Asthma

. 2022 Oct 13;1-11.

doi: 10.1080/02770903.2022.2129063. Online ahead of print.

CHECK – multilevel real-world pediatric asthma care coordination: results and lessons learned

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Affiliations expand

- PMID: 36151882

- DOI: 10.1080/02770903.2022.2129063

Abstract

Objective: Because asthma health disparities in children remain common, innovative approaches to obtain asthma health equity are essential. Comprehensive care coordination programs may address the social determinants of health that influence these disparities. This analysis aims to ascertain if receipt of Coordination of Healthcare for Complex Kids (CHECK) program services was associated with changes in school absence, cost, healthcare utilization, and controller prescription in children with asthma.

Methods: The CHECK program ran from December 1, 2014 through August 31, 2017. Engagement with community health workers was rolling and targeted based on risk level (low, medium, or high determined by healthcare utilization). This analysis included school-aged children with asthma (n = 2,629) and sufficient Chicago Public Schools attendance data (n = 430).

Results: Children engaged in CHECK were more likely to be female (p = .046) and to identify as Black and/or Hispanic/Latino than enrolled-only children. School absence was not different between the groups. Average total cost for engaged children was 21.3% more than enrolled-only children the first year (p = .027) but did not differ by the second year (p = .948). At baseline, 68.1% of the cohort had at least one ED visit 12 months prior to

CHECK, this reduced to 49.5% post-1 and 41.9% post-2. Engaged children were 21% more likely to visit an ED (p = .010) and 40% more likely to have a controller.

Conclusions: CHECK program receipt was associated with improved healthcare utilization and controller prescriptions. School attendance did not change. The CHECK model offers potential pathways to support low-income children with asthma.

Keywords: Health disparities; community health workers; health services research; multilevel interventions; patient navigators.

Eur Respir J

. 2022 Oct 13;60(4):2200543.

doi: 10.1183/13993003.00543-2022. Print 2022 Oct.

Interactions between spirometry and oscillometry in patients with moderate to severe asthma

Rory Chan[1], Brian Lipworth[2]

Affiliations expand

- PMID: 35981746

- DOI: 10.1183/13993003.00543-2022

No abstract available

Conflict of interest statement

Conflict of interest: R. Chan has nothing to disclose. B. Lipworth reports non-financial support (equipment) from GSK, equipment, consulting and talks from Thorasys, consulting, advisory board work and talks for Circassia, grants, personal fees (for consulting, talks and advisory board work) and other support (attending meetings) from AstraZeneca and Teva, grants, personal fees (consulting, talks and advisory board work) and other support from Chiesi, grants and personal fees (consulting, advisory board work and talks) from Sanofi and Circassia, in relation to the submitted work; personal fees (consulting) from Lupin, Vectura (prior to 2017), Dr Reddy and Sandoz, personal fees (consulting and talks) from Glenmark, grants, personal fees (consulting, talks and advisory board work) and other support (attending BTS) from Boehringer Ingelheim, grants and personal fees (advisory board work and talks) from Mylan, outside of the submitted work; and the son of B. Lipworth is presently an employee of AstraZeneca.

Review

J Investig Allergol Clin Immunol

. 2022 Oct 11;32(5):345-356.

doi: 10.18176/jiaci.0822. Epub 2022 May 6.

Major Allergen Content in Allergen Immunotherapy Products: The Limited Value of Numbers

S Becker[1], F Fassio[2], R Muñoz-Cano[3], L Klimek[4], C Vidal[5], M D Heath[6], T M Kündig[7], C Vogelberg[8], C Toran[9], E Jensen-Jarolim[10 11], E Heffler[12 13], P V Tomazic[14], M Feindor[6 15], S Hewings[6], T Carreno[6], M Morales[9], R Mösges[16], M A Skinner[6], A Graessel[6 15], D Hernandez[9], M F Kramer[6 15]

Affiliations expand

- PMID: 35522054

- DOI: 10.18176/jiaci.0822

Abstract

The prevalence of allergic disorders has increased drastically over the last 50 years to the extent that they can be considered epidemic. At present, allergen-specific immunotherapy (AIT) is the only therapy that targets the underlying cause of allergic disorders, and evidence of its superiority is based on data accumulated from clinical trials and observational studies demonstrating efficacy and safety. However, several aspects remain unresolved, such as harmonization and standardization of manufacturing and quantification procedures across manufacturers, homogeneous reporting of strength, and the establishment of international reference standards for many allergens. This article discusses issues related to the measurement of major allergen content in AIT extracts, raising the question of whether comparison of products from different manufacturers is an appropriate basis for selecting a specific AIT product. Allergen standardization in immunotherapy products is critical for ensuring quality and, thereby, safety and efficacy. However, lack of harmonization in manufacturing processes, allergen quantification (methodologies and references), national regulatory differences, clinical practice, and labeling shows that the comparison of AIT products based solely on major allergen amounts is not rational and, in fact, impossible. Moreover, when rating the information given for a specific product, it is necessary to take into account further inherent characteristics of products and their application in clinical practice, such as the state of extract modification, addition of adjuvant or adjuvant system, route of administration (sublingual/ subcutaneous), and cumulative dose as per posology (including the volume per administration). Finally, only convincing clinical data can serve as the basis for product-specific evaluation and cross-product comparability of individual products.

Keywords: AIT; Adjuvants; Immunotherapy; Major allergen content; Product comparability; Quality; Standardization methods.

RHINITIS

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Review

Eur Arch Otorhinolaryngol

. 2022 Oct 14.

doi: 10.1007/s00405-022-07694-z. Online ahead of print.

The gut microbiome and allergic rhinitis; refocusing on the role of probiotics as a treatment option

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Affiliations expand

- PMID: 36239785

- DOI: 10.1007/s00405-022-07694-z

Abstract

Introduction: In the industrialized world, the incidence of Allergic rhinitis (AR), often known as hay fever, and other allergic disorders continues to grow. Recent studies have

suggested environmental variables such as bacterial exposures as a potential reason for the rising prevalence of AR. With breakthroughs in our abilities to research the complex crosstalk of bacteria, the gut microbiomes' effect on human development, nutritional requirements, and immunologic disorders has become apparent METHODS: Three search engines, including Scopus, Medline, and PubMed, were searched for related published articles up to and including 1st July 2022.

Results: Several studies have investigated links between commensal microbiome alterations and the development of atopic diseases such as asthma and AR. Besides, studies using probiotics for treating AR suggest that they may alleviate symptoms and improve patient's quality of life.

Conclusion: Research on probiotics and synbiotics for AR suggests they may improve symptoms, quality of life, and laboratory indicators. A better treatment strategy with advantages for patients may be achieved using probiotics, but only if more detailed in vitro and in vivo investigations are conducted with more participants.

Keywords: Dysbiosis; Gut flora; Microbiota; Rhinitis.

- 71 references

SUPPLEMENTARY INFO

Publication types, Grant supportexpand

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J Allergy Clin Immunol

. 2022 Oct 9;S0091-6749(22)01333-1.

doi: 10.1016/j.jaci.2022.08.029. Online ahead of print.

Effects of combination treatment with tezepelumab and allergen immunotherapy on nasal responses to allergen: a randomized controlled trial

Jonathan Corren[1], David Larson[2], Matthew C Altman[3], R Max Segnitz[4], Pedro C Avila[5], Paul A Greenberger[5], Fuad Baroody[6], Mark H Moss[7], Harold Nelson[8], Allison J Burbank[9], Michelle L Hernandez[9], David Peden[9], Sarbjit Saini[10], Stephen Tilles[11], Iftikhar Hussain[12], Don Whitehouse[13], Tielin Qin[2], Miguel Villarreal[14], Michelle Sever[14], Lisa M Wheatley[15], Gerald T Nepom[16], Srinath Sanda[13], Immune Tolerance Network ITN057AD CATNIP Study Team

Affiliations expand

- PMID: 36223848

- DOI: 10.1016/j.jaci.2022.08.029

Abstract

Background: Thymic stromal lymphopoietin (TSLP) has been shown to play a central role in the initiation and persistence of allergic responses.

Objective: We evaluated whether tezepelumab, a human monoclonal anti-TSLP antibody, improved the efficacy of subcutaneous allergen immunotherapy (SCIT) and promoted the development of tolerance in patients with allergic rhinitis.

Methods: We conducted a double-blind parallel design trial in patients with cat allergy. A total of 121 patients were randomized to receive either intravenous tezepelumab plus subcutaneous cat SCIT, cat SCIT alone, tezepelumab alone, or placebo for 52 weeks followed by 52 weeks of observation. Nasal allergen challenges (NAC), skin testing, and blood and nasal samples were obtained throughout the study.

Results: At week 52, the NAC-induced total nasal symptom scores (TNSS) (calculated as an area-under-the-curve [AUC 0-1 hr] and as a peak score [peak 0-1 hr] during the first hour after nasal allergen challenge) were significantly reduced in patients receiving tezepelumab/SCIT compared with SCIT alone. At week 104, one year after stopping treatment, the primary endpoint TNSS AUC 0-1hr was not significantly different in the tezepelumab/SCIT group compared to SCIT alone, while TNSS peak 0-1 hr was significantly lower in those receiving combination treatment vs. SCIT. Transcriptomic analysis of nasal epithelial samples demonstrated that treatment with the combination of SCIT/tezepelumab, but neither monotherapy, caused persistent downregulation of a gene

network related to type 2 inflammation which was associated with improvement in NAC responses.

Conclusions: These results suggest that inhibition of TSLP augments the efficacy of SCIT during therapy and may promote tolerance following a one year course of treatment. (ClinicalTrials.gov Identifier: NCT02237196).

Keywords: Allergy; cytokine; epithelium; inflammation; late phase; lymphocyte; mast cell; rhinitis; thymic stromal lymphopoietin; tolerance; tryptase.

Review

Int Arch Allergy Immunol

. 2022 Oct 12;1-9.

doi: 10.1159/000526604. Online ahead of print.

Local Allergic Rhinitis: Lights and Shadows of a Mysterious Entity

Giulio Melone[1], Veronica Giorgis[2], Marina Di Pino[3], Corrado Pelaia[4], Emanuele Nappi[1 5], Enrico Heffler[1 5], Massimo Landi[6 7], Matteo Gelardi[8], Giovanni Paoletti[9 10]

Affiliations expand

- PMID: 36223735

- DOI: 10.1159/000526604

Abstract

Local allergic rhinitis (LAR) is, to date, a debated and complex entity, still orphan of global consideration and a multicentric approach. LAR does not seem to find a proper positioning in the classic classifications and phenotypes of chronic rhinitis, and its pathophysiology relies specifically on the presence of local IgE. These patients in fact have a suggestive clinical history of allergic rhinitis in the presence of negative skin prick tests and serum IgE tests for the suspect allergen. Nasal allergen challenge, assessment of local IgE, basophil activation test (BAT), and nasal cytology are, at the moment, the most used tests in the diagnostic approach to the disease, despite their limitations. Considering that the correct interpretation of diagnostic tests and their clinical relevance is fundamental in the assessment of the right diagnosis and the subsequent therapy, we propose a new diagnostic approach that encompasses all of these methodologies and suggest that several pragmatic randomized control trials as well as prospective, multicentric studies directed at the long-term follow-up of LAR be carried out to further investigate this debated entity.

Keywords: IgE; Local allergic rhinitis; Nasal allergen provocation test; Nasal cytology; Nonallergic rhinitis.

Clin Otolaryngol

. 2022 Oct 12.

doi: 10.1111/coa.13990. Online ahead of print.

Blood eosinophil count in the diagnosis of allergic-like rhinitis with chronic rhinosinusitis

Qiqi Luo[1], Siyi Zhou[1], Bo Yuan[1], Zeli Feng[2], Guolin Tan[1], Honghui Liu[1]

Affiliations expand

- PMID: 36222453

- DOI: 10.1111/coa.13990

Abstract

Background: Allergic rhinitis (AR) and nonallergic rhinitis (NAR) often are comorbid with chronic rhinosinusitis (CRS). Finding a convenient test that distinguishes these complex conditions is helpful for effective treatment. We aimed to analyze blood parameter differences between AR and NAR patients with/without CRS.

Methods: Eight hundred thirteen patients, including AR and NAR with different conditions (CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP)) were analyzed in this retrospective study. Patients with a nasal deviation alone were included as healthy controls (HC). ROC analysis was used to assess the value of blood parameters for diagnosing AR or NAR with/without CRS.

Results: Compared to nonallergic-like rhinitis (HC, CRSwNP and CRSsNP), the blood eosinophil count was significantly increased in the allergic-like rhinitis groups, except for NAR-CRSsNP (AR, AR-CRSwNP, AR-CRSsNP, NAR and NAR-CRSwNP). The NAR-CRSsNP group had a higher level of eosinophils than the HC and CRSsNP groups. Among allergic-like rhinitis patients, eosinophils were higher in allergic-like rhinitis patients with CRSwNP (AR-CRSwNP and NAR-CRSwNP) than in allergic-like rhinitis patients without CRSwNP (AR, AR-CRSsNP, NAR and NAR-CRSsNP). However, no difference in blood eosinophils was observed between AR and NAR. There was also no difference among nonallergic-like

rhinitis patients. Similar findings were found for the blood eosinophil proportion. Furthermore, the blood eosinophil count was a good predictor of allergic-like rhinitis, especially allergic-like rhinitis with CRSwNP.

Conclusion: The blood eosinophil count and proportion may be good diagnostic predictors of allergic-like rhinitis but cannot differentiate between AR and NAR. This indicator may be much better in predicting allergic-like rhinitis with CRSwNP. This article is protected by copyright. All rights reserved.

Keywords: allergic rhinitis; blood parameters; eosinophil; nonallergic rhinitis.

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Evolution of Eczema, Wheeze, and Rhinitis from Infancy to Early Adulthood: Four Birth Cohort Studies

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Collaborators, Affiliations expand

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Abstract

Rationale: The relationship between eczema, wheeze or asthma, and rhinitis is complex, and epidemiology and mechanisms of their comorbidities is unclear. **Objectives:** To investigate within-individual patterns of morbidity of eczema, wheeze, and rhinitis from birth to adolescence/early adulthood. **Methods:** We investigated onset, progression, and resolution of eczema, wheeze, and rhinitis using descriptive statistics, sequence mining, and latent Markov modeling in four population-based birth cohorts. We used logistic regression to ascertain if early-life eczema or wheeze, or genetic factors (*filaggrin [FLG]* mutations and 17q21 variants), increase the risk of multimorbidity. **Measurements and Main Results:** Single conditions, although the most prevalent, were observed significantly less frequently than by chance. There was considerable variation in the timing of onset/remission/persistence/intermittence. Multimorbidity of eczema+wheeze+rhinitis was rare but significantly overrepresented (three to six times more often than by chance). Although infantile eczema was associated with subsequent multimorbidity, most children with eczema (75.4%) did not progress to any multimorbidity pattern. *FLG* mutations and rs7216389 were not associated with persistence of eczema/wheeze as single conditions, but both increased the risk of multimorbidity (*FLG* by 2- to 3-fold, rs7216389 risk variant by 1.4- to 1.7-fold). Latent Markov modeling revealed five latent states (no disease/low risk, mainly eczema, mainly wheeze, mainly rhinitis, multimorbidity). The most likely transition to multimorbidity was from eczema state (0.21). However, although this was one of the highest transition probabilities, only one-fifth of those with eczema transitioned to multimorbidity. **Conclusions:** Atopic diseases fit a multimorbidity framework, with no evidence for sequential atopic march progression. The highest transition to multimorbidity was from eczema, but most children with eczema (more than three-quarters) had no comorbidities.

Keywords: asthma; atopic march; birth cohorts; eczema; wheeze.

Comment in

- Revisiting the Atopic March Current Evidence.
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SUPPLEMENTARY INFO

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CHRONIC COUGH

Mycopathologia

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Challenges, Characteristics, and Outcomes of Chronic Pulmonary Aspergillosis: A 11-Year Experience in A Middle-Income Country

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Affiliations expand

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Abstract

Objectives: Chronic pulmonary aspergillosis (CPA) is a research priority in fungal diseases with a need for new studies to reduce misdiagnosis with more common diseases, discuss improvement in diagnostic methods and better characterize gaps in antifungal and surgical treatments to improve clinical outcomes.

Methods: In this retrospective study, we reviewed medical records of patients diagnosed with CPA from January 2010 to June 2021 at University of São Paulo, São Paulo, Brazil. We evaluated clinical characteristics, radiological findings, serology, treatment, and outcomes.

Results: The study included 91 participants, with 43 (47.3%) patients who underwent surgery and 69 (75.8%) received antifungal therapy. We found a predominance of middle-aged adults (median 51 years), males (n = 58, 64%) with lower BMI (median 21.3 kg/m^2). The most common underlying lung disease was pulmonary tuberculosis (n = 70, 76.9%). The commonest symptoms were cough (n = 67, 74%), haemoptysis, and dyspnea (n = 63, 70%). The most common chest computerized tomography abnormalities were cavity (n = 86, 94.5%), with a predominance of mycetomas (n = 78, 91%). The serology was positive in 81% (61/75). The one-year mortality was low (3.3%). Clinical improvement and stability occurred in 89% of participants for constitucional symptoms and 86% for pulmonary symptoms. While serological improvement and stability occurred in 71%. Radiological improvement and stability occurred in 75%.

Conclusion: We observed a good outcome after 1-year follow-up, in which the majority had improvement or stability of pulmonary and constitutional symptoms, decrease in CIE titers and low mortality.

Keywords: Antifungal therapy; Chronic pulmonary aspergillosis; Outcomes; Surgery.

- 24 references

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Review

Lung

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Narrative Review of the Mechanisms and Treatment of Cough in Asthma,

Cough Variant Asthma, and Non-asthmatic Eosinophilic Bronchitis

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Abstract

Chronic cough is a debilitating condition affecting 10-12% of the general population and is one of the leading causes for referral to secondary care. Many conditions have been associated with chronic cough, including asthma, gastro-esophageal reflux disease and upper airways cough syndrome. Inflammatory airway conditions including cough variant asthma (CVA) and non-asthmatic eosinophilic bronchitis (NAEB) contribute to a significant proportion of presentations with chronic cough, with differing diagnostic criteria and different responses to commonly used asthma therapy for their respective diagnoses. Mechanistic studies in both animal models and humans have identified increased neuronal sensitivity and subsequent central sensitization. These mechanisms include inflammatory-mediated nociceptor sensitization and alterations of afferent nerve terminal excitability, phenotypic changes in the vagal afferent neurons over time, and central neuroplasticity resulting from increased synaptic signalling from peripheral afferents. The aim of this review is to discuss the mechanisms, neurophysiology, and management approaches currently available for patients presenting with chronic cough with underlying asthma, CVA, and NAEB and to shed a light on areas of further research required to elucidate the mechanisms of cough in this patient population.

Keywords: Asthma; Chronic cough; Cough variant asthma; Eosinophils; Nerves; Non-asthmatic eosinophilic bronchitis.

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