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COPD

Medicine (Baltimore)

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. 2022 Jul 22;101(29):e29261.

doi: 10.1097/MD.0000000000029261.

Evaluation of chest radiography and low-dose computed tomography as valuable screening tools for thoracic diseases

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Affiliations expand

- PMID: 35866756

- DOI: 10.1097/MD.0000000000029261

Abstract

Background: Recent studies have shown that low-dose computed tomography (LDCT) is effective for the early detection of lung cancer. However, the utility of chest radiography (CR) and LDCT for other thoracic diseases has not been as well investigated as it has been for lung cancer. This study aimed to clarify the usefulness of the veridical method in the screening of various thoracic diseases.

Methods: Among individuals who had received general health checkups over a 10-year period, those who had undergone both CR and LDCT were selected for analysis. The present study included 4317 individuals (3146 men and 1171 women). We investigated cases in which abnormal opacity was detected on CR and/or LDCT.

Results: A total of 47 and 124 cases had abnormal opacity on CR and LDCT, respectively. Among these, 41 cases in which the abnormal opacity was identified by both methods contained 20 treated cases. Six cases had abnormalities only on CR, and none of the cases required further treatment. Eighty-three cases were identified using LDCT alone. Of these, many cases, especially those over the age of 50 years, were diagnosed with thoracic tumors and chronic obstructive pulmonary disease, which required early treatment. In contrast, many cases of pulmonary infections have improved spontaneously, without any treatment.

Conclusion: These results revealed that LDCT allowed early detection of thoracic tumors and chronic obstructive pulmonary disease, especially in individuals over the age of 50 years. CR is still a useful imaging modality for other thoracic diseases, especially in individuals under the age of 49 years.

Conflict of interest statement

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

- 41 references

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J Physiol

. 2022 Jul 21.

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Exertional dyspnoea in patients with mild-to-severe chronic obstructive pulmonary disease (COPD): Neuromechanical mechanisms

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- DOI: 10.1113/JP283252

Abstract

Key points: Dyspnoea during exercise is a common and troublesome symptom reported by patients with chronic obstructive pulmonary disease (COPD) and is linked to an elevated inspiratory neural drive (IND). The precise mechanisms of elevated IND and dyspnoea across the continuum of airflow obstruction severity in COPD remains unclear. The present study sought to determine the mechanisms of elevated IND [by diaphragm EMG, EMGdi (%max)] and dyspnoea during cardiopulmonary exercise testing (CPET) across the continuum of COPD severity. There was a strong association between increasing dyspnoea intensity and EMGdi (%max) during CPET across the COPD continuum despite significant heterogeneity in underlying pulmonary gas exchange and respiratory mechanical impairments. Critical inspiratory constraints occurred at progressively lower ventilation during exercise with worsening severity of COPD. This was associated with the progressively lower resting inspiratory capacity with worsening disease severity. Earlier critical inspiratory constraint was associated with earlier neuromechanical dissociation and greater likelihood of reporting the sensation of 'unsatisfied inspiration'.

Abstract: In patients with COPD, exertional dyspnoea generally arises when there is imbalance between ventilatory demand and capacity, but the neurophysiological mechanisms are unclear. We therefore determined if disparity between elevated inspiratory neural drive (IND) and tidal volume (V_T) responses (neuromechanical dissociation) impacted dyspnoea intensity and quality during exercise, across the COPD severity

spectrum. In this two-centre, cross-sectional observational study, 89 participants with COPD divided into tertiles of FEV_1 %predicted (Tertile 1 = FEV_1 = 87 ± 9%, Tertile 2 = 60 ± 9%, Tertile 3 = 32 ± 8%) and 18 non-smoking controls, completed a symptom-limited cardiopulmonary exercise tests (CPET) with measurement of IND by diaphragm electromyography [EMGdi (%max)]. The association between increasing dyspnoea intensity and EMGdi (%max) during CPET was strong (r = 0.730, P < 0.001) and not different between the four groups who showed marked heterogeneity in pulmonary gas exchange and mechanical abnormalities. Significant inspiratory constraints (tidal volume/inspiratory capacity (V_T /IC) ≥ 70%) and onset of neuromechanical dissociation (EMGdi (%max):V_T /IC > 0.75) occurred at progressively lower $\dot{V}_E$ from Control to Tertile 3. Lower resting IC meant earlier onset of neuromechanical dissociation, heightened dyspnoea intensity and greater propensity (93% in Tertile 3) to select qualitative descriptors of 'unsatisfied inspiration'. We concluded that, regardless of marked variation in mechanical and pulmonary gas exchange abnormalities in our study sample, exertional dyspnoea intensity was linked to the magnitude of EMGdi (%max). Moreover, onset of critical inspiratory constraints and attendant neuromechanical dissociation amplified dyspnoea intensity at higher exercise intensities. Simple measurements of IC and breathing pattern during CPET provide useful insights into mechanisms of dyspnoea and exercise intolerance in individuals with COPD. Abstract figure legend As chronic obstructive pulmonary disease severity increases, worsening gas exchange and respiratory mechanical impairment causes increased afferent receptor stimulation, increasing inspiratory neural drive at a given ventilation. The widening disparity between progressively greater inspiratory neural drive and reduced ventilatory output causes, 'neuromechanical dissociation'. This is strongly associated with a rapid increase in the intensity of dyspnea during exercise, and the onset of the sensation of 'unsatisfied inspiration'. This article is protected by copyright. All rights reserved.

Keywords: COPD; cardiopulmonary exercise testing; dyspnoea; inspiratory neural drive; respiratory mechanics.

Respirology

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doi: 10.1111/resp.14325. Online ahead of print.

Treatable traits in the NOVELTY study

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Affiliations expand

- PMID: 35861464

- DOI: 10.1111/resp.14325

Abstract

Background and objective: Asthma and chronic obstructive pulmonary disease (COPD) are two prevalent and complex diseases that require personalized management. Although a strategy based on treatable traits (TTs) has been proposed, the prevalence and relationship of TTs to the diagnostic label and disease severity established by the attending physician in a real-world setting are unknown. We assessed how the presence/absence of specific TTs relate to the diagnosis and severity of 'asthma', 'COPD' or 'asthma + COPD'.

Methods: The authors selected 30 frequently occurring TTs from the NOVELTY study cohort (NOVEL observational longiTudinal studY; NCT02760329), a large (n = 11,226), global study that systematically collects data in a real-world setting, both in primary care clinics and specialized centres, for patients with 'asthma' (n = 5932, 52.8%), 'COPD' (n = 3898, 34.7%) or both ('asthma + COPD'; n = 1396, 12.4%).

Results: The results indicate that (1) the prevalence of the 30 TTs evaluated varied widely, with a mean ± SD of 4.6 ± 2.6, 5.4 ± 2.6 and 6.4 ± 2.8 TTs/patient in those with 'asthma', 'COPD' and 'asthma + COPD', respectively ($p < 0.0001$); (2) there were no large global geographical variations, but the prevalence of TTs was different in primary versus specialized clinics; (3) several TTs were specific to the diagnosis and severity of disease, but many were not; and (4) both the presence and absence of TTs formed a pattern that is recognized by clinicians to establish a diagnosis and grade its severity.

Conclusion: These results provide the largest and most granular characterization of TTs in patients with airway diseases in a real-world setting to date.

Keywords: COPD; airways; allergy; asthma; bronchitis; chronic obstructive pulmonary disease; emphysema; smoking.

- 36 references

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NPJ Prim Care Respir Med

. 2022 Jul 20;32(1):25.

doi: 10.1038/s41533-022-00288-6.

A descriptive cohort study of withdrawal from inhaled corticosteroids in COPD patients

Smit Patel[1], Scott Dickinson[2], Kevin Morris[2], Helen F Ashdown[3], James D Chalmers[4]

Affiliations expand

- PMID: 35859081

- PMCID: PMC9300648

- DOI: 10.1038/s41533-022-00288-6

Abstract

Inhaled corticosteroid (ICS) therapy is widely prescribed without a history of exacerbations and consensus guidelines suggest withdrawal of ICS in these patients would reduce the risk of side effects and promote cost-effective prescribing. The study describes the prescribing behaviour in the United Kingdom (UK) in relation to ICS withdrawal and identifies clinical outcomes following withdrawal using primary and secondary care electronic health records between January 2012 and December 2017. Patients with a history ≥12 months' exposure who withdrew ICS for ≥6 months were identified into two cohorts; those prescribed a long-acting bronchodilator maintenance therapy and those that were not prescribed any maintenance therapy. The duration of withdrawal, predictors of restarting ICS, and clinical outcomes were compared between both patient cohorts. Among 76,808 patients that had ≥1 prescription of ICS in the study period, 11,093 patients (14%) withdrew ICS therapy at least once during the study period. The median time without ICS was 9 months (IQR 7-14), with the majority (71%) receiving subsequent ICS prescriptions after withdrawal. Patients receiving maintenance therapy with a COPD review at withdrawal were 28% less likely to restart ICS (HR: 0.72, 95% CI 0.61, 0.85). Overall, 69% and 89% of patients that withdrew ICS had no recorded exacerbation event or COPD hospitalisation, respectively, during the withdrawal. This study provides evidence that most patients withdrawing from ICS do not experience COPD exacerbations and withdrawal success can be achieved by carefully planning routine COPD reviews whilst optimising the use of available maintenance therapies.

Conflict of interest statement

S.P., S.D., and K.M. are employees of Boehringer Ingelheim Ltd. Dr. J.C. has received research grants from Boehringer Ingelheim, AstraZeneca, GlaxoSmithKline and Pfizer. Dr. J.C. has also received fees for consultancy and speaking from Boehringer Ingelheim. Dr. Helen Ashdown’s academic department receives money for her role in a collaborative project with Boehringer Ingelheim Ltd. We declare that none of the authors has competing financial or non-financial interests as defined by Nature Portfolio.

- 47 references
- 4 figures

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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Adv Ther

. 2022 Jul 20.

doi: 10.1007/s12325-022-02234-x. Online ahead of print.

Comparative Efficacy of Umeclidinium/Vilanterol Versus Other Bronchodilators for the Treatment of Chronic Obstructive Pulmonary Disease: A Network Meta-Analysis

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Affiliations expand

- PMID: 35857184

- DOI: 10.1007/s12325-022-02234-x

Abstract

Introduction: Few randomised controlled trials (RCTs) have directly compared long-acting muscarinic antagonist/long-acting β_2-agonist (LAMA/LABA) dual maintenance therapies for patients with chronic obstructive pulmonary disease (COPD). This systematic literature review and network meta-analysis (NMA) compared the efficacy of umeclidinium/vilanterol (UMEC/VI) versus other dual and mono-bronchodilator therapies in symptomatic patients with COPD.

Methods: A systematic literature review (October 2015-November 2020) was performed to identify RCTs ≥ 8 weeks long in adult patients with COPD that compared LAMA/LABA combinations against any long-acting bronchodilator-containing dual therapy or monotherapy. Data extracted on changes from baseline in trough forced expiratory volume in 1 s (FEV_1), St George's Respiratory Questionnaire (SGRQ) total score, Transitional

Dyspnoea Index (TDI) focal score, rescue medication use and moderate/severe exacerbation rate were analysed using an NMA in a frequentist framework. The primary comparison was at 24 weeks. Fixed effects model results are presented.

Results: The NMA included 69 full-length publications (including 10 GSK clinical study reports) reporting 49 studies. At 24 weeks, UMEC/VI provided statistically significant greater improvements in FEV_1 versus all dual therapy and monotherapy comparators. UMEC/VI provided similar improvements in SGRQ total score compared with all other LAMA/LABAs, and significantly greater improvements versus UMEC 125 µg, glycopyrronium 50 µg, glycopyrronium 18 µg, tiotropium 18 µg and salmeterol 50 µg. UMEC/VI also provided significantly better outcomes versus some comparators for TDI focal score, rescue medication use, annualised moderate/severe exacerbation rate, and time to first moderate/severe exacerbation.

Conclusion: UMEC/VI provided generally better outcomes compared with LAMA or LABA monotherapies, and consistent improvements in lung function (measured by change from baseline in trough FEV_1 at 24 weeks) versus dual therapies. Treatment with UMEC/VI may improve outcomes for symptomatic patients with COPD compared with alternative maintenance treatments.

Keywords: COPD; Dual bronchodilators; Dual inhaler therapy; LABA; LAMA; Network meta-analysis.

Plain language summary

Bronchodilators are medicines that open the airways, allowing patients with chronic obstructive pulmonary disease (COPD) to breathe more easily. There are two different types of bronchodilators, namely long-acting muscarinic antagonists (LAMAs) and long-acting β_2-agonists (LABAs), which can be used on their own or combined (LAMA/LABAs). Only a few clinical trials have compared different LAMA/LABA combinations with each other, so it is unclear which LAMA/LABA combination provides the greatest benefits for patients.In this study, we used network meta-analysis to compare a LAMA/LABA combination medicine called umeclidinium and vilanterol (UMEC/VI) with other LAMAs and LABAs used alone or in combination to treat patients with COPD. Network meta-analysis is a way of comparing two or more medicines by analysing data from many studies. We systematically searched for evidence from clinical trials in adult patients with COPD that were at least 8 weeks long and that compared LAMA/LABA combinations with a LAMA, a LABA, or another LAMA/LABA combination. We analysed data from 49 clinical trials that met these criteria.We found that patients treated with UMEC/VI had better lung function than patients treated with alternative LAMA/LABA combinations or bronchodilators used on their own. Patients treated with UMEC/VI had better quality of life than those receiving some other treatments, but not all. All the medicines we compared had similar side effects.Our results suggest that treating patients with COPD with UMEC/VI might improve their lung function and quality of life more than alternative bronchodilators.

- 63 references

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Intern Emerg Med

. 2022 Jul 20;1-9.

doi: 10.1007/s11739-022-03048-z. Online ahead of print.

The predictive value of modified risk scores in patients with acute exacerbation of COPD: a retrospective cohort study

Buğra İlhan[1], Göksu Bozdereli Berikol[2], Halil Doğan[2]

Affiliations expand

- PMID: 35854207
- PMCID: PMC9296366
- DOI: 10.1007/s11739-022-03048-z

Abstract

This study aims to evaluate the performance of CREWS (Chronic Respiratory Early Warning Score), S-NEWS (Salford-National Early Warning Score), qNEWS (Quick National Early Warning Score), NEWS (National Early Warning Score), and qSOFA (Quick Sequential Organ Failure Assessment) scores in predicting mortality, intensive care unit (ICU) admission and the need for mechanical ventilation (MV) of patients presented with acute exacerbations of chronic obstructive pulmonary disease (AECOPD). This retrospective cohort study was conducted in the emergency department of a tertiary hospital between January 1 and December 31, 2019. The patients with AECOPD and aged ≥ 18 were included. Patients who were transferred from another center and whose data could not be reached were excluded. Demographic information, comorbid diseases, variables of the scores, laboratory results, and outcomes were recorded. A total of 575 consecutive patients were included. The 30-day mortality, ICU admission, and MV need rate were 5.7% (n = 33), 9.6% (n = 55), and 13.7% (n = 79), respectively. Each score had moderate-to-excellent performance in predicting MV need and ICU admission, while their performance in predicting mortality was poor. CREWS is the most successful score in predicting 30-day mortality (AUC 0.695), ICU admission (AUC 0.841), and MV need (AUC 0.924). ICU admission, age, and creatinine levels were associated with mortality ($p < 0.05$). All scores have better performance in predicting ICU admission and MV need than mortality. ICU admission, age, and creatinine levels may be the predictors of mortality among AECOPD patients.

Keywords: Acute exacerbation; Chronic obstructive pulmonary disease; Chronic respiratory disease; Early warning score; Emergency.

Conflict of interest statement

The authors declare that they did not have any potential conflicts of interest with regard to this research, or the authorship and publication of this article.

- 29 references
- 2 figures

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Lung

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. 2022 Jul 19.

doi: 10.1007/s00408-022-00554-x. Online ahead of print.

Effects of Pulmonary Rehabilitation Including Inspiratory Muscle Training in Patients with Chronic Obstructive Pulmonary Disease after Stratification by the Degree of Static Hyperinflation

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Affiliations expand

- PMID: 35852621

- DOI: 10.1007/s00408-022-00554-x

Abstract

Background: Inspiratory muscle training (IMT) improves inspiratory muscle strength, exercise capacity and health status in patients with chronic obstructive pulmonary disease (COPD). However, there is no additional effect on top of comprehensive pulmonary rehabilitation (PR). It is unclear whether patients with different baseline degrees of static hyperinflation respond differentially to IMT as part of a PR program. Therefore, the aim was to study the effects of IMT as an add-on on PR after stratification for baseline degrees of static hyperinflation.

Methods: In this single center retrospective study data were extracted between June 2013 and October 2020 of COPD patients who participated in a comprehensive PR program including IMT. IMT was performed twice daily, one session consisted of 3 series of 10 breaths and training intensity was set initially at a load of approximately 50% of patients' maximal static inspiratory mouth pressure (MIP). The primary outcome measure was MIP. Secondary outcomes were the distance achieved on the 6-min walk test (6MWD),

endurance cycling exercise capacity at 75% of the peak work rate (CWRT) and disease-specific health status using the COPD assessment test.

Results: 754 patients with COPD were screened for eligibility and 328 were excluded because of repeated PR programs, missing data or baseline residual volume (RV) > 350%. In total, 426 COPD patients were categorized into RV categories 50-130% (n = 84), 131-165% (n = 86), 166-197% (n = 86), 198-234% (n = 85) and 235-349% (n = 85). In the whole sample, MIP, endurance exercise capacity and health status improved significantly. The change in 6MWD was higher in the lowest baseline degree of static hyperinflation [+ 39 (9-92) m] compared with the baseline highest degree of static hyperinflation [+ 11 (- 18-54) m] ($p < 0.05$).

Conclusions: IMT as part of a PR program in patients with COPD with different baseline degrees improved MIP irrespective of the degree of static lung hyperinflation. Improvement in functional exercise capacity was significantly higher in the group with the lowest degree of static hyperinflation compared with the patients with the highest degree of static hyperinflation.

Keywords: Chronic obstructive pulmonary disease; Inspiratory muscle training; Maximal static inspiratory mouth pressure; Static hyperinflation.

- 32 references

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Editorial

Respirology

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. 2022 Jul 18.

doi: 10.1111/resp.14331. Online ahead of print.

Vaccination in patients with COPD: COVID has raised the bar

Grant Waterer[1]

Affiliations expand

- PMID: 35852029

- DOI: 10.1111/resp.14331

No abstract available

Keywords: COPD; COVID-19; chronic obstructive pulmonary disease; coronavirus disease; influenza and pneumococcal vaccination; pneumonia.

- 13 references

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Lung

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. 2022 Jul 18.

doi: 10.1007/s00408-022-00556-9. Online ahead of print.

Acute Effect of Bronchodilator on Intrathoracic Airway Wall Compliance in COPD Patients

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Affiliations expand

- PMID: 35851429

- DOI: 10.1007/s00408-022-00556-9

Abstract

Purpose: In patients with chronic obstructive pulmonary disease (COPD), bronchial responsiveness after acute administration of short acting bronchodilators is conventionally assessed by measuring the improvement of forced expiratory volume in the first second (FEV_1) during a maximal forced expiratory maneuver. This study aimed to measure the variation of intrathoracic airway wall compliance (AWC) after acute administration of short acting beta-2 agonist in COPD patients since this might influence the final modification of airway caliber during maximal expiratory effort and the resulting bronchodilation as inferred by FEV_1 changes.

Methods: In a group of 10 patients suffering from COPD, intrathoracic AWC was measured at middle (50% of Forced Vital Capacity (FVC) and low (75% of FVC) lung volumes using the interrupter method during forced expiratory maneuver in basal conditions and after acute inhalation of albuterol (salbutamol) (400 mcg by MDI). Ten healthy subjects were examined similarly as a control group.

Results: Lower values of baseline intrathoracic AWC at both lung volumes were found in COPD patients (1.72 ± 0.20 ml/cmH_2O and 1.08 ± 0.20 ml/cmH_2O, respectively) as compared to controls (2.28 ± 0.27 ml/cmH_2O and 1.44 ± 0.22 ml/cmH_2O, respectively) ($p < 0.001$). In COPD patients, AWC increased significantly at both lung volumes after salbutamol, amounting to 1.81 ± 0.38 ml/cmH_2O and 1.31 ± 0.39 ml/cmH_2O, respectively ($p < 0.01$), but the relative change was not different from that observed in controls.

Conclusion: In COPD patients, AWC is reduced compared to controls, but after bronchodilator, the intrathoracic airways become more compliant. The consequent increased collapsibility under high positive pleural pressure could limit the airway caliber improvement seen after bronchodilator, as assessed by the FEV_1 changes during the forced expiratory maneuver, underestimating the effective bronchodilation achieved in these patients.

Keywords: Airway wall compliance; Bronchial responsiveness; Bronchodilator; COPD; Chronic bronchiolitis.

BMJ Support Palliat Care

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Morphine for chronic breathlessness in COPD: improvement predictors-cross-sectional study

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- PMID: 35850961

- DOI: 10.1136/spcare-2022-003693

Abstract

Objective: Morphine is used as palliative treatment of chronic breathlessness in patients with chronic obstructive pulmonary disease (COPD). Part of the patients does not experience a clinically meaningful improvement of breathlessness and it is unclear which characteristics are related to a clinically meaningful improvement of breathlessness after morphine. Therefore, this study assessed whether sensory breathlessness description, demographic and clinical characteristics are related with this improvement.

Methods: Cross-sectional secondary analysis of the intervention arm of a randomised controlled trial. 45 patients with COPD and moderate-to-very severe chronic breathlessness despite optimal treatment received 20-30 mg oral sustained-release morphine daily for 4 weeks. Using binary logistic regression, the relationship between a clinically meaningful improvement in breathlessness (≥1 point on 0-10 numeric rating scale) and the baseline variables sensory breathlessness descriptors, age, breathlessness and body mass index (BMI) was assessed.

Results: Twenty-one participants (42%) showed a clinically meaningful improvement. Baseline breathlessness (OR 1.51, 95% CI 1.04 to 2.21, p=0.03) and BMI (OR 1.13, 95% 1.02-1.28, p=0.02) were significant associated to a clinically meaningful improvement of breathlessness, while age and sensory breathlessness descriptors were not.

Conclusions: Worse baseline breathlessness and higher BMI are associated to a clinically meaningful improvement of breathlessness in patients using 20-30 mg oral sustained-release morphine. Opioid treatment should be considered in patients with COPD with severe breathlessness, taking into account the patient's BMI.

Keywords: Chronic obstructive pulmonary disease; Drug administration; Dyspnoea.

Conflict of interest statement

Competing interests: MHJvdB-E reports personal fees from Kyowa Kirin and MSD, outside the submitted work. DJAJ reports grants from ZonMw, the Hague, the Netherlands, during the conduct of the study; personal fees from Boehringer Ingelheim, Novartis, and AstraZeneca, outside the submitted work.

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The influence of adverse drug effects on health-related quality of life in chronic obstructive pulmonary disease patients

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- PMID: 35849340

- DOI: 10.1093/ijpp/riac052

Abstract

Objectives: Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide. Concerns have been raised about the influence of adverse drug effects on patient's health-related quality of life (HRQoL) in COPD patients. This study aimed to evaluate the impact of COPD treatment-related adverse effects on HRQoL in COPD patients.

Methods: In a cross-sectional study, COPD patients aged 40 years or older were identified and interviewed during their hospital visits. The EuroQol 5 Dimension 5 Level (EQ-5D-5L) questionnaire was used for evaluating HRQoL. Potential treatment adverse effects were evaluated as experienced by participants during the last 2 weeks preceding the interview. The intensity of adverse effects was reported in the following categories: never, mild, moderate and severe. Multivariable linear regression model was performed to evaluate the influence of adverse drug effects on utility scores as an indicator of HRQoL.

Key findings: A total of 203 patients diagnosed with COPD were recruited in the current study. The mean utility score of the study sample was 0.68 (SD = 0.36). Moderate-severe constipation, moderate-severe confusion, mild urinary hesitation, moderate-severe urinary hesitation, moderate-severe dry eyes and moderate-severe drowsiness were significant predictors/determinants for the average utility scores (coefficients were -0.099, -0.191, -0.111, -0.157 and -0.144, respectively). In addition, having higher COPD Assessment Test scores and severe disease was negatively associated with average utility scores (coefficients were -0.287 and -0.124, respectively).

Conclusions: Higher intensity of COPD treatment-related adverse effects has a negative influence on HRQoL in COPD patients. Anticholinergic drug effects are of concern in COPD adults' population.

Keywords: COPD; HRQoL; Jordan; adverse drug effects.

Review

Adv Ther

. 2022 Jul 17.

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Fluticasone Furoate/Umeclidinium/Vilanterol (FF/UMEC/VI) Triple Therapy Compared with Other Therapies for the

Treatment of COPD: A Network Meta-Analysis

Afisi S Ismaila[1,2], Katrin Haeussler[3], Alexandrosz Czira[4], Ji-Hee Youn[5], Mia Malmenäs[6], Nancy A Risebrough[7], Jatin Agarwal[8], Maria Nassim[3], Raj Sharma[4], Chris Compton[4], Claus F Vogelmeier[9,10], MeiLan K Han[11], David M G Halpin[12]

Affiliations expand

- PMID: 35849317

- DOI: 10.1007/s12325-022-02231-0

Abstract

Introduction: Randomized controlled trials (RCTs) comparing triple therapies (inhaled corticosteroid [ICS], long-acting β_2-agonist [LABA], and long-acting muscarinic antagonist [LAMA]) for the treatment of chronic obstructive pulmonary disease (COPD) are limited. This network meta-analysis (NMA) investigated the comparative efficacy of single-inhaler fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) versus any triple (ICS/LABA/LAMA) combinations and dual therapies in patients with COPD.

Methods: This NMA was conducted on the basis of a systematic literature review (SLR), which identified RCTs in adults aged at least 40 years with COPD. The RCTs compared different ICS/LABA/LAMA combinations or an ICS/LABA/LAMA combination with any dual therapy (ICS/LABA or LAMA/LABA). Outcomes of interest included forced expiratory volume in 1 s (FEV_1), annualized rate of combined moderate and severe exacerbations, St George's Respiratory Questionnaire (SGRQ) total score and SGRQ responders, transition dyspnea index focal score, and rescue medication use (RMU). Analyses were conducted at 24 weeks (primary endpoint), and 12 and 52 weeks (if feasible).

Results: The NMA was informed by five trials reporting FEV_1 at 24 weeks. FF/UMEC/VI was statistically significantly more effective at increasing trough FEV_1 (based on change from baseline) than all triple comparators in the network apart from UMEC + FF/VI. The NMA was informed by 17 trials reporting moderate or severe exacerbation endpoints. FF/UMEC/VI demonstrated statistically significant improvements in annualized rate of combined moderate or severe exacerbations versus single-inhaler budesonide/glycopyrronium bromide/formoterol fumarate (BUD/GLY/FOR). At 24 weeks, the NMA was informed by five trials. FF/UMEC/VI showed statistically significant improvements in annualized rate of combined moderate or severe exacerbations versus UMEC + FF/VI and BUD/GLY/FOR. FF/UMEC/VI also demonstrated improvements in mean

SGRQ score versus other triple therapy comparators at 24 weeks, and a significant reduction in RMU compared with BUD/GLY/FOR (160/18/9.6).

Conclusion: The findings of this NMA suggest favorable efficacy with single-inhaler triple therapy comprising FF/UMEC/VI. Further analysis is required as additional evidence becomes available.

Keywords: Beclomethasone dipropionate/formoterol fumarate dihydrate/glycopyrronium bromide; Budesonide/glycopyrronium bromide/formoterol fumarate; COPD; Fluticasone furoate/umeclidinium/vilanterol; Indirect treatment comparison; Network meta-analysis; Triple therapy.

- 45 references

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. 2022 Jul 17;22(1):274.

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Determinants of depressive symptom trajectories in self-reported chronic obstructive pulmonary disease patients

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Affiliations expand

- PMID: 35843947

- PMCID: PMC9288686

- DOI: 10.1186/s12890-022-02060-5

Free PMC article

Abstract

Background: The depressive symptom trajectories of COPD individuals and its' predictors remain to be established. Therefore, this study aimed to explore the trajectories of depressive symptoms and predictors thereof in COPD patients.

Methods: A total of 1286 individuals over 45 years of age with self-reported COPD were assessed. Depressive symptoms were evaluated using the Center for Epidemiological Studies Depression Scale short form, with depressive symptom trajectories being identified via latent class growth analysis. The predictors of depressive symptom trajectories were then identified through multinomial logistic regression.

Results: Finally, three depressive symptom trajectories were identified: "steadily high", "consistently moderate", and "consistently low". Old age, longer night-time sleep duration, and high BMI were found to be associated with individuals being classified under the "consistently moderate" trajectory. Moreover, participants exhibiting more than two chronic conditions were more likely to be classified under the "consistently moderate" trajectory. Higher education and lower hand grip strength were important predictors of individuals classified in the "steadily high" trajectory.

Conclusions: To conclude, three depressive symptom trajectories were identified in self-reported COPD individuals. To ensure timely intervention aimed at preventing the worsening of depressive symptom progression among COPD individuals, health-care workers should regular analyze depressive symptoms and provide appropriate interventions when possible.

Keywords: COPD; Depressive symptoms; Latent class growth modeling; Trajectory pattern.

Conflict of interest statement

The authors declare that they have no competing interests.

- 35 references
- 1 figure

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Meta-Analysis

BMC Pulm Med

. 2022 Jul 17;22(1):275.

doi: 10.1186/s12890-022-02072-1.

Inhaled corticosteroids, COPD, and the incidence of lung cancer: a systematic review and dose response meta-analysis

Tyler Pitre[1], Michel Kiflen[2 3], Terence Ho[4], Luis M Seijo[5], Dena Zeraatkar[# 6], Juan P de Torres[# 7]

Affiliations expand

- PMID: 35843928
- PMCID: PMC9290283
- DOI: 10.1186/s12890-022-02072-1

Free PMC article

Abstract

Background: There has been debate on whether inhaled corticosteroids (ICS) reduce the incidence of lung cancer amongst patients with Chronic Obstructive Lung Disease (COPD). We aimed to perform a systematic review and dose-response meta-analysis on available observational data.

Methods: We performed both a dose response and high versus low random effects meta-analysis on observational studies measuring whether lung cancer incidence was lower in patients using ICS with COPD. We report relative risk (RR) with 95% confidence intervals (CI), as well as risk difference. We use the GRADE framework to report our results.

Results: Our dose-response suggested a reduction in the incidence of lung cancer for every 500 ug/day of fluticasone equivalent ICS (RR 0.82 [95% 0.68-0.95]). Using a baseline risk of 7.2%, we calculated risk difference of 14 fewer cases per 1000 ([95% CI 24.7-3.8 fewer]). Similarly, our results suggested that for every 1000 ug/day of fluticasone equivalent ICS, there was a larger reduction in incidence of lung cancer (RR 0.68 [0.44-0.93]), with a risk difference of 24.7 fewer cases per 1000 ([95% CI 43.2-5.4 fewer]). The certainty of the evidence was low to very low, due to risk of bias and inconsistency.

Conclusion: There may be a reduction in the incidence for lung cancer in COPD patients who use ICS. However, the quality of the evidence is low to very low, therefore, we are limited in making strong claims about the true effect of ICS on lung cancer incidence.

Keywords: COPD; Dose-response meta-analysis; ICS; Lung cancer.

Conflict of interest statement

None.

- 39 references
- 5 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Observational Study

Fam Pract

. 2022 Jul 19;39(4):570-578.

doi: 10.1093/fampra/cmab107.

Continuity of care for patients with chronic disease: a registry-based observational study from Norway

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Affiliations expand

- PMID: 34536072

- PMCID: PMC9295609

- DOI: 10.1093/fampra/cmab107

Abstract

Background: Continuity of care (CoC) is accepted as a core value of primary care and is especially appreciated by patients with chronic conditions. Nevertheless, there are few studies investigating CoC for these patients across levels of healthcare.

Objective: This study aims to investigate CoC for patients with somatic chronic diseases, both with regular general practitioners (RGPs) and across care levels.

Methods: We conducted a registry-based observational study by using nationwide consultation data from Norwegian general practices, out-of-hours services, hospital outpatient care, and private specialists with public contracts. Patients with diabetes mellitus (type I or II), asthma, chronic obstructive pulmonary disease, or heart failure in 2012, who had ≥2 consultations with these diagnoses during 2014 were included. CoC was measured during 2014 by using the usual provider of care (UPC) index and Bice-Boxerman continuity of care score (COCI). Both indices have a value between 0 and 1.

Results: Patients with diabetes mellitus comprised the largest study population (N = 79,165) and heart failure the smallest (N = 4,122). The highest mean UPC and COCI were measured for patients with heart failure, 0.75 and 0.77, respectively. UPC increased gradually with age for all diagnoses, while COCI showed this trend only for asthma. Both indices had higher values in urban areas.

Conclusions: Our findings suggest that CoC in Norwegian healthcare system is achieved for a majority of patients with chronic diseases. Patients with heart failure had the highest continuity with their RGP. Higher CoC was associated with older age and living in urban areas.

Keywords: Norway; chronic disease; continuity of care; general practice; healthcare system; observational study.

- Cited by 1 article
- 34 references
- 1 figure

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

FULL TEXT LINKS

OXFORD ACADEMIC

ASTHMA

Br J Sports Med

. 2022 Jul 21;bjsports-2022-105759.

doi: 10.1136/bjsports-2022-105759. Online ahead of print.

International Olympic Committee (IOC) consensus statement on acute respiratory illness in athletes part 1: acute respiratory infections

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Affiliations expand

- PMID: 35863871

- DOI: 10.1136/bjsports-2022-105759

Abstract

Acute illnesses affecting the respiratory tract are common and form a significant component of the work of Sport and Exercise Medicine (SEM) clinicians. Acute respiratory illness (ARill) can broadly be classified as non-infective ARill and acute respiratory infections (ARinf). The aim of this consensus is to provide the SEM clinician with an overview and practical clinical approach to ARinf in athletes. The International Olympic Committee (IOC) Medical and Scientific Commission appointed an international consensus group to review ARill (non-infective ARill and ARinf) in athletes. Six subgroups of the IOC Consensus group were initially established to review the following key areas of ARill in

athletes: (1) epidemiology/risk factors for ARill, (2) ARinf, (3) non-infective ARill including ARill due to environmental exposure, (4) acute asthma and related conditions, (5) effects of ARill on exercise/sports performance, medical complications/return-to-sport and (6) acute nasal/vocal cord dysfunction presenting as ARill. Several systematic and narrative reviews were conducted by IOC consensus subgroups, and these then formed the basis of sections in the consensus documents. Drafting and internal review of sections were allocated to 'core' members of the consensus group, and an advanced draft of the consensus document was discussed during a meeting of the main consensus core group in Lausanne, Switzerland on 11 to 12 October 2021. Final edits were completed after the meeting. This consensus document (part 1) focusses on ARinf, which accounts for the majority of ARill in athletes. The first section of this consensus proposes a set of definitions and classifications of ARinf in athletes to standardise future data collection and reporting. The remainder of the consensus paper examines a wide range of clinical considerations related to ARinf in athletes: epidemiology, risk factors, pathology/pathophysiology, clinical presentation and diagnosis, management, prevention, medical considerations, risks of infection during exercise, effects of infection on exercise/sports performance and return-to-sport guidelines.

Keywords: Consensus; IOC; Respiratory System.

Conflict of interest statement

Competing interests: None declared except for the following: RB who works as Director for the IOC Medical and Scientific Department, International Olympic Committee, Lausanne, Switzerland. LE who works as Head of Scientific Activities for the IOC Medical and Scientific Department, International Olympic Committee, Lausanne, Switzerland. UE who is the Chair of the Medical and Scientific Department, International Olympic Committee, Lausanne, Switzerland. TS who works as Scientific Manager for the IOC Medical and Scientific Department, International Olympic Committee, Lausanne, Switzerland.

J Allergy Clin Immunol Pract

. 2022 Jul 18;S2213-2198(22)00704-8.

doi: 10.1016/j.jaip.2022.07.005. Online ahead of print.

The role of social determinants of health in the use of telemedicine for asthma in children

Sarah P Justvig[1], Linda Haynes[1], Kristin Karpowicz[1], Fiona Unsworth[1], Sheila Petrosino[1], Alon Peltz[2], Bridgette L Jones[3], Madison Hickingbotham[4], Joanne Cox[1], Ann Chen Wu[5], Faye F Holder-Niles[6]

Affiliations expand

- PMID: 35863670

- DOI: 10.1016/j.jaip.2022.07.005

Abstract

Asthma is the most common chronic health condition among children in the United States. The adverse impacts of social determinants of health often manifest in unmet health-related social needs, potentially contributing to worse asthma outcomes. With the onset and rapid spread of COVID-19 and the identification of asthma as a potential risk factor for more severe disease, our asthma program quickly pivoted to a remote access telemedicine asthma population management platform to best meet the needs of our most at-risk patients. Our practice provides care to a large proportion of Black and Latino/a/e children in urban areas insured by the State Medicaid Program and impacted by unmet social needs. As we pivoted to telemedicine, we consistently reached a greater number of patients and families than pre-pandemic and observed decreased ED visits and hospitalizations. About 1 in 5 families received resource touch points spanning categories of transportation, food and supplies, clothing, utilities, and rent. Overall, families reported positive experiences with telemedicine, including the ability to connect remotely with our social work and resource teams. Telemedicine may be an effective strategy for addressing both the medical and social needs of children with asthma at risk for worse outcomes.

Keywords: COVID-19; asthma; pandemic; social determinants of health; telemedicine; virtual visits.

J Allergy Clin Immunol Pract

. 2022 Jul 18;S2213-2198(22)00701-2.

doi: 10.1016/j.jaip.2022.06.050. Online ahead of print.

Corticosteroid responsiveness following mepolizumab in severe eosinophilic asthma – a randomised, placebo-controlled crossover trial [MAPLE]

Freda Yang[1], John Busby[2], Liam G Heaney[2], Ian D Pavord[3], Chris E Brightling[4], Katie Borg[3], Jane P McDowell[2], Sarah E Diver[4], Rahul Shrimanker[5], Peter Bradding[4], Malcolm Shepherd[6], Rekha Chaudhuri[6], Medical Research Council: Refractory Asthma Stratification Programme (RASP-UK Consortium)

Affiliations expand

- PMID: 35863669

- DOI: 10.1016/j.jaip.2022.06.050

Abstract

Background: Mepolizumab inhibits interleukin-5 (IL-5) activity, reduces exacerbation frequency and maintenance oral corticosteroid (OCS) dosage in patients with severe eosinophilic asthma (SEA). Some patients remain dependent on OCS despite anti-IL-5 treatment suggesting residual corticosteroid responsive mechanisms.

Objective: We aimed to determine the clinical and anti-inflammatory effects of OCS in patients with SEA on mepolizumab.

Methods: We conducted a randomised, triple-blind, placebo-controlled crossover trial of prednisolone (0.5mg/kg/day, maximum 40mg/day, for 14±2 days) in adults with SEA after ≥12 weeks of mepolizumab. We compared change in asthma symptoms, quality of life, lung function measured by spirometry and airwave oscillometry, FeNO, and blood and sputum eosinophil cell count after prednisolone and placebo.

Results: 27 patients completed the study. Prednisolone did not improve ACQ-5 (mean difference in change for prednisolone vs placebo -0.23, 95% CI -0.58 to 0.11), mini-AQLQ (0.03, 95% CI -0.26 to 0.42), SGRQ (0.24, 95% CI -3.20 to 3.69) or VAS scores for overall asthma symptoms (0.11, 95% CI -0.58 to 0.80). The mean difference for FEV_1 in favour of prednisolone was 105ml (95% CI -4 to 213 ml); FEF_{25-75} 484ml/s (95% CI 151 to 816 ml/s); FeNO reduction 41% (95% CI 25 to 54%); blood eosinophil count reduction 49% (95% CI 31 to 62%); and percentage of sputum eosinophil reduction 71% (95% CI 26 to 89%).

Conclusion: OCS improved small airway obstruction and reduced biomarkers of type 2 inflammation but had no significant effect on symptoms or quality of life in patients with severe eosinophilic asthma receiving treatment with mepolizumab.

Keywords: Asthma; IL-5; T2; Type 2 inflammation; corticosteroid resistance; eosinophils; interleukin-5; mepolizumab; oral corticosteroids; prednisolone; severe eosinophilic asthma.

J Asthma

. 2022 Jul 21;1-14.

doi: 10.1080/02770903.2022.2103428. Online ahead of print.

Clinical burden related to oral corticosteroid treatment of severe asthma in Spain: LEVANTE study

Xavier Muñoz Gall[1], Javier Domínguez-Ortega[2], Silvia Pascual[3], Carlos Cabrera López[4], Resler Gustavo[5], Javier Nuevo[6], Gema Monteagudo[5]

Affiliations expand

- PMID: 35862653

- DOI: 10.1080/02770903.2022.2103428

Abstract

Background: Severe asthma treatment with oral corticosteroids (OCS) added to inhaled corticosteroids and a long-acting β2-agonist (ICS-LABA) may result in more treatment burden and increased adverse effects.*Objective and Methods***:** This ambispective multicenter observational study aimed at describing the clinical burden in patients with severe asthma on stable high-dose ICS-LABA who received OCS during ≥6 months (maintenance group) or ≥2 cycles in the previous 12 months (bursts group). Data collection comprised a retrospective 12-month baseline period and 2 follow-up visits at 3 and 6 months. *Results***:** Eighty-nine patients were evaluable (30 on maintenance, 59 on bursts). At baseline, mean (SD) daily prednisone equivalent exposure in the total population was 24.6 (14.7) mg: 13.8 (9.4) mg on maintenance and 29.9 (14.3) mg on bursts. During the 6-month follow-up period, mean (SD) daily dose in the total cohort was 22.5 (18.8) mg: 17.2 (18.6) mg on maintenance and 28.4 (20.6) mg on bursts. The overall annual severe exacerbations rate during the 12-month baseline period was 2.05 per patient-year and 1.5 per patient-year over the 6-month follow-up, and frequency of hospitalizations and emergency department visits were similar on both maintenance and bursts use. *Conclusions*: Results show a suboptimal control of severe asthma despite such high doses of OCS and persistence of disease burden regardless of the prescribing pattern in maintenance or bursts. There is therapeutic inertia to continue using OCS despite the increased risk of adverse effects and the availability of biologics.

Keywords: bursts; clinical burden; maintenance; oral steroids regimen; real-world; severe asthma; therapeutic inertia.

J Asthma

. 2022 Jul 21;1-10.

doi: 10.1080/02770903.2022.2103427. Online ahead of print.

Severe non-atopic asthma: omalizumab can reduce severe asthma exacerbations

Lise Melscoet[1], Naji Khayath[1,2], Nicolas Migueres[1], Marc-André Goltzene[3], Nicolas Meyer[3], Frédéric de Blay[1,2]

Affiliations expand

- PMID: 35862624

- DOI: 10.1080/02770903.2022.2103427

Abstract

Introduction: Humanized monoclonal anti-IgE antibody (omalizumab) has demonstrated efficacy in severe atopic asthma. However, few studies have assessed its efficacy in non-atopic and even less in T2-low severe asthma. The objective was to determinate the omalizumab response according to atopic status.**Methods**: This retrospective, real-world study was performed in the Chest Diseases Department of Strasbourg University Hospital from January 1, 2006, to June 30, 2017. The response to omalizumab was assessed in 139 patients 4, 6, and 12 months after treatment and compared to data collected prior to omalizumab initiation.**Results**: Forty-four patients (31.7%) had severe non-atopic asthma and 95 (68.3%) had a severe atopic asthma. In the non-atopic group, omalizumab significantly reduced the severe exacerbation rate by 44% (95% CI 18-64%, $p < 0.05$), 43% (CI 95% 20-60%, $p < 0.05$), and 54% (CI 95% 36-67%, $p < 0.05$), at 4, 6 and 12 months, respectively. A trend toward improvement in FEV1, asthma control and oral corticosteroid use was also observed. These results were not significantly different from those obtained in

atopic asthmatics except a more effective oral corticosteroid sparing in atopic group ($p < 0.05$). Similar reduction of severe exacerbation rates were observed in T2-low asthma subgroup (non-atopic, non-eosinophilic).**Conclusion**: Omalizumab was effective in severe asthma, regardless of atopic status.

Keywords: T2 inflammation; atopy; eosinophil; omalizumab; severe asthma.

J Asthma

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. 2022 Jul 21;1-20.

doi: 10.1080/02770903.2022.2103429. Online ahead of print.

Effects of aerobic exercise on asthma control and quality of life in adults: a systematic review

Joshua Ang[1], Ray Moussa[1], Safiya Shaikh[2], Sandra Mele[1]

Affiliations expand

- PMID: 35862617

- DOI: 10.1080/02770903.2022.2103429

Abstract

Objective: The aim of this study is to review the effects of aerobic exercise on asthma control and quality of life in adult patient populations.:**Data Sources**: Randomized controlled trials and prospective studies published between January 2012 and April 2022 were searched in Scopus, Web of Science, and PubMed databases.:**Study Selections**: We

followed pre-specified inclusion criteria and excluded manuscripts that studied pediatric populations and those that did not study asthma control or quality of life. We included ten randomized controlled trials and four prospective studies from a combined 2286 search results.:**Results**: Of the included studies, all but three studies found significant improvement in asthma control and quality of life after aerobic intervention. The method of measuring aerobic intervention varied among the studies. Statistical significance was consistent among studies that used maximal heart rate and peak power output to measure intervention.**Conclusion**: Aerobic exercise intervention can improve asthma control and quality of life in both the acute and chronic response phase. Aerobic activity can be measured by various methods, but in this review, there were no significant adverse events with activity. Higher quality studies are necessary to confirm these results.

Keywords: Control/Management; Prevention; Quality of Life; Reviews; Therapy.

JAMA

. 2022 Jul 21.

doi: 10.1001/jama.2022.12258. Online ahead of print.

Therapy for Mild to Moderate Asthma

Sarah E Gray[1], Adam S Cifu[1], Valerie G Press[1]

Affiliations expand

- PMID: 35862052

- DOI: 10.1001/jama.2022.12258

No abstract available

Review

J Biochem Mol Toxicol

. 2022 Jul 21;e23174.

doi: 10.1002/jbt.23174. Online ahead of print.

Exploring the role of antibiotics and steroids in managing respiratory diseases

Dinesh K Chellappan[1], Parteek Prasher[2], Shakti D Shukla[3,4], Tong W Yee[5], Tiong K Kah[5], Toh W Xyan[5], Tang W Kid[5], Teoh H Si[5], Ting S Weng[5], Nagashekhara Molugulu[6], Lakshmana P Sakthivel[7], Jestin Chellian[1], Thiagarajan Madheswaran[8], Himaja Malipeddi[9], Yogendra Singh[10], Harish Dureja[11], Deepak N Kapoor[12], Poonam Negi[12], Rohit Goyal[13], Lakshmi Thangavelu[14], Deepak Kumar[12], Piyush K Gupta[15], Niraj K Jha[16], Madhur D Shastri[17], Ronan MacLoughlin[18,19,20], Sachin K Singh[4,21], Monica Gulati[4,21], Gaurav Gupta[22,23,24], Kamal Dua[3,4,11]

Affiliations expand

- PMID: 35861662

- DOI: 10.1002/jbt.23174

Abstract

Respiratory diseases (RDs), such as chronic obstructive pulmonary disease, cystic fibrosis, asthma, and pneumonia, are associated with significant morbidity and mortality. Treatment usually consists of antibiotics and steroids. Relevant published literature reviews, studies, and clinical trials were accessed from institutional and electronic databases. The keywords used were respiratory diseases, steroids, antibiotics, and combination of steroids and antibiotics. Selected articles and literature were carefully reviewed. Antibiotics are often

prescribed as the standard therapy to manage RDs. Types of causative respiratory pathogens, spectrum of antibiotics activity, route of administration, and course of therapy determine the type of antibiotics that are prescribed. Despite being associated with good clinical outcome, treatment failure and recurrence rate are still high. In addition, antibiotic resistance has been widely reported due to bacterial mutations in response to the use of antibiotics, which render them ineffective. Nevertheless, there has been a growing demand for corticosteroids (CS) and antibiotics to treat a wide variety of diseases, including various airway diseases, due to their immunosuppressive and anti-inflammatory properties. The use of CS is well established and there are different formulations based on the diseases, such as topical administration, tablets, intravenous injections, and inhaled preparations. Both antibiotics and CS possess similar properties in terms of their anti-inflammatory effects, especially regulating cytokine release. Thus, the current review examines and discusses the different applications of antibiotics, CS, and their combination in managing various RDs. Drawbacks of these interventions are also discussed.

Keywords: antibiotics; corticosteroids; drawbacks; interactions; respiratory diseases.

- 212 references

SUPPLEMENTARY INFO

Publication typesexpand

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J Appl Physiol (1985)

. 2022 Jul 21.

doi: 10.1152/japplphysiol.00103.2022. Online ahead of print.

Small Airways Dysfunction is Associated with Increased Exacerbations in Patients with Asthma

Claire F O'Sullivan[1,2], Kris Nilsen[1,3], Brigitte M Borg[1,2], Matthew J Ellis[1], Pam Matsas[1], Frank Thien[2,4], Jo A Douglass[5], Chris Stuart-Andrews[1], Gregory G King[6], Gordon Kim Prisk[7], Bruce R Thompson[1,8]

Affiliations expand

- PMID: 35861519

- DOI: 10.1152/japplphysiol.00103.2022

Abstract

There is poor understanding of why some patients with asthma experience recurrent exacerbations despite high levels of treatment. We compared measurements of peripheral ventilation heterogeneity and respiratory system mechanics in participants with asthma who were differentiated according to exacerbation history, to ascertain whether peripheral airway dysfunction was related to exacerbations. Three asthmatic groups: "Stable" (no exacerbations for >12 months, n=18), "Exacerbation-prone" (≥1 exacerbation requiring systemic corticosteroids within the last 12 months, but stable for ≥1-month, n=9) and "Treated-exacerbation" (exacerbation requiring systemic corticosteroids within the last 1 month, n=12) were studied. All participants were current non-smokers with <10pack/years smoking history. Spirometry, static lung volumes, ventilation heterogeneity from multi-breath nitrogen washout (MBW) and respiratory system mechanics from oscillometry were measured. The Exacerbation-prone group compared to the Stable group had slightly worse spirometry (FEV_1 Z-score -3.58(1.13) vs -2.32(1.06), p=0.03), however acinar ventilation heterogeneity (S_{acin} Z-score 7.43(8.59) vs 3.63(3.88), p=0.006) and respiratory system reactance (X_{rs} $cmH_2O.s.L^{-1}$ -2.74(3.82) vs -1.32(1.94), p=0.01) were much worse in this group. The Treated-exacerbation group had worse spirometry but similar small airway function, compared with the Stable group. Patients with asthma who exacerbate have worse small airway function as evidenced by increases in S_{acin} measured by MBW and delta X_{rs} from oscillometry, both markers of small airway dysfunction, compared with those that do not.

Keywords: Asthma exacerbation; Peripheral airways; Ventilation heterogeneity.

SUPPLEMENTARY INFO

Grant supportexpand

Respirology

. 2022 Jul 21.

doi: 10.1111/resp.14325. Online ahead of print.

Treatable traits in the NOVELTY study

Alvar Agustí[1 2 3 4], Eleni Rapsomaniki[5], Richard Beasley[6], Rod Hughes[7], Hana Müllerová[8], Alberto Papi[9 10], Ian D Pavord[11], Maarten van den Berge[12], Rosa Faner[3 4], NOVELTY Study Investigators

Affiliations expand

- PMID: 35861464

- DOI: 10.1111/resp.14325

Abstract

Background and objective: Asthma and chronic obstructive pulmonary disease (COPD) are two prevalent and complex diseases that require personalized management. Although a strategy based on treatable traits (TTs) has been proposed, the prevalence and relationship of TTs to the diagnostic label and disease severity established by the attending physician in a real-world setting are unknown. We assessed how the presence/absence of specific TTs relate to the diagnosis and severity of 'asthma', 'COPD' or 'asthma + COPD'.

Methods: The authors selected 30 frequently occurring TTs from the NOVELTY study cohort (NOVEL observational longiTudinal studY; NCT02760329), a large (n = 11,226), global study that systematically collects data in a real-world setting, both in primary care clinics and specialized centres, for patients with 'asthma' (n = 5932, 52.8%), 'COPD' (n = 3898, 34.7%) or both ('asthma + COPD'; n = 1396, 12.4%).

Results: The results indicate that (1) the prevalence of the 30 TTs evaluated varied widely, with a mean ± SD of 4.6 ± 2.6, 5.4 ± 2.6 and 6.4 ± 2.8 TTs/patient in those with 'asthma', 'COPD' and 'asthma + COPD', respectively ($p < 0.0001$); (2) there were no large global geographical variations, but the prevalence of TTs was different in primary versus specialized clinics; (3) several TTs were specific to the diagnosis and severity of disease, but many were not; and (4) both the presence and absence of TTs formed a pattern that is recognized by clinicians to establish a diagnosis and grade its severity.

Conclusion: These results provide the largest and most granular characterization of TTs in patients with airway diseases in a real-world setting to date.

Keywords: COPD; airways; allergy; asthma; bronchitis; chronic obstructive pulmonary disease; emphysema; smoking.

- 36 references

SUPPLEMENTARY INFO

Grant supportexpand

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11

Review

Clin Exp Allergy

. 2022 Jul 21.

doi: 10.1111/cea.14207. Online ahead of print.

Pediatric asthma and non-allergic comorbidities: a review of current risk and proposed mechanisms

Bronwyn K Brew[1,2], Emma Caffrey Osvald[1,3], Tong Gong[1], Anna M Hedman[1], Kirsten Holmberg[4], Henrik Larsson[1,5], Jonas F Ludvigsson[1,6], Mwenya Mubanga[1], Awad I Smew[1], Catarina Almqvist[1,3]

Affiliations expand

- PMID: 35861116

- DOI: 10.1111/cea.14207

Abstract

It is increasingly recognised that children with asthma are at a higher risk of other non-allergic concurrent diseases than the non-asthma population. A plethora of recent research has reported on these comorbidities and progress has been made into understanding the mechanisms for comorbidity. The goal of this review was to assess the most recent evidence (2016-2021) on the extent of common comorbidities (obesity, depression & anxiety, neurodevelopmental disorders, sleep disorders and autoimmune diseases) and the latest mechanistic research, highlighting knowledge gaps requiring further investigation. We found the majority of recent studies from around the world demonstrates that children with asthma are at an increased risk of having at least one of the studied comorbidities. A range of potential mechanisms were identified including common early life risk factors, common genetic factors, causal relationships, asthma medication and embryologic origins. Studies varied in their selection of population, asthma definition and outcome definitions. Next steps in future studies should include using objective measures of asthma, such as lung function and immunological data, as well as investigating asthma phenotypes and endotypes. Larger complex genetic analyses are needed, including genome wide association studies, gene expression- functional as well as pathway analyses, or Mendelian Randomization techniques; and identification of gene-environment interactions, such as epi-genetic studies or twin analyses, including omics and early life exposure data. Importantly, research should have relevance to clinical and public health translation including clinical practice, asthma management guidelines and intervention studies aimed at reducing comorbidities.

Keywords: anxiety; asthma; children; comorbidity; depression; obesity; sleep.

Published Erratum

Nat Med

. 2022 Jul 20.

doi: 10.1038/s41591-022-01949-2. Online ahead of print.

Author Correction: Metabolomic profiling reveals extensive adrenal suppression due to inhaled corticosteroid therapy in asthma

Priyadarshini Kachroo[#1], Isobel D Stewart[#2], Rachel S Kelly[1], Meryl Stav[1], Kevin Mendez[1], Amber Dahlin[1], Djøra I Soeteman[1 3], Su H Chu[1], Mengna Huang[1], Margaret Cote[1], Hanna M Knihtilä[1 4], Kathleen Lee-Sarwar[1], Michael McGeachie[1], Alberta Wang[1], Ann Chen Wu[5], Yamini Virkud[6], Pei Zhang[7 8], Nicholas J Wareham[2], Elizabeth W Karlson[9], Craig E Wheelock[7 8 10], Clary Clish[11], Scott T Weiss[1], Claudia Langenberg[2 12], Jessica A Lasky-Su[13]

Affiliations expand

- PMID: 35859205

- DOI: 10.1038/s41591-022-01949-2

No abstract available

Erratum for

- Metabolomic profiling reveals extensive adrenal suppression due to inhaled corticosteroid therapy in asthma.
  Kachroo P, Stewart ID, Kelly RS, Stav M, Mendez K, Dahlin A, Soeteman DI, Chu SH, Huang M, Cote M, Knihtilä HM, Lee-Sarwar K, McGeachie M, Wang A, Wu AC, Virkud Y, Zhang P, Wareham NJ, Karlson EW, Wheelock CE, Clish C, Weiss ST, Langenberg C, Lasky-Su JA.Nat Med. 2022 Apr;28(4):814-822. doi: 10.1038/s41591-022-01714-5. Epub 2022 Mar 21.PMID: 35314841

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CPT Pharmacometrics Syst Pharmacol

. 2022 Jul 20.

doi: 10.1002/psp4.12842. Online ahead of print.

Integrated systems modeling of severe asthma: Exploration of IL-33/ST2 antagonism

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Affiliations expand

- PMID: 35857704

- DOI: 10.1002/psp4.12842

Abstract

Asthma is a complex, heterogeneous disease with a high unmet medical need, despite therapies targeting a multitude of pathways. The ability to quantitatively integrate preclinical and clinical data on these pathways could aid in the development and testing of novel targets and therapeutics. In this work, we develop a computational model of asthma biology, including key cell types and mediators, and create a virtual population capturing clinical heterogeneity. The simulated responses to therapies targeting IL-13, IL-4Rα, IL-5, IgE, and TSLP demonstrate agreement with clinical endpoints and biomarkers of type 2 (T2) inflammation, including blood eosinophils, FEV1, IgE, and FeNO. We use the model to explore the potential benefit of targeting the IL-33 pathway with anti-IL-33 and anti-ST2. Model predictions are compared with data on blood eosinophils, FeNO, and FEV1 from recent anti-IL-33 and anti-ST2 trials and used to interpret trial results based on pathway biology and pharmacology. Results of sensitivity analyses on the contributions of IL-33 to the predicted biomarker changes suggest that anti-ST2 therapy reduces circulating blood eosinophil levels primarily through its impact on eosinophil progenitor maturation and IL-5-dependent survival, and induces changes in FeNO and FEV1 through its effect on immune cells involved in T2 cytokine production. Finally, we also investigate the impact of ST2 genetics on the conferred benefit of anti-ST2. The model includes representation of a wide array of biologic mechanisms and interventions that will provide mechanistic insight and support clinical program design for a wide range of novel therapies during drug development.

Allergy

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. 2022 Jul 20.

doi: 10.1111/all.15448. Online ahead of print.

Selective eosinophil necroptosis contributes to airway inflammation and remodeling in asthma

Andong He[1], Jiaqian Chen[1], Jieying Guan[1], Yuye Huang[2], Huancheng Xie[1], Honglv Chen[1], Yuhuan Wen[1], Qile Chen[1], Shiyun Xie[1], Haoyang Li[1], Changxing Ou[3], Qingling Zhang[3], Ailin Tao[1], Jie Yan[1]

Affiliations expand

- PMID: 35855664

- DOI: 10.1111/all.15448

No abstract available

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. 2022 Jul 18;8(3):00670-2021.

doi: 10.1183/23120541.00670-2021. eCollection 2022 Jul.

Clinical response to biologicals for severe asthma: any relevance for sex in different age ranges?

Roberto Benoni[1], Silvia Panunzi[2], Veronica Batani[3], Francesca Moretti[1], Stefano Fuggini[1], Mattia Todesco[4], Gianenrico Senna[3,4], Albino Poli[1], Andrea Vianello[5], Marco Caminati[3]

Affiliations expand

- PMID: 35854871

- PMCID: PMC9289375

- DOI: 10.1183/23120541.00670-2021

Free PMC article

Abstract

Background: Whether sex can influence the clinical response to biological treatment in patients with severe asthma has not been fully addressed.

Aims and methods: The aim of this study was to investigate in patients with severe asthma undergoing biological treatment the individual evolution of lung function measurements and patient-reported asthma control scores over a 12-month follow-up period, in relation to patients' sex, in different age ranges. Second, the change in the administered dose of oral corticosteroids (OCS) before and after 12 months of treatment was investigated.

Results: 64 patients (58% female and 42% male) with a median age of 52 years were enrolled in the study. There were no relevant differences between sexes in terms of lung function, patient-reported asthma control, exacerbation rate and daily OCS dose within the study timeframe. A separate sub-analysis by biological treatment confirmed the same finding. Stratifying individuals by age, we showed that older men had lower lung function parameter values (forced expiratory volume in 1 s (FEV_1) % predicted and FEV_1/forced vital capacity index) than older women, whereas an opposite trend was observed in terms of Asthma Control Test score. No other relevant differences were detected after age stratification.

Conclusion: According to our findings, sex does not act as a determinant of treatment response to biologicals in people with severe asthma. Although to be confirmed in larger studies, our data suggest that neither sex nor age should limit biological treatment prescription, once the eligibility criteria for that therapy are satisfied.

Conflict of interest statement

Conflict of interest: None declared.

- 31 references
- 4 figures

FULL TEXT LINKS

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Review

Respir Care

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. 2022 Jul 19;respcare.09813.

doi: 10.4187/respcare.09813. Online ahead of print.

Effects of Inspiratory Muscle Training and High-Intensity Interval Training on Lung Function and Respiratory Muscle Function in Asthma

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Affiliations expand

- PMID: 35853706

- DOI: 10.4187/respcare.09813

Abstract

Background: Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. Although inspiratory muscle training (IMT) and high-intensity interval training (HIIT) are beneficial for patients with asthma, controversies persist. Therefore, we aimed to investigate the effects of IMT and HIIT on lung function and respiratory muscle function of subjects with asthma.

Methods: We searched PubMed, Embase, Web of Science, and the Cochrane Library databases up to May 2021. Inclusion criteria were randomized controlled trials (RCTs) of subjects with asthma who received either IMT or HIIT. The outcome measures were changes in lung function and respiratory muscle function.

Results: A total of 13 RCTs (10 in IMT and 3 in HIIT) were included, with a total of 598 subjects. The meta-analysis showed a significantly improved FEV_1 of the expected value (FEV_1%pred) (mean difference [MD] 4.49% [95% CI 2.31-6.67], $P < .001$; $I^2 = 13\%$), FVC of the expected value (FVC % pred) (MD 5.72% [95% CI 3.56-7.88], $P < .001$; $I^2 = 0\%$), FEV_1/FVC % (MD 5.01% [95% CI 2.45-7.58], $P < .001$; $I^2 = 25\%$), FVC (L) (MD 0.21 L [95% CI 0.03-0.40], $P = .02$; $I^2 = 0\%$), maximum inspiratory pressure (P_{Imax}) (MD 27.62 cm H_2O [95% CI 6.50-48.74], $P = .01$; $I^2 = 96\%$), and P_{Imax} (%pred) (MD 27.35% [95% CI 6.94-47.76], $P = .009$; $I^2 = 83.5\%$) in the IMT group. There was no statistical significance in maximum expiratory pressure.

Conclusions: IMT improved pulmonary function (FEV_1%pred, FVC) and inspiratory muscle strength in subjects with stable asthma. Due to the small number of RCT studies included and the limited outcome measures involving HIIT, we were unable to draw conclusions about whether HIIT was beneficial in this meta-analysis. Moreover, clinical heterogeneity exists in different areas such as population and training programs; the above conclusions still need to be confirmed in future studies.

Keywords: asthma; high-intensity interval training; inspiratory muscle training; meta-analysis; pulmonary function.

J Asthma

. 2022 Jul 19;1-16.

doi: 10.1080/02770903.2022.2102036. Online ahead of print.

Impact of mepolizumab in patients with high-burden severe asthma within a managed care population

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Affiliations expand

- PMID: 35853158

- DOI: 10.1080/02770903.2022.2102036

Abstract

Objective: To evaluate the real-world impact of mepolizumab on the incidence of asthma exacerbations, oral corticosteroid (OCS) use and asthma exacerbation-related costs in patients with high-burden severe asthma.*Methods:* This was a retrospective study of the MarketScan Commercial and Medicare Databases in patients with high-burden severe asthma (≥80th percentile of total healthcare expenditure and/or significant comorbidity burden). Patients were ≥12 years of age upon mepolizumab initiation (index date November 1, 2015-December 31, 2018) and had ≥2 mepolizumab administrations during the 6 months post-index. Asthma exacerbation frequency (primary outcome), use of OCS (secondary outcome), and asthma exacerbation-related costs (exploratory outcome) were assessed during the 12 months pre-index (baseline) and post-index (follow-up).*Results:* In total, 281 patients were analyzed. Mepolizumab significantly reduced the proportion of patients with any asthma exacerbation ($P < 0.001$) or exacerbations requiring

hospitalization (P = 0.004) in the follow-up versus baseline period. The mean number of exacerbations decreased from 2.5 to 1.5 events/patient/year (relative reduction: 40.0%; P < 0.001). The proportion of patients with ≥1 OCS claim also decreased significantly from 94.0% to 81.9% (relative reduction: 12.9%; P < 0.001), corresponding to a decrease from 6.6 to 4.7 claims/person/year (P < 0.001). Of the 264 patients with ≥1 OCS claim during baseline, 191 (72.3%) showed a decrease in mean daily OCS use by ≥50% in 117 patients (61.3%). Total asthma exacerbation-related costs were significantly lower after mepolizumab was initiated (P < 0.001).*Conclusions:* Mepolizumab reduced exacerbation frequency, OCS use and asthma exacerbation-related costs in patients with high-cost severe asthma. Mepolizumab provides real-world benefits to patients, healthcare systems and payers.

Keywords: corticosteroid use; costs; exacerbations; hospitalization; real-world; retrospective study.

Handb Exp Pharmacol

. 2022 Jul 20.

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Precision Medicine in Asthma Therapy

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- PMID: 35852633

- DOI: 10.1007/164_2022_598

Abstract

Asthma is a complex, heterogeneous disease that necessitates a proper patient evaluation to decide the correct treatment and optimize disease control. The recent introduction of new target therapies for the most severe form of the disease has heralded a new era of treatment options, intending to treat and control specific molecular pathways in asthma pathophysiology. Precision medicine, using omics sciences, investigates biological and molecular mechanisms to find novel biomarkers that can be used to guide treatment selection and predict response. The identification of reliable biomarkers indicative of the pathological mechanisms in asthma is essential to unravel new potential treatment targets. In this chapter, we provide a general description of the currently available -omics techniques, focusing on their implications in asthma therapy.

Keywords: Asthma; Biomarkers; Omics; Precision medicine.

Thorax

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. 2022 Jul 18;thoraxjnl-2022-219052.

doi: 10.1136/thorax-2022-219052. Online ahead of print.

Single dose of budesonide/formoterol turbuhaler compared to salbutamol pMDI for speed of bronchodilator onset in asthma: a randomised cross-over trial

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Affiliations expand

- PMID: 35851045

- DOI: 10.1136/thorax-2022-219052

Abstract

Objective: To compare bronchodilator response after to salbutamol and budesonide/formoterol in adults with stable asthma.

Methods: A double-blind, cross-over, single-centre, placebo-controlled, non-inferiority trial. Adults with stable asthma were randomised to different orders of two treatment regimens: two actuations of placebo via MDI and one actuation of budesonide/formoterol 200/6 µg via turbuhaler; and one actuation of placebo turbuhaler and two actuations of salbutamol 100 µg via MDI. The primary outcome measure was FEV_1 after 2 min. Secondary outcome measures included FEV_1, mBorg Dyspnoea Scale score and visual analogue score for breathlessness over 30 min.

Results: Forty-nine of 50 potential participants were randomised. One participant withdrew following the first intervention visit and another could not be randomised due to COVID-19 restrictions. The mean (SD) change from baseline FEV_1 2 min after treatment administration for budesonide/formoterol and salbutamol was 0.08 (0.14) L, n=49, and 0.17 (0.18) L, n=48, respectively, mean (95% CI) paired difference of -0.097 L (-0.147 to -0.047), p=0.07, against a non-inferiority bound of -0.06 L. In the secondary analysis, FEV_1 over 30 min was lower for budesonide/formoterol compared with salbutamol, difference (95% CI): -0.10 (-0.12 to -0.08) L, p<0.001. There were no differences in Visual Analogue Scale score or mBorg Dyspnoea Scale score between treatments.

Conclusion: The results do not support the primary hypothesis of non-inferiority at the boundary of -0.06 L for the difference between budesonide/formoterol 200/6 µg compared with salbutamol 200 µg for FEV_1 at 2 min, and could be consistent with inferiority with a p value of 0.07. For the secondary analysis of FEV_1 measurements over time, the FEV_1 was higher with salbutamol.

Trial registration number: Australian and New Zealand Clinical Trials Registry (ACTRN 12619001387112).

Keywords: asthma; inhaler devices.

Conflict of interest statement

Competing interests: RB has received research funding from Genentech, AstraZeneca and Health Research Council New Zealand and CureKids (NZ) and personal fees from AstraZeneca, Cipla, Avillion and Theravance all outside the submitted work.

Ann Rheum Dis

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Sequential rituximab and mepolizumab in eosinophilic granulomatosis with polyangiitis (EGPA): a European multicentre observational study

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Collaborators, Affiliations expand

- PMID: 35850947

- DOI: 10.1136/ard-2022-222776

No abstract available

Keywords: Biological Therapy; Epidemiology; Rituximab; Systemic vasculitis.

Conflict of interest statement

Competing interests: GE received consultation honoraria from GSK outside the current work. LD received consultation honoraria from GSK outside the current work. DJ's disclosures of commercial conflicts are as follows: AstraZeneca, Aurinia, BMS, Boehringer-Ingelheim, Chemocentryx, Chugai, CSL, GSK, Infla-RX, Janssen, Novartis, Roche/Genentech, Takeda and Vifor. LM received consultation honoraria from GSK outside the current work. PP received consultation honoraria from GSK, and Novartisand LEOPharma. Professor Camillo Ribi received consultation honoraria from GSK outside the current work. JS received Advisory Board fees from AstraZeneca and GSK. AV received consultation honoraria from GSK outside the current work. All other authors and collaborators declare no conflicts of interest.

Eur Ann Allergy Clin Immunol

. 2022 Jul 18.

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Can dose reduction be made in patients with allergic bronchopulmonary

aspergillosis receiving high-dose omalizumab treatment?

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Affiliations expand

- PMID: 35850503

- DOI: 10.23822/EurAnnACI.1764-1489.261

Free article

Abstract

Objective. To reduce the omalizumab dose in patients with allergic bronchopulmonary aspergillosis (ABPA) who were on long-term omalizumab treatment. **Methods.** Once asthma was controlled, two approaches were used to reduce total monthly omalizumab dose, 1) both extending dose intervals from 2 to 4 weeks and decrease omalizumab dose, 2) to reduce omalizumab dose while keeping dose intervals stable. **Results.** Thirteen patients with ABPA (8F/5M, mean age 53.4 ± 13.0 years) were included. Pre-omalizumab, mean blood eosinophil count was 723.1 ± 547.1 cells/mcL, mean numbers of attacks and hospitalizations were 2.5 ± 1.5 and 1.3 ± 0.8, respectively. Median total monthly omalizumab dose was 750 (min 300, max 900) mg. First and 2nd approach to reduce omalizumab dose was used in nine and four patients with a median time of reduction 32 (min 13, max 47) months. The 2nd dose reduction was made in four patients at median of 23.5 months. Pre-omalizumab, mean oral corticosteroid (OCS, as methylprednisolone) dose was 12.2 ± 10.4 mg daily, it decreased to 0.69 ± 0.95 mg (p = 0.001) in the 1st year of omalizumab and could be stopped in 11 patients. Attacks and hospitalizations decreased to 0.31 ± 0.86 (p less than 0.001) and 0 (p = 0.003), respectively, in the 1st year of omalizumab. Total omalizumab dose was reduced by median 40% (min 20, max 60) in 1st intervention and 50% (min 20, max 67) after 2nd intervention. After omalizumab reduction, asthma control did not deteriorate and there was no need to increase the omalizumab or OCS-dose. **Conclusions.** Decreasing the total omalizumab dose does not cause clinical deterioration in ABPA after the disease is controlled.

Keywords: ABPA; Asthma control; omalizumab; omalizumab dose reduction.

Eur Ann Allergy Clin Immunol

. 2022 Jul 18.

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Bronchospasm and iodinated contrast media (ICM): an accurate evaluation is mandatory

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Affiliations expand

- PMID: 35850502

- DOI: 10.23822/EurAnnACI.1764-1489.262

Free article

No abstract available

Keywords: Adverse drug reaction; bronchial asthma; bronchospasm; cholinergic tone; hypersensitivity; iodinated contrast media; psychological stress.

J Asthma

. 2022 Jul 18;1-14.

doi: 10.1080/02770903.2022.2103708. Online ahead of print.

The rationale of applying inspiratory/expiratory muscle training within the same respiratory cycle in children with bronchial asthma: A placebo-controlled randomized clinical investigation

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Affiliations expand

- PMID: 35849445

- DOI: 10.1080/02770903.2022.2103708

Abstract

Objective: Even though positive implications of inspiratory muscle training (In-MT) have been established in children and adolescents with bronchial asthma (C/AwBA), the role of combined inspiratory and expiratory muscle training (Ex-MT) within the same respiratory cycle (In/Ex-SC) is still unknown. This study was, therefore, set out to explore the effect of In/Ex-SC on respiratory muscle strength, pulmonary functions, and control of asthma symptoms in C/AwBA.**Methods:** This was a placebo-controlled randomized clinical investigation that included 51 C/AwBA (12-18 years). Participants were assigned randomly into three groups: Placebo, In-MT only, or combined In/Ex-SC training (n = 17, each group). The training was conducted for ~35 min, thrice/week over 12 weeks. The maximal inspiratory (IP_{max}) and expiratory (EP_{max}) pressure (indicating the strength of the inspiratory

and expiratory muscles, respectively), pulmonary functions [forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), and FEV_1/FVC index], and asthma control test (ACT) were assessed before and after the intervention.**Results:** The In/Ex-SC yielded larger increases in IP_{max} and EP_{max} than either the Placebo training (*P*=.031 and *P*=.009 respectively) or the In-MT (*P*=.029 and *P*=.032 respectively). Further, In/Ex-SC produced favorable improvement in FEV_1, FVC, and FEV_1/FVC compared to the Placebo training (*P*=.001, *P*=.004, and *P*=.0005 respectively) or In-MT (*P*=.038, *P*=.037, and *P*=.025 respectively) training. Furthermore, In/Ex-SC led to better control of asthma symptoms than the Placebo (*P*<.001) or In-MT (*P*=.002) training.**Conclusion:** This study provides evidence that combined In/Ex-SC can considerably improve respiratory muscle strength, enhance pulmonary function, and promote control over asthma symptoms in C/AwBA.

Keywords: Lung diseases; breathing exercises; bronchial asthma; respiratory function test; respiratory muscle training.

Expert Rev Respir Med

. 2022 Jul 18.

doi: 10.1080/17476348.2022.2099841. Online ahead of print.

Overprescription of short-acting β $_2$-agonists is associated with poor asthma symptom control: results from five Middle Eastern countries included in the SABINA International (III) study

Ashraf Al Zaabi[1], Nasser Busaidi[2], Saleh Al Mutairy[3], Arzu Yorgancıoğlu[4], Kurtuluş Aksu[5], Hamdan Al-Jahdali[6], Siraj Wali[7], Mohamed Elsayed[8], Maarten Jhi Beekman[9]

Affiliations expand

- PMID: 35848074

- DOI: 10.1080/17476348.2022.2099841

Abstract

Background: Although short-acting β_2-agonist (SABA) overuse is associated with poor treatment outcomes, data on SABA use in the Middle East are lacking.

Research design and methods: In this cross-sectional study in patients (aged ≥12 years) with asthma, data on disease characteristics and asthma treatments were collected from the Middle Eastern cohort of the SABA use IN Asthma (SABINA) III study. Patients were classified by investigator-defined asthma severity and practice type. Multivariable regression models analyzed the association between SABA prescriptions and clinical outcomes.

Results: Of 1389 patients (mean age, 46.7 years; female, 69.5%), 85.7% had moderate-to-severe asthma and 88.7% were treated by specialists. Overall, 51.3% of patients experienced ≥1 severe asthma exacerbation in the previous 12 months, with 58.2% having partly controlled or uncontrolled asthma. Notably, 47.1% of patients were prescribed ≥3 SABA canisters (considered overprescription). SABA canisters were purchased over the counter by 15.3% of patients. Higher SABA prescriptions (vs 1-2 canisters), except 3-5 canisters, were associated with increased odds of uncontrolled asthma ($p<0.05$).

Conclusions: SABA overprescription occurred in almost half of all patients in the Middle East, underscoring the need for healthcare providers and policymakers to adhere to the latest evidence-based recommendations to address this public health concern.

Keywords: Asthma; Middle East; prescription; public health; short-acting β2-agonists.

Plain language summary

Asthma is a long-term disease that causes inflammation of the airways in the lungs and affects both adults and children. Despite effective medicines, asthma remains poorly controlled in many patients. Inhaled steroids with anti-inflammatory properties are the most effective controller medications for asthma. However, many patients rely on rescue or reliever medications, including short-acting β_2-agonists (SABAs), as they provide immediate relief from symptoms. However, SABAs do not treat the underlying inflammation of asthma and their continued overuse may place patients at risk of asthma attacks and

hospitalization. The SABA use IN Asthma study, known as SABINA, examined SABA prescriptions in patients with asthma in 24 countries across 5 continents. As part of this study, data were collected on prescriptions for asthma medications (including SABA prescriptions) and the purchase of SABA over-the-counter (OTC) at the pharmacy without a prescription from 1389 patients aged at least 12 years across 5 countries in the Middle East (United Arab Emirates, Kuwait, Oman, Saudi Arabia, and Turkey). Nearly half of all patients were prescribed 3 or more SABA canisters in the previous 12 months, which is above that recommended by asthma treatment guidelines. SABA was also purchased OTC without a prescription by approximately 15% of patients, the majority of whom already received a high number of SABA prescriptions. Prescription of six or more SABA canisters was associated with poor asthma control. Therefore, there is an urgent need for healthcare providers to follow the latest treatment guidelines for asthma to reduce SABA prescriptions.

Tokai J Exp Clin Med

. 2022 Jul 20;47(2):79-84.

Effect of Post-nasal Drip on Overnight-cough Frequency and Cough Pattern in Children with Asthma

Kota Hirai[1], Chinami Kaiga, Tomofumi Otomo, Kenta Kuruma, Yuichi Kama, Koichi Yamaguchi, Masahiko Kato, Hiroyuki Mochizuki

Affiliations expand

- PMID: 35801553

Free article

Abstract

Objective: In children, post-nasal drip (PND)-induced cough is speculated. However, the relationship between PND and cough is still unclear.

Methods: During acute exacerbation of asthma, the number of overnight coughs and the cough pattern were compared in the children with atopic asthma with PND (n = 8) and the children with atopic asthma without PND (n = 27). All subjects had allergic rhinitis according to our original cough monitor.

Results: The total number of overnight coughs was significantly higher in the subjects with PND than in the subjects without PND ($P < 0.05$). In contrast, the overnight cough pattern of the subjects with PDN was found to be the same as in the subjects without PND, showing an increase in the number of coughs at the sleep onset and in the early morning.

Conclusion: Our results suggest that PND may increase the number of nighttime coughs in children with atopic asthma and allergic rhinitis. In contrast, the overnight cough pattern was the same in the two groups, suggesting that this specific cough pattern is due to allergic inflammation of the upper and lower airways.

SUPPLEMENTARY INFO

MeSH termsexpand

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Eur Respir J

. 2022 Jul 21;60(1):2102106.

doi: 10.1183/13993003.02106-2021. Print 2022 Jul.

The environmental impact of inhaled therapy: making informed treatment choices

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Affiliations expand

- PMID: 34916263
- PMCID: PMC9301054
- DOI: 10.1183/13993003.02106-2021

Free PMC article

Abstract

When selecting the best inhaler and drug combination for a patient with respiratory disease, a number of factors should be considered. While efficacy and safety of medical treatments are always a priority, in recent years the environmental impacts of all aspects of life have become an increasingly necessary consideration and inhaled therapies are no exception. The carbon footprint of an item, individual or organisation is one of the most important and quantifiable environmental impacts, assessed by the amount of greenhouse gases (often expressed in terms of carbon dioxide equivalents) generated throughout the life cycle. The two most commonly prescribed and manufactured inhaler types worldwide are pressurised metered-dose inhalers (pMDIs) containing hydrofluorocarbon (HFC) propellants and dry powder inhalers (DPIs). Most of the carbon footprint of current pMDIs is a result of the propellants that they contain (HFC-134a and HFC-227ea, which are potent greenhouse gases). In comparison, the powder in DPIs is dispersed by the patient's own inhalation, meaning DPIs do not contain a propellant and have a lower carbon footprint than most pMDIs currently available. Soft mist inhalers are another propellant-free option: the device contains a spring, which provides the energy to disperse the aqueous medication. In this review, we examine the published data on carbon footprint data for inhalers, providing an analysis of potential implications for treatment decision making and industry initiatives.

Conflict of interest statement

Conflict of interest: A. Woodcock is co-chair of the Montreal Protocol Technology and Economic Assessment Panel, and member of the Medical and Chemical Technical Options Committee; has received compensation for consulting activities from GlaxoSmithKline, Novartis and Sandoz UK; and has received compensation for speaker activities from Novartis, GlaxoSmithKline and Teva. Conflict of interest: K.M. Beeh and/or the institution he represents has in the past 5 years received compensation for services on advisory boards or consulting activities from AstraZeneca, Berlin-Chemie, Boehringer, Chiesi, Elpen, GlaxoSmithKline, Mundipharma, Novartis, Pohl Boskamp, Sanofi and Teva; compensation for speaker activities in scientific meetings supported by AstraZeneca, Berlin-Chemie, Boehringer, Chiesi, Elpen, ERT, GlaxoSmithKline, Novartis, Pfizer, Pohl Boskamp, Sanofi and Teva; compensation for design and performance of clinical trials from AstraZeneca, Boehringer, GlaxoSmithKline, Novartis, Parexel, Pearl Therapeutics, Teva and Sterna. Conflict of interest: H. Sagara has received compensation for speaker activities supported by AstraZeneca, GlaxoSmithKline, Novartis and Sanofi. Conflict of interest: S. Aumônier is employed by ERM, a global sustainability consulting company that undertakes engagements with a wide range of public sector companies, including many in the healthcare sector and including Novartis. Conflict of interest: E. Addo-Yobo is employed by the Kwame Nkrumah University of Science and Technology, in the Dept of Child Health, School of Medicine and Dentistry, and is Honorary Consultant Paediatrician at the Komfo Anokye Teaching Hospital, Kumasi, Ghana with special interest in paediatric asthma and respiratory care and research; has received compensation as a resource person for asthma educational activities supported by AstraZeneca in Ghana. Conflict of interest: J. Khan and/or the institution he represents has received a research grant from NIHR UK for work on Smokeless Tobacco and Campaign for Tobacco Free Kids for a pilot study on looking at smoking policies at restaurants in Karachi, and is a member of the Medical and Chemical Technical Options Committee. Conflict of interest: J. Vestbo has received honoraria for presenting and/or advising from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis and Teva. Conflict of interest: H. Tope is employed by Planet Futures, a consulting business providing services to government, industry and other nongovernmental organisations on climate change, ozone-depleting substances and other environmental issues. As an independent expert, she co-chairs the Medical and Chemicals Technical Options Committee, which provides technical and economic advice, including on inhalers, to the Montreal Protocol. The views expressed herein are those of the co-authors and do not represent those of the Medical and Chemicals Technical Options Committee.

- 66 references
- 3 figures

Observational Study

Fam Pract

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Continuity of care for patients with chronic disease: a registry-based observational study from Norway

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Affiliations expand

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- PMCID: PMC9295609

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Free PMC article

Abstract

Background: Continuity of care (CoC) is accepted as a core value of primary care and is especially appreciated by patients with chronic conditions. Nevertheless, there are few studies investigating CoC for these patients across levels of healthcare.

Objective: This study aims to investigate CoC for patients with somatic chronic diseases, both with regular general practitioners (RGPs) and across care levels.

Methods: We conducted a registry-based observational study by using nationwide consultation data from Norwegian general practices, out-of-hours services, hospital outpatient care, and private specialists with public contracts. Patients with diabetes mellitus (type I or II), asthma, chronic obstructive pulmonary disease, or heart failure in 2012, who had ≥2 consultations with these diagnoses during 2014 were included. CoC was measured during 2014 by using the usual provider of care (UPC) index and Bice-Boxerman continuity of care score (COCI). Both indices have a value between 0 and 1.

Results: Patients with diabetes mellitus comprised the largest study population (N = 79,165) and heart failure the smallest (N = 4,122). The highest mean UPC and COCI were measured for patients with heart failure, 0.75 and 0.77, respectively. UPC increased gradually with age for all diagnoses, while COCI showed this trend only for asthma. Both indices had higher values in urban areas.

Conclusions: Our findings suggest that CoC in Norwegian healthcare system is achieved for a majority of patients with chronic diseases. Patients with heart failure had the highest continuity with their RGP. Higher CoC was associated with older age and living in urban areas.

Keywords: Norway; chronic disease; continuity of care; general practice; healthcare system; observational study.

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Single-cell immunoprofiling after immunotherapy for allergic rhinitis reveals functional suppression of pathogenic Th2 cells and clonal conversion

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- PMID: 35863510

- DOI: 10.1016/j.jaci.2022.06.024

Abstract

Background: Allergic rhinitis is a growing problem worldwide. Currently, the only treatment that can modify the disease is antigen-specific immunotherapy; however, its mechanism(s) of action is not fully understood.

Objective: To comprehensively investigate the role and changes of antigen-specific T cells before and after sublingual immunotherapy (SLIT) for Japanese cedar pollinosis (JCP).

Methods: We cultured PBMCs obtained both before and at 1 year after initiating SLIT and used a combination of single-cell RNA sequence and repertoire sequencing. To investigate biomarkers, we used PBMCs from patients participating a phase II/III trial of SLIT tablets for JCP and PBMCs from good and poor responders in outpatients.

Results: Antigen-stimulated culturing after SLIT led to clonal expansion of Th2 and Treg cells, and most of these $CD4^+$ T cells retained their CDR3 regions before and after treatment, indicating antigen-specific clonal responses and differentiation secondary to SLIT. However, SLIT reduced the number of clonal functional Th2 cells but increased the Trans-type Th2 cell population that expresses musculin (MSC), TGF-β, and IL-2. Trajectory

analysis suggested that SLIT induced clonal differentiation of the Trans-type Th2 cells differentiated into Treg cells. Using real-time PCR, we found that the MSC levels increased in the active SLIT group and good responders after 1 year of treatment.

Conclusion: The combination of single-cell RNA sequencing and repertoire analysis helped reveal a part of the underlying mechanism-that SLIT promotes the expression of MSC on pathogenic Th2 cells and suppresses their function; MSC may be a potential biomarker of SLIT for allergic rhinitis.

Keywords: Allergic rhinitis; Japanese cedar pollinosis; T cell; musculin; repertoire sequencing; single-cell RNA sequence; sublingual immunotherapy.

J Biol Chem

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Helical remodeling augments 5-lipoxygenase activity in the synthesis of pro-inflammatory mediators

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- PMID: 35863431

- DOI: 10.1016/j.jbc.2022.102282

Abstract

The synthesis of pro-inflammatory leukotrienes implicated in asthma, allergic rhinitis, and atherosclerosis is initiated by the enzyme 5-lipoxygenase (5-LOX). The crystal structure of human Stable-5-LOX revealed a conformation where the catalytic iron was inaccessible to bulk solvent as two aromatic residues on a conserved helix-α2 (Hα2) plugged the substrate access portal. Whether 5-LOX can also adopt a more open conformation has not been resolved. Here, we present a new conformation of 5-LOX where Hα2 adopts an elongated conformation equivalent to that described in other animal lipoxygenase structures. Our observation of the sigmoidal kinetic behavior of 5-LOX, which is indicative of positive cooperativity, is consistent with a substrate-induced conformational change that shifts the ensemble of enzyme populations to favor the catalytically competent state. Strategic point mutations along Hα2 designed to unlock the closed conformation and elongate Hα2 resulted in improved kinetic parameters, altered limited-proteolysis data, and a drastic reduction in the length of the lag phase yielding the most active Stable-5-LOX to date. Structural predictions by AlphaFold2 of these variants statistically favor an elongated Hα2 and reinforce a model in which improved kinetic parameters correlate with a more readily adopted, open conformation. Taken together, these data provide valuable insights into the synthesis of leukotrienes.

Conflict of interest statement

Competing interests The authors declare that they have no conflicts of interest with the contents of this article.

Am J Rhinol Allergy

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Utilization of Nasal Mucus to Investigate the Pathophysiology of Chronic Rhinosinusitis

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- PMID: 35848564

- DOI: 10.1177/19458924221111830

Abstract

Background: Nasal mucus is proving to be a useful means by which to study the pathogenesis of chronic rhinosinusitis (CRS). Given the increase in publications examining nasal mucus and the lack of a review on this topic, we will focus on this noninvasive approach to studying CRS. Particular attention will be drawn towards inflammatory cytokines and biomarkers and their influence on disease severity.

Methods: A literature review of papers published in English pertaining to nasal mucus was performed using the PubMed database. The search utilized combinations of the following keywords: sinusitis, polyps, sample collection, nasal mucus, or nasal secretion. Studies solely on acute or bacterial sinusitis, allergic rhinitis, or cystic fibrosis were not included.

Results: A wide variety of materials and methods have been used to collect nasal mucus. Numerous assay types have been performed with the most common being ELISA, cytometric bead array, and proteomics. Most studies have focused on examining the levels of Th1/Th2 cytokines along with chemokines associated with type 2 immunity. Other factors identified include growth factors, senescence-associated proteins, complement, and antimicrobial defenses have also been identified. Nasal mucus cytokines have proven useful in cluster analysis and predicting postoperative improvement in Sino-nasal Outcome Test (SNOT-22) scores. One limitation of the use of nasal mucus is that some studies have suggested that nasal mucus does not always reflect the tissue microenvironment.

Conclusions: Nasal mucus represents a critical tool by which to examine the sinonasal microenvironment in a noninvasive manner. Unlike studies of tissue, it can be utilized in both surgically and medically managed patients and avoids the trauma of biopsies. However, studies are still needed to determine the most effective method for nasal mucus

collection. Studies should also take care to confirm that nasal mucus markers do, in fact, reflect the levels of the product studied in the tissue.

Keywords: chemokine; complement; cytokine; cytometric bead array; nasal mucus; nasal polyp; nasal secretion; olfaction; sinusitis; type 2 inflammation.

Tokai J Exp Clin Med

. 2022 Jul 20;47(2):79-84.

Effect of Post-nasal Drip on Overnight-cough Frequency and Cough Pattern in Children with Asthma

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- PMID: 35801553

Free article

Abstract

Objective: In children, post-nasal drip (PND)-induced cough is speculated. However, the relationship between PND and cough is still unclear.

Methods: During acute exacerbation of asthma, the number of overnight coughs and the cough pattern were compared in the children with atopic asthma with PND (n = 8) and the children with atopic asthma without PND (n = 27). All subjects had allergic rhinitis according to our original cough monitor.

Results: The total number of overnight coughs was significantly higher in the subjects with PND than in the subjects without PND ($P < 0.05$). In contrast, the overnight cough pattern of the subjects with PDN was found to be the same as in the subjects without PND, showing an increase in the number of coughs at the sleep onset and in the early morning.

Conclusion: Our results suggest that PND may increase the number of nighttime coughs in children with atopic asthma and allergic rhinitis. In contrast, the overnight cough pattern was the same in the two groups, suggesting that this specific cough pattern is due to allergic inflammation of the upper and lower airways.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

CHRONIC COUGH

J Paediatr Child Health

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'Long COVID': Symptom persistence in children hospitalised for COVID-19

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- PMID: 35851732

- DOI: 10.1111/jpc.16120

Abstract

Aim: We aimed to describe the long-term outcome with respect to symptom persistence amongst children hospitalised for COVID-19.

Methods: This was a follow-up study of 58 children and adolescents hospitalised with COVID-19. For all patients, the data were collected in a phone call to the family in December 2021 (9 months after the initial study and more than 13 months after their admission to hospital). We inquired about their current health status and obtained information, if the responding parent consented orally to participate and answer the questions.

Results: Fifty-one children and adolescents were studied. Only five patients (10%) had persistent symptoms compatible with long-COVID; the reported symptoms include fatigue in four (8%), weakness in three (6%), exercise intolerance in two (4%) and shortness of breath in two (4%) patients. Four patients (7.8%), who did not have any symptoms of long-COVID in phase 1 of the study, reported new-onset symptoms or complaints that are potentially compatible with the diagnosis of long-COVID (weakness, myalgia, excess sputum, cough, fatigue) in the current phase.

Conclusions: Symptom persistence of long-COVID is infrequent amongst children hospitalised for COVID-19. Most of the symptoms of long-COVID will resolve with the passage of time and the residual symptoms are often mild and tolerable. The scientific community should carefully and clearly define long-COVID and its natural course in order to facilitate and harmonise future studies.

Keywords: COVID-19; chronic; coronavirus; paediatrics.

- 21 references

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BMC Pulm Med

. 2022 Jul 18;22(1):276.

doi: 10.1186/s12890-022-02069-w.

The risk factors for urinary incontinence in female adults with chronic cough

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- PMID: 35850673

- PMCID: PMC9295435

- DOI: 10.1186/s12890-022-02069-w

Free PMC article

Abstract

Background: Female patients with chronic cough are more likely to suffer from urinary incontinence (UI). However, there are few data in regard of risks related with UI in female adults with chronic cough.

Method: We recruited female adult patients with chronic cough from the cough specialist clinic. Demographic information and clinical characteristics including age, BMI, duration of cough, severity of cough, nature and timing of cough, cough triggers, concomitant symptoms, comorbidities and UI condition were collected. The demographics and clinical features of patients with UI and those without UI were compared.

Result: A total of 700 female patients with the main symptom of chronic cough were included, of whom 351 (50.1%) presented with UI. As compared with patients without UI, patients with UI showed a longer mean age (years) (49.5 vs. 42.4, $p < 0.001$), a more severe cough symptom (median of cough Visual Analogue Scale: 65 vs. 50, $p < 0.001$), a higher prevalence of chronic sinusitis (17.6% vs. 8.6%, $p = 0.002$), and combined with a higher incidence of abdominal muscle pain due to cough (39.6% vs. 18.7%, $p < 0.001$).In addition,

patients in UI group whose cough were more easily triggered by exercise (28.2% vs. 17.2%, p = 0.048). Multivariate logistic regression analysis indicated the above five variables were risk factors for UI in female adult patients with chronic cough.

Conclusion: Urinary incontinence is a common complication in female patients with chronic cough. Older age, severe cough, combing with a higher proportion of chronic sinusitis and abdominal muscle pain, a cough easily triggered by exercise are identified as risk factors for urinary incontinence. We should pay more attention to female chronic coughers with these risk factors in clinics.

Keywords: Chronic cough; Female; Risk factors; Urinary incontinence.

Conflict of interest statement

The authors have no conflicts of interest to declare that are relevant to the content of this article.

- 44 references
- 2 figures

Indian J Pediatr

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doi: 10.1007/s12098-022-04303-z. Online ahead of print.

Thinking Beyond Tuberculosis in a Child with Chronic Cough

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Affiliations expand

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- DOI: 10.1007/s12098-022-04303-z

No abstract available

- 4 references

SUPPLEMENTARY INFO

Publication typesexpand

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