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Effect of theophylline as adjunct to inhaled corticosteroids on exacerbations in patients with COPD

Graham Devereux, Seonaidh Cotton, Shona Fielding, et al.
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COPD remains a growing global health concern, with exacerbations being associated with high morbidity and mortality. Research continues to explore novel, optimal therapeutic options for COPD patients to aid the improvement of COPD management and outcomes. Theophylline has long been used to treat COPD; however, high blood concentrations have been related to adverse effects. Recent data has highlighted a potential role for low-dose theophylline in combination with ICS, demonstrating up to a 10,000-fold increase in the anti-inflammatory effects of ICS therapy. Despite this, the evidence to support the clinical relevance of low-dose theophylline has not been fully established.

In this double-blind, placebo-controlled, randomised study, researchers aimed to investigate the clinical effectiveness of low-dose theophylline in combination with ICS therapy in patients with COPD and frequent exacerbations. The clinical trial recruited 1578 participants across 121 UK primary and secondary care sites, all of which had COPD with a FEV₁/FVC ratio of >0.7 and at least two exacerbations in the previous year. Patients were randomised into two groups: treatment (n=791) group, who received low-dose theophylline (200 mg) either once or twice a day for 1 year, or placebo (n=787) group.

Results demonstrated that the addition of low-dose theophylline to ICS therapy did not significantly decrease the number of recorded exacerbations (moderate to severe) in adults with COPD. A total number of 1727 exacerbations were recorded in the theophylline group, with 1703 exacerbations being recorded in the placebo group. Based on these findings, the researchers concluded that low-dose theophylline as an adjunctive therapy to ICS was not clinically effective in the prevention of COPD exacerbations.

Secondhand exposure to aerosols from electronic nicotine delivery systems and asthma exacerbations among youth with asthma

Jennifer Bayly, Debra Bernat, Lauren Porter, et al.
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E-cigarettes are continually rising as a favourable option for smoking cessation. However, a deep understanding of their long-term safety is still lacking. Recently, interest has grown in the impact of secondhand aerosol exposure to patient health, particularly in those affected by respiratory disease.

To address this question, this study examined the relationship between secondhand ENDS aerosol exposure and asthma exacerbations in the young. Using data collected from the 2016 Florida Youth Tobacco survey, researchers analysed participant asthma status and exposure to secondhand ENDS aerosol. Analyses were restricted to those aged 11–17 years old with a self-reported diagnosis of asthma (n=11,830).

Results demonstrated that of those surveyed, 21% of those with asthma reported an asthma exacerbation within the previous 12 months. In addition, 33% of those surveyed reported

secondhand exposure to ENDS aerosol. After controlling for demographics, tobacco product use (including ENDS) and secondhand tobacco smoke exposure, the association between secondhand ENDS aerosol exposure and asthma exacerbations remained significant.

Based on these findings, the researchers concluded that such exposure may be related to an increase in asthma symptoms in asthmatic patients between the ages of 11 and 17. However, although compelling, the researchers did emphasise that the findings only demonstrated an association as opposed to a causal relationship. Despite this, they emphasised the importance of counselling asthmatic youths on the potential risks associated with ENDS aerosol exposure.

Concomitant diagnosis of asthma and COPD: a quantitative study in UK primary care

Francis Nissen, Daniel Morales, Hana Mullerova, et al.
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An accurate diagnosis of asthma and COPD is essential for the treatment of patients, reducing the frequency and severity of exacerbations and improving the overall quality of life.

The differential diagnosis of asthma and COPD relies on clinical presentation, triggering factors and demonstration of airflow obstruction. The existence of ACOS is controversial, with some guidelines, for example, classifying asthma with chronic airways obstruction as COPD. Studies looking at unblended populations of patients with asthma and patients with COPD keep the diseases distinct, and the prevalence of a concomitant diagnosis varies greatly in different studies.

The aim of this quantitative study in UK primary care was to quantify concomitant prevalence and to determine the extent of possible misdiagnosis and missed opportunities for diagnosis.

UK electronic health records of diagnosed populations of only those patients with asthma and patients with COPD from two previous validation studies were used to define the prevalence of concomitant asthma and COPD.

Patients with validated asthma and patients with validated COPD were identified from the UK CPRD in separate validation studies, and confirmed with GP questionnaires. Data for asthma were collected for two years from December 2013, and for eight years from January 2004 for COPD. Prevalence of concurrent asthma and COPD was based on CPRD coding, GP questionnaires and additional requested information.

The study found that concurrent asthma and COPD diagnosis affects a minority of patients with either asthma (14.8%) or COPD (14.5%). The conclusion is that asthma may be over-recorded in people with COPD in electronic health records.

Novel pharmacist-led intervention secures the minimally important difference (MID) in Asthma Control Test (ACT) score: better outcomes for patients and the healthcare provider

Michela Tinelli, John White and Andrea Manfrin
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By 2025, an estimated 400 million people worldwide will be suffering from asthma, with a cost of €72 billion annually to the

28 countries of the European Union.

The long-term goals of asthma management, according to the GINA, are to achieve good symptom control and to minimise the risk of exacerbation, and therefore a key priority is the development of a simple and effective intervention for improving asthma control.

A previous C-RCT in Italy (n=1263) has previously measured the effectiveness and cost-effectiveness of an innovative pharmacist-led intervention. Its primary outcome was asthma control, as assessed using the ACT score (ACT \geq 20 representing good control) and its secondary outcomes were (1) the number of active ingredients, (2) adherence and (3) cost-effectiveness compared with usual care. The key results showed that firstly the intervention was effective: the median score was 19 before the intervention, 20 at three months post-intervention and 21 at six months post-intervention; and secondly the intervention was cost-effective – the probability of the intervention being more cost-effective than usual care was 100% at nine months.

The aim of Tinelli et al.'s study was to measure the impact of this intervention on the MID in asthma control, i.e. looking at the proportion of patients reaching a three-point improvement in the ACT score. It also looked at the benefits of reaching clinical MID in terms of health outcomes for the patient and economic savings for the healthcare provider. For this study, a subset of the former study was used (n=816).

In demonstrating a MID in the ACT, an improvement in patients' health outcomes and a reduction of costs to the NHS, the pharmacist-led intervention explored in this study promotes a shift in the approach to good asthma control.

Safety of benzodiazepines and opioids in interstitial lung disease: A national prospective study

Sabrina Bajwah, Joanna Davies, Hanan Tanash, et al.
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Chronic breathlessness is a near-universal symptom of advanced fibrotic ILD. Guidelines recommend the use of BZDs and/or opioids for symptomatic management; however, recent studies have suggested a link between the use of these therapies and increased hospital admission or death in COPD patients. This study is the first to examine the association of BZDs and opioids with these adverse outcomes in patients with fibrotic ILD.

The study included 1603 patients, all starting LTOT. BZDs were used by 196 (12%) patients, opioids by 252 (16%), and both by 59 (4%). There was no difference in baseline lung function between patients taking BZDs or opioids, compared with non-users.

Neither BZD nor opioid treatment had any significant association with hospitalisation rates. This was true even when looking at high- vs low-dose therapies. In general, opioids seemed to be associated with increased mortality, but this association disappeared when looking at adjusted risks for each dose level. BZD treatment was associated with increased mortality, in a dose-dependent fashion.

In summary, opioid treatment was not associated with increased risk of hospitalisation or death in advanced fibrotic ILD patients. High-dose BZD treatment was linked to increased mortality. However, the authors postulate that this could be confounded by the increased use of BZDs at the end of life, to relieve terminal anxiety-related breathlessness.

Overall, the use of BZD and opioids in fibrotic ILD was lower, suggesting that this patient group may be currently undertreated and could benefit from holistic management of symptomatic breathlessness.

What is the impact of GOLD 2017 recommendations in primary care? – a descriptive study of patient classifications, treatment burden and costs

Alicia Gayle, Scott Dickinson, Kevin Morris, et al.
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The GOLD classification of COPD patients has undergone several changes over the past few years. In 2013, it was overhauled to focus on symptoms and exacerbation history, in addition to airflow limitation. The recent 2017 report went one step further and uses *only* symptom and exacerbation frequency to guide treatment.

This population-based study uses the CPRD to examine whether a cohort of COPD patients could be classified into the new GOLD criteria based on their primary care records. It also evaluates the treatment cost implications of doing so.

A total of 19,268 patients were included. When GOLD 2017 grading was applied, there was a significant shift towards less severe grading compared to GOLD 2013. Under GOLD 2013, only 46% of patients were classified as GOLD A or B; with 2017 criteria, this increased to 86%. Most patients moved from group D to B (65%) and from C to A (74%).

Regarding treatment, 32% of all patients were prescribed triple therapy, including 22% of GOLD A and 43% of GOLD B patients. Total costs for all study patients under current therapy were estimated to be £8,614,020 per year. If the GOLD 2017 recommended treatments were applied, this could be reduced to £6,141,361 – a 29% decrease.

The findings of this study suggest that reviewing and reclassifying patients using medical records is possible in clinical practice. Revising therapy recommendations based on the new classification may reduce inappropriate prescribing of ICS and improve clinical outcomes.

Abbreviations/acronyms:

ACOS = asthma–COPD overlap syndrome
ACT = Asthma Control Test
BZD = benzodiazepine
COPD = chronic obstructive pulmonary disease
CPRD = Clinical Practice Research Datalink
C-RCT = cluster randomised controlled trial
ENDS = electronic nicotine delivery systems
FEV₁ = forced expiratory volume in the first second
FVC = forced vital capacity
GINA = Global Initiative for Asthma
GOLD = Global Initiative for Chronic Obstructive Lung Disease
ICS = inhaled corticosteroids
ILD = interstitial lung disease
LTOT = long-term oxygen therapy
MID = minimally important difference



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