JOURNAL CLUB

What's hot that the other lot got

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WHICH PATIENTS WITH BRONCHIECTASIS BENEFIT FROM LONG-TERM ANTIBIOTICS?

Current bronchiectasis guidelines recommend that long-term macrolide antibiotics should be given to patients with frequent exacerbations and those without *Pseudomonas aeruginosa* infection. This study attempts to address the calls from the European Respiratory Society and the Cochrane Collaboration for further work in identifying the subgroups of patients with bronchiectasis who will benefit most from macrolide treatment (Chalmers *et al*, *Lancet Respir Med* 2019;7;845). This systematic review and meta-analysis addresses this using individual patient data from three randomised controlled trials providing data on 173 subjects on macrolide therapy and 168 on placebo. Consistent with the individual trials, the analysis found that macrolide therapy was associated with a significant reduction in the frequency of exacerbations over 6–12 months (adjusted incidence rate ratio 0.49, 95% CI 0.36 to 0.66; p<0.0001). The authors examined prespecified subgroups and found no significant interaction effects of these subgroups except for the cause of bronchiectasis ($p_{interaction}$=0.034). Notably, there was similar efficacy of therapy in patients with and without *P. aeruginosa* in baseline sputum culture (incident rate ratio (IRR) 0.36, 95% CI 0.18 to 0.72, p=0.004, and IRR 0.53, 95% CI 0.38 to 0.74, p<0.0001, respectively; $p_{interaction}$=0.45). While this study provides evidence that long-term macrolide treatment is beneficial to groups of patients who are not undergoing prophylaxis based on current guidelines, the authors are careful to balance this against the wider context of the downsides and side effects of long-term antibiotic treatment and antimicrobial stewardship.

CAN VAPING HELP YOU QUIT?

The use of e-cigarettes as a means of harm reduction and smoking cessation tool remains controversial. Walker and colleagues' (*Lancet Respir Med* 2019: doi.org/10.1016/S2213-2600(19)30269-3) study examined the effectiveness of e-cigarette use with and without nicotine on patients who were motivated to quit and had no recent e-cigarette use. Participants (n=1124) were recruited from the general population and were assigned using stratified block randomisation (4:4:1) to (1) patches plus an 18 mg/L nicotine e-cigarette, (2) patches plus a nicotine free e-cigarette and (3) nicotine patches only. In each group, the carbon monoxide-verified continuous abstinence at 6 months was 7%, 4% (risk difference (RD) 2.99, 95% CI 0.17 to 5.81) and 2% (RD 4.60, 95% CI 1.11 to 8.09), respectively. Although the study had a high withdrawal or lost-to-follow-up rate (50% in the patches-only group, 33% in the nicotine free e-cigarette group and 32% in the nicotine e-cigarette group), the per-protocol analysis was consistent with the primary intention-to-treat analysis. The serious adverse event rate was low, with none adjudged to be treatment related. This study adds to the body of evidence surrounding e-cigarettes as a smoking cessation tool. While the evidence is still scarce, this study underscores that we should not be quick to dismiss tools available to our patients in their fight to quit smoking.

CAN WE TARGET EOSINOPHILIC INFLAMMATION TO REDUCE CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) EXACERBATIONS?

There is increasing recognition that eosinophilic inflammation plays an important role in a subset of patients with COPD. Criner *et al* (*NEJM* 2019;381:1023) present data from two trials examining benralizumab, an interleukin-5 receptor alpha-directed cytolytic monoclonal antibody targeting eosinophilic-mediated inflammation. Patients with moderate to severe COPD, frequent exacerbations despite dual or triple inhaled bronchodilator therapy and a blood eosinophil count of >220/mm^3 were randomised to two double-blind, placebo-controlled parallel-group phase III trials (GALATHEA and TERRANOVA). Patients with an active diagnosis of asthma were excluded, and previous asthma was present in <10% of the trial populations. Patients were randomly assigned to receive either benralizumab or placebo every 4 weeks for three doses and then every 8 weeks. GALATHEA randomised dosage of benralizumab to 30 or 100 mg, whereas TERRANOVA randomised dosage to 10, 30 or 100 mg. There was no significant difference in the annual exacerbation rate ratios for any dose of benralizumab compared with placebo and no trend in dose response. Previous reported data for the anti-IL-5 antibody mepolizumab indicated a significant but modest reduction in exacerbation rates. These benralizumab trials were larger, had higher eosinophil count cut-offs and had well characterised the patients' history of asthma. It remains to be proven if a subgroup of patients with COPD can be identified who benefit from add therapy such as anti-IL5 and it remains the preserve of clinical trials.

CHRONIC RESPIRATORY SYMPTOMS WITHOUT AIRFLOW LIMITATION: WHAT'S THE RISK?

The importance of chronic respiratory symptoms in patients with no evidence of airflow obstruction is debated and the category was removed from recent Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. Çolak *et al*. (*Eur Respir J* 2019;54:1900734) present a large population-based cohort study of 108 246 individuals in Denmark examining the risk of hospitalisation due to exacerbations of airway disease, pneumonia, respiratory and all-cause mortality over a period of 15 years. Normal spirometry was defined as FEV_1/FVC of ≥0.7. There was a high prevalence of chronic respiratory symptoms with normal spirometry (32% of all patients without known respiratory disease) with these patients at increased risk of hospitalisation due to an exacerbation (HR 1.62, 95% CI 1.20 to 2.18) and due to pneumonia (HR 1.26, 95% CI 1.17 to 1.37). They were also at high risk of respiratory (HR 1.59, 95% CI 1.22 to 2.06) and all-cause mortality (HR 1.19, 95% CI 1.13 to 1.25). While this evidence may not describe the risk of these patients progressing to obstructive airway disease, it does quantify the risk attributable to chronic respiratory symptoms. The diligent respiratory clinician should note the importance of such unexplained symptoms and look beyond spirometry for a diagnosis and focus support for smoking cessation where relevant.

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