JOURNAL CLUB SUMMARIES

What's hot that the other lot got

George William Nava

MEPOLIZUMAB FOR EOSINOPHILIC CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Mepolizumab is a monoclonal antibody that interferes with interleukin-5 signalling to reduce blood eosinophil level and is licenced for use in severe refractory eosinophilic asthma. The clinical relevance of eosinophilic inflammation in chronic obstructive pulmonary disease (COPD) is being increasingly recognised. Pavord *et al* (*NEJM* 2017;377:1613–1629) describe the METREX and METREO trials, which evaluated the effect of mepolizumab in frequent exacerbator phenotype patients with COPD. METREX and METREO were international, phase 3, double-blinded, randomised clinical trials. Patients with COPD on triple inhaled therapy who had had at least two moderate or one severe exacerbation in the preceding year were recruited and stratified by blood eosinophil level. Non-eosinophilic patients were excluded from METREO. Eight hundred and thirty-seven (METREX) and 675 (METREO) patients were randomised to receive 4 weekly mepolizumab (METREX: 100 mg, METREO: 100 mg or 300 mg assigned 1:1) or placebo as add on to their COPD therapy for 52 weeks. The primary end point of both studies was annual rate of moderate or severe exacerbations. Secondary end points included time to first exacerbation, frequency of hospital attendance and changes to patient-reported outcomes. The data were analysed in a modified intention-to-treat population. In METREX, exacerbation frequency and time to first exacerbation were significantly reduced in the eosinophilic group in patients receiving mepolizumab compared with placebo (1.40 vs 1.71 per year, adjusted P=0.04; 192 vs 141 days, P=0.04). There were no significant differences in any other secondary end points. No significant difference in exacerbation rate was identified in METREO. Mepolizumab was well tolerated with a similar adverse event rate as placebo. These data suggest the potential of targeted antieosinophil therapy to improve outcomes in a subpopulation of patients with COPD supporting further work on phenotyping and personalised medicine.

PHYSIOTHERAPY BREATHING RETRAINING FOR ASTHMA: A RANDOMISED CONTROLLED TRIAL

Breathing retraining is beneficial to asthmatics as an add on to pharmacological therapies. A finite number of specialist physiotherapists means that this is a limited NHS resource. Bruton *et al* (*Lancet Respir Med* 2018;6:19–28) performed an observer-blinded, parallel group, randomised control trial to evaluate whether breathing retraining could be effectively delivered as a digital, audiovisual self-help programme. Six hundred and fifty-five patients with clinically diagnosed asthma from 34 UK general practices were randomised to a self-guided breathing retraining programme via a DVD and booklet (DVDB), to physiotherapist-led breathing retraining or to normal care. The primary outcome was 12-month Asthma Quality of Life Questionnaire (AQLQ) score compared with baseline. Secondary outcomes include spirometry, fraction of exhaled nitric oxide, questionnaire measures of asthma control and asthma-related health resource use. The data were analysed with an intention-to-treat population. The adjusted mean AQLQ in the DVDB group showed an improvement compared with usual care (0.28, 95% CI 0.11 to 0.44). This improvement was seen across emotion, symptoms, activities and environment subdomains. No differences were found when DVDB was compared with the face-to-face intervention (0.04, 95% CI −0.16 to 0.24). There were no notable significant differences found in the secondary outcomes. The authors conclude that this cheap self-training programme can be used alongside current medications to improve quality of life in asthmatics.

TIOTROPIUM IN EARLY-STAGE CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Many patients with mild and moderate COPD do not take medications for COPD because they do not have clinically significant symptoms. The potential benefits of medication at these early stages of COPD are unknown. Zhou *et al* (*NEJM* 2017;377:923–935) performed a phase 4, double-blind, multicentre, randomised placebo controlled trial in China examining the effect of 2 years of inhaled tiotropium on patients with Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage 1 or 2 COPD. The primary outcome was prebronchodilator FEV_1 at 24 months. Secondary outcomes included annual decline in FEV_1, change in FVC, FEV_1/FVC ratio, exacerbation frequency and severity and COPD assessment test (CAT) scores. An intention-to-treat population of 771 was included in the full analysis. The tiotropium group had a significantly higher prebronchodilation FEV_1 at 2 years than the placebo group (157 mL, 95% CI 123 to 192; P<0.001). Significant reductions in exacerbation frequency (risk ratio 0.53, 95% CI 0.39 to 0.73; P<0.001) and hospitalisation (0.03 vs 0.07 hospitalisations per patient-year, P=0.009) were demonstrated in the tiotropium group along with improvement in quality of life (mean difference in CAT 1.2, 95% CI 0.5 to 1.9, P=0.0011). There was no difference in the frequency of serious adverse events, although oropharyngeal discomfort was more common in the tiotropium group (63 vs 28 patients, P<0.001). The authors conclude that the use of tiotropium in mild COPD (GOLD 1 or 2) improves lung function and quality of life, decreases exacerbation frequency and may attenuate FEV_1 decline. It is not clear from the data whether tiotropium prevents underlying disease progression or merely delays it.

ASSOCIATION OF OCCASIONAL SMOKING WITH TOTAL MORTALITY IN THE POPULATION-BASED TROMSØ STUDY, 2001–2015

Smoking is a known risk factor for many health conditions; however, the impact of occasional smoking on mortality is not known. The Tromso Study (Lochen *et al*, *BMJ Open* 2017;7:e019107. doi:10.1136/bmjopen-2017-019107) is a population-based, prospective, multipurpose study consisting of seven surveys between 1974 and 2016. This analysis concerns 7053 residents of Tromso who completed a physical examination, blood tests and two questionnaires in 2001 that included questions about smoking habits. The

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subjects were followed up for an average of 12.5 (0.2–14.3) years, and their deaths were recorded. A total of 1648 participants died during the follow-up period. Self-reported current or ex-smokers were found to have increased all-cause mortality when compared with non-smokers. Mortality was increased in occasional smokers compared with non-smokers (HR 1.38, 95% CI 1.08 to 1.76) when data were adjusted for age, gender, education, body mass index, serum cholesterol and serum triglycerides. There was a dose response effect seen with higher mortality found in consistent daily smokers than in occasional smokers. The authors discuss multiple possible confounders to their data but conclude that while mortality is improved, occasional smoking cannot be considered a safe alternative to daily smoking.

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