Journal club

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THE RISE OF THE NOVEL ANTIHYPERGLYCAEMIC AGENTS: ARE PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE THE NEXT TO BENEFIT?

The role of novel antihyperglycaemic drugs in cardiology and diabetes is well recognised, and laboratory studies have suggested possible mechanisms by which these drugs could reduce chronic obstructive pulmonary disease (COPD) exacerbations in patients with type 2 diabetes mellitus. A population-based cohort study by Pradhan *et al* (*BMJ* 2022;379:e071380) used primary care and hospital databases to compare 3 novel antihyperglycaemic drugs (glucagon-like peptide 1 (GLP-1) receptor agonists, n=1252; dipeptidyl peptidase 4 (DPP-4) inhibitors, n=8731 and sodium-glucose co-transporter-2 (SGLT2) inhibitors, n=2956) to sulphonylureas (n=14 259, 18 204 and 10 841, respectively, for each comparison). After adjustment for confounders, GLP-1 receptor agonists were associated with a 30% lower risk of a severe COPD exacerbations (3.5 vs 5.0 events per 100 person years; HR 0.70, 95% CI 0.49 to 0.99) and SGLT2 inhibitors were associated with a 38% decrease. (2.4 vs 3.9; HR 0.62, 95% CI 0.48 to 0.81). There was no significant difference between sulphonylureas and DPP4 inhibitors. The weight-inducing effects of sulphonylureas could have impacted their role as a comparator, and the use of a database relying on correct classification of illness could lead to inaccuracies. A randomised control trial will help to confirm the role of SGLT2 inhibitors and DPP-4 inhibitors in COPD management.

RITUXIMAB VERSUS CYCLOPHOSPHAMIDE: PROVIDING AN ALTERNATIVE FOR CONNECTIVE TISSUE DISEASE-INTERSTITIAL LUNG DISEASE

Cyclophosphamide is recommended in international guidelines for connective tissue disease (CTD)-associated interstitial lung disease (ILD). The RECITAL trial, a double-blind, double-dummy, randomised control trial, compared rituximab to cyclophosphamide for CTD-ILD (*Lancet Respir Med* 2022;11:45). The authors hypothesised that rituximab would be superior based on existing retrospective cohort and small open-label studies. Eligible patients had a diagnosis of systemic sclerosis, idiopathic inflammatory myositis or mixed CTD with associated severe or progressive ILD. Recruitment stopped early due to the covid pandemic with 101 patients randomised of which 97 received at least 1 dose of therapy, fewer than the 104 required to adequately power the study. The primary end-point was rate of change in forced vital capacity (FVC) from baseline at 24 weeks. There was an improvement in FVC with a mean increase of 99±329 mL and 97±234 mL in the cyclophosphamide and rituximab groups, respectively, but there was no significant difference between the two therapies (mean difference −40 mL, 95% CI −153 to 74; p=0.49), and no difference in overall survival or progression-free survival. More severe adverse events were seen in the cyclophosphamide group (33 vs 29 events). With similar efficacy and a marginal better safety profile rituximab is an alternative option for treatment of severe or progressive CTD-ILD.

OMALIZUMAB MAY HAVE BENEFITS BEYOND DISCONTINUATION, BUT FOR WHICH PATIENTS?

Omalizumab is licensed for the treatment of severe allergic asthma. The impact of long-term discontinuation of omalizumab therapy on asthma control and healthcare resource use (HCRU) is unclear. This nationwide population-based study (*Eur Respir J* 2022;60:2103130) investigated the impact of omalizumab discontinuation on HCRU and asthma control. The French Healthcare Database System was used to gather information about outpatient and hospital care for 19 203 adults and children who had been treated with omalizumab for asthma and had a prolonged (1-year) period without omalizumab indicating a presumed intentional cessation of therapy. HCRU at the start of omalizumab initiation, through treatment and after discontinuation, was compared. In adults, there was a reduction in hospital admissions by 73.8%, and oral corticosteroid consumption by 27.9%. 23.6% of adults had asthma control at omalizumab discontinuation, and of these patients, 69.8% remained controlled at a year, 39.4% at 2 years and 24.3% at 3 years. In children, 40.9% had asthma control at omalizumab discontinuation, and of these 75.8%, 44.1% and 32.6% remained controlled at 1, 2 and 3 years, respectively. The lack of information on reasons for omalizumab discontinuation limits interpretation of the findings. Without analysis looking at which patients are likely to benefit from ongoing asthma control on omalizumab discontinuation, it is difficult to integrate these findings into clinical decision-making. A comparative study between omalizumab versus a control may further allow for associations to be made between ongoing asthma control after discontinuation of omalizumab as opposed to this representing the natural course of the disease.

THE VIRTUAL PATH FORWARD: USING VIRTUAL BRONCHOSCOPY NAVIGATION TO DIAGNOSE SOLITARY PULMONARY NODULES

Diagnostic yield of CT-guided transthoracic biopsy of peripheral solitary pulmonary nodules (SPNs), the current gold standard, is approximately 75%, but when the lesion is more distant from the pleura it carries significant risk of pneumothorax and pulmonary haemorrhage with a lower diagnostic yield. The NAVIGATOR observational cohort study (*Lung Cancer* 2023;117:37) looked at an alternative approach. The authors recruited 35 patients over a 1-year period, who underwent virtual bronchoscopy navigation (VBN) for diagnosis of a suspicious SPN>6 mm, in the parenchymal tissue >5 mm from the pleura and considered accessible by VBN. Included SPNs were not accessible by other means, or other diagnostic procedures were considered less appropriate. Ninety-four per cent were solid lesions, and 66% had a diameter over 20 mm. Following VBN no patients had a pneumothorax or respiratory failure, although one did have late-presenting subcutaneous emphysema. Haemorrhage occurred in 26% of participants, 6% of which was grade 3 requiring bronchoscopy haemostasis with full recovery. Diagnostic yield was 77% overall and rose to 89% in those whose biopsy was accessed via an airway path. This definitive diagnosis changed the treatment plan in two-thirds of the patients; however, there is no information on why other procedures had been deemed unsuitable or had been unsuccessful, and therefore, possibility of selection bias. Utilisation of VBN may reduce the amount of SPNs treated without diagnostic certainty. Larger-scale comparison studies looking at the diagnostic yield and adverse event profiles of different procedures will be beneficial.

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