Journal club

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PSEUDOMONAS ERADICATION IN CYSTIC FIBROSIS: ORAL THERAPY CHEAPER AND JUST AS GOOD AS INTRAVENOUS THERAPY

Chronic *Pseudomonas aeruginosa* infection remains a leading cause of morbidity and mortality in cystic fibrosis (CF), despite this, there is a lack of consensus regarding optimum antibiotic regimen for eradication. Langton-Hewer and colleagues (*Lancet Respir Med* 2020;8:975) report on TORPEDO-CF; a multicentre, parallel group, open-label, randomised controlled trial comparing 14 days of intravenous ceftazidime and tobramycin to 12 weeks of oral ciprofloxacin for the eradication of *P. aeruginosa* (both cohorts received 12 weeks of nebulised colistimethate sodium). *Pseudomonas* naive or *pseudomonas*-free children and adults, from 61 CF centres, were randomised to intravenous (n=137) or oral (n=149) therapy. The primary outcome of successful eradication of *P. aeruginosa* at 3 months and remaining infection free at 15 months was achieved by 44% of the intravenous and 52% of the oral group (relative risk 0.84, 95% CI 0.65 to 1.09; p=0.18). There was no statistically significant difference in quality of life questionnaires or absenteeism from school or work between the groups. Health economic evaluation showed a cost saving of £5939 per patient in the oral group, predominantly due to costs of hospital inpatient days for intravenous treatment. The study failed to demonstrate any clinically significant benefit of intravenous over oral therapy in eradicating *P. aeruginosa* with cost-saving favouring oral treatment. However, caution is advised when extrapolating these results to the adult CF population, as only 15 of 286 recruited participants were 18 years or older.

MORTALITY IN PATIENTS WITH CANCER AND COVID-19: THE RISK IS NOT EQUALLY SPREAD

When the COVID-19 pandemic began individuals with cancer diagnoses were identified as clinically vulnerable and advised to shield. However, the diagnosis of cancer encompasses a diverse group of patients with different disease types and varying prognoses. Lee *et al*. (*Lancet Oncol* 2020;21:1309) investigated COVID-19 prevalence and mortality across tumour subtypes in the UK cancer population. They designed a prospective, observational cohort study comparing 1044 adults enrolled in the UK Coronavirus Cancer Monitoring Project (UKCCMP) with a non-COVID-19 UK cancer control population (UK Office for National Statistics 2017; ONS). Overall mortality of patients with active cancer assessed for hospital admission with COVID-19 was 30.6% (92.5% attributed to COVID-19). The all-cause case-fatality rate was significantly associated with male sex and increasing age. Those with haematological malignancies were significantly overrepresented in the UKCCMP population compared with the control ONS population. Following multivariate analysis, patients with leukaemia were identified to have a significantly higher case-fatality rate (OR 2.25, 95% CI 1.13 to 4.75, p=0.023) than the median UKCCMP case-fatality rate. In contrast, there was no increased case-fatality rate within the lung cancer population compared with UKCCMP median, which may be attributable to good shielding adherence. The data suggest a significant variation in risk of COVID-19 and the risk of poor outcomes between different cancer diagnoses. Clinicians can use the data to support joint decision-making with patients regarding level of social isolation and shielding.

NOCTURNAL OXYGEN FOR PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE WITH ISOLATED NOCTURNAL HYPOXIA: LITTLE TO SUGGEST BENEFIT

The role of oxygen therapy for isolated nocturnal hypoxaemia in chronic obstructive pulmonary disease (COPD) remains unclear. Lacasse and colleagues (*N Engl J Med* 2020:383;12) aimed to determine whether nocturnal oxygen, in patients with COPD experiencing nocturnal oxygen desaturation (defined as oxygen saturation <90% for ≥30% of the night), improves survival or reduces progression to requirement of long-term oxygen therapy (LTOT). This was an international, double-blinded, placebo-controlled, randomised clinical trial. Participants were randomised 1:1 to nocturnal oxygen (n=123) or ambient air (n=120) via a sham oxygen concentrator. At 3 years of follow-up, 39.0% of the nocturnal oxygen cohort and 42% of the placebo cohort met the composite primary outcome of meeting criteria for LTOT or death (difference −3.0% points, 95% CI −15.1 to 9.1; p=0.64). No difference in exacerbation rates, hospitalisation or quality of life scores was identified between the cohorts. Due to recruitment and retention difficulties, recruitment was halted after 243 of the planned 600 participants. Therefore, the trial was significantly underpowered, resulting in wide CIs surrounding the absolute risk difference, which included the prespecified minimum clinically important difference. The authors completed a meta-analysis with previously published trials, which also does not provide evidence of benefit of nocturnal oxygen. Considered in isolation and in the context of previously published trials, this trial does not demonstrate a clinical benefit for nocturnal oxygen therapy in patients with COPD who do not meet requirements for LTOT.

REALITI-A STUDY OF MEPOLIZUMAB FOR SEVERE ASTHMA: CONFIRMS TREATMENT EFFECT

Monoclonal antibody therapies such as mepolizumab have demonstrated efficacy in randomised clinical trials but data from more heterogeneous populations are sparse. Harrison *et al* (*Eur Respir J* 2020;56:2000151) report initial analysis from REALITI-A study, a global, prospective, observational cohort study evaluating mepolizumab in severe asthma. Patients with physician initiated treatment with mepolizumab, who had not already received mepolizumab or a novel trial drug in the last 12 months, were enrolled (n=368). These initial results report on the first year of follow-up and were compared with the 12 months pretreatment. Results demonstrate a 69% reduction in exacerbation rate, falling from 4.63 to 1.43 exacerbations per person per year (rate ratio 0.31 95% CI 0.27 to 0.35; p<0.001). Additionally, the hospitalisation rate fell by 77%. A significantly higher proportion of patients had no exacerbations during the 12-month follow-up period (48% vs 7% pre-mepolizumab treatment, OR 12.13 95% CI 8.03 to 18.33, p<0.001). These effects were observed across eosinophil count subgroups. Notably, 34% of patients were able to discontinue maintenance oral corticosteroids during the 12-month follow-up. During the study, 70 patients (19%) discontinued mepolizumab, with nine patients (2%) suffering an adverse event that led to treatment cessation. Importantly, the safety profile was in line with trial data. The results from this observational study demonstrate that mepolizumab efficacy and safety data from clinical trials translate to the more heterogeneous clinic population.

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