COMBINATION ALBUTEROL–BUDESONIDE RESCUE THERAPY FOR UNCONTROLLED ASTHMATICS ON MAINTENANCE INHALED GLUCOCORTICOIDS: REDUCED EXACERBATIONS AND GOOD SAFETY PROFILE

Short-acting β agonists (SABA) are a core component of asthma management as rescue medication. However, there are long-standing safety concerns regarding reliance on SABA alone. Papi et al (NEJM 2022; 386:2071) conducted a phase 3, multinational, double-blinded randomised clinical trial to examine the safety and efficacy of albuterol-budesonide combination reliever inhaler in children and adults with uncontrolled moderate to severe asthma and an exacerbation in the previous 12 months. Patients with chronic obstructive pulmonary disease, used systemic glucocorticoids or had biologics in the last 3 months, were excluded from the study. Participants (n=3132) were randomised (1:1:1) to one of three groups: higher-dose combination (budesonide 160 μg and albuterol 180 μg), lower-dose combination (budesonide 80 μg and albuterol 180 μg) or albuterol (180 μg) alone. The primary efficacy end point of the study was the first episode of severe asthma exacerbation. In the time-to-event analysis, a higher-dose combination therapy was associated with a lower risk of severe exacerbation (rate ratio 0.74, 95% CI 0.62 to 0.89, p=0.001) compared with albuterol alone whereas there was only a borderline effect with lower dose combination therapy (rate ratio 0.84, 95% CI 0.71 to 1.00, p=0.052). Safety analysis revealed low and similar adverse event rates across groups with discontinuation rates of ~1%. Therefore, the authors conclude that using a higher-dose budesonide–albuterol combination as a rescue medication along with maintenance steroids should be considered as a safe and effective alternative to SABA alone.

MANAGEMENT OF ACUTE RESPIRATORY FAILURE IN IMMUNOCOMPROMISED PATIENTS: NON-INVASIVE VENTILATION OR HIGH-FLOW THERAPY PRODUCE SIMILAR OUTCOMES

Acute respiratory failure is a common complication in the care of patients with immunocompromise and carries a high mortality (~1 in 3). Current guidelines recommend the use of Non-Invasive ventilation to reduce intubation and subsequent mortality but this guidance has been called into question with the development of oxygen enriched high-flow therapy (HFT). Couroy et al (Lancet Respir Med 2022;10:641) conducted the FLORALI-IM study (HFCN alone or associated with NIV for immunocompromised patients admitted to ICU for acute respiratory failure), a multicentre, open-label, randomised trial conducted in the Danish ICU and France. Immunocompromised adults with acute hypoxemic respiratory failure were considered eligible if they had a respiratory rate of more than 25 and PaO₂ to FiO₂ ratio of ≤300 mmHg while spontaneously breathing on standard O₂. Patients with a low Glasgow coma scale, severe shock, CO₂ higher than 50 mmHg were excluded. The study randomised 300 patients to either NIV (n=146) or the HFT (n=154). A single patient withdrew from the NIV group and was excluded from the analysis. In the NIV group, alternating treatment with HFT was allowed with the aim of 12 hours of NIV per day in 4-hour sessions. The primary outcome of the study was mortality at day 28 with longer-term mortality, intubation rates and length of stay as secondary outcomes. Mortality at day 28 was 36% in the HFT group compared with 35% in the NIV group (mean difference 1.2%, 95% CI –9.6 to 11.9, p=0.83). The study was adequately designed and powered for a 15% absolute difference in mortality and so small differences between treatment arms cannot be excluded and may still be considered clinically significant. However, the study demonstrates that the choice of NIV or HFT in this patient population.

DOMICILIARY HFT IN COPD: POTENTIAL COST SAVING TO HOSPITAL SYSTEMS

Chronic obstructive pulmonary disease (COPD) is a common progressive disease which is a common cause of hospital admissions with high associated costs. HFT delivers high flow humidified air with or without oxygen enrichment and has been shown to reduce admissions with exacerbations of COPD when delivered at home in high-risk patients. Milne et al (IJCOPD 2022;17:1311) used data from a previous randomised clinical trial of HFT performed in Denmark on 200 patients (100 control, 100 HFT) with COPD requiring LTOT and performed budget impact based on the New Zealand hospital system with a 5-year horizon. Hospital admissions due to COPD exacerbation in the Danish study were compared with the admissions in Middlemore Hospital, NZ, using a matched cohort of 30 patients. Compared with the baseline of 12 months before the study, it was noted there was significant reduction in hospital admissions of 9% in the HFT group compared with a 7% rise in the control group. This study calculates the hospital admission costs for NZ with a linear regression analysis, which was estimated to be US$8699. Thereafter, keeping into account the device cost and the average usage, the projected hospital savings were $18,025 per device over a 5-year period. The study demonstrates a potential cost saving by introduction of a new therapy in this group of patients with significant care burden with the health system.

VENOUS THROMBOEMBOLISM PROPHYLAXIS FOR ACUTE MEDICAL PATIENTS: META-ANALYSIS SUPPORTS INTERMEDIATE DOSE LOW-MOLECULAR-WEIGHT HEPARIN AS TREATMENT OF CHOICE

Venous thromboembolism (VTE) in patients who have been admitted to hospital with acute medical problems is a major cause of morbidity and mortality. The use of anticoagulant prophylaxis is common but choice of agent, precise efficacy and safety profile are in need of further data. Eck et al (BMJ 2022;378:e070022) report a systematic and network meta-analysis examining the risks vs benefits in using various anticoagulants for the prevention of VTE. The study examined four primary outcomes: all-cause mortality, symptomatic VTE, major bleeding and adverse effects over 90 days. A total of 44 studies including 90,095 patients published between 1973 and 2016 contributed to the network analysis. Symptomatic VTE was reported in 32 trials (84,903 participants) with an incidence of 0.9%. Although pentasaccharides, intermediate dose low-molecular-weight heparin (LMWH), unfractionated heparin and direct oral anticoagulants reduced the risks of VTE compared with placebo the only conclusive estimate was for LMWH. In 29 trials (84,483 participants) reported major bleeding complications with highest rates seen with unfractionated heparin (OR 2.62) and direct oral anticoagulants (OR 2.31). The meta-analysis evaluates a range of randomised clinical trial data and the authors conclude that intermediate dose LMWH provides the best balance of risk and benefit for VTE prophylaxis in patients admitted with acute medical problems, however, they also acknowledge that the overall quality of the evidence was only low to moderate.

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