DOES ANTIBIOTIC TREATMENT IMPROVE OUTCOMES FOR PATIENTS WITH ASTHMA EXACERBATIONS?

Antibiotic therapy is commonly prescribed to patients with acute exacerbations of asthma, despite scarce evidence and consensus guidelines advocating limited prescribing. Stefan and colleagues (JAMA Intern Med 2019; E1-E7; doi:10.1001/jamainternmed.2018.5394) investigated the outcomes of antibiotic therapy in hospitalised patients with asthma exacerbations treated with corticosteroids using a retrospective cohort study design.

Data were collected from an administrative database in the USA. A propensity score matched analysis was conducted in an attempt to minimise the influence of confounding factors. Additionally, exposure to antibiotics was assessed in the first 2 days of admission to avoid association of subsequent deterioration. The authors included 19 811 adults from 542 acute care hospitals. Patients with a potential indication for antibiotics (eg, COPD, bronchiectasis, pneumonia, etc) were excluded.

In the first 2 days of hospital admission, 8788 patients (44.4%) received antibiotics. The median hospital stay in those treated with antibiotics was 4 (3–5) days, compared with 3 (2–4) days in those untreated (p<0.001). Treatment failure rates in the whole cohort was low (5.6%) and did not differ between the groups. Rates of antibiotic-associated diarrhoea were low (1.4% treated vs 1.1% untreated). Suggested mechanisms for the prolongation of the hospital stay include unmeasured confounders (mitigated by trial design) and patients not being discharged until they had completed their course of antibiotics. These results support the current recommendations for limited antibiotic prescribing in non-infective asthma exacerbations and highlights the importance of good antimicrobial stewardship.

OMADACYCLINE VERSUS MOXIFLOXACIN FOR COMMUNITY-ACQUIRED BACTERIAL PNEUMONIA

Omadacycline is a new tetracycline-based antibiotic with a spectrum of actions, making it an appealing option for empirical treatment of community-acquired pneumonia (CAP). Stets and colleagues (NEJM 2019;380:517 doi:10.1056/NEJMoa1800201) conducted a phase III, double-blind, non-inferiority randomised control trial at 86 sites worldwide over a 15-month period (November 2015–February 2017), comparing omadacycline and moxifloxacin for the treatment of radiologically confirmed CAP in hospitalised patients. Trial participants comprised 774 adult patients who predominantly had moderately severe pneumonia (defined by pneumonia severity index risk III to IV). Those immunocompromised, with severe pneumonia (pneumonia severity index risk class V) or clinically significant liver or renal insufficiency were excluded. The omadacycline group comprised 386 participants randomised to a 7–14-day course (100 mg intravenously), with 77.2% converting to oral 300 mg once daily dose after ≥3 days. In the moxifloxacin group, there were 388 participants who received 400 mg intravenously, with 75.8% subsequently stepping down to 400 mg orally once daily after ≥3 days. The trial analysis was to demonstrate non-inferiority of omadacycline in early clinical response (blind investigator assessed) at 72 to 120 hours post initial dose with further secondary outcomes for end of treatment and follow-up clinical response (30–37 days post initial dose). Treatment success rates were high in both groups; at 81.1% with omadacycline and 82.7% with moxifloxacin. Omadacycline was non-inferior to moxifloxacin at early (mean difference −1.6%; 95% CI −7.1 to 3.8%), end of treatment (−0.7%; 95% CI −5.7% to 4.3%) and follow-up (1.9%; 95% CI −4.6 to 8.3%) clinical assessments. Frequency of adverse effects were similar between the two groups. However, a higher incidence of diarrhoea was reported with moxifloxacin (8.0%), in contrast to omadacycline (1.0%), with increased rates of Clostridium difficile infection in the moxifloxacin group (2.1%) compared to 0 cases in the omadacycline group. Omadacycline offers a potentially viable treatment for mild to moderate severity CAP in hospitalised patients and may have benefits in those at higher risk of gastrointestinal side effects.

LIBERAL OXYGEN THERAPY IN PATIENTS WITH ACUTE ILLNESS

Despite evidence regarding the deleterious impact of hyperoxia, excess oxygen is frequently given to patients in acute care. Chu and colleagues (Lancet 2018;391:1693) published a systematic review and meta-analysis of 25 randomised clinical trials including more than 16 000 adult patients with acute illness, comparing liberal oxygen therapy (median FiO2 0.52, ranging 0.28–1.00) and conservative oxygen therapy (median FiO2 0.21, ranging 0.21–0.50). Patients with acute illness were defined as those who may be exposed to supplemental oxygen, requiring non-elective hospital admission (eg, trauma, sepsis, myocardial infarction, etc). Patients undergoing elective operations, hyperbaric oxygen therapy and with chronic respiratory conditions were excluded.

An intention-to-treat analysis and modified Cochrane risk of bias assessment tool were applied to reduce bias. Liberal oxygen administration demonstrated an increased risk of both in-hospital (relative risk 1.21, 95% CI 1.03 to 1.43, p=0.020) and 30-day (RR 1.14, 95% CI 1.01 to 1.28, p=0.033) mortality, in comparison with conservative oxygen therapy. A similar finding was reported for long-term mortality (median 3 months follow-up, RR 1.10, 95% CI 1.00 to 1.20, p=0.044). Meta-regression analysis showed a dose–response relationship between SpO2 and mortality in the liberal oxygen therapy group (slope 1.25, 95% CI 1.00 to 1.57, p=0.0080). No significant differences were observed between the two groups in morbidity (neurological outcome or disability) or in the incidence of hospital-acquired pneumonia. Greater awareness of the harmful effects of hyperoxia should be raised in clinical practice, with emphasis on targeted oxygen therapy for patients with acute illness.
WOULD TRACHEOSTOMISED PATIENTS AT RISK OF WEANING FAILURE BENEFIT FROM HIGH-FLOW OXYGEN THERAPY?

High-flow oxygen via nasal cannula (HFNC) is increasingly used for its range of physiological (improved oxygenation, decreased work of breathing, improved mucociliary clearance) and clinical (de novo hypoxaemic respiratory failure, post-extubation, post-cardiothoracic surgery) benefits. In a single-centre, unblinded cross-over study, conducted by Stripoli et al (Intensive Care 2019;9:4: doi:10.1186/s13613-019-0482-2), 14 patients were enrolled from an intensive care unit in Italy. Inclusion criterion was adults with prolonged ventilatory weaning according to WIND study (ie, after more than 7 days from first ventilator separation attempt). Those with neuromuscular pathologies, phrenic nerve dysfunction and signs of paradoxical abdominal movement or accessory muscle use were excluded. If patients passed a spontaneous breathing trial, they were disconnected from the ventilator for the study protocol. Subsequently they received high-flow oxygen therapy through the tracheostomy (HF-T) at 50 L/min, followed by conventional oxygen therapy via T-piece, and back to HF-T, with each phase lasting for 1 hour. The delivered FiO₂ was adjusted for target SpO₂ (94%–98%, unless known COPD then 88%–92%). Detailed respiratory physiological assessment was conducted during the intervention periods, including diaphragm electromyogram, used to calculate the pressure-time product of the respiratory muscles, providing a validated estimate of work of breathing. Despite the small sample size, attrition rate and unblinded non-randomised study design, it yielded an interesting conclusion that HF-T did not improve physiological parameters (respiratory rate, PaO₂/FiO₂, PaCO₂ or work of breathing), in comparison with conventional oxygen therapy. The contrast between HF-T and HFNC is interesting and mechanistically insightful; the failure to improve the respiratory physiology demonstrates that the ability of HFNC to washout the airway dead-space is vital to its function. Further work is needed to assess the impact on comfort and airway clearance with HF-T to indicate if there is a clinical role for this therapy.

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