Journal club

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DEXMEDETOMIDINE OR PROPOFOL FOR SEDATION IN SEPSIS: PAY YOUR MONEY AND MAKE YOUR CHOICE

Dexmedetomidine has been shown to have superior anti-inflammatory and immunomodulatory properties compared with propofol. However, clear clinical benefits remain unproven. Hughes and colleagues (NEJM 2021;384:1424) explore if dexmedetomidine may be superior to propofol in patients with critical illness due to sepsis requiring targeted sedation. This multicentre double-blinded, non-inferiority trial conducted over 13 sites in the USA enrolled 432 patients, who were randomised in a 1:1 ratio with a total of 422 receiving a trial drug. Overall, there was no difference in the primary endpoint of days alive without delirium or coma during the intervention period of 14 days (adjusted median 10.7 vs 10.8 days; OR 0.96; 95% CI 0.74 to 1.26). Moreover, there was no difference between the secondary endpoints of ventilator-free days at 28 days (adjusted median 23.7 vs 24.0 days; OR 0.98; 95% CI 0.63 to 1.51) and death at 90 days (38% vs 39%; HR 1.06; 95% CI 0.74 to 1.52). Key statistics from the trial demonstrate the complexity of achieving appropriate sedation with patients in both groups only spending 57%–60% of the time at target sedation and up to half of the patients in both groups having rescue doses of midazolam. To conclude, this trial reinforces current sedation guidance.

TREATMENT OF ACUTE RESPIRATORY FAILURE: NO CLEAR WINNER BETWEEN HIGH-FLOW NASAL CANNULA AND NON-INVASIVE POSITIVE PRESSURE VENTILATION

Acute respiratory failure requiring invasive ventilation carries a high mortality. Yasuda and colleagues (Journal of Intensive Care 2021;9:32) compared the effectiveness of conventional oxygen therapy (COT), for example, low-flow nasal cannula and venturi masks, high-flow nasal cannula (HFNC) and non-invasive positive pressure ventilation (NPPV) in patients with acute respiratory failure. The meta-analysis included 27 randomised controlled trials which compared either COT, NPPV or HFNC, with a total of 4618 patients. Twenty studies were included for the primary outcome analysis of 90-day mortality. There were trends to improved mortality over COT for NPPV (relative risk (RR) 0.88 (95% CI 0.76 to 1.01); low certainty) and HFNC use (RR 0.93 (95% CI 0.80 to 1.09); low certainty). Of note, no significant difference was observed between NPPV and HFNC use for mortality (RR 0.94 (95% CI 0.78 to 1.15); low certainty), however there were only three studies of direct comparison. Twenty-six studies were included in the analysis for the rate of endotracheal intubation. Both NPPV (RR 0.81 (95% CI 0.72 to 0.91); low certainty) and HFNC (RR 0.78 (95% CI 0.68 to 0.89); low certainty) reduced intubation rate compared with COT with no significant difference between NPPV and HFNC (RR 1.04 (95% CI 0.88 to 1.22); low certainty). Despite this meta-analysis, the low certainty of the evidence and high degree of statistical heterogeneity fail to provide a definitive answer on the best method of respiratory support for acute respiratory failure prior to invasive ventilation.

CLINICAL PROGRESS AND MANAGEMENT OF PATIENTS WITH COVID-19 REQUIRING INVASIVE VENTILATION: PERHAPS PRONE EARLIER?

COVID-19 may lead to severe acute hypoxaemic respiratory failure leading to intensive care unit (ICU) admission. Patel and colleagues (Intensive Care Medicine 2021 47:549) undertook a UK-based, multicentre, observational cohort study describing clinical characteristics and management of COVID-19 from 1 March to 31 August 2020. The study incorporated machine learning and explainable artificial intelligence methods to 'characterise the evolution of clinical parameters'. Out of 1130 screened patients, 633 met the criteria for inclusion in the study. Overall, ICU mortality was 43.3%, as expected this was significantly higher in those with refractory hypoxaemia over first 7 days of their admission (60.4% vs 17.6%; $p<0.001$). Moreover, the median arterial oxygen pressure/fractional inspired oxygen on the day of death was 12.3 (8.9 to 18.4) kPa, indicating that many patients died with or from refractory hypoxaemia. Interestingly, despite widespread suggestion of benefit, proning was not implemented in 50.5% of the patients, despite the fact that 76% had an episode of moderate and 46% of severe hypoxaemia during their admission. Patients who had 'resolved' hypoxaemia were proned earlier (2 (1–5) days vs 4 (2–7) days; $p=0.007$) suggesting a possible early benefit from this intervention. However, over 75% remained in static or worsening hypoxaemia despite application of Acute Respiratory Distress Syndrome (ARDS) interventions, signifying that many patients' disease was refractory to approved ARDS interventions.

CYTOKINE RESORPTION DURING EXTRACORPOREAL MEMBRANE OXYGENATION IN PATIENTS WITH COVID-19: JUST SAY NO

A causative role has been suggested for a 'cytokine storm' in the development of ARDS secondary to COVID-19 with elevated serum interleukin-6 (IL-6) levels associated with higher mortality. Previous data in non-COVID-19 ARDS have been generated indicating a possible beneficial impact of the removal of this excess cytokine load. Supady and colleagues (Lancet Respiratory Medicine 2021;9:755) used a single-centre, open-label, randomised controlled trial to assess cytokine removal in patients with COVID-19 requiring extracorporeal membrane oxygenation (ECMO) with the use of a Cytosorb device. A total of 34 patients with COVID-19 requiring ECMO were eligible and were randomly assigned (1:1) to receive either a Cytosorb device or not. The primary endpoint was 72-hour serum IL-6 concentration after initiation of ECMO. Interestingly, the 72-hour median serum IL-6 concentrations was similar in the Cytosorb group (95% CI −0.70 to 1.30, $p=0.54$) compared with no intervention. Also, the secondary endpoint of 30-day survival was significantly lower in the cytokine adsorption group (3 of 17 (18%) patients vs 13 of 17 (76%); $p=0.0016$). The authors were unable to determine from the data collected the reason behind the negative impact on survival but did suggest that the Cytosorb device could cause activation of coagulation pathways or be removing protective host factors as well as those contributing to the inflammatory process. Overall, despite the small size of the study, it is clear that currently cytokine adsorption should not be used in patients with COVID-19 during the first days of ECMO support.

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Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Commissioned; internally peer reviewed.

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Check for updates

To cite Sainsbury H. *Thorax* 2021;**76**:1064.

Thorax 2021;**76**:1064.
doi:10.1136/thoraxjnl-2021-218122

Thorax: first published as 10.1136/thoraxjnl-2021-218122 on 17 September 2021. Downloaded from http://thorax.bmj.com/ on April 24, 2024 by guest. Protected by copyright.