ICU MANAGEMENT & PRACTICE

ICU Volume 13 - Issue 3 - Autumn 2013 - Country Focus:France

Hot Topics in Critical Care in France

Authors

Catherine Paugam- Burtz, *MD,PHD*

Anaesthesia and Critical Care Department

AP-HP Hôpitaux Universitaires Paris Nord Val de Seine Hôpital Beaujon,

Clichy, France

Diderot University Paris, France

catherine.paugam@bjn.aphp.fr

Samir Jaber, *MD, PHD*

Anaesthesia and Critical Care Department B

Saint Eloi Teaching Hospital Unité INSERM U1046

Centre Hospitalier Universitaire Montpellier

Montpellier, France

This article briefly reviews selected recent French critical care medicine studies that currently impact medical practices.

Introduction

Clinical research activity in the field of intensive care and perioperative medicine in France has been very productive in the last two years. In this review article, we provide a state-of-the-art update on the recent main French published randomised controlled trials (RCTs) as well as reviewing some promising completed trials for which the results should be published in the next few weeks.

ARDS Clinical Trials

Despite its high incidence and devastating outcomes, acute respiratory distress syndrome (ARDS) has no specific treatment, with effective therapy currently limited to minimising potentially harmful ventilation. Until 2012, lung protective mechanical ventilation strategies were the only supportive therapy that clearly improved survival in patients with ARDS. Lung protective ventilation combines limited low tidal volume (5-6 ml/kg of ideal body weight) and positive end-expiratory pressure (PEEP from 5 to 20 cm H2O) with respect to limited plateau pressure lower than 30cm H2O. Two recent major French multicentre RCTs gave new insights, which permit improved ARDS mortality (Papazian et al. 2010; Guerin et al. 2013).

• Neuromuscular Blockade and ARDS: The ACURASYS Study

Lung protective ventilation can be achieved in the majority of patients without using neuromuscular blocking agents (NMBA). However, in the severely hypoxaemic ARDS patient (PaO2/FiO2 < 150 mmHg), NMBA may permit lower pressure, lower tidal volume ventilation with a consequent reduction in ventilator-induced lung injury. These beneficial effects led to the ACURASYS multicentre, randomised, placebo-controlled trial to assess the effect of NMBA upon mortality (Papazian et al 2013). This trial was the first to report decreased mortality by using a pharmacological agent in ARDS. The ACURASYS study included 340 hypoxaemic ARDS patients (PaO2/FiO2 <150 mmHg with PEEP >5cm H2O). A control group without NMBA was compared to an intervention group who received early infusion with cisatracurium besylate within 48 hours of mechanical ventilation. The conclusion of the study was that in patients with severe ARDS early use of NMBA for a short period (<48h) significantly improved mortality at 28-day (23.7% vs 33.3% (P=0.05)) and also improved 90-day survival (31.6% vs 40.7% (p= 0.08)).

• Prone Position and ARDS: The PROSEVA Study

Prone position (PP) in ARDS patients has proved to improve oxygenation and lung recruited volume. Until 2013, previous RCTs involving patients with ARDS failed to show a beneficial effect of PP during mechanical ventilator support on outcomes, although there were significant improvements in oxygenation.

The PROSEVA study evaluated the effect of early application of PP on outcomes in patients with severe ARDS (PaO 2/FiO2 <150 mmHg with PEEP >5 cm H2O) (Guerin et al. 2013). In this multicentre, prospective, randomised, controlled trial, 466 patients were randomly assigned to undergo PP sessions of at least 16 hours (n=237) or to be left in the supine position (n=229). The conclusion of the study was that, in patients with severe ARDS, early application of prolonged PP sessions significantly decreased 28-day (16% vs 33%; p<0.001) and 90-day mortality (24% vs 41%; p<0.001).

Other Published Clinical Trials

• Lung Protective Ventilation in Operating Room In Patients with Healthy Lungs: The IMPROVE Study

In our opinion, preventive strategies should also include protective ventilation with low tidal volume in patients at risk, such as from elective abdominal surgery. Although one physiological study supports this approach, until 2013 no RCT has evaluated the effect of a lung protective strategy on postoperative complications in patients with uninjured lungs in the operating room for abdominal surgery. The IMPROVE trial was a multicentre, double- blind, parallel group trial, which randomly assigned 400 adults at intermediate to high risk of pulmonary complications after major abdominal surgery to either nonprotective mechanical ventilation (tidal volume 10- 12 ml/kg ideal body weight and no PEEP) or a strategy of lung protective ventilation (tidal volume 6-8 ml/kg ideal body weight and PEEP 6-8 cm H2O with recruitment manoeuvres) (Futier et al 2013). The primary outcome was a composite of major pulmonary and extrapulmonary complications occurring within the first seven days after surgery.

The study conclusion was that, compared with a practice of nonprotective mechanical ventilation, the use of a lung protective ventilation strategy in intermediate-risk and high-risk patients undergoing major abdominal surgery was associated with improved clinical outcomes and reduced health care utilisation.

• Stress-Dose Hydrocortisone in Trauma Patients: The HYPOLYTE Study

The HYPOLYTE trial was a multicentre, randomised, double-blind, placebo-controlled study, which evaluated the efficacy of hydrocortisone therapy in trauma patients (Roquilly et al. 2011). The study included 150 patients with severe trauma. Patients were randomly assigned to a continuous intravenous infusion of either hydrocortisone (200 mg/d for five days, followed by 100 mg on day six and 50 mg on day seven) or placebo. The treatment was stopped if patients had an appropriate adrenal response. The primary endpoint was hospital-acquired pneumonia within 28 days. Secondary outcomes included the duration of mechanical ventilation, hyponatraemia, and death. The conclusion of the study was that, in intubated trauma patients, the use of an intravenous stress-dose of hydrocortisone, compared with placebo, resulted in a decreased risk of hospital-acquired pneumonia (36 vs 54%; P=0.01).

• Cardiopulmonary Resuscitation and Patients' Family

The effect of family presence during cardiopulmonary resuscitation (CPR) on the family members themselves and the medical team remains controversial. A multicentre RCT enrolled 570 relatives of patients who were in cardiac arrest and were given CPR by 15 pre-hospital emergency medical service units (Jabre 2013). The units were randomly assigned either to systematically offer the family member the opportunity to observe CPR (intervention group), or to follow standard practice regarding family presence (control group). The primary endpoint was the proportion of relatives with post-traumatic stress disorder (PTSD)-related symptoms on day 90. The frequency of PTSD-related symptoms was significantly higher in the control group than in the intervention group, and the conclusion of the study was that family presence during CPR was associated with positive effects on psychological variables and did not interfere with medical efforts, increase stress in the healthcare team, or result in medicolegal conflicts.

Promising Completed Trials

Besides this recent literature, several promising French multicentre studies have been completed, and these trials may provide us with interesting results for practice. Asehnoune and coworkers have studied traumatic brain injured patients, who frequently suffered from glucocorticoid insufficiency associated with an increase in the rate of pneumonia, responsible for significant burden. Corti-TC study is a double-blinded RCT supported by the French Anaesthesia and Critical Care Society (SFAR), designed to assess the treatment of glucocorticoid insufficiency (hydrocortisone associated with fludrocortisone) for prevention of post-trauma pneumonia in a population of severe traumatic brain injury patients (Nantes University Hospital).

To come also are the results of the STATIN VAP study by Papazian et al. on the effect of the association of a statin to antibiotics on hospital mortality of patients presenting with a suspicion of ventilator-associated pneumonia (Assistance Publique Hopitaux De Marseille). Another study to come is focused on fluid resuscitation. The CRISTAL study by Annane et al. is a large multinational open randomised trial designed to compare the effects on hospital mortality of crystalloids and colloids when given for fluid resuscitation in critically ill patients (University of Versailles). There is no doubt that this study will probably boost the debate about fluids in ICU.

The last study is dedicated to the evaluation of the streamlining of antimicrobial therapy after the identification of the pathogen responsible for infection. Even if it is a classical guideline, few randomised clinical trials have tested this strategy prospectively. In the DEA (Désescalade) study, Leone et al. are conducting a randomised clinical trial comparing a strategy based on de-escalation (streamlining of the empirical antimicrobial

therapy) and a conservative strategy (continuation of the empirical antimicrobial therapy) (Assistance Publique Hopitaux De Marseille). They aim to show that a strategy based on de-escalation is not inferior to a conservative strategy in terms of intensive care unit length of stay.

Conclusion

Clinical research in intensive care and perioperative medicine in France is very productive. Recently it has addressed relevant questions, providing us with interventions associated with a positive impact on the outcomesof critically ill patients. Results of further studies are awaited in the hope of continued improvement of our daily clinical practice.

Acknowledgements

No financial sponsor

Published on : Wed, 2 Oct 2013