ICU UPDATE FOR THE ANAESTHETIST

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The following topics and papers from the last year have relevance in Intensive Care and Anaesthesia practice.

Trauma

Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial from the CRASH-2 trial collaborators.

The Lancet, Volume 376, Issue 9734, Pages 23 – 32, 3 July 2010

This randomised controlled trial was undertaken in 274 hospitals in 40 countries. 20,211 adult trauma patients with, or at risk of, significant bleeding were randomly assigned within 8 hours of injury to either tranexamic acid (loading dose 1g over 10 min then infusion of 1g over 8 h) or matching placebo. The primary outcome was death in hospital within four weeks of injury, and was described with the following categories: bleeding, vascular occlusion (myocardial infarction, stroke and pulmonary embolism), multiorgan failure, head injury, and other.

Results: 10,096 patients were allocated to tranexamic acid and 10,115 to placebo, of whom 10,060 and 10,067, respectively, were analysed. All-cause mortality was significantly reduced with tranexamic acid (1,463 [14.5%] tranexamic acid group vs 1,613 [16.0%] placebo group; relative risk 0.91, 95% CI 0.85–0.97; p=0.0035). The risk of death due to bleeding was significantly reduced (489 [4.9%] vs 574 [5.7%]; relative risk 0.85, 95% CI 0.76–0.96; p=0.0077).

Interpretation: Tranexamic acid safely reduced the risk of death in bleeding trauma patients in this study. On the basis of these results, tranexamic acid should be considered for use in bleeding trauma patients.

Shock

Comparison of dopamine and norepinephrine in the treatment of shock.

N Engl J Med. 2010 Mar 4; 362(9): 779-89

Background: Both dopamine and norepinephrine are recommended as first-line vasopressor agents in the treatment of shock. There is a continuing controversy about whether one agent is superior to the other. In this multicenter, randomised trial, patients with shock were assigned to receive either dopamine or norepinephrine as first-line vasopressor therapy to restore and maintain blood pressure. When blood pressure could not be maintained with a dose of 20 mcg/kg/min of dopamine or a dose of 0.19 mcg/kg/min of norepinephrine, open-label norepinephrine, epinephrine, or vasopressin could be added. The primary outcome was the rate of death at 28 days after randomisation; secondary end points included the number of days without need for organ support and the occurrence of adverse events.

Results: The trial included 1,679 patients, of whom 858 were assigned to dopamine and 821 to norepinephrine. The baseline characteristics of the groups were similar. There was no significant between-group difference in the rate of death at 28 days. However, there were more arrhythmic events among the patients treated with dopamine than among those treated with norepinephrine (207 events [24.1%] vs. 102 events [12.4%], P<0.001). A subgroup analysis showed that dopamine, as compared with norepinephrine, was associated with an increased rate of death at 28 days among the 280 patients with cardiogenic shock but not among the 1,044 patients with septic shock or the 263 with hypovolaemic shock.

Conclusions: Although there was no significant difference in the rate of death between patients with shock who were treated with dopamine as the first-line vasopressor agent and those who were treated with norepinephrine, the use of dopamine was associated with a greater number of adverse events.

Efficacy and safety of dopamine versus norepinephrine in the management of septic shock.
Shock. 2010 Apr; 33(4): 375-80

This single centre study demonstrated similar findings.

Glucose Control

Intensive versus Conventional Glucose Control in Critically Ill Patients.
The NICE-SUGAR Study Investigators N Engl J Med 2009; 360:1283-1297

NICE-SUGAR (Normoglycemia in Intensive Care Evaluation–Survival Using Glucose Algorithm Regulation) showed that intensive glucose control in critically ill patients was associated with increased hypoglycaemia and increased mortality, suggesting that this strategy should be discarded.

Background: After a study reported decreased mortality and other benefits with an intensive glucose-control protocol in postoperative patients in the ICU, many professional organisations recommended tight glucose control as routine in ICUs. The study, however, was done at a single centre, did not study medical patients in the ICU definitively, and routinely administered substantial amounts of glucose as part of postoperative care. Although a benefit of intensive glucose control was not seen in multiple subsequent studies or in a meta-analysis, an increased risk for hypoglycaemia was found, and the relative risks and benefits of aiming to maintain normoglycaemia in critically ill patients are debated.

Study Design: A multicenter, international RCT of 6,104 critically ill medical and surgical patients compared insulin infusion protocols aimed to achieve intensive glucose control (target blood glucose level, 4.5 to 6.0 mmol/L [81 to 108 mg/dL]) or conventional glucose control (target <10.0 mmol/L [<180 mg/dL]). The primary end point was death from any cause at 90 days.

Findings: The groups were similar at baseline and included patients with a range of medical and surgical problems (37% were surgical patients, 20% had diabetes, 31% had an Acute Physiology and Chronic Health Evaluation II score greater than 25, 21% had severe sepsis, and 93% received mechanical ventilation). At 90 days, 27.5% in the intensive-control group had died, compared with 24.9% in the conventional-control group (OR for intensive control, 1.14 [CI, 1.02 to 1.28]; P = 0.02). Subgroup analysis suggested that the results did not differ between surgical or medical patients or whether the patient had diabetes or severe sepsis. The median survival time was lower in the intensive-control group than in the conventional-control group (HR, 1.11 [CI, 1.01 to 1.23]; P = 0.03). Severe hypoglycaemia (≤ 2.2 mmol/L [≤40 mg/dL]) occurred in 6.8% of patients in the intensive-control group and 0.5% in the conventional-control group (OR, 14.7 [CI, 9 to 25]; P < 0.001).

Implications: Despite earlier enthusiasm and recommendations for widespread implementation, intensive glucose control has not been substantiated as beneficial in critically ill patients. Insulin therapy aiming to achieve normoglycaemia results in increased mortality compared with a goal of less than 10.0 mmol/L (<180 mg/dL) and an increased risk for hypoglycaemia. The study reminds us of the need for a more cautious approach to the adoption of widespread recommendations, including awaiting confirmation of preliminary findings from additional studies.

NICE-SUGAR TBI

Awaiting publication as there maybe some benefit of tighter glucose control in traumatic brain injury.

Fluids

A Comparison of Albumin and Saline for Fluid Resuscitation in the ICU.

The SAFE Study Investigators. N Engl J Med 2004; 350: 2247-56.

In this clinical trial in critically ill patients in the intensive care unit, the use of albumin and saline resulted in similar outcomes at 28 days. With equivalent clinical outcomes, the decision about which fluid to use should be determined by physician preference, safety, and cost.

Saline of Albumin Fluid Resuscitation in Patients with Traumatic Brain Injury

The SAFE Study Investigators. N Engl J Med 2007; 357(9): 874-884

A post-hoc analysis of the SAFE Study to determine the effect of saline versus albumin for fluid resuscitation in patients with traumatic brain injury.

460 patients, of whom 231 (50.2%) received albumin and 229 (49.8%) received saline. The subgroup of patients with GCS scores of 3 to 8 were classified as having severe brain injury (160 [69.3%] in the albumin group and 158 [69.0%] in the saline group). Demographic characteristics and indexes of severity of brain injury were similar at baseline.

Results: At 24 months, 71 of 214 patients in the albumin group (33.2%) had died, as compared with 42 of 206 in the saline group (20.4%) (relative risk, 1.63; 95% confidence interval [CI], 1.17 to 2.26; P = 0.003). Among patients with severe brain injury, 61 of 146 patients in the albumin group (41.8%) died, as compared with 32 of 144 in the saline group (22.2%) (relative risk, 1.88; 95% CI, 1.31 to 2.70; P<0.001); among patients with GCS scores of 9 to 12, death occurred in 8 of 50 patients in the albumin group (16.0%) and 8 of 37 in the saline group (21.6%) (relative risk, 0.74; 95% CI, 0.31 to 1.79; P = 0.50).

Conclusion: In this post hoc study of critically ill patients with traumatic brain injury, fluid resuscitation with albumin was associated with higher mortality rates than was resuscitation with saline.

SAFE TBI II (unpublished)

This study involves a retrospective chart review of the SAFE TBI cohort, examining potential mechanisms behind the detrimental effect of fluid resuscitation with albumin. The study examined whether increased ICP associated with albumin resuscitation lead to therapies with toxic side effects that increased mortality.

Another study with more relevance to anaesthesia fluid choice is presently underway. It is the comparison of crystalloid vs. colloid fluid for resuscitation. This has predefined subgroups in trauma, TBI and sepsis.

Crystalloid versus Hydroxy-Ethyl Starch Trials – CHEST

Background: Fluid resuscitation is a fundamental component of the haemodynamic management of critically ill patients and the choice of fluid is a longstanding issue of debate. Broadly, resuscitation fluids can be divided into colloids (eg 6% hydroxyethyl starch (130/0.4)) and crystalloids (eg saline). Currently there is little high quality evidence available to clinicians in order to guide their clinical decision-making when choosing resuscitation fluids.

Aim: The primary aim of the CHEST study is to compare the 90-day all-cause mortality between patients assigned 6% hydroxyethyl starch (130/0.4) compared to 0.9% sodium chloride (saline).

Design: The CHEST study is a prospective, multicentre, concealed, randomised controlled trial of 6% hydroxyethyl starch (130/0.4) in 0.9% sodium chloride for intravascular volume resuscitation in the Intensive Care Unit (ICU) compared to those 0.9% sodium chloride (saline) alone. The study is a collaboration of The George Institute For International Health, The ANZICS Clinical Trials Group and the University of Sydney.

Methods: In this study, 7000 patients will be recruited in over 25 Intensive Care Units throughout Australia and New Zealand. Participants will be randomised to receive either 6% hydroxyethyl starch (130/0.4) or saline for all resuscitation episodes whilst in the intensive care unit for up to 90 days.

Renal Failure

Acute kidney injury in the intensive care unit: An update and primer for the intensivist.

Critical Care Medicine 2010; 38:1: 261-275

Acute kidney injury is common in critically ill patients and is associated with significant morbidity and mortality. Acute kidney injury (AKI), previously termed acute renal failure, refers to a sudden decline in kidney function causing disturbances in fluid, electrolyte, and acid–base balance because of a loss in small solute clearance and decreased glomerular filtration rate (GFR). The nomenclature shift to AKI more accurately represents the spectrum of disease from subclinical injury to complete organ failure. More than 35 definitions of AKI currently exist in the literature. The Acute Dialysis Quality Initiative convened in 2002 and proposed the RIFLE classification (risk, injury, failure, loss, end-stage kidney disease) specifically for AKI in critically ill patients. Using serum creatinine and urine output, the RIFLE criteria define three grades of severity and two outcome classes.

More recently the Acute Kidney Injury Network (AKIN), an international multidisciplinary organisation composed of nephrologists and intensivists, further modified the RIFLE criteria recognizing that even very small changes in SCr (>=0.3 mg/dL) adversely impact clinical outcome. According to AKIN, the most current consensus diagnostic criteria for AKI is “an abrupt (within 48 hrs) reduction in kidney function currently defined as an absolute increase in serum creatinine of more than or equal to 0.3 mg/dL (>=26.4 μmol/L), a percentage increase in serum creatinine of >=50% (1.5-fold from baseline), or a reduction in urine output (documented oliguria of <0.5 mL/kg/hr for >6 hrs).” Importantly, the AKIN definition and classification system incorporates creatinine, urine output, and time. Both the RIFLE and AKIN criteria were developed to facilitate clinical investigation and comparison across study populations. Epidemiologic data comparing the RIFLE and AKIN criteria have demonstrated concordance in critically ill patients.

Perioperative acute kidney injury: risk factors, recognition, management, and outcomes.

BMJ 2010; 341: c3365

In this article the authors outline the risk factors for perioperative AKI and discuss how to recognise the condition, manage it, and improve outcomes, focusing on the non-specialist surgery setting and using evidence from randomised trials, retrospective studies, meta-analyses, and expert reviews, as well as the recommendations of recent guidelines. AKI is both important and all too often ignored. Most cases of AKI that occur in the perioperative period are associated with relative hypoperfusion of the kidney and / or exposure of the kidney to nephrotoxins, and not with primary intrinsic renal disease.

Tips for the Anaesthetist

- Perioperative AKI increases surgical mortality and morbidity and increases hospital costs.
- Careful preoperative assessment can identify patients at particular risk of AKI and could allow for additional monitoring and planning.
- Perioperative AKI rarely indicates an isolated renal problem but rather a physiologically unstable patient who may deteriorate further and must not be ignored.
- The successful prevention and management of AKI involves timely recognition of perhaps subtle abnormalities, basic clinical assessments and observations, and quick and appropriate reaction to information, including getting senior and specialist help.
- Ensure that the patient with a diagnosis of AKI is normovolaemic, has an adequate mean arterial pressure, and preferably is not exposed to nephrotoxins.
- Many surgical patients have a history of ventricular dysfunction, and optimisation of cardiac function may require inotropic support.
- Renal tract obstruction must be excluded radiologically within 24 hours of a diagnosis of AKI.

Post Operative Respiratory Failure

Postoperative Noninvasive Ventilation.

Anesthesiology 2010; 112: 2: 453-46

This paper gives an excellent review of the literature with respect to: epidemiology, surgery and anaesthesia-induced respiratory changes, definitions and principles of NIV, application and results within post op groups (cardiac, thoracic and abdominal) both with preventive and curative NIV. An example is below –

> How to Set NIV and Duration of Trial: NIV works best in patients relaxed and prepared. CPAP pressures of 7–10 cm H2O are required to keep tracheal pressure positive during the entire respiratory cycle and to consistently improve gas exchange. These CPAP pressures are safe, and no adverse haemodynamic effects were observed. In PSV + PEEP, patient comfort and interface acceptance may be gained by starting with PEEP alone and then slowly increasing the PSV level once the mask is applied. We recommend starting with a PSV of 3–5 cm H2O and increasing in increments of 2 cm H2O to achieve a 6–10 ml/kg expiratory tidal volume, a decrease in the patient's respiratory rate, and a comfort improvement. The PEEP is started at 3–5 cm H2O and increased as needed to improve oxygenation without adverse haemodynamic effects up to 10 cm H2O. The insufflation pressure (PSV + PEEP level) applied should be less than 25 cm H2O. These setting recommendations are based solely on clinical experience without any formal data to support the superiority of one technique over another. A surgical complication arises in nearly half the cases of acute respiratory failure (ARF). The treatment is usually reintervention, management of ARF is only symptomatic, and there is no reason to use NIV to avoid intubation because the patient requires intubation for anaesthesia.