

CONGRESS REPORT

Hot topics in intensive Care 2015

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On 7 October 2015, on the final day of the ESICM annual conference in Berlin, the Hot Topics session was scheduled. A fully crowded room, everyone eager to hear the latest results of large multicentre ICU studies. For those who could not be there and have not yet had time to read the paper on the presented studies, we provide a summary of this session. If you want to see the presentations 'live' please go to: <http://www.esicm.org/news-article/LIVES-2015-HOT-TOPICS-FULL-PRESENTATIONS>

SPLIT trial

The results of the SPLIT trial were presented by Paul Young from Wellington.⁽¹⁾ In the SPLIT trial, the effect of a buffered crystalloid fluid (balanced solution) versus 0.9% saline on renal complications in ICU patients was investigated. The hypothesis was that buffered solutions would reduce the risk of acute kidney injury. A double-blind, cluster randomised, double-crossover trial was conducted in four ICUs in New Zealand. This means that a collaborating centre used either one of the fluids for a period of seven weeks in all ICU patients during that period. After these seven weeks the crossover was made to the other type of fluid. Patients admitted during the buffered solutions period remained in that group. The total study duration was 28 weeks. Bags with fluids were coded A and B so that the treating team did not know what was administered. Any ICU patient requiring crystalloid infusions who did not need dialysis due to established renal injury or was admitted for palliative care was included. In total 2262 patients were included. In the buffered crystalloid group, 102 of 1067 patients (9.6%) developed acute kidney injury within 90 days after enrolment compared with 94 of 1025 patients (9.2%) in the saline group (absolute difference 0.4% [95% CI -2.1% to 2.9%]; relative risk, 1.04 [95% CI 0.80 to 1.36]; $p=0.77$). No difference was found in the need for renal replacement therapy or any of the other endpoints. Also, in the pre-defined subgroup analyses, no differences were seen

between different ICUs, more or less severely ill (Apache II scores) patients or between patients with and without sepsis. The conclusion of this study was that the use of buffered crystalloid solutions did not reduce the risk of acute kidney injury in ICU patients.

EPO-TBI trial

The double-blind, placebo-controlled EPO-TBI trial was presented by Craig French from Melbourne.⁽²⁾ Erythropoietin (EPO) is thought to have neuroprotective effects, but is also thought to increase the incidence of thromboembolic events. This study investigated the effect of EPO on neurological recovery, mortality and venous thrombotic events in patients with moderate or severe traumatic brain injury. Patients in the EPO group received epoetin alfa 40,000 IU as a subcutaneous injection. The first dose was administered within 24 hours after traumatic brain injury. EPO was repeated weekly for a maximum of three doses or as long as the patient stayed on the ICU. Placebo consisted of 0.9% NaCl. In a period of almost five years, 606 patients were randomised. Finally, 302 patients were available for analysis in the erythropoietin group and 294 in the placebo group. No differences were found for the primary endpoint of neurological outcome nor for any of the secondary outcomes. Furthermore, no differences were seen in adverse events, especially no increase in the number of thromboembolic events.

I-VNICTUS study

Results of the French study on noninvasive ventilation (NIV) versus oxygen therapy in critically ill immunocompromised patients were presented by Virginie Lemiale.⁽³⁾ In this multicentre randomised trial, patients were randomised to NIV, started immediately after randomisation. The hypothesis was that NIV would lead to a decrease in mortality in this severely ill population. Noninvasive ventilation was recommended for 60-minute sessions every four hours, for at least two days. In

both groups high flow nasal oxygen was used. The primary outcome for this study was all-cause mortality within 28 days after randomisation. The need for intubation was used as a secondary endpoint. Based on the assumption that the 28-day mortality would be 35% in the study population, 187 patients were needed in both groups. In 19 months the collaborating 28 French ICUs included 374 patients, 183 were randomised to the oxygen alone group, 191 received NIV. The vast majority of the patients were cancer patients; half of the patients in both groups were treated with chemotherapy. No differences were found for any of the endpoints in this study. The authors conclude that early NIV did not reduce 28-day mortality in immunocompromised critically ill patients. However, as mortality was lower than expected in the control group (27 instead of 35%) it is likely that the sample size of this study was too small to answer the question. Furthermore, the use of high flow nasal oxygen in both groups limits the differences between the two treatment arms and may influence the results.

VANISH trial

The acronym VANISH is used for the VAsopressin versus Noradrenaline as Initial vasopressor therapy in Septic shock study, which was presented by Anthony Gordon from London (not yet published). This study investigated whether the use of vasopressin or noradrenaline reduced renal dysfunction in septic shock patients. A secondary question was whether an interaction existed between vasopressin and the use of corticosteroids. A multifactorial (2 x 2) double-blind randomised control trial was performed. Patients were randomised to vasopressin (0-0.06 U/min) or noradrenaline 0-0.12 µg/min and, if the maximum dose of these drugs was exceeded, patients were then randomised to receive hydrocortisone (50 mg four times a day) or placebo. Eighteen British hospitals collaborated in this study and included 412 patients in two years. The baseline characteristics were well balanced between the four treatment groups. The results showed no difference in the occurrence of renal dysfunction between any of the groups, but a reduced need for renal replacement therapy was seen in the vasopressin group. No differences in mortality or duration of shock were found.

Eurotherm3235 trial

Peter Andrews from Edinburgh presented the results of the prematurely stopped Eurotherm3235 study.⁽⁴⁾ In this randomised control trial, the effectiveness of hypothermia in patients with traumatic brain injury and increased intracranial pressure was investigated. The aim was to enrol 600 patients in this study. Patients with intracranial pressure monitoring after traumatic brain injury were eligible for this study when the intracranial pressure increased to >20 mmHg for at least five minutes after stage 1 treatment. Stage 1 treatment consisted of sedation and analgesia, CSF drainage if possible and surgical

removal of space occupying lesions. Patients were randomised to hypothermia to reduce intracranial pressure or to treatment with mannitol or hypertonic saline. If, despite this treatment, the intracranial pressure remained high or increased further, stage 3 therapies were used. These consisted of barbiturate therapy or decompressive craniectomy. After inclusion of 387 patients in 47 centres in 18 countries, the study was stopped as advised by the safety monitoring board. The hypothermia group consisted of 195 patients, the control group 192 patients. Baseline characteristics were well balanced between the groups. Stage 3 strategies were more often needed in the control patients than in the hypothermia-treated group, indicating a beneficial effect of hypothermia on intracranial pressure. However, after a follow-up of 6 months, a statistically significant decrease in the number of patients with a good outcome was seen in the hypothermia group. More patients died in the hypothermia group. A trial stopped early has a significant risk of bias, but the trend of increased mortality in the hypothermia group was already seen in the first interim analysis and increased further after inclusion of more patients. In conclusion, hypothermia does affect intracranial pressure but does not improve outcome after traumatic brain injury.

CLEAN trial

The last trial presented was the CLEAN trial, by Jean-Francois Timsit from Paris, which investigated the effect of skin antisepsis with chlorhexidine-alcohol versus povidone iodine-alcohol with and without skin rubbing for the prevention of intravascular catheter-related infection.⁽⁵⁾ This was an open-label, multicentre, two-by-two factorial design study. Catheter-related infections remain a serious problem in critically ill patients, leading to an increase in the length of ICU stay, mortality and costs. It is likely that most infections can be avoided by relatively simple strategies such as optimal skin antisepsis. The best solution to achieve skin antisepsis and the best method to apply remains to be established. The hypotheses of this study were that 1) use of chlorhexidine-alcohol would be more effective than povidone iodine-alcohol to prevent short-term catheter-related infections and 2) that scrubbing of the skin would not reduce catheter colonisation compared with just the application of the antiseptic. The main endpoint of the study was the incidence of catheter-related infections; both central venous lines and haemodialysis lines were included. Patients were followed until 48 hours after discharge from the ICU. When the central venous line was no longer needed, it was removed. Inclusion of patients started in October 2012 and finished in February 2014 when 2349 patients had been enrolled by the collaborating French centres. In the chlorhexidine-alcohol group (1181 patients, 2547 catheters) the incidence of catheter-related infections was much lower (0.28 per 1000 catheter days) compared with the incidence in the povidone iodine-alcohol group (1168 patients, 2612 catheters; 1.77 per 1000

catheter days) . A similar effect was found for catheter-related blood stream infections, but this did not lead to a difference in length of stay on the ICU or mortality. No effect of scrubbing or no scrubbing was found on any of the outcome parameters. No difference in systemic adverse events was seen, but skin reactions were more frequent and more severe in chlorhexidine-treated patients. The authors concluded that the results clearly showed a favourable effect of skin antisepsis with chlorhexidine-alcohol on the incidence of catheter-related infections and advocate the inclusion in guidelines and treatment bundles.

Disclosure

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References

1. Young P, Bailey M, Beasley R, et al. Effect of a Buffered Crystalloid Solution vs Saline on Acute Kidney Injury Among Patients in the Intensive Care Unit The SPLIT Randomized Clinical Trial. *JAMA*. 2015; 314:1701-10.
2. Nichol A, French C, Little L, et al. Erythropoietin in traumatic brain injury (EPO-TBI): a double-blind randomised controlled trial. *Lancet*. 2015; Oct 6. pii: S0140-6736(15)00386-4. doi: 10.1016/S0140-6736(15)00386-4. [Epub ahead of print]
3. Lemiale V, Mokart D, Matthieu Resche-Rigon, et al. Effect of Noninvasive Ventilation vs Oxygen Therapy on Mortality Among Immunocompromised Patients With Acute Respiratory Failure A Randomized Clinical Trial. *JAMA*. 2015;314:1711-9.
4. Andrews PJ, Sinclair HL, Rodriguez A, et al. Hypothermia for intracranial hypertension after traumatic brain injury. *New Engl J Med*. 2015; Oct 7. [Epub ahead of print].
5. Mimoz O, Lucet JC, Kerforne T, et al. Skin antisepsis with chlorhexidine-alcohol versus povidone iodine-alcohol, with and without skin scrubbing, for prevention of intravascular-catheter-related infection (CLEAN): an open-label, multicentre, randomised, controlled, two-by-two factorial trial. *Lancet*. 2015 Sep 17. pii: S0140-6736(15)00244-5. doi: 10.1016/S0140-6736(15)00244-5.

NVIC CONFERENCE AND COURSE AGENDA

COURSES AND CONFERENCES | NVIC

NVIC Intensivistendagen 2016

Thursday 21 January – Friday 22 January 2016

NVIC Cursus echografie

Tuesday 8 March – Wednesday 9 March 2016

NVIC Cursus luchtwegmanagement op de IC

Thursday 9 June – Friday 10 June 2016

NVIC Najaarscongres

Thursday 22 September – Friday 23 September 2016

COURSES AND CONFERENCES | OTHER

ISICEM Brussels

Tuesday 15 March – Friday 18 March 2016

ICEM Cape Town

Monday 18 April – Tuesday 21 April 2016

ESICM annual congress

Saturday 1 October – Friday 5 October 2016