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HOT TOPICS

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On the final day of the annual congress of the European Society of Intensive Care Medicine (ESICM) in Berlin, results of leading research from the previous year were presented. Below I will summarize the presentations given and highlight the most important conclusions drawn from this research.

Elie Azoulay presented the results of the palliative non-invasive ventilation (NIV) study in critically ill patients with acute respiratory failure when the policy is not to intubate or the goal is to provide comfort care during the last phase of life [1]. His research question was: does palliative NIV increase the duration of life or does it extend the process of dying? The investigators designed the study to see how often palliative NIV is used in intensive care units (ICU) and what palliative NIV implies for the quality of life of patients and their families. The study was a longitudinal observational multicentre study in 61 ICUs in France and Belgium. Seven hundred and eighty patients receiving NIV were included and in 206 (26.4%) cases palliative NIV was applied. Of these, 134 (17.2%) because of a not to intubate policy, and 72 (9.2%) because of comfort care. Mortality was 44% in the not to intubate policy cases and 94 % for those receiving comfort care. Quality of life, as expressed through symptoms of anxiety, depression and stress, did not decrease in survivors or relatives at day 90. This suggests that palliative NIV does not only prolong the process of dying.

The role of extracorporeal membrane oxygenation (ECMO) in acute respiratory distress syndrome (ARDS) is still controversial. Kathy Rowan presented the results of a recent ECMO study [2]. The aim of this study was to compare the mortality for patients that were referred, accepted, and transferred to ECMO centres in the United Kingdom because of H1N1- related ARDS, with carefully matched non-ECMO referred patients. During the influenza pandemic of 2009-2010, no randomized clinical trials for patients with H1N1 were funded, established or completed. Data for this study were obtained from the Swine Flu Triage Study (SWIFT) which was a prospective cohort study of patients with suspected or confirmed H1N1 who had been referred and assessed as requiring critical care. The investigators used three types of matching to minimize confounding results when estimating effectiveness from observational data. There were 80 patients referred, accepted and transferred to an ECMO centre during the study period, and there were 195 potential non-ECMO referred patients. The hospital mortality rate was 23.7% for ECMO patients and 52.5% (RR 0.45 [95% CI 0.26 -0.79]) for non-ECMO patients after individual matching, 24.0% vs 46.7% (RR 0.51 [95% CI 0.31-0.84]) after propensity score matching and 24.0% vs 50.7% (RR 0.47 [95% CI 0.31-0.72]) after so-called GenMatch matching. Hence, the study suggests that transfer to an ECMO centre for patients with H1N1- related ARDS is associated with a lower mortality compared with matched non- ECMO referred patients.

The current definition of acute lung injury (ALI) / ARDS dates from the American-Europe Consensus Conference in 1994 and consists of bilateral infiltrates of acute onset on chest radiography and a pulmonary artery wedge pressure of less than 18 mm Hg or absence of signs of left atrial hypertension. This definition can, however, be criticized since sensitivity is only 84 % and specificity 51% when compared with post mortem studies. With the current criteria, ARDS is under-recognized by clinicians and consequently patients may not receive the best treatment. ESICM convened an international panel with experts to create an update of the current definition. Marco Ranieri reported the objectives of the new definition [3]. The objectives were to update the ARDS definition using a systematic analysis of current epidemiologic evidence, physiological concepts and results of clinical trials. Syndrome definitions must fulfil three criteria: feasibility, reliability and validity. In the new definition there are three stages of ARDS: mild/moderate/severe. The new definition takes issues like acute onset and the oxygenation ratio in combination with positive end-expiratory pressure (PEEP) into account. Respiratory failure should not be fully explained by cardiac failure or fluid overload. To improve the interobserver agreement of the judgement of the chest radiographs, a training set is available. To fulfil the new criteria there must be an accepted risk factor for ARDS, either direct or indirect. Now that the new definitions have been formulated, the next step is to see if they are fulfilling the criteria for face validity and predictive validity.

The omega-3 (n-3) fatty acids docosahexaenoic acid and eicosapentaenoic acid, along with γ-linolenic acid and antioxidants, may modulate the systemic inflammatory response and improve oxygenation and outcomes in patients with acute lung injury (ALI). The interpretation of previous studies on this subject is limited by their small sample sizes. The aim of the study presented by Todd Rice [4] was to test the hypothesis that omega-3 fatty acids and antioxidant supplementation compared with placebo improves the clinical outcomes in patients with ALI/ARDS by attenuating systemic inflammation. The primary end point was ventilator-free days at day 28. Secondary end points

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were mortality prior to hospital discharge up to day 60, ICU-free days up to day 28, organ failure-free days up to day 28 and changes in serum/urine inflammatory biomarkers. After the first interim analysis (after 272 patients had been included) the study was stopped because of futility. There were more ventilator-free days in the control group (17.2 vs 14, P = 0.02). Also, ICU- free days were fewer in the control group (16.7 vs 14, P = 0.04) and mortality was 26.6% in the treatment group versus 16.3 % in the control group (P = 0.054). The outcomes were in contrast with those of previous studies. Differences may be explained by a potential bias because of exclusion criteria in previous studies, and by the different composition of the nutritional supplement used in the control group, which may have had a pro-inflammatory effect in previous studies.

Hypoalbuminaemia is a predictor for a poor outcome associated with severe disease. There are several arguments in favour of the administration of albumin in these patients: an elevation of oncotic pressure, improvement of drug transport and delivery, antioxidative and anti inflammatory actions and cardiac protection by albumin. However, the administration of albumin may also be harmful; it is an expensive blood product that may cause renal failure and pulmonary oedema. The Early Albumin Resuscitation during Septic Shock study presented by Jean-Paul Mira is a randomised prospective, multicentre, open, study in France [5]. The aim of the study was to investigate the efficacy and safety of early administration of hyperoncotic albumin in patients with septic shock. The patients in the albumin group received 20 gram of 20 % albumin three times daily, while the control group received 100 ml NaCl 0.9% three times daily. There were 792 patients included, 399 received albumin and 393 received saline. The plasma concentration of albumin at baseline was 17.8 vs 18.1 g/l. the administration of 60 grams of albumin over three days increased the albumin level, but not above 25 g/l in 36 % of cases. There was no difference in mortality between the groups, 24.1% vs 26.3 %. Also, secondary end-points, incidence of nosocomial infections, length of stay in the ICU and in the hospital, and of renal failure did not differ between the groups. However, the groups differed in catecholamine-free days, 24 (albumin) vs 23 (saline) days on the average (P= 0.038). In conclusion, there was neither advantage nor disadvantage related albumin administration in septic patients.

Colloids may be harmful for kidney function, for coagulation, inducing a risk of bleeding, and may cause itching following tissue storage. Bertrand Guidet was one of the investigators of the CHRYSTalloids Morbidity Associated with severe Sepsis study. (CHRYSTMAS), a randomised double blind multicentre parallel group study to compare colloids with saline [6]. The colloid group received Voluven 6% at a dose of 50 ml/kg on day and 25 ml/kg on day 2-4. The control group received the same amount of NaCl 0.9%. One hundred and ninety-six patients with severe sepsis were randomised (Voluven n=100, control n=96). It took 11.8 hours in the Voluven group and 14.3 hours, on average, in the control group to achieve haemodynamic stability, which was a primary outcome variable. This difference was not significant, however. The volume of study drug to initial haemodynamic stabilisation was 1379 ml in the Voluven group and 1709 ml in the saline group (P = 0.0185). The latter outcome is statistically significant but is it also clinically significant? Indeed, it may be clinically more important to reach haemodynamic stability two hours earlier in the Voluven than in the control group, even if statistical significance is not reached. No differences were seen in the use of catecholamines, mortality and length of stay in the ICU or hospital. The safety variables, including renal function, coagulation and frequency of itching, did not differ between the two groups.

Ventilator-associated pneumonia (VAP) is a problem in our ICUs and, on average, prolongs ICU stay by at least four days; it is also responsible for more than half of the prescriptions for antibiotics on ICUs. Mortality rates for VAP are high. Thiago Lisboa and colleagues designed a care bundle for preventing VAP and designed a prospective multicenter study (FADO project) to determine the impact of implementing this bundle for the prevention of VAP on the duration of ventilation and length of stay in the ICU [7]. The bundle includes hand hygiene, interruption of sedation, a weaning protocol, oral care with chloorhexidine every 4 hours, intracuff pressure control and prevention of changes in the ventilatory circuit unless absolutely indicated. Nine hundred and ten patients (3,845 ventilator days) were included. The incidence risk ratio of VAP was 0.78 (95% CI 0.15-0.99) using care bundles, despite the very low compliance to the bundle elements (14.8% - 34 %). Better compliance to the bundle care may possibly decrease the incidence of VAP even more.

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