Meeting report

Meeting Report from the 20th International Symposium on Intensive Care and Emergency Medicine, Brussels, Belgium, 21–24 March 2000

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Received: 28 March 2000
Accepted: 31 March 2000
Published: 14 April 2000

Crit Care 2000, **4**:169–171

The opening session

This year's conference opened with a session influenced by millennial spirit, reflecting on the 'coming of age' of Intensive Care Medicine, taking stock of the speciality and in particular, how it can and perhaps should, be evaluated, as well as speculating about the future.

As in previous years, a round table conference had taken place over the two days preceding the symposium. This focused on 'Evaluating Critical Care: Using health services research to improve quality.' This sobering macroscopic view of the cost benefit ratio of intensive care, especially when compared with much cheaper and more efficacious interventions, forced all present to reflect on our work and justify it. The report was timely, when set against the background of escalating demands for clinical governance and external audit, both in the UK and Internationally. This led appropriately, to a presentation and examination of End of Life management in the intensive care unit (ICU), which focused on the financial costs. The clear take home message from the speaker, Derek Angus (Pittsburgh, USA), was that this sometimes neglected area requires a much higher priority, which in turn is likely to increase costs further.

Immunology and molecular biology were given their dues with presentations describing the current theories of pro- vs anti-inflammatory cytokines, and a valuable update on a groundbreaking area of innate immunity. The cytokine picture, already complicated to the non-expert, was plunged further into confusion by new evidence suggesting that the earlier classification of cytokines into pro- and anti-inflammatory is at best misleading, and at worst entirely useless. In direct opposition, the discovery of an intermediate branch of the immune system, which bridges the gap between the innate and adaptive systems was refreshingly simple, offering significant promise for future interventions. In essence, it appears that even fruit flies make specific IgM to a few common antigens, and humans seem to do the same. These constitutive forms of specific immunological molecules appear to have important roles in the activation and modulation of the inflammatory process.

Also noteworthy, was the presentation entitled, 'Attributable mortality of hypoxaemia' by Duncan Young (Oxford, UK). He presented a series of retrospective analyses which supported the hypothesis that arterial oxygenation has no correlation with mortality in adult ICU patients. He argued that this may explain the negative results of recent studies such as those into the effects of inhaled nitric oxide and that further studies into interventions that improve arterial oxygenation are therefore, equally unlikely to reveal any outcome benefits [1].

Heart–lung interactions

This short session of 3 presentations examined the clinical applications of the cardiovascular physiology of mechanically ventilated patients. Experimental work was presented confirming that simple analysis of arterial systolic pressure variation with respiratory phase accurately predicts biventricular preload. This technique dramatically outperforms the conventional markers of preload, central venous pressure (CVP) and pulmonary artery wedge pressure (PAWP) [2].

ACTH = adrenocorticotrophic hormone; ARDS = acute respiratory distress syndrome; CO = cardiac output; CT = computed tomography; CVP = central venous pressure; CVVHF = continuous venovenous haemofiltration; eNOS = endothelial nitric oxide synthase; ICU = intensive care unit; LPS = lipopolysaccharide; NO = nitric oxide; PAWP = pulmonary artery wedge pressure; PEEP = positive end-expiratory pressure; TNF = tumour necrosis factor.

Hepatology

Julia Wendon (London, UK), gave three excellent presentations covering acute liver failure, the hepatorenal syndrome [3] and liver trauma. The era of extracorporeal liver support appears to be tantalisingly close, although current best practice utilising high flow bicarbonate continuous venovenous haemofiltration (CVVHF) appears to offer considerable benefit and is not that far short of this therapeutic goal. Hepatectomy as a bridge to transplantation is increasingly being employed with the anhepatic state surprisingly well tolerated for short periods, often leading to the stabilisation and improvement of acute liver failure patients. The early results of vasopressin analogue trials in the hepatorenal syndrome were presented. These show encouraging results, albeit with a high incidence of severe side effects. As regards liver trauma, this can often be best managed conservatively. The value of repeated computed tomography (CT) imaging and interventional angiography was also demonstrated.

Hyperosmotic–hyperoncotic intravenous fluids

A short series of presentations on these comparatively new fluids demonstrated the theoretical benefits that they offer and the results of several recent positive trials [4]. There appears to be a clear role emerging for these fluids both in the resuscitation of trauma patients and perioperatively. Their role in other ICU patients awaits further evaluation.

Pressure–volume curves, open lung ventilation and recruitment

A great number of sessions were devoted to these issues, which remain controversial. Direct visualisation, using a variety of radiological techniques, of the pressure volume changes seen in differing patterns of lung injury seem to confirm the suspicion that the pressure volume curve is a poor determinant of optimal ventilatory parameters, especially the level of positive end-expiratory pressure (PEEP). The debate on how to best optimise PEEP continues, although both speakers and the majority of delegates appear to advocate relatively high values. Several speakers confirmed the value of lung recruitment, although the method and frequency of such manoeuvres remains contentious. The consensus view appears to favour more frequent, less aggressive manoeuvres than previously recommended. The impact of the acute respiratory distress syndrome (ARDS) Network trial [5] awaits full consideration as few of the speakers had had sufficient opportunity to review it. However the universal adoption of low tidal volumes in ARDS patients seems likely.

Myocardial dysfunction in sepsis

We normally associate the septic patient with a high cardiac output (CO), but it is also recognised that these patients may present with a normal or low CO due to myocardial dysfunction. This session was devoted to the mechanisms and clinical implications of this phenomenon. Keith Walley (Vancouver, Canada) gave an enthusiastic insight into the role of the leukocyte in contributing to this combination of reduced systolic contractility and diastolic stiffness. In his pig model of septic shock, capillaries in the heart were plugged with leukocytes, retained after an inflammatory response, and caused actual myocardial damage. Further experiments using an isolated heart preparation showed that the use of a leukocyte filter blocked this reduction in contractility. He concluded that a variety of mechanisms probably existed to explain why the retained leukocytes ultimately caused this myocardial depression including reactive oxygen intermediates, nitric oxide (NO) and tumour necrosis factor (TNF)α.

Jean-Luc Balligand (Brussels, Belgium) gave an overview of the complicated picture for NO modulating myocardial contractility in sepsis. Perhaps the most interesting message from this speaker was his description of the recently found β_3-adrenoceptor pathway [mediated via endothelial nitric oxide synthase (eNOS)] which opposes the classical pathway of positive inotropy mediated by β_1 & β_2-adrenoceptors. The expression of this β_3-adrenoceptor is increased when lipopolysaccharide (LPS) is injected into mice and this may partly explain the hyporesponsiveness of the heart to inotropes in sepsis. The search is now on for a β_3-adrenoceptor blocker to treat the failing heart in sepsis.

Alexandre Mebazaa (Paris, France) summarised the other factors thought to affect myocyte function in sepsis. The cyclooxygenase-2 enzyme is found in abundance after endotoxin is injected into rabbits and it is therefore likely that prostaglandins are important mediators. The role of endothelin is more controversial since although it is found to be elevated in the plasma of septic rats and patients, it is well known that its concentration in the plasma does not reflect its paracrine role in the heart. However, it does appear to induce a time-dependant reduction in cardiac function.

Andrew Rhodes (London, UK) gave an excellent account of the dobutamine stress test, which provides information about the intrinsic metabolic function of cells. Mortality was virtually universal in those patients who were unable to show an increase in oxygen consumption and delivery following a short dobutamine infusion.

Finally Lambert Thijs (Amsterdam, The Netherlands) summarised the clinical implications of our knowledge of the mechanisms involved in sepsis. A variety of historical experimental approaches were alluded to. The hope is that haemofiltration may be helpful in the future for removing these inflammatory mediators of sepsis and reducing myocardial dysfunction.

Steroids in septic shock and ARDS

This was an excellent session following the history of this subject and demonstrating how a reduction in dose and

prolonging the duration of steroid administration has changed a potentially harmful therapy into an exciting approach to septic shock and ARDS for the 21st century. Charles Sprung (Jerusalem, Israel) explained his early involvement in the treatment of septic shock with large doses of steroids given late in the course of sepsis. Several studies were unable to show any differences in outcome in sepsis and ARDS, and a meta-analysis nearly halted the enthusiasm for the use of steroids, since there was a suggestion that they increased mortality in patients with sepsis.

However, Umberto Meduri (Memphis, USA) presented his data following prolonged (day 9–28) methylprednisolone therapy for the management of unresolving ARDS . Infection surveillance was detailed, and although the study only involved small numbers, those receiving methylprednisolone showed improvements in lung injury scores, reduced ventilator days a reduction in pro-inflammatory cytokines and an increase in anti-inflammatory cytokines.

Piere Bollaert (Nancy, France) discussed the 'relative' adrenocortical deficiency seen in 6–20% patients with sepsis/septic shock. High basal cortisol levels (>34 μg/dl) and low stimulated cortisols to the short adrenocorticotrophic hormone (ACTH) test (<9 μg/dl) are high predictors of death in septic patients. However, neither the low (1 μg) or conventional (250 μg) short ACTH tests are sensitive enough in predicting who will benefit from steroid therapy in sepsis, and the benefits of steroids may not be related to this 'relative' deficiency. At this point the audience was surveyed to find that many intensivists were already using physiological doses of steroids in septic shock, but that only 50% were performing ACTH stimulation tests in this group.

Herwig Gerlach (Berlin, Germany) described his crossover study exploring the use of physiological doses of steroids, given for 3 days, in septic shock. A reduction in noradrenaline doses was seen in the steroid treated group reflecting the reversal in vasodilatation. Investigations to determine the mechanisms behind this effect revealed reduced nitrite/nitrate production (a surrogate marker of NO production), reductions in cytokines and leukocyte adhesion in the steroid group, but interestingly no evidence of immunosuppression. Unfortunately numbers were too small to show any outcome benefits.

Finally Djillali Annane (Garches, France) presented his exciting preliminary data on the results of the Phase III multi-centre, randomised, double-blind trial of low dose hydrocortisone (50 mg, 6 hourly) and fludrocortisone (50 μg/day) in septic shock. A second safety analysis, following the recruitment of 220 patients, showed an impressive 28 day reduction in mortality in the steroid treated group (placebo 63%, steroid 50%, $P=0.029$). However because the primary efficacy variable (mortality in non-responders to the ACTH stimulation test) did not reach significance ($P=0.051$), the study was completed to enrol all 300 patients. Full results will be available later in the year.

Summary

Once again this International Symposium lived up to its reputation for providing a diverse mixture of 'state of the art' lectures, seminars and tutorials. Both the clinician and scientist involved in the critically ill would have found an abundance of 'hot-off-the-press' material to digest prior to the 21st symposium.

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