

Meeting report

European Society of Intensive Care Medicine 14th Annual Congress, 30 September–3 October 2001, Geneva, Switzerland

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Abstract

The European Society of Intensive Care Medicine Annual Congress offers the opportunity for basic scientists and clinicians to share recent findings. Apart from the large number of free communications, several sessions of the congress were dedicated to state-of-the-art tutorials given by established speakers. The areas of interest of the attendees were widely distributed as usual, a reflection of the large array of so-called 'critical illnesses'. The results of clinical trials and experimental findings using recently developed drugs were presented, essentially in the fields of inflammation, sepsis, and acute lung injury. The benefits of several new compounds observed experimentally need to be confirmed clinically. The European Society of Intensive Care Medicine Congress is well established as a unique opportunity to implement and to promote a collaboration between European basic scientists and clinicians.

Keywords acute lung injury, ethics, multi-resistant microorganisms, sepsis, vasopressin

The Annual Congress of the European Society of Intensive Care Medicine (ESICM) gathered 2500 registered participants, mainly physicians, nurses and physiotherapists working in the intensive care unit (ICU). This number was slightly lower than in previous meetings of the ESICM, probably because of the tragic events in the United States only 3 weeks before. Nonetheless, most sessions had a large audience, allowing numerous interactive discussions. Although clinically oriented, this meeting also offers the opportunity for basic scientists to present data relevant to the pathophysiology or to new therapeutic approaches of common complications occurring in critically ill patients. Six hundred abstracts were accepted for the main program, and 28 for the nursing and physiotherapy sessions. The 3-day program included 39 thematic sessions, 72 sessions dedicated to oral or poster presentations of abstracts, and nine educational sessions. The major sponsors (pharmaceutical and technological companies) organized seven additional sessions during lunchtimes. The physiotherapy and nursing section of the ESICM organized nine thematic sessions and four oral or poster sessions.

The main topics covered included acute respiratory failure, ethics, sepsis, cardiovascular dysfunction, nutrition, metabolism, renal support therapies, and the management of neurotrauma, presented as well-balanced mixtures of clinical and experimental findings. The results of experimental data on the effects of several new compounds, mainly used in the fields of sepsis and acute lung injury, were presented. A European Sepsis Network was implemented during the meeting.

New technological approaches, including recently developed monitoring and therapeutic tools, have been assessed in patients and were reported. In addition, a growing numbers of abstracts were dedicated to typically clinical topics, including ethics, outcome/quality of life, costs of ICU care, sedation, and new technologies. For instance, the results of the ETHICUS audit, a European survey of the current practice of end-of-life decisions, were presented for the first time.

Sepsis

Nitric oxide pathway inhibitors

The role of nitric oxide (NO) in the cellular alterations of septic shock is intensively investigated. For instance, Dr Singer *et al.*, from University College of London, UK, demonstrated a close correlation between circulating levels of the stable byproducts of NO, the severity of septic shock, and the activity of the mitochondrial complex I and ATP levels measured in muscle biopsies of septic patients. Comparing 1400W and GW273629 (two selective inhibitors of the inducible isoform of the NO synthase enzyme) with a NO scavenger (carboxy-PTIO), with a guanylate cyclase inhibitor (ODQ), and with L-NAME, a non-selective NO synthase inhibitor, Singer *et al.* reported that the contractile hyporesponsiveness of isolated rat arterial rings to phenylephrine was reversed by all agents but the NO scavenger. In human arteries exposed to interleukin-1 and endotoxin, 1400W but not L-NAME administration reversed the hyporesponsiveness to phenylephrine. Dr Siegemund *et al.*, from the University of Basel, Switzerland, also found that 1400W inhibitor restored gut perfusion, decreased functional oxygen shunting, and increased coronary blood flow and myocardial microvascular oxygenation in a porcine model of endotoxemia. Likewise, in another pig model of endotoxemia, Dr Radermacher *et al.*, of the University of Ulm, Germany, found an improved gut perfusion following administration of 1400W.

The toxicity of NO probably involves the activation of poly-(ADP-ribose)-synthetase enzyme by peroxyxynitrite. The effects of a novel poly-(ADP-ribose)-synthetase inhibitor (PJ34) were assessed in a rabbit model of endotoxic shock in the laboratory of Dr Vincent of the Free University of Brussels, Belgium. Significant improvements in hemodynamic parameters and serum gut lactate concentrations were reported, suggesting a protective role of this agent in the cellular alterations of endotoxic shock. The effects of a poly-(ADP-ribose)-polymerase (3-aminobenzamide) were evaluated in a rat model of myocardial ischemia by Dr Liaudet *et al.* from CHUV University Hospital, Lausanne, Switzerland. Promisingly, the size of the infarcted area was reduced and left ventricular function was preserved following the administration of 3-aminobenzamide.

The cardiovascular effects of a continuous infusion of methylene blue, a guanylate cyclase inhibitor, during septic shock in patients was described by Dr Kirov of Northern State Medical University, Arkhangelsk, Russia. The already described positive inotropic and vasoconstrictive effects of this agent appeared to be sustained, and appeared not to be associated with significant side effects.

Antibiotics

The growing emergence of multi-resistant microorganisms was confirmed in several countries, although the appropriateness of the initial antibiotherapy administered to septic patients was confirmed in several studies presented during this ESICM meeting. However, changes in antibiotic policies are probably

mandatory to reduce the occurrence of multi-resistant bacteria. A prospective observational study, presented by Dr Lorente of the University Hospital of Las Canarias, Spain, evaluated the effects of a patient-to-patient rotation policy. Compared with the data from the European Prevalence of Infection in Intensive Care study, the incidence of infections – related to multi-resistant Gram-negative bacteria and fungi infections – was lower after implementing the rotation policy. The rate of antibiotic resistance was also lower.

Dr Kollef *et al.* of Washington University School of Medicine, Missouri, USA, found that the topical oral administration of Iseganan, a synthetic analog of the protegrin antimicrobial peptides, decreased the oral microbial burden of intubated patients. Although promising, this approach warrants confirmation in large-scale studies.

Vasopressin and related analogs

Several teams investigated the effects of vasopressin and related analogs, both experimentally and clinically. In non-septic rabbits, Dr Payen *et al.* of McGill University, Montreal, Canada, studied the effects of arginine vasopressin on arterial pressure and renal hemodynamics. Arginine vasopressin was found to influence the systolic renal blood flow more than the diastolic renal blood flow, and to influence medullar more than the cortical flow. In an ovine model of endotoxic shock, Dr Bone *et al.* from the University of Munster, Germany, carefully studied the dose–effect relationships of vasopressin and terlipressin (a long-acting vasopressin analog) and confirmed the potent vasoconstrictive effects of these compounds. In a sheep model of cecal ligation and puncture, Dr Vincent *et al.* of the Free University of Brussels, Belgium, compared vasopressin with norepinephrine. Administration of vasopressin was associated with an improvement in tissue oxygenation, assessed by blood lactate concentrations and PCO₂ gap. In contrast, Dr Chioléro, from CHUV University Hospital, Lausanne, Switzerland, presented clinical data recorded in patients with vasoplegia (septic shock or postcardiopulmonary bypass). Along with a large increase in vascular resistance, an increase in PCO₂ gap was reported. Hence, in clinical conditions, the effects of vasopressin on gastrointestinal perfusion needs to be further clarified. In another clinical study – performed by Dr Dunser of Leopold Franzens University, Innsbruck, Austria – the administration of arginine vasopressin was devoid of significant hemodynamic side effects in patients with postcardiotomy distributive shock. In another clinical study performed in patients with severe septic shock by Dr Singer *et al.* from University College of London, UK, a single bolus of terlipressin was followed by a long-lasting vasoconstriction that allowed a reduction of the dose of norepinephrine. The issues of safety and clinical usefulness of vasopressin and analogs require confirmation in larger clinical studies.

Others

Dr Schmidt *et al.* from the University of Heidelberg, Germany, presented compelling evidence for the involvement of a sero-

tonin-mediated pathway in leukocyte-independent plasma extravasation, in keeping with previous findings of this laboratory. The new experiments demonstrated that methysergide (a mixed 5-HT_{1/2} receptor antagonist) was as efficient as cinanserin (a selective 5-HT₂ receptor antagonist) and ketanserin (a 5-HT_{2A} receptor antagonist) in treating microvascular hyperpermeability, assessed by intravital gut microscopy in endotoxemic rats. The authors suggest the effects of serotonin are mainly mediated via the activation of 5-HT_{2A} receptors.

Another recently described pathophysiological mechanism of intestinal ischemia-induced shock involves the translocation of pancreatic proteases across the injured gut barrier. Accordingly, Dr Fitzal *et al.* of the Ludwig Boltzmann Institute, Vienna, Austria, reported, in a model of gut ischemia/reperfusion, that intestinal lavage with gabexate mesilate (a serine protease inhibitor) decreased leukocyte activation and decreased local and remote organ damage.

Dr Radermacher *et al.* of the University of Ulm, Germany, used ATP-MgCl₂ in a porcine hyperdynamic model of endotoxemia. This agent had already been found to decrease cellular damage in several models of low cardiac output. Consistently, the data presented during this meeting confirmed a decrease in the PCO₂ gap without a concomitant change in mucosal microcirculation.

Dr Petillot *et al.* of the University of Lille, France, assessed the efficacy of the caspase inhibitor, zVAD.fmk – which was previously reported to attenuate septic myocardial dysfunction – in reducing apoptosis. Indeed, the uptake of iodinated Annexin V by rat myocardium was reduced following treatment with the caspase inhibitor, although it was not restored to normal values recorded in non-septic hearts.

Dr Vincent of the Free University of Brussels, Belgium, presented new data from the PROWESS study; it demonstrated an improvement in survival of patients with severe sepsis following the administration of Activated Protein C (drotrecogin alfa [activated]). In a subgroup analysis after stratification according to the severity of disease, the reduction in mortality was significant in all groups except those in the first APACHE II quartile. However, given that this quartile had a low disease severity – as defined by clinical and biochemical measures – as well as a low rate of adverse events and complications, Dr Vincent concluded the drug's effect in this quartile was consistent with that observed in the overall trial population.

Acute lung injury

Inhalation of a nebulized water-soluble NO donor (DS1) was assessed in a sheep model of endotoxin-induced acute lung injury in the laboratory of Dr Bjertnaes of the University of Tromsø, Norway. The major effects were decreases in pulmonary hypertension, vascular resistance and microvascular

pressure, and extravascular lung water, and a progressive improvement in arterial oxygenation.

Dr Koh of the University of Ulsan, Seoul, Korea, and Dr Xiao-Li, Fujian of the Medical University, FuZhou, China, explored several putative mechanisms of endotoxin-induced lung injury in rats. The data presented during the congress indicate that pretreatment with itraconazole, anisodamine, and ramipril attenuated the severity of endotoxin-induced pulmonary inflammatory response, namely via a decrease in the production of interleukin-1.

Ethics

The results of the ETHICUS study, a European survey designed to describe the current practice of end-of-life procedures, were presented. Thirty-seven centers from 17 countries screened the outcome of ICU patients during 18 months. A total of 4280 deaths out of 31,417 screened patients occurred during the ICU stay or up to 2 months after discharge. The patients were categorized as 'failed cardiopulmonary resuscitation' (approximately 20%), 'brain death' (approximately 8%) or 'end-of-life decision (withholding, withdrawing, or shortening of the dying process)' (approximately 72%). Interestingly, the doctor's religion contributes to the clinical decision-making process. For instance, withholding treatment was almost four times more common among Protestant physicians than Greek Orthodox physicians. The physicians were aware of the patient's wishes in only 20% of the cases, and the thoughts of the families about end-of-life procedures were ascertained in about 50%, although the decision was communicated in 90%. The end-of-life decision was written in two-thirds of the cases. Large variations in the procedure of end-of-life decisions and in the communication of decisions to the patient's relatives and to ICU staff also exist between the north and the south of Europe.

Summary

This ESICM Congress gathered a wide array of European ICU professionals, and successfully covered the hot topics related to the care of critically ill patients. Most novel data related to new pharmacological tools were assessed in the fields of the so-called 'malignant inflammation' and provided several promising approaches that require clinical evaluation. Interestingly, the issues of ethics and outcome are gaining considerable interest, as ICU practitioners clearly need to compare their own practices. Similarly, the need to share the local policies of antibiotherapy should be encouraged in order to face the persistent emergence of multi-resistant microorganisms, a major public health problem that is particularly challenging in most European ICUs.

Competing interests

None declared.