Oral Presentations
ARDS – 172–177

172

INDICES OF PULMONARY OXYGENATION IN ACUTE RESPIRATORY DISTRESS SYNDROME

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INTRODUCTION. Inclusion of PaO_2/FiO_2 in the American European Consensus Document (AECD) on Acute Respiratory Distress Syndrome (ARDS) leads to the erroneous view that it is the 'preferred method' to quantify oxygenation (1) thus creating a potential risk of misuse. PaO_2/FiO_2 should be interpreted cautiously particularly when applied over long periods. We revisit this subject comparing an alternate oxygen content based index Qs/Qt_{RA} [substituting oxygen content of right atrial (RA) blood in the shunt equation] and PaO_2/FiO_2 against venous admixture (Qs/Qt).

METHODS. Four serial simultaneous samples of arterial, mixed venous (MV) and RA blood were obtained from 24 patients 12 hours apart and the corresponding PaO_2/FiO_2, Qs/Qt and Qs/Qt_{RA} were derived. From 96 sets of measurements changes in each parameter between adjacent time points were derived. The mean change in Qs/Qt (n = 24) for the entire 48 hour period was then compared with corresponding changes in Qs/Qt_{RA} and PaO_2/FiO_2.

RESULTS. The mean age and APACHE II score were 54 years and 17 respectively. Changes in Qs/Qt were reflected by corresponding changes in Qs/Qt_{RA} ($r^2 = 0.6$). In two patients a mean increase in Qs/Qt was associated with a paradoxical increase in PaO_2/FiO_2 and in 5 patients reduction in Qs/Qt was associated with a reduction in PaO_2/FiO_2. Within and between patient standard deviation in RA oxyhaemoglobin saturation was 5.3% and 12.5% respectively (5.2% and 15.3% for MV blood).

CONCLUSION. Our results show that Qs/Qt_{RA} is a suitable index to quantify oxygenation in the absence of a pulmonary artery catheter. Variations in RA / MV saturation preclude simple algorithms that derive MV saturation from RA samples. There is now a clear need to clarify the AECD oxygenation criteria (2,3).

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173

ENDOTRACHEAL SUCTIONING (ES) IN PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS): COMPARISON OF 3 TECHNIQUES

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INTRODUCTION. ES is necessary in mechanically ventilated patients but may result in deleterious effects on lung volume, especially in hypoxemic patients. The aim of this study was to evaluate the effect of 3 techniques of ES on respiratory mechanics and lung volumes in patients with ARDS.

METHODS. In 9 ARDS patients, 3 techniques of ES were studied in a random order: 1) patient's disconnection from the ventilator (D); 2) no disconnection, using the connector's opening (ND); 3) closed system (C). Suctioning-induced changes in oxygen saturation (ΔSaO_2) and functional residual capacity (ΔFRC) were measured with the 3 techniques. Pressure-volume (PV) curves from PEEP and from ZEEP were acquired before and after each ES. Alveolar recruitment (Vrecr) was measured as the volume difference between the PV curve at PEEP and at ZEEP.

RESULTS. Both ΔSaO_2 and ΔFRC with D were greater than with ND and C (respectively, –9.8 vs –2.5 vs –3.1% for ΔSaO_2, $p < 0.01$, and –1.46 vs –0.73 vs –0.53 L for ΔFRC, $p < 0.01$). Similarly, just after ES, the residual ΔFRC was greater with D compared to ND and C (-1.12 vs –0.28 vs –0.12 L respectively, $p < 0.01$). After ES, Vrecr was significantly decreased with D and ND (180 vs 274 ml and 199 vs 254 ml respectively, $p < 0.05$), while it did not change with C. Chord compliance of the PV curve from ZEEP and total PEEP were not modified by any ES.

CONCLUSION. 1) In ARDS patients, ES should be performed without patient's disconnection from the ventilator. 2) The 2 ES techniques without disconnection (ND and C) are comparable, but the closed system allows a lower lung volume drop, a preservation of the PEEP-induced alveolar recruitment and a faster lung volume recuperation.

174

ACUTE RESPIRATORY DISTRESS SYNDROME IN CRITICALLY ILL CANCER PATIENTS DURING NEUTROPENIA RECOVERY

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INTRODUCTION. Although neutropenia recovery (NR) is associated with a high risk of acute respiratory distress syndrome (ARDS), no studies designed to identify risk factors for ARDS in this situation have been published.

METHODS. We conducted a study to describe critically ill cancer patients (CICPs) with ARDS during NR (defined as the seven-day period centered on the day the neutrophil count rose above 1000/mm3 [day0]) and to compare them with CICPs without ARDS during NR.

RESULTS. During a 10-year period, 62 CICPs recovered from neutropenia, of whom 21 experienced ARDS during NR, with a median time of –1 days (-2.5–1) between day 0 and ARDS. In-ICU mortality in these 21 patients was 61.9%. As compared with non-ARDS patients, ARDS patients were less likely to have myeloma and more likely to have leukemia/lymphoma treated with adriamycin, a history of pneumonia before neutropenia, and a neutropenia duration greater than ten days; they had a shorter time since malignancy diagnosis and a longer time from chemotherapy to neutropenia. Neither the leukocyte counts on day 0 nor those during the six-day NR period were predictive of ARDS.

CONCLUSION. Patients with acute respiratory failure after prolonged neutropenia complicated by pneumonia are at increased risk for ARDS.

REFERENCE. Rinaldo JE, Borovetz H. Deterioration of oxygenation and abnormal lung microvascular permeability during resolution of leukopenia in patients with diffuse lung injury. Am Rev Respir Dis 1985; 131(4): 579–83.

175

INFLUENCE OF PRONE POSITION ON THE INCIDENCE OF VAP AND THE OUTCOME OF ARDS PATIENTS

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INTRODUCTION. The presented work was prospectively designed in order to evaluate the effects of prone position on the incidence of pneumonia and the outcome of ARDS patients.
METHODS. From 1994 to 1999, all ARDS patients admitted to a medical and surgical ICU were included (n = 139). The ventilatory strategy was not modified during this period: objectives of SaO_2 greater than 95%, of pH greater than 7,25 and pressure of plateau < 35 cmH_2O. The low level of PEEP giving the best oxygenation was applied. A treatment by inhaled NO, almitrine or prone position was left to the choice of the clinician. All patients were tracheostomised, sedated and paralysed during the intial phase of ARDS. The diagnosis of ventilator-associated pneumonia (VAP) was obtained by the association of radiological, clinical and microbiological criteria (quantitative cultures of BAL, protected mini-BAL and/or tracheal aspirates). The antibiotic strategy was uniform for all patients: treatment directed against microorganisms identified on prior routinely tracheal aspirates, modified or stopped according to the results of the cultures. The patients turned at least once in prone position (6 H min) were included in group SDRA-PP (n = 65), the others in the control group (SDRA-C, n = 74). Demographic and clinical data, SAPS II, LIS, SOFA, gazometric and ventilatory parameters were analyzed. The results are expressed on average ± SD. To analyze the effect of prone position on the occurrence of VAP and ICU mortality, we used a Cox proportional hazards model. A p-value below 0.05 indicated significance.
RESULTS. The incidence of VAP was not different between the two groups (52% vs 47%). Mortality was lower in the SDRA-PP group. Indeed, 22 patients SDRA-DV died (33,8%) as compared with 43 in group SDRA-C (58%), (p = 0.003). Cox proportional hazards model identified duration of mechanical ventilation as the unique risk factor associated with the acquisition of a VAP in ARDS patients (p = 0.0001). Cox proportional hazards model identified four independent factors influencing prognosis (Table). Two factors (age and SOFA score the day of ARDS) were significantly associated with an overmortality, while PEEP and prone position exhibited a protective effect against death. When mortality was adjusted according to SAPS II score, prone position was always found as protective against death (Odds ratio 0.41, 95% confidence interval: 0.20–0.82).

	OR	95% IC	p
Age	1.02	1.00–1.04	0.049
SOFA (day 1 of ARDS)	1.1	1.01–1.19	0.021
PEEP level	0.88	0.77–0.99	0.044
prone position	0.55	0.30–0.98	0.045

CONCLUSION. Prone position does not influence the incidence of VAP. The present work suggests that prone position could improve the outcome of ARDS patients.

176

ABSENCE OF MODIFICATION OF EXTRA-VASCULAR LUNG WATER AFTER SIX HOURS OF PRONE POSITION IN ARDS PATIENTS

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INTRODUCTION. Prone positioning of ARDS patients is one of the new strategies proposed in the treatment of the hypoxemia. A decrease of lung water content has been proposed as one of the mechanisms that could explain the improvement in oxygenation related to prone position. The aim of this prospective study was to evaluate the effects of a 6-h trial of prone position on extra-vascular lung water.

METHODS. Prone positioning was performed on special mattresses using a dynamic flotation system incorporating an automate sensor pad (Nimbus Prone Nursing, Huntleigh Healthcare, Luton, UK). This work was approved by our local ethical committee and concerned 33 patients (50 ± 14 years, SAPS II: 35 ± 11) presenting an ARDS (Lung Injury Score: 3.1 ± 0.3). The ARDS was of pulmonary origin in 29 cases. Upon inclusion, PEEP level was 11 ± 2 cmH_2O and tidal volume was 7.3 ± 1.8 ml/kg. Respiratory parameters were not modified throughout the study period. The patients were equipped with an arterial catheter positioned in the aorta (Pulsiocath, Pulsion Medizintechnik) and with a pulmonary arterial catheter. Extra-vascular lung water (EVLWI) was measured by the double indicator technique (Cold, Pulsion Medizintechnik).

RESULTS. Prone position caused an improvement of the PaO_2/FiO_2 ratio [from 127 ± 50 to 205 ± 80 mmHg ($p < 0.001$)]. There were no modification of PVC, POAP, cardiac index and intrathoracic blood volume related to posture changes. $PaCO_2$ remained unchanged (42.3 ± 8.4 to 43.0 ± 10.8 mmHg). No modification of EVLWI related to posture changes was observed (10.4 ± 5.9 ml/kg in supine position, 10.8 ± 6.3 ml/kg in prone position). No difference was found between responders and non responders to prone position concerning the baseline value of EVLWI (in supine position). The amount of EVLWI remained stable after 6 hours of prone position in both responders and non responders to prone position.

CONCLUSION. This work seems to indicate that a modification of the EVLWI evaluated by a double-dilution method is not implied in the improvement of oxygenation related to the prone position. That does not prejudge possible regional modifications of the EVLWI, but underlines the complexity of the mechanisms explaining the improvement in oxygenation related to prone position.

177

A MULTICENTER RANDOMIZED CONTROLLED TRIAL OF EARLY PRONE POSITIONING OF PATIENTS WITH ACUTE RESPIRATORY FAILURE: INTERIM ANALYSIS

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INTRODUCTION. Since December 14, 1998 a multicenter prospective randomized controlled trial is ongoing in 17 ICUs in France comparing early prone positioning (PP) versus supine position (SP) in patients intubated and mechanically ventilated for acute respiratory failure.

METHODS. The design has been already described (1). After a 12–24-hour therapeutic optimization period, the patients were randomized into a SP group in which they remained in SP or a PP group in which they were turned to PP for at least 8 hours per day. Changing from SP to PP was allowed for those patients allocated to SP in case of severe hypoxemia. The primary end-point was the mortality at D 28 after randomization.

RESULTS. This reports the results of the interim analysis on the first 382 patients included. Between SP (n = 185) and PP (n = 197) groups, on the day of randomization, there was no difference for age (62 ± 14 vs 61 ± 16 years), medical admission (83 vs 80%), SAPS II (47 ± 18 vs 45 ± 16), organ system failure (2.4 ± 1 vs 2.2 ± 1), PEEP (8 ± 3 cm H_2O in both groups), PaO_2/FiO_2 (154 ± 57 vs 149 ± 61 mm Hg), Murray lung injury score (2.2 ± 0.6 vs 2.2 ± 0.7), ARDS (29 vs 28%). The D 28 mortality rate was not different between the two groups.

CONCLUSION. Trial is continuing to include the 380 patients per group required to verify the hypothesis of reduction of mortality from 40% to 30% in PP group, with a 0.05 and β 0.20.

REFERENCE. AJRCCM 2000;161: A380

Oral Presentations
Models for new therapeutic approaches (I) – 178–183

178

SELECTIVE BLOCKADE OF INOS BY 1400W, BUT NOT BY LNMA, IS BENEFICIAL TO MYOCARDIAL OXYGENATION AFTER ENDOTOXAEMIA

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INTRODUCTION. NO produced by endothelial cells is an important mediator of blood flow distribution and oxygen supply in the coronary microcirculation. Therefore therapeutic agents blocking the production of NO during experimental and clinical sepsis will affect the microcirculatory oxygenation. We investigated the influence of selective nitric oxide synthase (NOS) inhibition (1400W) compared to unspecific blockade (LNMA) on myocardial microvascular oxygenation ($\mu PcorO_2$).
METHODS. After anaesthesia and installation of haemodynamic monitoring 7 pigs underwent thoracotomie. After fenestration of the pericard the animals were monitored with an ultrasonic flow probe around the left anterior descending artery (Qcor; ml/min/kg) and a catheter in the interventricular vein. The μPO_2 (mmHg) of the myocard was measured by the oxygen dependent quenching of phosphorescence technique via an optical fiber over the apex of the heart. After baseline measurements (BL) LPS (1 µg/kg/h) was infused via the mesenteric vein until the mean arterial pressure dropped below 60 mmHg. After a shock phase of 30 minutes (Shock), the pigs received fluid resuscitation guided on wedge pressure and an infusion of 0.5 µg/kg/h of 1400W for 3 hours (T1-T3). In the last 30 minutes the animals received 5 mg/kg N^G monomethyl-L-arginine.
RESULTS. Both NOS blocking drugs increased coronary artery flow (ml/kg/min) above baseline levels. Cardiac index (CI; ml/kg/min) decreased below shock values after the infusion of LNMA(Table). For statistical analysis Friedman test and Dunns test were applied. A $p < 0.05$ was considered statistical significant. All data are mean ± SD.

	BL	S	T1	T2	T3	B > LNMA
CI	165±26	107±11*	141±13**	135±11	139±23	95±17.1*
Qcor	0.74±0.24	0.46±0.08	1.08±0.28**	1.11±0.48**	0.84±0.36	0.92±0.37
$PcvO_2$	25±3.3	29±2.2	31±3.3*	31±5.1	30±7.5	31±5.1
$\mu PmyoO_2$	26±2.5	19±3.4*	22±2.5	23±5.1	20±3	16±8.7*

Mean ± SD, * = $p < 0.05$ versus baseline; ** = $p < 0.05$ versus S2

CONCLUSION. The selective blockade of iNOS by 1400W increased coronary flow over baseline and partially the myocardial μPO_2 over the values of endotoxic shock. In contrast the vasoconstriction due to LNMA decreased CI and $\mu PmyoO_2$ below shock values, although it increased the coronary artery flow above baseline. This finding suggest that LNMA increased the functional microcirculatory shunting of oxygen to the venous compartment in the heart.
REFERENCE. Siegemund M. (1999) Assesment of tissue oxygenation. Intensive Care Med.

179

PHAGOCYTOSIS ASSISTANCE IN A PIG MODEL OF SEPSIS

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INTRODUCTION. One major reason for the development of a systemic infection is the impairment and dysfunction of the host immune system including phagocytosis. The aim of the presented study was to show the efficacy and compatibility of bioartifical extracorporeal phagocytosis assistance in a pig model of Gram-positive sepsis.

METHODS. Human hematopoetic precursor cells have been expanded and stimulated to differentiate towards functional granulocytic cells. In an animal-model of sepsis, similar to the one described by Lee et al. 1998 (1), 21 female immature landscape-swines (weight: 7,5–12 kg) were given 8x109 cfu/kg living Staph. aureus i. v. and for 7 days clinical parameters and survival time were monitored. After a 1 hour infusion of bacteria and a 30 minutes waiting period the pigs were treated for 6 hours by an extracorporeal plasmaperfusion model containing a membrane – based bioreactor(Nylon, pore-size: 20 µm) with 2,9 x E + 9 cells. Group I was treated without cells (Untreated-Group = UG, n = 7), group II with cells (Treated-Group = TG, n = 7) and group III with cells, but without bacteria (Control-Group = CG, n = 7).

RESULTS. All animals of the UG died (between 2,3 and 110,25 hours), but two pigs of the TG and all pigs of CG survived the whole observation – time (survival-time TG between 23,75 and 168 hours; Breslow-test: TG-UG p = 0.041). The other clinical parameters showed marked benefit for the cell – treated animals (TG) compared with the UG (see table below). No adverse effects were observed that could be accounted to the presence of human phagocytes.

Clinical Parameters	Untreated-Group (UG n = 7)	Treated-Group (TG n = 7)	Control-Group (CG n = 7)
Survival-Time	31.1 h	78.1 h	168 h
Bacterial Count in Blood (cfu/ml)	360000±900000	1900±2200	0
AT III (%)	66.43±24.13	88.09±11.22	116.86±15.04
Quick (%)	83.64±39.94	112.29±8.65	117.09±45.82
Fibrinogen (g/l)	1.27±0.74	2.46±075	2.31±1.26
Lactat (mmol/l)	16.86±5.35	7.8±5.9	2.8±0.8
Thrombocytes (/microliter)	129.728±60.965	191.371±168.607	434.428±159.669
p C02 (mmHg)	46.43±16.23	37.2±2.38	42.2±5.44
p 02 (mmHg)	59.59±18.66	66.4±11.61	80.3±7.86
Sp02 (%)	79.4±20.22	94.9±1.63	93.5±7.5

Clinical Parameters as mean, after 168 h or before death

CONCLUSION. Bioartificial phagocytosis assistance may improve the outcome of systemic and severe infection.

REFERENCE. Lee et al. Crit Care Med, (1998), Vol.26, No.4, 730–737

180

EFFECT OF UNFRACTIONATED AND LOW MOLECULAR WEIGHT HEPARINS ON MICROCIRCULATORY ANTITHROMBIN EFFECTS DURING ENDOTOXAEMIA

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INTRODUCTION. A recent prospective randomized clinical sepsis trial (Kybersept study) shows a reduction in 90-day mortality by antithrombin (ATIII) only in the prospectively defined subgroup of patients without simultaneous heparin treatment. To investigate whether this clinically observed heparin-ATIII antagonism is caused by a heparin-related reversal of ATIII effects on the microcirculation during endotoxaemia (1), experimental ATIII administration was combined with administration of different heparins at a clinically relevant dose.

METHODS. In skin fold preparations of the Syrian hamster, normotensive endotoxaemia was induced by i. v. administration of 2 mg/kg endotoxin (LPS, E. coli, 2 mg/kg), whereby intravital video fluorescence microscopy allowed determination of venular adherent leukocyte count (VALC) and functional capillary density (FCD), which served as a measure of capillary perfusion. ATIII (ATIII group, n = 6, Kybernin, 250 IU/kg i. v.) was substituted 5 min before LPS administration. Another group simultaneously received intravenous unfractionated heparin (ATIII + Hep, n = 5, sodium heparin, 100IE/24 h, i. v.), whereas additional animals received low molecular weight heparin (ATIII + LMWH, n = 5, fraxiparin, 5 yl/kg, 2 h before LPS, s. c.). Controls: Saline-treated animals receiving only LPS.

RESULTS. LPS induced a massive increase in VALC with a maximum at 8 h and a decrease in FCD ($p < 0.01$ vs. baseline). Both LPS effects were effectively prevented by ATIII ($p < 0{,}01$), whereas ATIII + Hep and ATIII + LMWH animals showed microcirculatory disturbances comparable to that observed in endotoxemic controls.

CONCLUSION. In accordance with the clinical finding that beneficial AT III effects during sepsis are antagonized by concomitant heparin administration, our study indicates a relevant in-vivo adverse effect of heparins on microcirculatory AT III effects during endotoxaemia .

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181

INOSINE REDUCES SYSTEMIC INFLAMMATION AND IMPROVES SURVIVAL IN SEPTIC SHOCK INDUCED BY CECAL LIGATION AND PUNCTURE

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INTRODUCTION. Inosine, a naturally occurring purine formed from the breakdown of adenosine, exerts anti-inflammatory effects in vitro and in vivo. Septic shock is characterized by an overwhelming systemic inflammatory response leading to multiple organ dysfunction. Here, we have evaluated the effects of inosine in a murine model of polymicrobial sepsis induced by cecal ligation and puncture (CLP).

METHODS. Anesthetized mice (n = 197) were subjected to CLP using a large bore (18-gauge) needle. The animals were treated with inosine (100 mg/kg i. p.) or vehicle 1 h before and 6 h after CLP. After 12 h, TNF-a, IL-6, and IL-10 were measured in plasma. Biochemical markers of organ damage, liver NAD + /NADH (indicator of the mitochondrial redox state), plasma nitrate, tissue myeloperoxidase (MPO, indicator of neutrophil accumulation) and malondialdehyde (MDA, indicator of lipid peroxidation), ex vivo vascular reactivity in aortic rings, and the levels of the chemokines MIP-1 a and MIP-2 in the lung and liver were also measured. In a second set of studies, mice challenged with CLP were killed after 24 h for quantitative bacterial cultures in blood, liver and spleen. In a third set of studies the mortality of CLP was investigated in mice receiving inosine either as a pretreatment (100 mg/kg ip, 1 h before, 6 and 12 h after CLP), or a posttreatment (inosine 100 mg/kg ip 1, 12 and 24 h after CLP) with or without antibiotics (gentamycine 10 mg/kg and clindamycine 300 mg/kg subcutaneously twice daily for 3 days).

RESULTS. Mice treated with inosine had significantly lower levels of circulating cytokines. Organ damage was significantly reduced by inosine treatment, which was associated at the tissue level by an increased hepatic NAD + /NADH ratio, a decreased MPO activity in the lung and a reduced MDA formation in the gut and liver. Furthermore, inosine significantly improved endothelium-dependant relaxant responses of aortic rings, and reduced the expression of MIP-1 a and MIP-2 in the lung and liver. In contrast, inosine had no particular influence on the bacterial load in blood, liver and spleen 24 h after CLP. These effects were associated with a significant improvement of the survival of CLP in mice receiving inosine either as a pre- or a postreatment, especially when inosine was associated with antibiotics.

CONCLUSION. Our data show that inosine reduces systemic inflammation, organ damage, tissue dysoxia, vascular dysfunction and tissue chemokine expression, resulting in an improved survival in CLP. Inosine warrants further investigation as a potential useful adjunct for the therapy of clinical septic shock.

182

TITRATION OF TERLIPRESSIN AND VASOPRESSIN IN ENDOTOXAEMIC SHEEP

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INTRODUCTION. Patients suffering from vasodilatatory shock are usually treated with vasoactive drugs in order to optimise the haemodynamic state[1]. Purpose of this study was to elucidate if the V1-agonists vasopressin (VP) and terlipressin (TP) beneficially inverse the haemodynamic alterations due to sepsis. Furthermore we wanted to mimic the clinical szenario with the complicated selection of the right drug and the appropriate dosage.
METHODS. In this trial, 20 ewes were instrumented for chronic study. Subsequent to a preseptic baseline measurement, sepsis was induced by an infusion of Salmonella typhosa endotoxin ($10\ ng \cdot kg^{-1} \cdot min^{-1}$) for 16 hours. Thereafter, the sheep received either one of the two V1-agonists or norepinephrine (NE, control group) as a titrating infusion. The main aim was to increase the MAP by 20 mm Hg or to investigate the concentration obtaining the maximum pressure raise. The titration of TP (Glycylpressin®) was started with $10\ \mu g \cdot kg^{-1} \cdot h^{-1}$ and was raised by $5\ \mu g \cdot kg^{-1} \cdot h^{-1}$ every 15 minutes until the desired haemodynamic effect was reached. In analogy, the administration of VP (Pitressin®) was begun with $0{,}6\ U \cdot h^{-1}$ and was increased by $0{,}6\ U \cdot h^{-1}$. The animals receiving NE (Arterenol®) got an initial rate of $0{,}2\ \mu g \cdot kg^{-1} \cdot min^{-1}$, which was raised by $0{,}1\ \mu g \cdot kg^{-1} \cdot min^{-1}$. After the titration period of collectively 90 minutes, the infusion of TP or VP, respectively was continued with the ascertained target dose and simultaneously with NE ($0{,}2\ \mu g \cdot kg^{-1} \cdot min^{-1}$) for additional 90 minutes, whereas the control group only received NE. Data are expressed as mean ± SEM. Significance was accepted with $p < 0.05$.
RESULTS. Three sheep died due to sepsis, whereas the surviving animals were characterised by a hyperdynamic circulation (increase in HR, CI, MPAP and PVRI; decrease in MAP and SVRI). With an infusion rate of $0{,}54 \pm 0{,}09\ \mu g \cdot kg^{-1} \cdot min^{-1}$, four of the five sheep treated with NE reached the aimed MAP. With an average rate of $2{,}4 \pm 0{,}66\ U \cdot h^{-1}$, five of the six animals which got VP, achieved the desired pressure enhance, as well. With regard to the sheep receiving TP, a ceiling effect was observed. In only three of the six ewes, the intended MAP could be attained. The utmost alteration could be induced with an infusion of $29{,}17 \pm 8{,}01\ \mu g \cdot kg^{-1} \cdot h^{-1}$. Apart from these changes, the titration of NE significantly enhanced the SVRI. The administration of VP and TP improved the haemodynamic state by a significant reduction in CI and HR, as well as by an increase in SVRI. In all study groups, the titration was not associated with a statistically relevant enhance of MPAP. Even an additional treatment with NE did not deteriorate the MPAP of the ewes receiving VP and TP.
CONCLUSION. These results implicate that the titration of V1-agonists can be useful in vasodilatatory shock. We demonstrated that a gradually administration, even in a combination with NE is not associated with a significant increased MPAP. In particular, vasopressin procured a convincing vasopressor activity and reversed the haemodynamic alterations due to endotoxic shock.
REFERENCE. Critical Care Medicine 1996, 24: 525–537

183

HEMODIAFILTRATION DOES NOT IMPROVE PULMONARY HAEMODYNAMICS IN A PORCINE MODEL OF ENDOTOXIN SHOCK

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INTRODUCTION. Some experimental and clinical evidences suggest that high ultrafiltration rate hemofiltration (200 ml/kg/h) can improve pulmonary haemodynamics during septic shock (1). Unfortunately, high ultrafiltration rates are difficult to target in humans. Therefore, we tested wether combining dialysis and hemofiltration (HDF) but with ultrafiltration rates easier to achieve (30 ml/kg/h) would have beneficial effects on pulmonary haemodynamics.

METHODS. 12 anesthetized pigs received a 0.5 mg/kg endotoxin infusion over 30 min. After a 30 minutes interval at the end of the endotoxin infusion period (T60), HDF was started during 5 hours in six randomly chosen animals (HDF group). The remaining six animals (Control group) served as control. A four-element windkessel model was used to describe pulmonary haemodynamics (2).

RESULTS. Endotoxin insult led to a complex pulmonary vascular response involving a dynamic, time-dependent interplay between characteristic resistance (R1), peripheral resistance (R2), and vascular compliance (C). R1 was significantly higher in HDF group from the start of HDF (0.02 ± 0.005 vs 0.03 ± 0.005 mmHg.s/ml) until T150 (0.024 ± 0.009 vs 0.028 ± 0.006 mmHg.s/ml). Three hours after the start of endotoxin infusion (T180), R2 of HDF group increased at a significantly higher value than R2 of Control group (0.58 ± 0.1 vs 0.78 ± 0.1 mmHg.s/ml)). HDF did not affect C. Two animals in the control group and four animals in the HDF group died from acute right heart failure before the end of the experiment.

CONCLUSION. In the early phase of septic shock, HDF must be used cautiously since it amplifies the pulmonary vascular response to the endotoxin insult. Such an increase in pulmonary vascular resistance can precipitate right heart failure and lead to death. This increase in pulmonary vascular resistance is probably mediated by a humoral mediator.

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Oral Presentations
Novel haemodynamic interventions (II) – 184–189

184

ATP-MGCL2 EFFECTS ON HEPATO-SPLANCHNIC HAEMODYNAMICS AND METABOLISM DURING HYPERDYNAMIC PORCINE ENDOTOXAEMIA

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INTRODUCTION. We tested the hypothesis whether ATP-$MgCl_2$ allows to improve liver haemodynamics, O_2 exchange and metabolic balance during hyperdynamic porcine endotoxaemia characterized by a sustained increase in cardiac output.
METHODS. 12 h after starting continuous i. v. endotoxin (LPS), pigs received either placebo (CON = 8) or 0.3 Δmol/kg/min of ATP-$MgCl_2$ (ATP = 9). Before as well as at 12 and 24 h of LPS, we assessed hepatic artery (Qha) and portal vein (Qpv) blood flows, (Doppler flow probes), liver O_2 delivery (hDO_2) and uptake (hVO_2) as well as liver lactate flux (hep-Q-lactate).
RESULTS. Data are median (25 %;75 %), *p < 0.05 versus pre-shock (Friedman) and § p < 0.05 versus CON (Mann-Withney). In contrast to the CON animals changes in liver lactate uptake rate were significantly (r: 0.87, p < 0.0001) correlated to those of liver lactate influx in the ATP-$MgCl_2$ group.

	Before LPS	12 h LPS	24 h LPS
CON MAP (mm Hg)	92 (91;97)	101 (97;106)	97 (87;107)
ATP MAP (mm Hg)	94 (90;96)	99 (91;115)	78 (74;87)*§
CON CI (ml/kg/min)	116 (106;123)	148 (117;165)*	148 (140;171)*
ATP CI (ml/kg/min)	112 (90;140)	134 (120;148)*	175 (156;204)*
CON Q ha (ml/kg/min)	4.1 (2.8;6.2)	2.5 (2.2;3.2)	5 (4.2;5.5)*
ATP Q ha (ml/kg/min)	2.1 (1.4;5.8)	2.2 (1.8;3.2)	2.3 (1.5; 10.4)
CON Qpv (ml/kg/min)	22 (18;23)	25 (22;28)*	28 (26;31)*
ATP Q pv (ml/kg/min)	19 (18;24)	22 (20;29)	42 (36;45)*§
CON hDO_2 (ml/kg/min)	2.3 (1.7;2.5)	2.2 (2.0;2.8)	2.4 (2.2;3.2)
ATP hDO_2 (ml/kg/min)	1.8 (1.5;2.5)	1.7 (1.7;2.7)	2.8 (2.7;3.2)*
CON hVO_2 (ml/kg/min)	0.8 (0.6;1.1)	0.8 (0.6;1)	0.7 (0.5;0.9)
ATP hVO_2 (ml/kg/min)	1 (0.6;1.5)	0.9 (0.8;1)	0.7 (0.6;0.9)
CON Hepatic vein pH	7.47 (7.45;7.48)	7.34 (7.31;7.36)*	7.34 (7.31;7.38)*
ATP Hepatic vein pH	7.43 (7.40;7.46)	7.34 (7.32;7.38)*	7.33 (7.29;7.37)*
CON Hep-Q-lactate (mmol/kg/min)	15.4 (11.5;20)	9.8 (7.7;12.1)	6.9 (4.2;11.9)*
ATP Hep-Q-lactate (mmol/kg/min)	11.3 (9.9;16.8)	10.7 (10.1;13.1)	14.5 (12.7;16) §

CONCLUSION. ATP-$MgCl_2$ blunted the decrease in hepatic lactate clearance thus preserving the metabolic coupling between lactate release from the intestine and lactate utilization by the liver.

185

EFFECT OF CLONIDINE AND DEXMEDETOMIDINE ON GUINEA PIG SMALL BOWEL MOTILITY IN VITRO

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INTRODUCTION. Recently, we demonstrated an inhibitory effect of different catecholamines on guinea pig small bowel motility in vitro (1). This inhibitory effect is partly mediated via α2-receptors in the gut. Clonidine is frequently used in the clinical setting (2,3). Dexmedetomidine, a newer α2-receptor agonist, is now available in the USA. The aim of our study was to evaluate the direct effect of clonidine and dexmedetomidine alone and in combination with yohimbine, an α2-receptor antagonist, on guinea pig small bowel motility in vitro.

METHODS. Segments of small bowel excised from guinea pigs were mounted in a tissue bath (Temp. 37 °C) in Tyrode solution and bubbled with 95 %O_2/5 %CO_2. Luminal perfusion was provided with the same solution at a rate of 0.5 ml/min. Peristalsis was recorded via changes in the intraluminal pressure. The test drugs (clonidine, dexmedetomidine, yohimbine and drug combinations) were added to the tissue bath. Dose response curves were constructed. One and two way ANOVA was used for statistics. p < 0.05 was considered statistically significant.

RESULTS. Clonidine and dexmedetomidine alone revealed a dose dependent inhibitory effect on guinea pig small bowel motility. This effect was due to an increase of the pressure threshold, the intraluminal pressure which triggers peristaltic contractions. A complete block of peristalsis was seen at a concentration of 300 nM for clonidine and at 30 nM for dexmedetomidine. In combination with yohimbine at 0.3 nM the inhibitory effect of clonidine was completely abolished. This was seen even at a concentration of 1 μM of clonidine when combined with 0.3 nM yohimbine. The inhibitory effect of dexmedetomidine in combination with yohimbine 0.3 nM was decreased, but not completely abolished. A blockade of peristalsis was now found at 100 nM dexmedetomidine in combination with yohimbine.

CONCLUSION. Both tested α2-receptor agonists have dose-dependent inhibitory effects on small bowel motility. A complete blockade of peristalsis was seen at high concentrations. This action reflects the direct effect on peristalsis independent of the substances central effects on α2-receptors. The α2-receptor antagonist yohimbine was able to prevent the blockíng effect of clonidine, but not of dexmedetomidne. The absent capability to neutralize the blockade of peristalsis might be due to the higher affinity of dexmedetomidne on α2-receptors.

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186

MUCOSAL DYSOXIA IN ENDOTOXIN SHOCK CAN BE DETECTED BY LUMINAL MICRODIALYSIS BUT NOT BY REGIONAL L/P RATIOS

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INTRODUCTION. Gut mucosal dysoxia may contribute to the development of multiple organ dysfunction in septic shock. We investigated lactate and pyruvate metabolism and ketone body ratios over the viscera in order to determine where the signs of dysoxia occur first during endotoxin shock.
METHODS. 14 pigs were randomised into two groups: endotoxin shock (ETX) for 12 hours induced by E. Coli LPS infusion (n = 7) or controls (n = 7). We cannulated regional veins and femoral artery. Microdialysis capillaries were introduced into the lumen of stomach, jejunum and mid-colon. Arterial and regional blood samples for lactate, pyruvate, ketone bodies were collected every 2 hours. Intestinal luminal microdialysate (MD) [1] was collected in 30 minutes fractions. Results are presented as median (quartiles). Non-parametric test for repeated measurements (Friedman) was used.
RESULTS. In hyperdynamic, hypotensive shock lactate gradient over gastric wall turned negative (p = 0.025). Mesenteric and colonic lactate gradients decreased (p = 0.0001 and p = 0.0001). L/P ratios tended to increase (Table 1), while pyruvate gradient changes indicated visceral uptake (Table 2). MD-lactate increased to 0.4 (0.2,0.5) mmol/L in colon after 11–12 hours (p = 0.001), while MD-lactate remained low in stomach and jejunum (p = 0.2 and p = 0.1). Ketone body ratios over small bowel (p = 0.13) and stomach (p = 0.22) remained low and decreased over colon (p = 0.03) and liver (p = 0.002).

		baseline	4 h	8 h	12 h	p
L/P(gastr)	ETX	7(5.8)	11(9.13)	13(11.15)	17(15.19)	0.105
	Control	7(6.9)	7(7.7)	7(6.9)	8(6.9)	0.87
L/P(mes)	ETX	10(9.12)	14(12.16)	15(13.17)	15(15.20)	0.079
	Control	11(10.12)	9(9.12)	9(7.10)	10(9.11)	0.098
L/P(col)	ETX	14(12.15)	17(16.19)	17(14.18)	20(18.22)	0.053
	Control	1(-12.9)	6(-25.13)	1(-9.11)	–8(-13.7)	0.9
Dpyr(gastr)	ETX	14(6.38)	–13(-35.24)	–21(-32.4)	4(-21.20)	0.6
	Control	9(7.30)	–3(-17.21)	–8(-14.17)	–2(-7.11)	0.4
Dpyr(mes)	ETX	16(1.18)	–20(-38.1)	–31(-43.–21)	–29(-44.–17)	0.012
	Control	1(-12.9)	6(-25.13)	1(-9.11)	–8(-13.7)	0.9
Dpyr(col)	ETX	10(-1.19)	–30(-42.–14)	–38(-42.–30)	–65(-72.–26)	0.017
	Control	18(1.40)	10(-1.23)	3(-4.15)	–12(-23.7)	0.38

CONCLUSION. Endotoxin shock induces mucosal epithelial dysoxia first in colon based on luminal microdialysis, whereas small intestine and stomach show no signs of dysoxia during 12 hours of endotoxaemia . Endotoxin induces pyruvate uptake in the viscera and therefore interpretation of regional L/P ratios is difficult.
REFERENCE. Tenhunen JJ et al (1999) Anesthesiology 91: 1807–1815

187

EFFECT OF ENTERAL FEEDING ON THE ASSESSMENT OF SPLANCHNIC PERFUSION BY GASTRIC TONOMETRY: A RANDOMIZED STUDY

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INTRODUCTION. Objective: To determine whether enteral feeding modifies gastric intraluminal pCO_2 values measured by gastric tonometry.

METHODS. We carried out a prospective trial in critically ill patients ready to begin with enteral feeding. A gastric tonometer was placed in the stomach. Patients were randomized to receive standard enteral feeding (an initial bolus of 100 ml and them 80 ml/h)or control, with or without previous ranitidine administration (50 mg IV). Gastric intramucosal pCO_2 measured by tonometry, clinical characteristics, available haemodynamic parameters, gastric juice ph, and blood gas analysis were determined at baseline (120 min after ranitidine administration when appropriate), and 30, 60, and 120 min after the onset of enteral feeding.

RESULTS. 37 patients were included: 16 out of 37 received enteral feeding. Gastric intramucosal pCO_2 did not change (table), independently of the previous administration of ranitidine. Results are mean (SD).

intramucosal	pCO_2 baseline	pCO_2 30 min	pCO_2 60 min	PCO_2 120 min
Enteral feeding n = 16	46 (9)	43 (5)	42 (10)	49(6)
No enteral feeding n = 21	46 (21)	49 (12)	51 (8)	49 (10)

CONCLUSION. Enteral feeding does not seem to modify the assessment of gastric intramucosal pCO_2 by tonometry. These result suggest that gastric intramucosal pCO_2 monitoring can be maintained in spite of early administration of enteral feeding.

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188

EFFECT OF THREE DIFFERENT RESUSCITATION REGIMENS ON JEJUNAL TISSUE OXYGEN SUPPLY AFTER HAEMORRHAGIC SHOCK

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INTRODUCTION. Effects of resuscitation fluids on microcirculatory blood flow and tissue oxygen supply are still a matter of intense clinical discussion. In this study we evaluated effects of blood (B; n = 7), gelatine (G; n = 8) and Ringer's lactate (R; n = 8) resuscitation on jejunal microvascular blood flow (PU), tissue microvascular hemoglobin oxygen saturation (HbO_2t) and jejunal mucosal tissue oxygen tension (PO_2muc) after severe haemorrhage (50% of estimated blood volume) in pigs.
METHODS. Animals were anaesthetised, paralysed, and normoventilated. A small segment of the jejunal mucosa was exposed by midline laparotomy and antimesenteric incision. PO_2muc was measured using Clark-type surface oxygen electrodes. HbO_2t and PU were determined by tissue reflectance spectrophotometry and laser doppler velocimetry. Systemic haemodynamics, mesenteric-venous acid base and blood gas variables as well as systemic acid base and blood gas variables were recorded. Measurements were performed after a resting period, after a 50 minutes period of haemorrhage (H) and after resuscitation with B, G and R to achieve baseline pulmonary capillary wedge pressures at 70, 90, 110 and 130 minutes, respectively. An analysis of variance for repeated measurements was performed to analyse differences in mean values between and within groups. Multiple comparisons were done by two tailed Dunnett's t-test followed by Bonferoni correction. $P < 0.05$ was considered significant. Data are presented as means + SD.
RESULTS. H resulted in significant hypotension and decreased systemic blood flow which was reversed after resuscitation in all groups. At baseline we observed no differences in PO_2muc (B: 29 + 5.9 mmHg), HbO_2t (B: 48.5 + 6.7%) and microvascular blood flow (B: 253 + 66 PU) between groups. H equally and significantly decreased PU, PO_2muc and HbO_2t in B,G, R animals. However, after resuscitation R animals had significantly lower HbO_2t (time point 130 min; R: 25 + 9%) when compared with B and G animals (time point 130 min; B: 39 + 9%; G: 33 + 10%). PO_2muc decreased similar in B and R animals after resuscitation (time point 130 min; B: 15 + 6 mmHg; R 14 + 7 mmHg). However, in G animals a trend towards higher PO_2-muc values (time point 130 min; G: 20 + 9 mmHg) was observed during resuscitation. There were no differences concerning microvascular blood flow during resuscitation.
CONCLUSION. Resuscitation after severe haemorrhage using whole blood, Ringer's lactate or gelatine results in distinct changes of jejunal tissue oxygen supply. Whole blood resuscitation favourably preserved HbO_2t without affecting PO_2muc while use of gelatine only, demonstrated a trend towards higher PO_2muc values when compared with R and B animals. Therefore type of resuscitation fluid seems to have some impact on tissue oxygen supply within the gastrointestinal tract.

189

INHIBITION OF POLY(ADP-RIBOSE) POLYMERASE REDUCES INFARCT SIZE AND IMPROVES LONG-TERM VENTRICULAR FUNCTION IN A RAT MODEL OF MYOCARDIAL ISCHAEMIA-REPERFUSION INJURY

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INTRODUCTION. The nuclear enzyme poly (ADP-ribose) polymerase (PARP) plays an important role in the pathogenesis of various forms of ischaemia/reperfusion injury and circulatory shock. Recent studies demonstrated that inhibition or genetic inactivation of PARP is beneficial in the early phase of myocardial reperfusion injury. However, there are no data regarding long-term functional consequences of PARP inhibition after acute myocardial infarction. Here we have evaluated whether pharmacological suppression of PARP would influence left ventricular dysfunction in a rat model of myocardial infarction (MI).
METHODS. Acute MI was induced in anesthetized, intubated and mechanically ventilated rats (n = 111) by occlusion of the left anterior descending (LAD) coronary artery. The occlusion was maintained for 1 h, followed by reperfusion for up to 24 h. 10 min before reperfusion, the animals received an intraperitoneal injection of the PARP inhibitor 3-aminobenzamide (3-AB, 20 mg/kg) or vehicle (saline, 1 ml), repeated 2, 4 and 6 h after reperfusion. A group of rats (sham rats) had the same surgical procedure, but the LAD was not occluded. After 24 h, the rats were reanesthetized and a Millar catheter was inserted into the left ventricle via the right carotid artery for the measurement of left ventricular (LV) haemodynamics (systolic and diastolic pressure and dp/dt max). Plasma creatine-kinase (CK, MB fraction) was also measured. Infarct size was determined by the Evans blue-triphenyltetrazolium method. In a subset of animals, hearts were harvested for the immunohistochemical localization of PARP activation, using a mouse monoclonal antibody against poly(ADP-ribose). Immunohistochemistry was also performed in a group of rats subjected to 1 h LAD occlusion and 2 h reperfusion, treated or not with 3-AB (20 mg/kg ip).
RESULTS. 3-AB significantly reduced infarct size (47.1 ± 5.6% vs 62.0 ± 3.8% of the area at risk, $p < 0.05$, unpaired t test) and plasma CKMB activity 24 h after LAD occlusion. This was associated with a suppression of LV systolic dysfunction (dp/dt max: sham: 5800 ± 211 mm Hg/sec; MI: 3670 ± 278 mm Hg/sec; MI-3-AB: 5125 ± 150 mm Hg/sec; $p < 0.05$ vs. MI; p = NS vs. sham, ANOVA), and a non significant reduction of LV end-diastolic pressure. In addition, immunohistochemical data showed that PARP was massively activated, both 2 and 24 h after MI, and was mainly localized to cardiomyocytes in the peri-infarction area. This pattern of immunostaining was markedly attenuated by 3-AB.
CONCLUSION. PARP activation takes place early (2 h) and is maintained as long as 24 h after acute MI. Suppression of PARP activation with 3-AB not only reduces infarct size but also markedly improves LV systolic function 24 h after MI. This supports the concept that pharmacological inhibition of PARP might represent a novel approach in the therapy of myocardial ischaemia-reperfusion injury.

Oral Presentations
Appropriateness of antibiotic therapy: Impact upon prognosis – 190–195

190

THE INFLUENCE OF INADEQUATED EMPIRICAL ANTIMICROBIAL TREATMENT ON CRITICALLY PATIENTS WITH BLOODSTREAM INFECTIONS

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INTRODUCTION. Previous studies have demonstrated a significant relationship between the inadequate antimicrobial treatment of bloodstream infections and hospital mortality due to nosocomial infections with adquired antibiotic resistance (1). The patterns of such resistance clearly vary among hospitals (2). The aims of this study were to determine the occurrence of inadequate antimicrobial therapy among critical ill patients with bacteremia, to know which microorganisms were most frequently inappropiated treated and to determine the relationship between inadequate treatment and patients outcome.
METHODS. During a three year period, from June 1995 to May 1998, we have evaluated all clinical significant ICU-bacteremias of a teaching hospital. Inadequate antimicrobial treatment of bloodstream infection was defined as the microbiological documentation of infection that was not being effectively treated at the time the causative microorganism and its antibiotic susceptibility were known. Clinical and microbiological variables were studied. An univariate analysis was performed to compare patients who received inadequate treatment with patients adequately treated using SPSS package (9.0).
RESULTS. Among 154 intensive care unit-bacteremias, 37 (24%) of them received inadequate antimicrobial treatment. The mean age of these patients were 64.3 ± 13.5 years. Fifty-nine percent of these patients were men and 41% were women. Ninety-two percent of bacteremias were hospital acquired. Eight percent showed septic shock. An ultimately fatal underlying disease was present in 30% of the patients. CNS (32%) and Acinetobacter baumannii (30%) were the microorganisms more frequently isolated. The most frequent source of bacteremia was unknown (52%) . Global mortality rate was 54% and attributable mortality was 27% . We did not find any statistically significant differences between the patients who received inadequate treatment and those who received adequately antibiotic therapy in any of the studied variables.
CONCLUSION. Inadequate empirical antimicrobial treatment to critically ill patients with bloodstream infections is not associated with a higher mortality in our study, probably this was caused by local microbiological factors.
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191

FIRST ANTIBIOTHERAPY IN SEPTIC SHOCK

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INTRODUCTION. The first antibiotitherapy prescribed in septic shock patients may influence mortality and number of organ failures (1). The goal of the present study was to evaluate the adaptation of this first antibiotherapy prescribed in septic shock patients.

METHODS. Patients with septic shock of a medico-surgical intensive care unit (ICU) were prospectively included for three years. Antibiotherapy which was prescribed by senior staff members consisted of a beta-lactamin (including or not Pseudomonas aeruginosa), an aminoside and a glycopeptide in case of suspicion of methicillin-resistant Staphylococcus. Bacteriological results, from samples collected before antibiotherapy beginning, were compared with the spectrum of antibiotherapy. Adaptation was successful if one or more antibiotic was effective.

RESULTS. 107 patients (61 ± 16 yrs) were included. The overall mortality was 59%. A bacteriological information was valid in 78 cases. Antibiotherapy was effective in 69 patients and ineffective in 9 patients. Between these two groups, no difference occured in IGS2, Knaus, and number of catecholamines. Failures in treatment were linked to: yeasts presence (3 cases), methicillin-resistant Staphylococcus (2 cases), penicillin-intermediate Pneumococcus (1 case), enterobacteriacae with cephalosporinase (1 case), multi-resistant Pseudomonas aeruginosa (1 case), and mycobacterium (1 case). Mortality was increased if first antibiotherapy was ineffective (78 vs 56%).

CONCLUSION. Antibiotherapy was effective in near of 90% of cases. This successful adaptation may be explained by the fact that the prescriptions were performed by senior staff members in collaboration with the laboratory of bacteriology staff members. The ineffectiveness of first antibiotherapy lead to an overmortality of 29%, which was no statistically significant because of small enrollment, but clinically important.

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192

SEVERE COMMUNITY-ACQUIRED PNEUMONIA: IMPACT OF INITIAL ANTIMICROBIAL THERAPY ON INTENSIVE CARE UNIT MORTALITY

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INTRODUCTION. The choice of initial empiric antimicrobial therapy to treat severe community adquired pneumonia (SCAP) is controversial. We examined the impact of antibiotics regimen on patients hospitalized with SCAP.
The objective was to determine the relationship between initial empiric antibiotic treatment usage intra intensive care units (ICUS) in patients with SCAP and mortality.

METHODS. Data base from two multicenter studies realized in different Spanish ICUS during two periods 1995 and 1998 was examined. All patients had SCAP. Patient characteristics included demographic dates, comorbid illnesses, mechanical ventilation used, shock and antibiotic treatment. The initial antimicrobial regimens were putting into six groups: Group I: (Pseudomonal third – generations cephalosporins only, Macrolides only, Second – generation cephalosporins plus macrolides, Non pseudomonal third – generation cephalosporins plus macrolides, betalactam/beta lactamase inhibitors plus macrolides) Reference group; Group II: (Antimicrobial regimen with aminoglycosides); Group III: (Non pseudomonal third – generation cephalosporins only); Group IV: (First and Second – generation cephalosporin only, betalactam/betalactamase inhibitors only); Group V: (Fluorquinolones only) and Group VI: (Other antimicrobial regimens).

RESULTS. A total of 460 patients (p) with SCAP were admitted to de ICU. The global mortality was 29.5%. Initial distribution antimicrobial regimens'and mortality (M) was: Group I: 292 p (25% M); Group II: 65 p (40% M); Group III 31 p (35.4% M); Group IV: 23 p (26% M); Group V: 11 p (27.3% M) and Group VI: 38 p (44.7% M). Use of an antimicrobial regimens: Group IV (HR 1.0; 95% CI, 19.7 – 17.5), and Group V (HR 2.2; 95% CI, 29.1 – 24.5) were independently associated with lower mortality than the mortality in the reference group. However, Group II was independently associated with a higher mortality (HR 15; 95% CI, 27.9 – 2.1).

CONCLUSION. This study suggests that the initial empiric antibiotic regimens'used to treatment SCAP should incuyed macrolides and fluorquinolones plus a betalactam/betalactamase inhibitors. However, the regimens with aminoglycosides are advised against.

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193

EFFICACY OF ADEQUATE EMPIRIC ANTIBIOTIC THERAPY IN VENTILATOR-ASSOCIATED PNEUMONIA (VAP): IMPACT OF THE BASELINE SEVERITY OF PATIENTS

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INTRODUCTION. VAP occurs in about 25% of patients requiring mechanical ventilation for more than 48 hours1. It is responsible for high mortality rates and an increased length of stay in intensive care units2.But despite VAP beeing a common issue, there is still no general agreement concerning its management. Particularly, whether antibiotics should be given early in the course of VAP and what empiric antibiotic therapy(AB) should be chosen remain controversial.Our aim was to compare the outcome of patients with VAP according to their baseline severity and the adequacy of initial AB.
METHODS. All patients with microbiologically confirmed VAP were prospectively included in this 8 month period, multicentric study.The impact of early adequate AB was tested separatly in the less and most severe patients according to the median LOD score.
RESULTS. Our results are shown in tables 1 and 2.

	Adequate AB N = 63	Inadequate AB N = 79	P
Age	66±14 (68)	65±15 (67)	0.53
SAPS II on admission	46.7±16 (45)	51±16 (50)	0.1
LOD on admission	5.1±2.5 (5)	5.6±2.6 (6)	0.15
SAPS II at VAP onset	44.7±15.8 (42)	40±12.6 (39)	0.12
LOD at VAP onset	5.4±2.9 (5)	4.5±2.5 (4)	0.07
Day of VAP	9.8±8.6 (7)	10.1±8.8	0.47
ICU death	36.5%	45.6%	0.31
Hospital death	47.6%	52%	0.73

General characteristics

		Adequate AB	Inadequate AB	P
LOD > 4	ICU death(%)	72	56	0.81
	Hospital death(%)	86	61	0.31
LOD = < 4	ICU death(%)	7	37	0.006
	Hospital death(%)	15	44	0.01

Influence of adequacy of initial AB according to the severity when VAP occurred

CONCLUSION. Our results suggest that initial adequate AB improves the prognosis of VAP among patients with the lowest baseline severity. As a consequence, an early broad-spectrum empiric AB should be systematically considered in these patients.
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194

INCIDENCE AND CONSEQUENCES OF THE INADEQUACY OF ANTIBIOTHERAPY FOR THE TREATMENT OF ICU-ACQUIRED PNEUMONIA

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INTRODUCTION. The severity of infections and co-morbidities in the critically ill patient lead us to use empiric antibiotherapy as early as possible. Several studies proved that empiric antibiotherapy is often inadequate and that adequacy of antibiotherapy is one of the main factors for success. The goals of our study were to assess the adequacy of our first line empiric antibiotic regimen for ICU-acquired pneumonia (VAP) and consequences of inadequacy.

METHODS. Retrospective analysis of prospectively collected data of all microbiologically documented (MD) VAP occurring in a 12-bedded Intensive Care Unit of an Emergency Department of an University Hospital in Porto, from the 1st January 1999 to the 31st December 2000. MD-VAP was a pneumonia acquired more than 48 hours after admission to the ICU in which a plausible pathogen was isolated in bronchial secretions and/or blood cultures. Antibiotherapy was considered adequate if the microorganism that caused the pneumonia was susceptible to the antibiotic used. Chi-Square and Mann-Whitney tests were used for statistical analysis.

RESULTS. 107 MD-VAP were studied; S. aureus and P. aeruginosa were the more frequent pathogens and beta-lactam with beta-lactamase inhibitor the more frequently used antibiotherapy. Antibiotherapy was inadequate in 18% of the cases. Results regarding the assessment of consequences of inadequacy of the first line antibiotic regimen were:

	Adequate n = 88	Inadequate n = 19	p =
Duration of antibiotherapy for MD-VAP	8	10	NS
Days of mechanical ventilation after MD-VAP	8	7,5	NS
Days of ICU stay after MD-VAP	11	10	NS
Mortality caused by MD-VAP	30%	37%	NS
Global ICU mortality	25%	21%	NS
Global hospital mortality	8%	5%	NS

CONCLUSION. Empiric decisions on antibiotherapy for VAP are sometimes wrong, but, when comparing patients submitted to adequate versus inadequate first-line empiric antibiotic regimen, no difference could be found in the outcome parameters studied.

195

EPIDEMIOLOGY OF NON-RESPONDING NOSOCOMIAL PNEUMONIA

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INTRODUCTION. Nosocomial pneumonia (NP) represent one of the major concerns in the ICU with a prevalence ranging from 10 to 65% and a mortality rate up to 50%. Furthermore, about 30% of patients with NP fail to respond to the empirical antibiotic treatment. The aims of our study were the establish the clinical characteristics, the bacteriological profile and the outcome of non-responding NP.
METHODS. Inmunosupressed patients were excluded. A total of 71 correlative cases of NP have been reported prospectively in five IUCs of our hospital. Demographic data, bacteriological results, treatment and outcome have been recorded for each patient. After 72 hours of empirical antibiotic treatment (based on ATS guidelines) all patients were re-evaluated for response. Non-responding NP was defined by the following criteria (at least one required): persistent body temperature > 38°C and purulent tracheobronchial secretion; an increase of 50% of radiographic infiltrates; development of septic shock or multiorgan failure; death probably or definitely due to pneumonia. All patients with clinical suspicion of NP were investigated based on the following protocol: chest radiograph and/or CT scan; blood culture; endotracheal aspirate (ETA), protected specimen brush (PSB) and bronchoalveolar lavage (BAL); stain of respiratory samples for Gram organisms, fungi, mycobacteria, P. carinii; quantitative culture of respiratory samples and susceptibility tests; serology (CMV, Aspergillus); urinary antigen for Legionella; blood levels of cytokines. Non-responders were investigated again on third day. Cause of non-response was addressed following a pre-established criteria.
RESULTS. Forty three patients (61%) with nosocomial pneumonia did not respond to empirical treatment. Concerning to risk factors there were no differences in terms of age (media 62 years in both groups), previous days of mechanical ventilation (5 vs 6 days), baseline intubation (40 vs 46%), previous antibiotic treatment (70 vs 71%), baseline oxygenation (PaO_2/FiO_2 ratio 174 vs 195 mmHg), APACHE-II score at ICU admission (14.3 vs 15.6), comorbidities (2.1 vs 2.7) and baseline MODS (3.5 vs 3.3). Baseline IL-6 levels (1028 ± 357 vs 231 ± 49 pg/mL)were significatively higher in non-reponders. The microorganisms more common isolated were *P. aeruginosa*, *S. aureus*, *H. influenzae*, *E. coli* and *S. pneumoniae*; MRSA was more frequently associated to non-responders. The main reasons for non-response to empirical antibiotic treatment were the infection by a microorganism not covered by the empirical treatment and the presence of ARDS. Mortality (51 vs 7%;$p < 0.001$) and ICU stay (21 vs 13 days;$p = 0.003$) were higher in non responders.
CONCLUSION. Non-responding NP was associated with a high mortality and morbidity. Infection by a multiresistant microorganism (specially MRSA) and presence of ARDS were the main reason for non-response to empirical treatment. IL-6 level at baseline is a good predictive factor.

Oral Presentations
End-of-life decisions – 196–201

196

PERCEPTIONS OF END-OF-LIFE DECISIONS BY PHYSICIANS AND OTHER HEALTHCARE PROFESSIONALS IN INTENSIVE CARE UNITS: A FRENCH NATIONAL STUDY

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INTRODUCTION. No guidelines about end-of-life (EOL) decisions have been issued in France. Few studies have evaluated and compared perceptions by physicians (P) and nonphysician healthcare professionals (NPHCPs) of EOL decisions in ICU patients.
METHODS. Questionnaire sent to 6300 NPHCPs and 950 Ps in 270 ICUs.
RESULTS. Completed questionnaires were sent back by 49.7% of the NPHCPs (n = 3134) and 54.8% of the patients (n = 521), in 130 ICUs. Ethics were an explicit concern in the ICU according to 64% of the NPHCPs and 79% of the patients ($P < 0.05$); 44% of the NPHCPs and 97% of the patients felt their opinion was sought on this point ($P < 0.05$). Thirty-one per cent of the NPHCPs and 80% of the patients indicated that the opinions of NPHCPs were consistently taken into account ($P < 0.05$). Current EOL procedures were considered satisfactory by 32% of NPHCPs and 75% of patients ($P < 0.05$). EOL decisions were usually taken collegially according to 27% of NPHCP and 49% of patients ($P < 0.05$) and by a physician alone according to 14% of NPHCPs and 4% of patients ($P < 0.05$); 91% of NPHCPs and 80% of patients felt EOL decisions should be taken collegially (NS), 43% of NPHCPs and 33% of patients felt that NPHCPs should shoulder part of the responsibility of making EOL decisions ($P < 0.05$), and 58% of patients felt that an EOL decision can be made despite disagreement among NPHCPs. Futility was the main criterion for EOL decisions according to 38% of NPHCPs and 73% of patients ($P < 0.05$). Suffering, whether psychological or physical, was a criterion for 29% of NPHCPs versus only 5% of patients ($P < 0.05$). Age (3% vs. 0.8%), cost (0.1% vs. 0%), former quality of life (5% vs. 6%), and family preferences (1.7% vs. 0.4%) were not criteria for either the NPHCPs or the patients. Among EOL decisions, withdrawing endotracheal mechanical ventilation was acceptable to 29% of NPHCPs and 28% of patients (NS), withdrawing amines to 85% of NPHCPs and 93% of physicians (NS), and withdrawing fluids to 22% of NPHCPs and 27% of patients (NS). According to 81% of NPHCPs and 91% of patients, an increased risk of death was not a valid reason for limiting sedative dosages (NS). Implementation of the EOL decision by an NPHCP was deemed acceptable by 63% of NPHCPs and 93% of patients when the decision was amines withdrawal ($P < 0.05$), by 55% of NPHCPs and 64% of patients when it was decreasing the FiO_2 ($P < 0.05$), by 31% of NPHCPs and 31% of patients when it was withdrawing endotracheal ventilation (NS), and by 52% of NPHCPs and 95% of patients when it was increasing sedative dosages ($P < 0.05$).
CONCLUSION. Major differences in perceptions about EOL decisions exist within French health care teams. French NPHCPs are dissatisfied with current procedures. These findings indicate a need for greater collegiality when making EOL decisions.
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197

SEVERITY SCORING SYSTEMS DO NOT PREDICT END OF LIFE DECISIONS

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INTRODUCTION. Severity scoring systems are designed to predict outcome among ICU population. Some authors proposed them to predict outcome in individual patients. Using scoring systems in that way could interact with end of life decisions. In this study we observed physicians behaviour during end of life process in a population of general intensive care patients stratified according to their risk of death determined by the APACHE II, SAPS II and LOD score.

METHODS. Observational study over a 14 month period in a single university hospital. APACHE II, SAPS II and LOD were measured on admission for all patients. A questionnaire was filled prospectively for any patient in whom end of life decision was taken. Statistical analysis were processed using Chi square test for contingency tables.

RESULTS. From January 1999 to April 2000, 1800 patients were admitted in the ICU. An end of life questionnaire was completed for 192 patients, 181 of them died. End of life decisions did not vary significantly among risk stratification with either scoring system. However there was a trend for less SDP decision in patient with higher risks of death (ROD > 80%) determined by APACHE II ($p = 0.06$) and LOD ($p = 0.08$). When patients were stratified according to their ICU stay, we observed that withholding decisions were more frequent in longer ICU stay ($p < 0.005$). When patient were stratified according to their age, withholding decisions appear to increase with the age ($p < 0.05$) and there was a trend for less CPR decisions in older patients($p = 0.09$).

CONCLUSION. In this study we observed that patient severity admission, assessed by scoring systems had very little impact – if any – on physician behaviour regarding end of life decisions. Conversely patient ICU lengh of stay and age had an impact on withholding decisions.

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198

THE IMPACT OF DO NOT RESUSCITATE (DNR) ON ICU PRACTICE: A SAUDI ARABIAN EXPERIENCE

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INTRODUCTION. DNR was not a common practice in our ICU till 1998 when our ethical hospital committee approved and implemented a new DNR policy, this study is to evaluate the impact of DNR on ICU practice.

METHODS. We reviewed all deaths occurs in our 12 beds medical-surgical adult ICU from January 1997 – December 1999, whether the patient died with or without DNR orders.

RESULTS. The number of patients dying with DNR orders in 1998 (84) and 1999 (86) was increased compare to 1997 (32), 70.6% vs 31.7% ($P < 0.0001$) and 72.9% vs 31.7% ($P < 0.0001$) respectively; on the other hand the average length of stay in ICU was reduced from 9.7 days in 1997 to 7.4 days and 6.1 days in 1998 and 1999 respectively.

	Total No. of ICU Admissions	Total No. of ICU Deaths	% Total Deaths / Total Admissions	No. of Deaths with DNR Orders	% Death with DNR / Total Deaths
Year 1997	475	101	21.3%	32	31.7%
Year 1998	587	119	20.3%	84	70.6%
Year 1999	640	118	18.4%	86	72.9%

CONCLUSION. The implementation of a new hospital DNR policy was very helpful in increasing the number of patients dying in ICU with DNR orders allowing critically ill patients with irreversible terminal illnesses to die with dignity in ICU; we observed in our study that DNR may have an impact on reducing the average length of stay in ICU, however, more study may be needed.

199

A PROSPECTIVE STUDY OF LIMITATION OF LIFE SUPPORT IN CHINESE PATIENTS: INCIDENCE, PROCESS AND FAMILY ACCEPTANCE

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INTRODUCTION. Despite modern intensive therapy, 10–20% of patients admitted to ICU will not survive [1,2]. The incidence of death preceded by limitation of life support therapy (LOT) varies from 50–90% [1–4]. The incidence, process and family acceptance may vary depending on cultural factors. It has been suggested that cultural factors, particularly family influences, may alter the process of LOT in Chinese patients [5]. The purpose of this study was to prospectively record the process of LOT in Chinese patients and identify the views of the family regarding acceptance of the process of LOT.
METHODS. A database was prospectively completed on all patients following a decision for LOT in the ICU. Demographic data, reasons for LOT, person initiating discussion, patients pre-ICU admission wishes, type (withholding or withdrawing), and time taken to achieve family or patient agreement for LOT were prospectively recorded. Consent for a telephone interview was obtained from the representative of families whose relative had died following LOT. Four weeks later the representative was contacted by telephone. Relatives were questioned on whether they agreed with the LOT decision.
RESULTS. Of 101 patients that died during the study period, death was preceded by LOT in 67(66%). Withholding occurred in 35(52%), withdrawing in 16(24%) and withholding followed by withdrawing in 16(24%). Only 3 patients (5%) had expressed a wish to limit therapy prior to ICU admission. The decision for LOT was initiated by the ICU physician (85% of occasions), family (9% of occasions), and the patient only once (2%). Poor acute prognosis and poor premorbid status were the most frequently cited reasons for withdrawal. Time from initial interview at which LOT was introduced to acceptance of LOT by 50% of patients and families was 3 hours or less and > 90% agreed within one day. LOT did not occur without patient and family agreement. Telephone follow-up questioning revealed that 81% still agreed with the LOT decision, 9% were neutral and 10% disagreed with the decision.
CONCLUSION. Despite cultural differences in the population served, the incidence and process of LOT is similar to that practiced in Western countries. Despite initially agreeing to LOT 10% of family members no longer agree with the decision to limit therapy four weeks after the event.
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200

DESIGNATION OF ICU PATIENT SURROGATES ACCORDING TO PATIENTS AND FAMILIES

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INTRODUCTION. A current ethical problem in France is the absence of legal alternatives to informed consent in intensive care unit (ICU) patients without decision-making capacity (DMC).

METHODS. Questionnaire study in ICU patients who lost then recovered their DMC and in family members of ICU patients without DMC.

RESULTS. 20 patients and 50 family members studied prospectively. No subjects declined to participate. Family (M/F: 1.5): 30% spouses, 30% siblings, 20% children. Ninety per cent were deeply worried about the patient and evaluated severity at 8.5 on a 0-to-10 scale; 20% knew the patient's preferences; 90% wanted to be fully informed about medical problems; and 85% did not know what a legal surrogate is. Designating a surrogate to speak for a patient with a transient loss of DMC was believed to be indispensable by 70%, useless by 10%, and prescribed by law by 10% of family members; 50% were opposed to mandatory designation of a surrogate. All family members believed the surrogate should participate in medical decisions, even those carrying a risk of causing or hastening death, and should not go against medical decisions, whether or not he/she knew the patient's preferences; 65% felt the surrogate should make decisions about participation of the patient in research studies. Ninety per cent of family members believed the surrogate should be designated by the family, 70% that he/she should be a family member, and 50% that more than one surrogate could be designated; 20% said they would decline to be the surrogate. Patients (20 M, SAPS II: 31 [20–40]): 10% had expressed their preferences prior to admission, 70% believed their family should be informed of their medical history, and 100% stated that designation of a surrogate should be mandated by law. All 20 patients felt the surrogate should accept medical decisions, even those carrying a risk of causing or hastening death; 60% believed the surrogate should decide about participation in a research study. 80% of patients felt the surrogate should be a family member and 40% that more than one surrogate could be designated. 65% expressed regret that no surrogate was designated at their admission.

CONCLUSION. French ICU patients and their family members are massively in favor of designating a surrogate. Our results reflect a preference for informed consent, with no tendency to challenge medical decisions.

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201

LOSS OF DECISION-MAKING CAPACITY IN INTENSIVE CARE PATIENTS

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INTRODUCTION. Assessing the decision-making capacity of intensive care unit patients is crucial but difficult. The objectives of this study were (1) to evaluate the prevalence of loss of decision-making capacity (DMC) in patients within 8 days of ICU admission, (2) to validate simple criteria for assessing DMC, and (3) to assess the role ascribed to family members.

METHODS. During a two-month period, DMC was assessed in all patients admitted to two ICUs, once a day from D0 to D7 and/or discharge, by nonphysician health-care professionals (NPHCPs) and using a ten-item test (T) validated against the MMSE(1). The following were recorded: psychopathology, SaO_2 < 90%, pH < 7.35, SBP < 90 mmHg, mottling, amines, temperature < 36 °C or > 39 °C, tracheal prosthesis and/or CV, sedation, Glasgow Coma Score (GCS), whether the patient designated a surrogate, and whether the patient or family were told of a decision to withdraw treatment.

RESULTS. 84% of patients had no DMC during 100% of the study period. On D0, 81% of patients had no DMC according to T and 79% according to NPHCPs; corresponding percentages at discharge were 43% and 48%.All patients with a GCS < 15 (P < 0.001), sedation (P < 0.001), hypotension (P = 0.03), amine therapy (P < 0.003), or mottling (P = 0.008) had lost their DMC. In 49% of cases, no surrogate was designated and all family members were informed. A surrogate was designated by the family in 31% of cases, the physician in 6.5%, and the patient in 1.8%. Eleven per cent of the patients received no visits. Of the 13 decisions to withdraw treatment, five were communicated to the family and none to the patients.

CONCLUSION. Loss of DMC was extraordinarily common in our ICU patients. Withdrawal of life support treatment in patients without DMC raises the problem of whom to inform when the law provides no surrogates to patient consent.

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Oral Presentations
Health informatics – 202–207

202

AN INTEGRAL AUTOMATIZED WATCHING SYSTEM FOR INTENSIVE CARE UNITS

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INTRODUCTION. The system was developed to help intensivists in their everyday practice. It is able to integrate the flow of critical care data from bedside monitors, ventilators, laboratory and other equipment with a digital output. The system includes a set of algorithms and programs for data processing, syndrome diagnostic and predicative mortality. Presenting data in an ergonomically correct and easily assimilated format is useful for interpretation and decision support.
METHODS. We examined 155 patients with abdominal sepsis during postoperative period. Sixty parameters (blood circulation, respiratory, base-acid balance, laboratory and others) were analyzed. Mathematical statistic (elementary statistic, histogram construction, frequency analysis, correlation analysis, nonparametric tests, T-test, regression analysis, discriminant and cluster analysis) and expert approach have been used for algorithm construction. Software was developed as database with friendly interface and written in Turbo C + + programming language.
RESULTS. The sequel of our research and technical performance is the power tool helping a physician in all his activities. The system provides typing, storage and printing in the standard form all sort of the text information. Doctor can prescribe treatment individually or from editable templates. Fluid balance, quantity of calories and electrolytes is counted automatically. All of quantity parameters can be displayed as graphical trends with normal limits. The main distinction of the system is the possibility of integrity assessment haemodynamic, respiratory and base-acid balance through automatically drawing polar diagrams and writing expert conclusion [1]. Furthermore, the system includes the diagnostic algorithm for precise determining of ARDS stage [2]. Probability of favourable or unfavourable outcome can be calculated by means our own prognostic indexes for every day and all days after surgery [3].
CONCLUSION. The system minimize spending physician's time and allow him to be more near patients. It gathers the big flow of data and relieves its interpretation. Including algorithms provide efficiency treatment and improve outcome.
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203

MANAGEMENT SOFTWARE IN ICU: A POWERFUL TOOL

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INTRODUCTION. Management of an ICU is a subject of interest, because the ratio profit: cost. Few areas have the level of complexity of an ICU and the staff, generally, has less information about the performance. If we give more managerial information, we could create a major partnership among the team and improve the performance.
To show a management software that we have developed in our ICU, which analise the performance and its change in function of new decisions.

METHODS. We have created a software in Access Microsoft environment. It runs in a PC inside ICU. Monthly, we put in circulation a report which studies the performance of the ICU, as a whole, and some specific variables of great impact (the "A" curve). The period of study was from January to December 2000, including 720 admissions; the data could be presented in tables, grafics and curves, with one or more variables. We calculated the median of each variables, that give us a tendency.

RESULTS. The performance of our ICU and how the variables changed is presented (exemples attached); they are: number of patients admitted, percentage of each insurance company, number of discharges, average time of stay in ICU, real percentage of deaths compared with the predicted by the Apache II score, rates of ICU acquired infection, average TISS, total number of days in ICU, incomes per day, total cost, cost per day, contribution rate, cost for medical material and drugs, ratio material and drugs: incomes. We'll see the impact of some decisions or politics, as cost control or income changes, in the performance.

CONCLUSION. Information is power. If we don't know how we work, then we are weak. A software which we can, easily, analise every important variable that impacts the performance of ICU is of great value, offering reliability and accuracy in an almost real-time. As we work in an open environment, the variables can be easily and quickly changed, according to the interest and needs.

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204

INTRANET: THE DISSEMINATION OF THE INFORMATION IN AN ICU

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INTRODUCTION. Nowadays, all the staff of an ICU need permanent atualization. To keep uptodated is a challenge, mainly in an "in developing country" as Brazil. There are many resources to disseminate knowledge and the criative use of the new technologies must to help us. To show a local solution of disseminate knowledge with a creation of a tool based on a web environment with an intranet.

METHODS. We have created an intranet to our ICU; the process began in May, 1996, with the implement of an electronic data recording; after, we added an electronic mail, a forum, where we discuss many doubts, put queries, and a kind of journal club, where the staff has the opportunity to learn about the new trials published in the medical literature focused on ICU.

RESULTS. The system was first introduced 1996, without sucess. There was no interest with the project. We then identify fear and discomfort, because many member haven't work with computers until the beginning of the project. Then our strategy was to advance slowly. First of all, we develop an email software only to improve communication. It was a very important phase because slowly each member develop some confidence and curiosity with the computer. . Nowadays there is no resistence and we could also introduce an on-line forum, an electronic library, a journal club, a lot of protocols and guidelines, some portals (ex. MDConsult, Connectmed) and an address book. In the year 2001, we started an electronic section called "Talk to the head"; it is an area, every staff member could write about problems and give suggestion to the head, without identification. Nowadays, the intranet is coming to be an essential part of our ICU.

CONCLUSION. The informatization process of an ICU must be slow and progressive. We have to be clear with the customer; the targets will be reached if every member was seen as an essential part and he must work together with the head, which stimulates all the process. The training activities improved with the use of resources from databank, as well as the technical and managerial information.

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205

MANAGING COST IN ICU: A REPORT OF AN EXPERIENCE

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INTRODUCTION. Costs have a huge impact in ICU bills and are a subject of many articles in the medical literature. To reduce costs without decreasing quality is a challenge. To demonstrate a cost management program in a 12 bed ICU in a general hospital with 110 beds. We've chosen some drugs of great impact in the bill and we've established a program which racionalized or replaced these drugs and a way to control, if there were some negative impact on quality.

METHODS. The period of the study was from January 1998 to January 1999. The drugs chosen were human albumin, omeprazole and midazolan. To decide when and how to use albumin and omeprazole, we employed evidence-based medicine concepts; with midazolan, we changed to diazepam, in equivalent dosis, and controlled the "ideal dosis" by the Ramsay scale.

RESULTS. We achived a considerable reduction in global costs, specifically US$ 20,000 for albumin, US$ 3200 for omeprazole and US$ 2000 for midazolan, each month. The economy was US$ 277,000 in the first year. The amount of money that could be expended, if we had mainteined the old pratice until now was US$ 881,400. We didn't find major mortality (compared to predicted by the Apache II score), higher length of stay (LOS), discomfort or difficulties inside the medical group. The benefits are maintained until now (38 months later).

CONCLUSION. Control costs without loss of quality is a challenge and a duty. We proved that this is possible without any problem. It's necessary to have clear targets and scientific basis, as evidence-based medicine, in conducting the protocols. After this study, other areas was included in this approach in our group (labs tests, for ex.). This kind of approach creates a "cost awareness" in the staff with many secondary benefits like money saved and less discomfort to the patient.

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206

DEVELOPMENT OF A DISCRETE EVENT SIMULATION MODEL TO PREDICT BED REQUIREMENTS FOR CRITICAL CARE

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INTRODUCTION. It is extremely difficult to quantify the number of beds required for a critical care unit because of the unpredictable case-mix. Moreover, the optimal size of a critical care unit depends on the complexity of services offered within the hospital, patterns of emergency workload, and the availability of intermediate care facilities. Given the significant resources involved in providing critical care, it is important that the supply of beds is matched to the demand for beds. Any mismatch between the two can result in unnecessary patient transfers or cancellation of major surgery. As a result, it is important that a method for predicting the optimal number of beds is developed. The aim of this study was to see whether discrete event simulation modelling could be used to determine critical care bed requirements.

METHODS. A semi-structured questionnaire was used to determine the availability and reliability of routinely collected patient data in twenty geographically adjacent critical care units. A common minimum dataset was then devised which consisted of the following: date and time of critical care admission, source of admission, admitting specialty, emergency/elective status, date and time of critical care discharge and subsequent destination. These data were sought for the 10,071 patients treated in the participating centres over a one-year period. Data on the number of staffed beds was also collected. Lanner Group's Witness modelling software was used to develop individual models for the critical care units. Witness uses discrete event simulation to model a real system, to understand the behaviour of a system, and to investigate 'what if' scenarios to determine the effects of changes in model parameters [1].

RESULTS. Models were developed that simulated patient flows through the twenty critical care units. Patients were characterised according to their emergency/elective status, source of admission and admitting specialty. The flow of patients was generated according to patients' time and day of admission, length of stay profile according to their specific characteristics, the decision making process of admission and discharge and the number of staffed beds. The model was capable of simulating twelve months' data from one critical care unit in less than 30 seconds using a standard laptop computer. The twenty models were linked together to form a region-wide model that was able to simulate the incidence of patient transfers given different scenarios of bed configuration.

CONCLUSION. A computerised discrete event model has been developed to simulate patient flows through twenty critical care units in the UK. This model can be used to determine the amount of time beds are occupied, the effects of increased demand for critical care, and consequently, which critical care units require additional resources.

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207

MEDICAL SIMULATION IN INTENSIVE CARE

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INTRODUCTION. Simulation technology is successfully employed in civil aviation (1). In the medical field, simulation has been used in the training of anaesthetists and operating room teams (2). The usefulness of simulator training in intensive care has not been determined. The aim of our project was to evaluate whether 1) high fidelity full scale medical simulation can be achieved in the settings of intensive care and, 2) simulator training is accepted by health-care workers in intensive care.
METHODS. A commercially available patient simulator was placed in our intensive care unit. A room was equipped in order to resemble as closely as possible the settings in the real unit. The scenario employed is that of a observed cardiac arrest due to ventricular fibrillation. Nurses, residents, and medical staff participate in the scenarion. The institutional target is that within a year every health care worker (n = 100) of the intensive care unit participate at least once in a simulator session. Simulator sessions are videotaped. A debriefing session, fascilitated by two instructors, follows immediately after the completion of the simulation. During the debriefing videotapes are reviewed by all participants. The debriefing should be an interactive event and participants are encouraged to share their experiences during simulation. At the end of the debriefing, participants are asked to evaluate their simulator training.
RESULTS. Simulator training was started in January 2001. Currently, 4 to 6 simulator sessions are conducted every month involving five participants each. Following this schedule should allow us to reach our target of at least one simulator session per health care worker per year. The analysis of the videotapes is well suited to discuss the team performance in relation to the existing algorithms of cardiopulmonary resuscitation. In addition, the analysis of the videotapes reveals information on issues as teambuilding, leadership, and communication. Participants' evaluation revealed favourable marks for the realism of the scenarios and the realism of team behaviour. In addition, the perceived usefulness of the simulator training is rated highly.
CONCLUSION. The Medical Intensive Care Unit of the University in Basel is the first intensive care unit in the world that has access to a patient simulator placed within the unit itself. Our preliminary data suggest that high fidelity full scale medical simulation can be achieved in the settings of intensive care. Regular simulator training for all health care worker of the unit appears to be a realistic target. Analysis of videotapes reveals quality of both medical performance and behavioural performance of the teams and individuals involved. Participants rated the realism of the scenarios and the realism of team behaviour with favourable marks, indicating that participants found not only their own behaviour, but also the behaviours of others to highly resemble that of the real intensive care unit. Participants' ratings of the perceived usefulness of medical simulator training in intensive care compare well with the ratings of aircraft pilots for their sessions in the flight simulator.
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