Dear Congress Participants, Readers and Colleagues

This issue of Biomedical Papers (Vol. 146, No 1) contains abstracts of the scientific papers to be presented at the 1st Central European Congress on Intensive Care Medicine.¹ The abstracts appear in order of presentation from Thursday 13 through Saturday 15 June 2002. This abstract book would have been impossible to produce without the help of several people from organizing and scientific committee, special thanks must be given to the Editorial Board of Biomed. Papers, which provided immense help toward successful completion of accepted papers. Our thanks also must go to people from Publishing Centre of Palacky University.

On behalf of Organizing and Scientific Committee of 1st Central European Congress on Intensive Care Medicine we wish you a pleasant stay at Olomouc.

Vladimír Černý, MD, PhD, FCCM
Chairman of the Scientific Committee

Oldřich Marek, MD
Chairman of the Organising Committee

¹ Each lectures agreed to provide a written version or synopsis of the lecture for this abstract book. Despite request, we regret that the speaker did not provide a written text of the lecture. Editors
June 13, Thursday  
15.00–17.00  
Room B  
Section: Ethics  

Chair: Drábková, Sprung, Ruokonen, Nalos

Invited speakers: (30 + 10 min)

1. **Sprung C.** (Israel)  
   End of life decisions

2. **Drábková J.** (Czech Republic)  
   Is there a difference in ethical access to critical patients without severe premorbidity and with chronic disabling comorbidity?

3. **Nalos D., Pařížková R., Novák I., Černý V.** (Czech Republic)  
   End of life decisions in critically ill – current status in Czech republic

4. **Ruokonen E.** (Finland)  
   How quality is monitored in Finnish ICU’s – benchmarking and quality control

Discussion

Workshop

1. Transfusion-Alternative strategies

   Break

Oral presentation (10 + 5 min)

1. **Pařížková R., Černý V., Dostál P.** (Czech Republic)  
   Limiting of life support in critically ill patients: a retrospective analysis of frequency and practice

2. **Wiedermann J., Smolka V., Reitinger J., Klásková E.** (Czech Republic)  
   Current state of intensive care in pediatrics and some ethic aspects

3. **Škulec R., Linhart A., Hnátek T., Špundová H., Mrázek V., Holm F., Aschermann M.** (Czech Republic)  
   Effect of statin therapy on long-term health-related quality of life in patients after acute myocardial infarction treated by PTCA

4. **Forró M., Mándli T., Gondos T.**  
   Experience in selection of liver transplantation recipients in anaesthetic aspect based on the first 100 cases

Discussion

Panel discussion

( Drábková, Sprung, Ruokonen, Nalos)
June 14, Friday  
8.30–12.30  
Room A  
Section: Infection

Chair: Romand, Zandstra, Eggiman, Ševčík

Invited speakers: (30 + 10 min)

1. **Romand J. A.** (Switzerland)  
   Infection versus colonization and implications for antibiotic therapy
2. **Zandstra D. F.** (The Netherlands)  
   Future perspectives of the selective decontaminations of the digestive tract with emphasis on the control of the emergence of resistance in the critically ill
3. **Eggiman P.** (Switzerland)  
   Catheter-related infections in the ICU, with special emphasizes on prevention
4. **Ševčík P.** (Czech Republic)  
   Ventilator-associated pneumonia: never ending story

Discussion

Workshop

1. **Maurer E.** (Germany)  
   Value of clinical examination EEG and evoked potential monitoring in ICU
2. **Adamus M., Adamus P.** (Czech Republic)  
   Automatic control of neuromuscular blocker delivery during general anaesthesia Datex-Ohmeda Workshop

Break

Oral presentation (10 + 5 min)

1. **Kolář M., Látal T., Berta E., Marek O., Čermák P., Blahut L. and Working Group** (Czech Republic)  
   Frequency of gramnegative bacterial pathogens in bloodstream infections in the Czech Republic
2. **Sobanska D., Stryjski A., Mazurek J., Stryjska M.** (Poland)  
   Bacterial and mycotic infections after oesophagus carcinoma operations
3. **Balík M., Kolář M., Šedivý J., Hendl A.** (Czech Republic)  
   Can bioimpedance measurement of extracellular water help to estimate the distribution volume of antibiotics in severe capillary leak syndrome?
4. **Kapš R., Starič S., Furlan P., Avšič-Županc T.** (Slovenia)  
   Hemorrhagic fever with renal syndrome in the Dolenjska region of Slovenia a 10-year survey
5. **Zvoniček V., Ondrovčík P., Sas I., Novák I., Šrámek V.** (Czech Republic)  
   Cryptococcus neoformans on ICU – case reports

Discussion

Panel discussion  
(Romand, Zandstra, Eggiman, Ševčík)
June 14, Friday
8.30–12.30
Room B
Section: Metabolism

Chair: Leverve, Gašparović, Phelan, Novák

Invited speakers: (30 + 10 min)

1. **Leverve X.** (France)
   Energy metabolism in critically ill patients: lactate is a major substrate

2. **Novák I., Rokyta R. jr., Matějovič M., Kroužecký A.** (Czech Republic)
   Early enteral nutrition in critically ill patients: where is a benefit?

3. **Gašparović V.** (Croatia)
   Continuous hemofiltration as a tool for control of homeostasis: renal support or renal replacement?

4. **Phelan D.** (Ireland)
   Catheter related sepsis and metabolic complications in TPN patients

Discussion

Workshop

1. **Černý V.** (Czech Republic)
   Activated protein C – a Novel agent for severe sepsis

Break

Oral presentation (10 + 5 min)

1. **Rokyta R. jr., Matějovič M., Kroužecký A., Novák I.** (Czech Republic)
   Effects of early postpyloric enteral nutrition on hepatosplanchnic hemodynamics and metabolism in severe sepsis

2. **Balík M., Jabar A., Kolář M., Hendel A.** (Czech Republic)
   Monitoring of the residual renal functions during continuous renal replacement therapy – the application of the analysis of cystatin C and natriuretic peptides

3. **Král J., Šetina M., Králová I., Tesařík R.** (Czech Republic)
   Acute renal failure requiring renal replacement therapy after cardiac surgery

4. **Suk J., Hruda J., Zvoníček V., Šrámek V.** (Czech Republic)
   Low urine output in acute renal dysfunction diagnosis in long term ICU patients

5. **Studená A., Bračoková I., Firment J.** (Slovakia)
   Hemorrhagic hypovolemia and some of its markers in experimental and clinical medicine

Discussion

Panel discussion
(Leverve, Gašparović, Phelan, Novák)

Poster session:

1. **Adorján K., Donáth K.** (Hungaria)
   Fluid and electrolyte disturbance resulting in tonic-clonic seizures, respiratory and renal failure (a case report)

2. **Balík M., Plašil P., Stehlíková M.** (Czech Republic)
   The diagnosis and therapy of heparin induced thrombocytopenia thrombocytopenia syndrome in a Czech general ICU
June 14, Friday  
14.00–17.00  
Room A  
Section: Cardiovascular dynamics  
Chair: Hasibeder, Černý, Voga

Invited speakers: (30 + 10 min)

1. Hasibeder V., Dünser M., Mayr A., Friesenecker B. (Austria)  
   Arginine vasopressin in vasodilatory shock
2. Černý V. (Czech Republic)  
   Hemodynamic goals in septic shock
3. Voga G. (Croatia)  
   Myocardial dysfunction in sepsis and MOF
4. Briegel J. (Germany)  
   Steroids in septic shock

Discussion

Break

Oral presentations (10 + 5 min)

1. Illias W. (Austria)  
   Non-invasive haemodynamic monitoring in intensive care and anesthesia
2. Balík M., Pachl J., Hendl J. (Czech Republic)  
   Influence of the degree of tricuspid regurgitation on cardiac output measurements by thermodilution
   Papillary muscle rupture with severe acute mitral regurgitation – rare complication of acute myocardial infarction.  
   Our experience with three consecutive patients.
4. Fazakas J., Gondos T., Horovitz P. (Hungary)  
   Relationships between conventional hemodynamic and blood volume monitoring during and after orthotopic liver transplantation
5. Mándli T., Forró M. (Hungary)  
   Application of continuous autotransfusion system during liver transplantation

Discussion

Panel discussion  
(Černý, Hasibeder, Voga, Briegel)

My “first line” approach to treat unstable patients with septic shock?

Poster session:

   Diagnosis of shock due to massive pulmonary embolism
June 14, Friday
14.00–17.00
Room B
Section: Systemic inflammation and sepsis
Chair: Radermacher, Träger, Trenkler, Matějovič

Invited speakers: (30 + 10 min)

1. Radermacher P. (Germany)
   Goal-directed therapy in the treatment of severe sepsis and septic shock: does it exist?
   Sepsis, septic shock and multiple organ dysfunction: new thinking about their pathophysiology
3. Träger K., Radermacher P. (Germany)
   Gastrointestinal tract resuscitation in critically ill patients
4. Trenkler Š. (Slovakia)
   Genetics behind sepsis

Discussion

Break

Oral presentation (10 + 5 min)

   Differentiation between local and systemic bacterial infection: the value of procalcitonin
2. Fazakas J., Gondos T., Sárvári E., Varga M., Horovitz P. (Hungaria)
   The systemic and regional procalcitonin serum level changes during and after liver transplantation
3. Borkowski J., Jedynak S., Wolczynski S., Siemiatkowski S., Czaban S. L. (Poland)
   Luteinizing hormone, prolactin and testosterone plasma levels in patients with septic shock
   Hypermyoglobinemia in critically ill patients: what does it mean?
5. Dziurdzik P., Krawczyk L., Jalowiecki P., Dudek-Dyczikowska D., Kondera-Anasz Z. (Poland)
   Serum interleukin-10 in patients with isolated acute intracranial lesions
6. Hruda J., Šrámek V. (Czech Republic)
   The impact of oversedation on septic shock severity

Discussion

Panel discussion
(Radermacher, Träger, Trenkler, Matějovič)
June 15, Saturday  
8.30–12.30  
Room A  
Section: Acute respiratory failure

Chair: Mutz, Putensen, Šrámek, Pavlík, Nalos jr.

Invited speakers: (30 + 10 min)

1. **Putensen C.** (Germany)  
   Patophysiology of ALI and ARDS
2. **Nalos M., Růžička J., Šrámek V., Novák I.** (Czech Republic)  
   Respiratory mechanics at the bedside
3. **Pavlík M.** (Czech Republic)  
   Open lung maneuvers – how to perform, how to monitor, possible side effects
4. **Šrámek V.** (Czech Republic)  
   Non-invasive ventilation in acute respiratory failure
5. **Mutz N.** (Austria)  
   Muscle fatigue and respiratory failure

Discussion  
Break

Oral presentation (10 + 5 min)

1. **Matuška P., Pilařová O., Merta Z., Skříčková J., Dušek L.** (Czech Republic)  
   The influence of co-morbidity on the outcome of non-invasive ventilatory support in patients with acute respiratory failure in chronic obstructive pulmonary disease
2. **Rindoš R., Hamžík J., Piovarčí D., Havelka V.** (Slovakia)  
   Postintubation tracheal lesions with acute respiratory failure – Serious problem of the intensive care today
3. **Kolek V., Marek O.** (Czech Republic)  
   Stent insertion in benign stenoses of central airways
4. **Pachl J., Zabrodský V., Roubík K., Waldau P., Krejzl J.** (Czech Republic)  
   Criteria for prediction of HFOV treatment efficiency in adult patients with ARDS

Discussion

Panel discussion  
(Mutz, Putensen, Šrámek, Pavlík, Nalos jr.)

Poster session:

1. **Pavlík M., Štětka P., Šrámek V.** (Czech Republic)  
   ARDS due to fat embolism – a case with a prolonged course
2. **Škulec R., Bělohlávek J., Pšenička M., Holm F., Aschermann M.** (Czech Republic)  
   Diffuse alveolar hemorrhage – unusual complication of combined antiaggregation therapy for acute myocardial infarction
3. **Řehořková D., Bosáková H., Horký P., Hude P., Wendsche P.** (Czech Republic)  
   The prone position as a part of the respiratory management in tetraplegic patients
4. **Bosáková H., Řehořková D., Horký P., Hude P., Wendsche P.** (Czech Republic)  
   Respiratory management of patients with spinal cord injuries (SCI)
END OF LIFE DECISIONS

Sprung C.

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No abstract available.

IS THERE A DIFFERENCE IN ETHICAL ACCESS TO CRITICAL PATIENTS WITHOUT SEVERE PREMORBIDITY AND WITH CHRONIC DISABLING COMORBIDITY?

Drábková J.

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Modern intensive care has an enormous technical and medical potential. The demand for intensive care has increased especially in patients at advanced disease stages with a steeply increasing proportion of elderly patients. The sequelae are rising costs, prolonged length of stay and increasing numbers of specialized staff and personnel. All these factors are confronted with limited economic resources and not always with positive clinical outcome. Ethical principles in evidence based intensive medicine have to withstand economic pressures, to assist in formulations of up-to-date definitions and in benchmarking of indicated versus abundant therapy; to support the ideas of appropriate aftercare; to describe the borderline between shared decision making and benevolent paternalism etc.

Ethical aspects, principles and expectations

Common medical and ethical expectations of conscious adult critical patients:

– state-of-the-art activities of the attending physicians and all health care providers,
– preservation of dignity,
– absence of pain and suffering,
– holistic medical care with optimal prognostic outcome.

The patients don't feel responsibility for the economic burden. Their main focus is concentrated on successful outcome, future quality of life, even on favourable quality adjusted life years. Protracted and complicated life crisis in the ICU increases abolition of circadian rhythmity, emotional stress, depression, dysexecutive syndrome or posttraumatic stress syndrome. In very rare cases patients insist on being told mere true facts on hopeless prognosis with a rapid shortage of life expectancy or with severe disability. The emotional stability of these informed patients can nevertheless change abruptly afterwards in an unexpected way. Light sedation without amnestic effect is the best choice.

The physician’s view is rather different. He is out of his patient's life crisis but he is engaged in the doctor-patient relationship. His view is a combination of several factors:

– his own ethical principles and compassion capacity,
– professional ethics with rules of beneficence, non-maleficence, respect for patient's autonomy and medical justice, cited by Beauchamp and Childress (1989, 1994),
– medical evaluation of his patient's physiologic reserve, his response to therapy, genetic and gender predisposition, diagnosis, complications, family background, age and personality.

Ethics and bioethics are not isolated theoretical sciences. Their performance is visible in all activities of intensive care personnel, in behaviour of all patients without brain traumatic or non-traumatic injuries. Actual ethical principles and individual behaviour and inter-relations influence the entire team in the ICUs or step-down units.

Specific features in the ICUs

– 50 % of survivors do not remember their stay and time in the intensive care due to primary unconsciousness or heavy sedation. This gap can afterwards stimulate the posttraumatic stress syndrome.
– 30 % do feel the ICU environment as a distressing factor; approximately 50 % of them estimate this could be improved if the carers had more ethical compassion and empathy.
– Previously healthy subjects, mainly from the group of younger males, feel shocked, embarrassed, deeply surprised, depressive or agitated. They are overwhelmed with fear of death, loss of autonomy and integrity. They suddenly have communication difficulties. The feeling of life insecurity can lead to loss of trust in the attending staff. Lack of uninterrupted sleep or long-term sedation provoke loss of orientation in time and space. All these negative impressions disturb the ethical stereotypes and barriers. In elderly patients they can completely disintegrate the previous personality.

Ethics and psychologic changes

Bioethics and psychology are tightly bound to each other especially in chronically limited, ill and disabled patients. This is more manifest in young patients, in males, in dominant personalities. Without scrutiny they can demand “best available care”, “rooming-in of their beloved ones”, iterative consultations and discussions considering their health status and future life style, compensatory equipment, participation of invited healers etc. On the other side elderly patients with chronic diseases feel depressed, taken aback with no perspective to be dismissed and return home as non-dependent on assistance of others as they were used to. Nevertheless they don’t express their more hidden feelings with such vivid vitality as the former group. Extreme reaction is mental apathy and nearly passive suicide rejecting medications, mobilization, weaning-off the ventilator.

Physicians and nurses have to handle both types of patients with identical ethical access. The longer the stay of these patients in the ICU or HDU the more relevant is the ethical background of the triangle patient-relatives-attending carers. Iterative complications, chronic ventilator therapy, immobilization, lack of good prognosis and new interests, lost of voice with tracheostomy can lead to disruption of ethical barriers and depress the social threshold of the patient and his relatives; their adverse reactions induce escalation of the burn-out syndrome in health care providers. Impatience and hostile feelings of carers are directed not only to the actual patient, they generate mental discomfort in the
ICU. Prophylactic measures have to be taken in time excluding the participation of clinical psychologist dealing with patients, relatives and personnel.

**Ethics and decision-making process**

Ethics is connected not only to psychology, deontology and human relations in units with acute or long-term critical patients. It is implemented in the decision-making process of physicians considering evaluation of anamnestic data, clinical history of the present injury or dec complication of a progressive chronic disease, comorbidity, age, presumed quality adjusted life years, amount of economic/financial resources, event. legal prospective wishes and directives in different countries. Professional ethics is not different in its basic principles but the actual role in different situations in emergency medicine, in intensive medicine and palliative care has distinct individual features.

**CPR and ethics**

CPR in the field is a typical example of a postponed definite decision. The overall survival rate of patients dismissed from the hospital is 3–5% in the USA. If we judge the patient's perception of the benefit of outcome as the most important element, we have to admit a rather ambivalent reality, that 35% survivors of myocardial infarction are living in constant fear of another coming attack, reducing their daily activities and 42% of them complaining of stressful social isolation. After CPR in the field results and outcome in adults are still worse; 54% of resuscitated patients do not survive already at the scene, 25% die during the transport and 4% are dismissed neurologically disabled. Especially poor outcome we see in trauma patients. Neverthe less even these statistical data (Kettler) don't justify general omission of CPR. In countries with high and lawful respect to patients autonomy and capacity to determine own destiny 41% elderly and limited patients opt for CPR if they lead an active life. This percentage is dropping to 11% if they are chronically ill and the progress of their dominant disease offers the life expectancy less than 1 year. Severe comorbid ity in elderly patients with discomfort decreases the option for CPR to 5%. Respect for autonomy in CPR and other rescue manoeuvres is not the only principle and should not be overvalued if it conflicts with other aspects. Autonomy cannot replace beneficence. Justice in the field is considered as CPR, helicopter transport in polytrauma emergencies and severe burns etc. to appropriate intensive care establishment. The exact evaluation of prognosis and the final decision is postponed to the hospital and to the moment of sufficient information.

**Intensive care and ethics**

In the intensive care ethical principles are based on positive motivation of patients towards favourable prognosis. Ideally, patients with no chance of recovery should be identified prior to their admission to intensive care (Booth 2002) and care decisions should be made on data, proven by means of evidence based medicine, using dynamic prognostic scoring systems merely as basic support for individually tailored decisions. Otherwise public will fear premature computer rationing and withholding or withdrawing of futile therapy only as a tool due to economic restriction. In the acute period the patient is incompetent for serious discussions concerning his real prognosis and for expression of directives, informal consent or disagreement. In our country best interest of the patient concerning the decision making process and treatment is directed to his attending physician. Guidance on healthcare ethical issues is the role of ethics committees, exceptionally of a state attorney. Legislation changes are expected with our membership in the European Union. Topics with ethical background enclude numerous issues – some of them general and some with different medicolegal validity in different countries:
- extent of therapy, life prolonging treatments and treatments to alleviate suffering, withholding and withdrawing therapy and its selected elements,
- issues of palliative care and basic life support,
- assistance of prognostic criteria as a result of dynamic scoring systems,
- criteria of brain death and donor programme,
- dimension of withholding/withdrawing crucial therapy encl. mechanical ventilation in respiratory insufficiency during end-stage chronic untreatable illness,
- definition of futile therapy,
- omission or refusing indicated therapy,
- rescue therapy and manoeuvres,
- off label medications and alternative care,
- moral difficulties in giving information to the patient, his relatives, insurance companies, police; scientific evaluation in congresses and periodicals etc.
- clinical trials of new drugs and methods in the non-autonomous patient,
- the role of relatives, the patient's proxy and surrogate,
- patient's prospective directives concerning CPR, emergency and intensive care,
- iterative informed consent and signature of directive of a mentally competent patient demanding euthanasia.

**Conclusion**

There is a difference between patients formerly healthy and patients with severe diseases after a recent primary hit. Basic ethical issues are common, no civilian triage is used, rationing is supported with state-of-the-art criteria. More sophisticated ethical image and reactions of patients, their relatives and carers differ excluding validation of specific features: stage of severe chronic and ultimately untreatable disease, decreased reserve of elderly people etc. Patient-carer relationship and behavior is judged ethically from both sides. Ethics has many topics in emergency and intensive medicine. Only few of them are covered and can be covered by legislature. Professional ethics is rather independent, its basic human principles are valid and economic restriction cannot beat them. Evidence based medicine offers new views to implement more exact arguments and definitions to individual topics; we don't expect radical change of ethical principles in peaceful and developed countries for next future. In Czech Republic topics of specific professional bioethics, ethical behavior of staff and personnel, moral difficulties, economic aspects, redefinition of legislature in emergency and intensive care form a burning challenge just now and for coming days.

**References**

**End of Life Decisions in Critically Ill – Current Status in Czech Republic**

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End of life decision (EOLD), is a constant component of decision making in ICUs. The role of EOLD has been increasing in USA, Europe in last decade. The Czech Association of Intensivist is beginning to discuss this issue. The main reasons for the controversy are: dignity of dying process and economic arguments.

The society relation to death and dying process is multifactorial. We assume that national and local traditions, intensity and differences of religions, living standards and accessibility of literary sources, play a major role.

Only after many years rapid economic and political changes reflect in lifestyle and ethics standards. The non-medical society is not yet prepared to adapt EOLD principals. Some rules of socialist relationship between patients and medical staff are continuing nowadays. The former assumption that “Health is a matter of the whole society”, is the main cause of strong medical paternalism as well as very low autonomy feeling of the patient.

Medical students have learned at medical faculty a lot about saving the lives, but constantly only few about dignity of dying. Medical staff has not accepted the basic concept and principles of EOLD yet. Technical and pharmacological standards of ICUs reached European level in the last decade. The number of patients who has met the criteria of futile treatment is rising currently. The amount of EOLD is increasing nowadays. Although I have only fragmentally data I will try to define the current situation in EOLD in the Czech republic in comparison to published data.

Article from American ICUs (Prendegast and Luce) reported an increase in withdrawal of life support from 51 % to 90 % in the period between 1988 and 1993. In a French study Ferrand et al have reported that 53 % of the ICU deaths were preceded by a decision to withdraw or withhold life support therapies. Last year Esteban et al. published the following data: 34.3 % of patients in Spanish ICUs died following withholding or withdrawing order. We assumed that consideration of dying process is extremely various in ICUs in Czech republic.

We present data from three different Czech ICUs using withholding and withdrawing order.

In ICU No. 1 The incidence of withholding and withdrawing order were 23 % of all admitted patients in the two years period between 2000 and 2001.

In ICU No. 2 In 2001 foregoing live-sustaining treatment occurs in 11 % of patients admitted in ICU and in 43 % of dying patients.

In ICU No3 the withholding and withdrawing was performed in 61 % patients before death.

ICU No 1 and 2 were participated on Ethics study. ICU No 3 not gained ethics committee agreement for Ethics study nevertheless they had all data for Ethics study available.

Participation on European studies can fundamentally contribute to better provision of dying process and help us in making difficult ethical decisions for critically ill.
Conclusion

End-of-life care is an important part of high-quality intensive care unit. The rate of withdrawing or withholding therapy decisions in dying patients occurred more frequently comparing to some studies. Increasing proportion of employment of ventilatory support withdrawal has been found in years 2000 and 2001.

References


CURRENT STATE OF INTENSIVE CARE IN PEDIATRICS AND SOME ETHIC ASPECTS

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Intensive care in the present-day paediatrics is featured by rigid organisation structure while it is given a minimum personal and technical background.

Primary concerns of the intensive and resuscitating care (IRC) continue to be focused on solution of urgent states but for the last decade there has been increasing number of patients suffering from irreversible organ alterations and chronic diseases that require chronic IRC to be applied. Such care is performed in IRC regional centres.

Patients mentioned above include in particular: a) those affected by CNS hypoxia b) those suffering from sequela resulting from urgent care complications c) those suffering from progression of a basic disease of degenerative type that cannot be influenced d) those suffering from progression of a basic disease of chronic type that cannot be influenced.

Present-day IRC in paediatrics is furthermore distinguished by: 1) increasing proportion of relapsing chronic diseases 2) enhanced intensity of pre-hospital treatment of urgent states 3) changing spectrum of urgent states in favour of doubtful complex multi-factorial emergent states (proportion of typical respiratory and gastro-intestinal diseases decreases) 4) growing influence of effects of perinatal patology on the development of urgent states in later age.

Trends in the present-day IRC in paediatrics are:

- Strict INDICATION OF INVASIVE TREATMENT TO BE APPLIED
- PREVENTION FROM COMPLICATIONS – technical, infective, toxic
- Emphasis given to performance of all interventions in ANALGOSEDATION
- Application of SCORING SYSTEMS
- Introduction of STANDARD PROCEDURES IN TREATMENT AND DIAGNOSTICS
- Growing role of CHRONIC INTENSIVE AND RESUSCITATING CARE

Ethic problems in IRC are related chiefly to states of irreversible failure of organ functions, which in particular require patient’s involvement and patient prevention from any “harm” to be taken into consideration. In the light of the current theoretical knowledge the extent of the offered care is limited by economic conditions. There is some endeavur to solve this antagonism (of “what we wish to and what we actually can”) by categorising the patients according to the care to be offered:

1) standard – maximum therapy 2) nonexpanding therapy – “withholding” 3) limiting therapy – “withdrawing”. In Scandinavia, in particular, the protocols of limited care are developed for states with unfavourable prognosis based on the scoring. In our opinion maximum therapy should be offered initially (72 to 96 h). This view is supported by the difference between real (0.009) and predicted (0.039) mortality in the IRC patient file at the Clinic of Paediatrics of FNO we have traced during evaluation of PRISM in 2001.

Increasing parental involvement in childcare is in accordance with the Charter of Hospitalised Children’s Rights. Contacts between parents and patients are constantly improving and the room for parental attendance even in IRC is increasing. But close contacts between parents and child-patient may cause pressure and subsequent conflicts with IRC ward staff.

Conflicts are: a) positive – stimulating b) negative – demotivating.

07

EFFECT OF STATIN THERAPY ON LONG-TERM HEALTH-RELATED QUALITY OF LIFE IN PATIENTS AFTER ACUTE MYOCARDIAL INFARCTION TREATED BY PTCA

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Purpose of study

Beneficial effect of statine treatment in patients with acute coronary syndrome has been studied. However, a little is known about its effect on long term health-related quality of life (HRQOL). Thus, we decided to analyze impact of statine therapy on HRQOL in patients who underwent direct or rescue percutaneous coronary angioplasty (PTCA) because of acute myocardial infarction (AMI).

Methods

We performed a retrospective single-center study in 127 patients who underwent direct or rescue PTCA because of AMI in 2nd Dep. of Internal Medicine, 1st School of Medicine, Charles University, Prague in the year 2000. 11 (SD ± 3.2) months after the procedure the patients were sent by the 36-Item Short-Form Health Survey (SF-36) and the questionnaire about actual symptomatology of coronary artery disease and concomitant medication. SF-36 quantifies HRQOL in eight parameters: physical functioning (PF), role limitations as a result of physical health problems (RP), bodily pain (BP), general health perceptions (GH), vitality (VT), social functioning (SF), role limitations caused by emotional health problems (RE), and general mental health (MH). All parameters were scored from 0 (worst score) to 100 (best score).

Results

Response-rate was 52 %. 95.5 % of responses were evaluable. 22.7 % of responders were women. Average age was 62.8 years (SD ± 10.8). Responders (47.6 %) were treated by statines in the time of completing the questionnaire, 52.3 % were not. We found out a significantly
better score in the statine treated group then in the group without statine treatment in PF (77.9 vs 64.8), RP (64.1 vs 36.5), BP (83.1 vs 68.8) (p < 0.05) and borderline score in SF (84.2 vs 73.0) (p < 0.05).

Conclusions

Statine treatment in patients who underwent PTCA because of AMI is associated with improved quality of life in several parameters. Confirmation of this finding requires further investigation.

08

APPLICATION OF CONTINUOUS AUTOTRANSFUSION SYSTEM DURING LIVER TRANSPLANTATION

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Purpose

The advantages and disadvantages of continuous autotransfusion during liver transplantation are investigated in our study compared with blood saving and traditional cell saving techniques.

Methods

Patients were divided into three groups in this retrospective study; Group 1 (n = 14): continuous autotransfusion was applied; in Group 2 (n = 14): no blood saving technique used; in Group 3 (n = 14): Haemonetics cell saver was used. Age, body weight, diagnosis, Child-Pugh score, level of haemoglobin and clotting factors, activated clotting time (ACT), duration of hepatectomy, blood replacement therapy, post-operative respiration time, treatment time and mortality were examined.

Results

In Group 1 the number of Child B patients was significantly higher than Child C patients (p < 0.05). The initial values of haemoglobin were significantly lower in Groups 1 and 3 (89 ± 19 vs. 103 ± 17 vs. 90 ± 16.8 g/l; p < 0.03). During hepatectomy in Group 1 lower haemoglobin values were detected than in the other two groups (96 ± 7 vs. 104 ± 16 vs. 106 ± 16.6 g/l; p < 0.05). The quantity of total blood utilisation (donor + autotransfusion) was significantly higher in Group 3 than Group 2 and in Group 1 than Group 2 (21.06 ± 11.2 vs. 11.07 ± 3.8 vs. 30.71 ± 18 U; p < 0.001). Comparing the values of ACT in each group during operation periods no significant difference was found. Treatment time on the ICU of the patients in Group 3 was significantly longer than in the other two groups (11.08 ± 7.8 vs. 9.17 ± 3.5 vs. 26.62 ± 14.6 days; p < 0.03).

Conclusion

We found that applying CATS is advantageous during liver transplantation, as the device reduces donor blood requirement. No significant complication was observed.

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EXPERIENCE IN SELECTION OF LIVER TRANSPLANTATION RECIPIENTS IN ANAESTETIC ASPECT BASED ON THE FIRST 100 CASES

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Purpose

Analysing preoperative parameters were for predict the outcome of liver transplantation.

Methods

Patients were divided retrospectively into two groups: Group 1. uncomplicated cases (n = 50), Group 2.: patients with severe complications (infection, rejection, organ failures etc.) (n = 29). Cases with primary surgical complications (bleeding, thrombosis of hepatic artery, problems of bile duct etc.) and acute retransplantations were excluded (n = 21) Age, BMI, Child-Pugh score, incidence of concomitant diseases, perioperative lab data, central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), systemic vascular resistance (SVR), requirement of intraoperative transfusion, treatment time in ICU, duration of mechanical ventilation and haemodynamic monitoring, need of cardiac support, incidence of perioperative infections, MOF score and mortality were compared between the two groups.

Results

Lower level of preoperative haemoglobin (104 ± 27 vs. 121 ± 21 g/l p = 0.003), PCWP (16.8 ± 9.6 vs. 12.6 ± 5 p = 0.02), higher requirement of intraoperative transfusion (12.6 ± 5 vs. 16.8 ± 9.6 U p = 0.02), longer ventilation time (31.3 ± 32 vs. 50 ± 42 days p = 0.03) longer staying in ICU, (7.8 ± 2.5 vs. 28.3 ± 22.9 days p = 0.0003), higher frequency of cardiac monitoring (15/50 vs. 23/29 cases p = 0.0001), higher MOF score (0.24 ± 0.5 vs. 2.65 ± 1.76 p < 0.002), and lower mortality (2 vs. 56.3 % p = 0.0001) were found in Group 2 than Group 1. Remaining parameters were not showed any significant differences.

Conclusion

It was found mortality and morbidity of liver transplantation are lower in case the recipients are well-hydrated and have good cardiac compensation ability.
INFECTIONS VERSUS COLONIZATION AND IMPLICATIONS FOR ANTIBIOTIC THERAPY
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FUTURE PERSPECTIVES OF THE SELECTIVE DECONTAMINATIONS OF THE DIGESTIVE TRACT WITH EMPHASIS ON THE CONTROL OF THE EMERGENCE OF RESISTANCE IN THE CRITICALLY ILL
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CATHETER-RELATED INFECTIONS IN THE ICU, WITH SPECIAL EMPHASIZES ON PREVENTION
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Catheter-related infection remains a leading cause of nosocomial infections, particularly in intensive care units (ICUs). It includes colonization of the device, skin exit-site infection and device -- or catheter-related bloodstream infection. The latter represents the most frequent life-threatening associated complication of central venous catheter use and is associated with significant patient morbidity, mortality and extra hospital costs. The incidence of catheter-related bloodstream infection ranges from 2 to 14 episodes per 1000 catheter-days. On average microbiologically-documented device-related bloodstream infections complicate 3 to 5 per 100 central venous line uses, but they only represent the visible part of the iceberg and most clinical sepsis are nowadays considered to be catheter-related.
We briefly review the pathophysiology of these infection, highlighting the importance of the skin insertion site and of intravenous line hub as principal sources of colonization. Principles of therapy are shortly reviewed. The most recent preventive approach are presented in more details, including the possible benefit of recently developed impregnated catheters and the positive impact of educational programs and/or global preventive strategy based on strict application of preventive measures and on a careful control of all factors associated with catheter-related infection.
Preliminary data from our institution showing a positive long term impact of these measures will be discussed. This may help clinicians to determine the eventual necessity to incorporate them in their own practice.

VENTILATOR-ASSOCIATED PNEUMONIA: NEVER ENDING STORY
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Introduction
The human body consists from approximately $10^{14}$ cells. Most of them, 90%, are microorganisms. In other words, only 10% of human body cells are of eucaryotic type. In adult, almost 1 kg of microorganisms, most of them bacteria, is present, particularly in the gut. In normal situation, 99.9% of bacteria in the large intestine are anaerobs. In critically ill patient the ecology of intestinal flora changes significantly and plays important role in the development of nosocomial infections. Nosocomial pneumonia is the second most common nosocomial infection and the most common nosocomial infection in intensive care units. Compared to most hospitalized patients, rates of nosocomial pneumonia are 10- to 20-fold higher in intensive care unit patients, and 7- to 21-fold higher in the intubated patients. Therefore, intubated and artificially ventilated patients in intensive care units are in the highest risk of nosocomial pneumonia. Most of the published studies report the incidence rate of the ventilator-associated pneumonia (the number of cases of ventilator-associated pneumonia per 100 hospitalized patients). The incidence of ventilator-associated pneumonia (VAP) ranges from 9% (some pediatric ICUs) to more than 50% in patients with ARDS. These rates fail to adjust for the duration of ventilation and are therefore difficult to interpret. Device-associated incidence density rates of VAP, that is, the number of cases of VAP per 1000 ventilator-days, are reported only for small amount of studies and range from 10 to 30 per 1000 ventilator days. In our study done in midle 90s (261 patients, general medical-surgical ICU, APACHE II score 21.76 ± 7.15) we observed 18.2 VAP per 1000 ventilator days, or, VAP developed in 24.2% of ventilated patients. On average, VAP rates are 9.3 times higher than nonventilator-associated pneumonia rates, ranging from 2.6 times higher in respiratory ICUs to 19 times higher in burn ICUs.
Nosocomial pneumonia is not only common, but also deadly. Estimates of its crude mortality range from 28 to 37%. In our study, the mortality of patients with nosocomial pneumonia was significantly higher (39.3%) than the mortality of patients without pneumonia (16.1%, p < 0.01). Some have argued that these high crude mortality
rates merely reflect the severity of patients underlying illnesses. However, several studies have shown that a large proportion of the mortality (approximately 30% for intubated patients) is directly attributable to the pneumonia. VAP caused by antibiotic-resistant bacteria was associated more closely with excess hospital mortality. In addition to increasing mortality, nosocomial pneumonia has an important economic impact. Intubated ICU patients require mechanical ventilation for 18 to 22 more days. They stay 10 to 13 days longer in the hospital. In our study, patients with pneumonia stay on average 11 day longer in ICU. It is estimated in USA that healthcare providers in DRG system lose $ 5800 per case of nosocomial pneumonia because of uncompensated extra costs.

**Pathophysiology**

Soon after admission, hospital-acquired bacteria appear in gastric secretions, the oropharynx, and the endotracheal tube. Nasogastric intubation and supine body position allow bacteria-laden secretions to reflux into the endotracheal tube. These colonizing bacteria usually come from the patients themselves rather than from the mechanical ventilator. Usual community pathogens such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, methicillin-sensitive *Staphylococcus aureus*, *Moraxella catarrhalis* may be responsible for early onset nosocomial pneumonia, multiresistant Gram-negative bacilli (*Pseudomonas, Enterobacteriaceae*), Gram-positive cocci (MRSA) or fungi are responsible for late onset nosocomial pneumonia.

**Definition and diagnosis of nosocomial pneumonia**

Nosocomial pneumonia (NP) is difficult to define. It may be defined as an infection of lung parenchyma that was neither present nor incubating at the time of hospital admission. The criteria for nosocomial pneumonia diagnosis are clinical and include fever, cough, purulent sputum, in combination with radiological evidence of a new or progressive pulmonary infiltrate, a suggestive Gram’s stain, and positive cultures of sputum, tracheal aspirate, pleural fluid, or blood. Although clinical criteria together with cultures of tracheal specimens may be sensitive for bacterial pathogens, they are not specific, especially in patients with artificial ventilation. Conversely, positive blood or pleural fluid cultures have very low sensitivity but are generally quite specific for nosocomial pneumonia. Much of misdiagnosis of VAP arises from the inaccuracy of traditional diagnostic criteria. In the previously healthy outpatient the findings of fever, leukocytosis, purulent respiratory secretions, and new radiographic lung infiltrates have identified pneumonia well. VAP caused by antibiotic-resistant bacteria was associated more closely with excess hospital mortality. In addition to increasing mortality, nosocomial pneumonia has an important economic impact. Intubated ICU patients require mechanical ventilation for 18 to 22 more days. They stay 10 to 13 days longer in the hospital. In our study, patients with pneumonia stay on average 11 day longer in ICU. It is estimated in USA that healthcare providers in DRG system lose $ 5800 per case of nosocomial pneumonia because of uncompensated extra costs.

**Risk factors**

Many aspects of a patient’s health status may predispose him or her to nosocomial pneumonia. These include old age, poor nutrition, chronic diseases such as chronic obstructive pulmonary disease and neuromuscular disease. Acute changes in health, such as decreased consciousness, impaired airway reflexes, aspiration, injury, particularly to the head or chest, may also increase risk of pneumonia. Investigators have identified several therapeutic measures as important risk factors for nosocomial pneumonia — endotracheal intubation (particularly performed in emergency), long-term mechanical ventilation, thoracic and/or upper abdominal surgery, nasogastric tube placement, recurrent position of the patient, treating patients with antacids or H2 receptor antagonists, antibiotics. Intensivists cannot change patient’s underlying illnesses; however, they may help prevent more severe infections by decreasing unnecessary antibiotic use.

**Preventive measures**

Education of healthcare workers is essential part of the control program. Body position — semirecumbent position may reduce aspiration of oropharyngeal secretions. Oral intubation has been shown to decrease the incidence of VAP and hospital mortality compared with nasal intubation. Reducing the duration of tracheal intubation has been associated with lower rates of VAP. Subglottic secretion drainage may reduce the incidence of nosocomial pneumonia. New techniques are undergoing development to prevent biofilm formation on endotracheal tubes, which have been implicated in the pathogenesis of VAP. Changing ventilator circuits — not every day but in 3- to 7-day intervals. Stress ulcer prophylaxis — agents that do not raise gastric pH are advocated (sucralfate). Selective decontamination of digestive tract (SDD) is matter of discussion. Some investigators have reported an increase in highly antibiotic resistant Gram-negative bacteria, others have noted greater patient colonization with Gram-positive cocci.

**Antibiotic treatment**

The optimal antibiotic treatment of VAP is unknown. In general, when a decision is made to treat VAP, antibiotics with demonstrable in vitro activity against the causative bacteria should be used. Unnecessary antibiotic treatment should be avoided to limit the emergence of resistance. Ibrahim et al. demonstrated that 7 days of antibiotic treatment is as effective as 14 days of treatment in patients with VAP. Several clinical studies have found that anaerobic bacteria are un-
common in the lower airway of patients with VAP or aspiration pneumonia occurring in the hospital setting. This may explain the lack of greater efficacy among antibiotic regimens with intrinsic anaerobic activity for patients with VAP.

Conclusion

Nosocomial pneumonia remains a challenge for intensivists and infection-control team. Many of the factors that increase patient’s risk of pneumonia are unalterable (underlying diseases, age, essential medical procedures), but some of them are preventable. Knowing the risk factors for nosocomial pneumonia may help intensivists prevent future cases. It is possible to reduce pneumonia rates by educating healthcare personnel about the importance of such simple measures as hand washing or body position. Clinicians practicing in the intensive care unit should support the development and routine implementation of interventions aimed at preventing VAP and encouraging rational use of antibiotic therapy.

References


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FREQUENCY OF GRAMNEGATIVE BACTERIAL PATHOGENS IN BLOODSTREAM INFECTIONS IN THE CZECH REPUBLIC

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Aim of the study

To determine the incidence of gramnegative bacterial pathogens in bloodstream infections in the Czech Republic.

Material and methods

The study was organized in twelve hospitals in the Czech Republic in the months June – October, 2001. The criteria for the participation were the location of facilities and their size, so that the study covered the whole area of the country and equal numbers of small and big (university type) hospitals were involved. The length of study was five months. Maximum number of strains from one facility was one hundred successive gramnegative isolates from blood, corresponding to the criteria of choice.

Results

During the period of observation, 831 bacterial strains (i.e. clinical cases) were registered (one strain = one patient with unequivocal bacterial bloodstream infection). In the total, 584 strains (70 %) were isolated in the group of big hospitals, and 247 strains (30 %) in the small hospitals. The most frequently, the strains of Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa were identified as etiologic agents (66 %). The incidence of other bacterial strains was lower than 7 %. A statistically significant difference (p = 0.05) was registered at Escherichia coli strains, the frequency of which was higher by 10 % in the group of small hospitals. As for Acinetobacter sp. strains, their incidence was lower in the small facilities. Stenotrophomonas maltophilia strains were isolated in big hospitals only.

Conclusions

In spite of the increasing incidence of grampositive bacteria (staphylococci and enterococci), gramnegative bacteria are to be considered as very dangerous pathogens causing bloodstream infections, namely in relation to the possibility of endotoxin reaction, more frequent development of sepsis and higher mortality of patients. The results show that among the gramnegative bacterial pathogens, the strains of
**BACTERIAL AND MYCOTIC INFECTIONS AFTER OESOPHAGUS CARCINOMA OPERATIONS**

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**Introduction**

Esophageal carcinoma belongs to the diseases of predominantly unfavourable prognosis. The first symptoms such as difficult or painful swallowing appear relatively late, the disease being already in advanced stage. This neoplasm occurs in elderly patients, tobacco smokers and people with heavy alcohol intake. Alcohol and nicotine are common risk factors which contribute to postoperative complications.

**The purpose of the study**

The aim of the study is to assess an effectiveness of prophylaxis as well as antibacterial and antimycotic treatments in patients of ITD subjected to oesophagus carcinoma operations.

**The subjects studied**

The subjects studied were 31 patients aged 45–76 (59 on the average, 5 female and 26 male) after oesophagus carcinoma operation, treated in ITD of Greatpoland Cancer Center. The ASA of these patients was classified as III. As an indicator of a nourishment condition an albumine content was taken, the standard value of which is >3.5, as well as total number of lymphocyte (c1l) per 1 mm3 of peripheral blood (standard > 1500 mm3). For every patient bacteriological and mycological assays were made by culture method and all were administered preventive antibiotic: Metronidasol 0.5g 3 times a day for 3 days, Biotaxym 1.0g 4 times a day or Netromycyne 0.3g 1 time a day. To patients with clinical or laboratory symptoms of mycosis Diflucan 0.2g 1 time a day was given.

**Results**

In 18 (58%) patients after operative procedures a decrease of the albumine content was observed. In 9 (19%) persons Candida albicans was cultured (also in these with bacterial infections). 12 patients (39%) revealed bacterial infection and in their bacteriological cultures Escheria coli, Staphylococcus epidermidis, Staphylococcus aureus, Staphylococcus auricularis, Staphylococcus warneri, Staphylococcus haemolyticus, Haemophilus parainfluenzae, Streptococcus pyogenes, Enterobacter cloacae, Streptococcus faecalis and Streptococcus agalacti were found. Occurrence of the infection contributed to eventration in 1 (3%) patient. In 3 (9%) patients pneumonia was recognized in spite of intensive motor and respiratory rehabilitation.

**Conclusions**

The patients subjected to operational treatment of esophageal carcinoma showed a decreased lymphocyte number (48%) and albumine content (58%). These developments facilitated the occurrence of mycotic (19%) and bacterial (39%) infections despite the antibiotic prophylaxis and antimycotic treatment.
Conclusion

Bioimpedance measurement can help to estimate the increased distribution volume and clearance in particular of vancomycin in severe sepsis with capillary leak syndrome. The correlation between the ratio ECW/TBW and Vd-area and CI of van and between ECW/TBW and V1 of net represents probably better penetration of van into the tissues in comparison to net. The antibiotics are distributed poorly into the extravascular space and routine treatment may lead to significant overdose. The next steps should be directed towards monitoring of the tissue level of the antibiotics.

Reference


HEMORRHAGIC FEVER WITH RENAL SYNDROME IN THE DOLENJSKA REGION OF SLOVENIA – A 10 YEAR SURVEY

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Authors describe the investigation of clinical findings for larger series of patients with hemorrhagic fever with renal syndrome (HFRS) who were infected with Dobrava virus. From 1985 to 1995, 38 patients with serologically confirmed HFRS were hospitalised at the regional hospital in Novo mesto in the Dolenjska region of Slovenia. On the basis of results of serological examination, 24 patients had Dobrava virus infection, and 14 patients had Puumala virus infection. Complete clinical data were available for 31 patients. Eleven patients underwent hemodialysis for treatment of acute oliguric or anuric renal failure. Four patients, all infected by Dobrava virus, had signs of shock and severe bleeding. Three severely ill Dobrava virus-infected patients died of hemorrhagic complications. We have demonstrated that Dobrava and Puumala virus coexist in a single region of endemicity and are capable of causing HFRS with significant differences in severity.

CRYPTOCOCCUS NEOFORMANS ON ICU – CASE REPORTS

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Cryptococcal infection affects usually immunocompromised patients1–3.

Methods

We reviewed medical records of 3 patients with cryptococcal meningoencephalitis hospitalized during 2000–2001 in 2 different ICUs. 1. Immunocompromised patient 7 weeks after uncomplicated liver transplantation. 2. Nonimmunocompromised patient. 3. Meningoencephalitis after penetrating head trauma.

Results

Lung as the principal route of entry of infection and CNS dissemination was documented in case 2. In case 3 direct entry of cryptococcus into CNS tissue was suspected. Clinical picture of infection varied in our cases, meningeal symptomatology was always present, in two cases changes in gray matter on brain MR images were found. In two patients the disease was diagnosed by microscopic analyse of CSF, in one cryptococcal antigen in CSF was detected. The diagnosis of infection was revealed relatively late in the course of disease and this may explain the fatal outcome in 2 cases.

Conclusion

Cryptococcal meningoencephalitis may occur in immune competent patients. Direct microscopic detection of cryptococcus in CSF may help to reveal the cryptococcal meningitis early in the course of disease and may potentially improve the outcome.

References

ENERGY METABOLISM IN CRITICALLY ILL PATIENTS: LACTATE IS A MAJOR SUBSTRATE

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Lactic acid, which is mostly present in biological fluids as its dissociated cationic form (lactate\(\beta\)), is widely distributed among the pathways involved in the intermediary metabolism of living systems. While, from the physiologist point of view, it is one of the most crucial intermediate of carbohydrate and non-essential aminoacid metabolisms, for most physicians it is merely considered as a marker of bad prognosis significantly related to high mortality rate in acutely ill patients. Although several works in the literature have shown the safety, and sometimes the usefulness, of administration of exogenous lactate, it is very often considered as a highly “toxic” compound. Even in sport physiology the “lactic threshold” as marker demonstrating a sharp switch from aerobic to anaerobic metabolism is very popular and lactate increase is often believed as the cause of side effects observed after exhausting exercise. Of course it is clear that high lactate infusion is actually safe, even in very sick patients, it is indeed a metabolite like glucose, aminoacids, fatty acids or ketones. Nevertheless, lactate is often intuitively considered as “the devil in metabolism” by many physicians or scientists, this resulting probably from confusion between cause and consequence.

Lactate is alternatively consumed and produced in the body, as it is the case for every intermediate involved through the vast circuit of the intercellular and interorgan metabolic interplay. This notion is actually the basis of the concept of “milieu interieur” as described by the French physiologist Claude Bernard more than a century ago. Hence, when released from one cell, lactate can be considered as a waste product, but when taken up by another cell, it becomes a very useful substrate. In fact, the extent of lactate turnover in vivo in man is of similar order of magnitude than that of glucose, alanine or glutamine, i.e. it is amongst the highest recycling rates in intermediary metabolism. Therefore, the main question remains as to understand precisely the role of lactate as one of the main actors of the energetic homeostasis in both physiological and pathological conditions.

Lactate is actually a metabolic “cul de sac” because it is metabolized by one single enzyme, lactate dehydrogenase. But, since the first description many decades ago by Cori, of an interorgan glucose-lactate recycling, it is clear that lactate has a real physiological meaning. The role energetic shuttle is classically considered between organs responsible for a net lactate release and the liver. Every organ is able to release lactate since all cells do contain the different enzymes allowing the conversion of glucose into lactate, pancreatic \(\beta\)-islets is an exceptional since they are deficient in lactate dehydrogenase. However quantitatively, muscle and red blood cells are probably the main tissues in physiological conditions other organs, as the lung for instance, could be of importance in pathological states. If the liver is often regarded as main organ for lactate disposal because of its prominent role in the gluconeogenesis, the kidney, although recognized for a long time as gluconeogenic organ as well, has been probably underestimated. Moreover, it was recently shown that even during the anhe-
leaving large amount of amino acids into the circulating pool for distribution to the liver, intestine, bone marrow, and injured or healing tissues. Enteral nutrition (EN) is the currently recommended technique of artificial nutrition in critically ill patients. EN has many advantages over parenteral nutrition such as maintenance of gut mucosal barrier function, reduction of incidence of nosocomial infection, better tolerance to carbohydrates, and reduced systemic inflammatory response (SIRS) to inflammation or infection. Hepatosplanchic region (gastrointestinal tract and liver) plays pivotal role in the pathophysiology and pathogenesis of shock states. EN activates a series of physiological responses involving the digestive, cardiovascular, respiratory and immune systems. Progress in intensive care has allowed prolonged survival of patients suffering from protracted catabolic disease such as sustained sepsis and multiple organ dysfunction (MODS). Hence, severe malnutrition, slowing down recovery and increasing ICU and hospital stay, is often present in such patients. A growing body of evidence suggests that, in the presence of a functional gut, nutrition should be administered by the enteral route whenever possible (concept of early enteral nutrition is to start during 48 hours after admission). Indeed, it is becoming increasingly clear that the consequences of enteral nutrition (EN) go beyond the supply of energy and proteins to the body, other beneficial effects including modulation of the host’s immune response and the provision of fuel and protein to maintain gut integrity and possibly prevent bacterial translocation. In healthy subjects the digestion and absorption of nutrients induce typical hemodynamic changes, consisting of an increase in both cardiac output and mesenteric blood flow. The timing of initiation and the dose of EEN in circulatory compromised patients is a matter of controversy. In terminal cardiac failure the decreased cardiac output leads to splanchnic hypoperfusion and malnutrition, the so-called cardiac cachexia. The purpose of this review is to focus on the assessment of the early systemic and splanchnic hemodynamic and metabolic changes in conjunction with EEN.

Rationale for enteral nutrition

Nutritional support for critically ill patients should be considered as an integral component of treatment.

Decisive factors for commencing of nutritional support

1. Route of feeding
2. Timing
3. Composition of feeding
4. Amount of feeding
5. The way of delivery (continuous vs. bolus)

The concept, that early enteral feeding should be preferred, whenever possible is gaining growing acceptance. During last two decades nutritional support has emerged as a vital component of the management of critically patients.

The hazards of parenteral nutrition compared to enteral nutrition

1. Immune compromise
2. Increased rate of infections
3. Overfeeding
4. Increase length of stay
5. Costs

Indeed, complete bypass of the gut leads to adverse structural and functional modifications of the mucosal barrier, which can be reversed by enteral feeding. This favourable effect stems from factors such as the stimulation of epithelial cell metabolism by direct contact with nutrients, increased in mucosal blood flow, and secretion of enterotrophic gastrointestinal hormones such as gastrin and enteroglucagon. Preventing mucosal atrophy is certainly an important goal, as animal studies indicate that the associated increase in gut permeability can induce translocation of bacteria from the gut lumen to the circulation, although there is no evident and convincing proof of such an occurrence in critically ill patients. Many critically ill, injured, and post-operative patients develop gastroparesis with abnormalities in intestinal motility. This phenomenon is responsible for limitation of ability to tolerate gastric feeding. However, it is now recognized that small bowel function and the ability to absorb nutrients remains intact, despite critical illness and the presence of gastroparesis. In patients with intolerance of gastric feeding is possible to introduce the post pyloric feeding. It has been suggested that EEN may reduce septic and non-septic complications.

Failure of gut barrier

Failure of the gut barrier function after injury may result in increased intestinal permeability with the risk of bacterial and endotoxin translocation as has been showed in both animal and human studies. An increase in intestinal permeability has been shown in patients with severe injuries and burns, ischemia – reperfusion, after cardiac surgery, and in those receiving only parenteral nutrition. EEN decreased intestinal permeability in some groups of critically ill. Pape studied gut permeability in multiply injured patients with respect to the development of multiple organ failure (MOF). Two groups were defined according to MOF score (threshold 10 points) as to whether MOF developed (group 1; n = 11, four deaths) or did not (group 2; n = 21, no death). Gut permeability was determined from the ratio of urinary excretion of enterally administered lactulose and mannitol. Serum elastase concentrations were also determined. Gut permeability was abnormal during the entire study. Severe injury led to increased intestinal permeability, which was related to a systemic inflammatory response. Roumen has shown in patients after elective or emergency aortic aneurysm repair a significant increase in intestinal permeability by a dual sugar absorption test, with lactulose and mannitol as markers. It has been suggested that this is mainly due to reperfusion injury rather than the ischemic period of the intestine itself. Hadfield reported the study comparing the effects of TPN and EN on GIT function. Twenty-four critically ill patients were randomly allocated to receive TPN or EN. The ratio between urinary recovery of lactulose and L-rhamnose (L/R) was used to measure GIT mucosal permeability. In the EN group, the L/R ratio displayed a progressive, significant fall. In the TPN group, no significant change in the L/R ratio occurred. This study demonstrated that GIT dysfunction is evident in critically ill patients and suggested that loss of GIT mucosal integrity is reversed by the institution of EN. As Fink pointed out that a variety of pre-mucosal and post-mucosal factors might influence the urinary excretion of an enterally administered probe (e.g. intestinal transit time, glomerular filtration rate). Clinical tests of gastrointestinal permeability that rely on the urinary recovery of enterally administered probes can yield invalid results in critically ill patients. Adams has proven that hemorrhagic shock-induced lung injury depends on gut injury and mesenteric lymph appears to be the route by which gut-derived toxic factors exit the gut to cause lung injury. Endothelial cell injury by polymorphonuclear neutrophils respiratory burst after trauma and hemorrhagic shock predisposes subjects to acute respiratory distress syndrome and multiple organ failure. In animal model mesenteric lymph injured endothelial cell and lymph duct ligation before trauma or hemorrhagic shock prevented pulmonary injury. Mesenteric lymph mediates post shock PMN dysfunction.
Translocation in human subjects

Translocation as a pathogenic mechanism is well established, but still the number of publications actually demonstrating this mechanism in human subjects is few. The classic publication demonstrates a prevalence of 5% in patients without distal intestinal obstruction or inflammatory bowel disease undergoing explorative laparotomy. A relationship is also described between translocation, in patients undergoing laparotomy, and the risk of developing postoperative complications. In patients with distal intestinal obstruction or with inflammatory bowel disease the incidence is higher. In neonates the immature intestine probably allows for translocation. At least, there is evidence that translocation and septicaemia occurs in infants requiring long-term parenteral nutrition. Also in intestinal transplantation there are a number of risk factors involved, which makes translocation a highly likely event. Evidence of intestinal transplantation in children suggests a higher incidence in particular involving bacterial species from the intestinal tract. However, there is another publication demonstrating a prevalence of 5% in patients without distal intestinal obstruction or inflammatory bowel disease undergoing explorative laparotomy. A relationship is also described between translocation, in patients undergoing laparotomy, and the risk of developing postoperative complications. In patients with distal intestinal obstruction or with inflammatory bowel disease the incidence is higher. In neonates the immature intestine probably allows for translocation. At least, there is evidence that translocation and septicaemia occurs in infants requiring long-term parenteral nutrition. Also in intestinal transplantation there are a number of risk factors involved, which makes translocation a highly likely event. Evidence of intestinal transplantation in children suggests a higher incidence in particular involving bacterial species from the intestinal tract.

Translocation and nutrition

There is a considerable amount of data from humans showing that patients who could not be provided nutrition by the enteral route have more organ failures in the intensive care unit, have a less favourable prognosis and have a higher frequency of septicaemia, in particular involving bacterial species from the intestinal tract. However, there is little evidence that this is connected with translocation or bacterial species in humans. When interpreting studies comparing enteral and parenteral nutrition one must keep in mind that failure to provide nutrition by the enteral route in many cases is related to an impaired intestinal function due to the underlying disease. Therefore, in many studies comparing enteral and parenteral nutrition, the underlying disease may contribute, to a substantial degree, to the prevalence of translocation. There is considerable evidence that bacteria of enteral origin are present in the blood, but their way into the blood is not well described. Furthermore, as pointed out in two recent overviews the evidence that parenteral nutrition in itself is associated with bacterial translocation in man is weak. Animal studies have shown that long-term total parenteral nutrition leads to intestinal mucosal atrophy, however, this contrasts with human studies in which this relationship is less clear. Furthermore, there is very little documentation from humans to support the hypothesis that enteral nutrition inhibits translocation. Also, animal data are not convincing. The high incidence of sepsis from gut origin in premature neonates is suggested to be reduced by parenteral or enteral nutrition containing a high concentration of glutamine.

Risk of early enteral nutrition

Controversy persists as to the optimal means of providing nutritional support. The aim of MacFie’s study was to compare enteral nutrition (EN) and parenteral nutrition (TPN) in terms of adequacy of nutritional intake, septic and no septic morbidity, and mortality. This was a prospective pragmatic study, whereby the route of delivery of nutritional support was determined by the attending clinician’s assessment of gastrointestinal function. Patients considered to have inadequate gastrointestinal function were given TPN (group 1), while those deemed to have a functioning gastrointestinal tract received EN (group 2). Patients in whom there was reasonable doubt as to the adequacy of intestinal function were randomised to receive either TPN (group 3) or EN (group 4). A total of 562 patients were included in the study. Gastrointestinal function on entry into the study was considered inadequate in 267 patients who were given TPN (group 1) and adequate in 231 whom received EN (group 2). There was clinical uncertainty about the adequacy of gut function in 64 patients (11.4%) who were randomised to receive either TPN (group 3, 32 patients) or EN (group 4, 32 patients). The incidence of inadequate nutritional intake was significantly higher in group 4 compared with group 3 (78% versus 25%). Complications related to the delivery system and other feed-related morbidity were significantly more frequent in both EN groups compared with the respective TPN groups. EN was associated with a higher overall mortality in both nonrandomised and randomised patients. There were no significant differences observed in the incidences of septic morbidity between patients receiving TPN and those given EN. EN was associated with a higher incidence of inadequate nutritional intake, complications related to the delivery system, and other feed-related morbidity than TPN. There is no evidence from this study to support a difference between the two modalities in terms of septic morbidity.

EEN is contraindicated

**Absolute**
1. Non functional gut: anatomic disruption, obstruction, gut ischemia, toxic megacolon
2. Generalized peritonitis
3. Severe shock states

**Relative**
1. Expected short period of fast, except in severely injured patients
2. Abdominal distension during EN
3. Localised peritonitis, intraabdominal abscess, severe pancreatitis
4. Patients with terminal disease
5. Extremely short bowel (less than 30 cm)

There is clinical consensus that severe hemodynamic instability is a contraindication to EN, based on the hypothesis that feeding the hypoperfused gut might result in worsening of gut ischemia. The main weak point of this hypothesis is how to define hemodynamic instability. Revelly assessed the hemodynamic and metabolic adaptations to EN in patients with hemodynamic compromise. This prospective study compared fasted with continuous EN condition. Nine patients requiring hemodynamic support by catecholamines (dobutamine and/or norepinephrine) 1 day after cardiac surgery under cardiopulmonary bypass were enrolled. Isoenergetic EN via a postpyloric tube while catecholamine treatment remained constant. Baseline (fasted) condition was compared to continuous EN condition. The introduction of EN in these postoperative patients increased cardiac output and splanchnic blood flow, while the metabolic response indicated that nutrients were utilized. These preliminary results suggest that the hemodynamic response to early EN may be adequate after cardiac surgery even in patients requiring inotropes. Rokya studied the influence of low dose postpyloric EEN on hepatosplanchnic perfusion and energy metabolism in medical critically ill patients with severe sepsis and/or septic shock (8 mechanically ventilated). In our study was concluded that the initiation of low dose postpyloric EN in septic patients requiring low dose norepinephrine does not compromise hepatosplanchnic blood flow. On the other side early high calorie enteral feeding might lead to a mismatch between oxygen delivery and oxygen consumption of the intestine. EN generates a dose and substrate dependent increase on intestinal oxygen consumption whereas overall organ perfusion is markedly diminished.

Functional intestinal complaints occur frequently but generally respond to alteration of the infusion rate or tube feeding formula. Occasionally,
however, non-specific signs of intestinal disturbance progress to a syndrome of abdominal distension, hypotension, and hypovolemic shock resulting in extensive small bowel necrosis. Schunn has reported that small bowel necrosis is a rare but highly morbid complication associated with postoperative jejunal tube feeding. Early high calorie enteral feeding might lead to a mismatch between oxygen delivery and oxygen consumption of the intestine. Kies tested the hypothesis in a rat model that delivery of enteral nutrients to the hypoperfused jejunum increases oxidative demand beyond that available, thereby exacerbating intestinal hypoxia. The results indicated that provision of metabolizable nutrients to the hypoperfused intestine exacerbates hypoxia and potentially leads to intestinal ischemia. Tappenden proved in rat model that the provision of luminal nutrients exacerbates the loss of gastrointestinal barrier function during hypoxia. Although early enteral nutrition is an important intervention after trauma, care must be taken to ensure adequate intestinal perfusion. Nonocclusive bowel necrosis (NOBN) is a rare, but potentially fatal complication, related to EN in acutely stressed patients. Marvin showed that NOBN developed in 0.3% of trauma patients. Onset occurred in the second week in patients who have had a period of EN tolerance. Clinical findings resembled bacterial sepsis with tachycardia, fever, and leukocytosis. Gastrointestinal specific signs were not consistent or occurred late. Gastric carbon dioxide tonometry occurred in the second week in patients who have had a period of EN tolerance. Clinical findings resembled bacterial sepsis with tachycardia, fever, and leukocytosis. Gastrointestinal specific signs were not consistent or occurred late. Gastric carbon dioxide tonometry may detect a vulnerable subgroup of patients. There are 3 major components, which could explain aetiology of NOBN (fig. 1):

1. Metabolic stress
2. Dysmotility of intestine
3. Dysmicrobia with bacterial colonization

**Methods to treat or prevent gut ischemia/reperfusion injury**

The main task at the beginning of treatment is to reach hemodynamic stability and restore adequate perfusion on regional level as soon as possible. Microcirculatory recruitment is crucial for the fate of critically ill. The first step in the therapeutic management (volume resuscitation) is followed by ischemia/reperfusion injury. Mechanisms of injury are not so far fully explained. It has been proposed i.e. damage from oxygen free radicals, neutrophil-derived enzymes, platelet-activating factor, and protein kinase C and/or mucosal cell dysfunction caused by cytokines or lipid mediators. Treatments tend to focus on minimizing injury by reducing the duration or severity of the ischemic event. There are two principle routes how to treat the effects of ischemia/reperfusion injury:

**Intravenous route**

Intravenous treatment is familiar for intensivists. Pyruvate has been shown to be protective in numerous in vitro and in vivo models of oxidant-mediated cellular or organ system injury. In an effort to take advantage of the ability of pyruvate to scavenge reactive oxygen species while avoiding the problems associated with the instability of pyruvate in solution. Sims has used a simple derivative, ethyl pyruvate and assessed in animal model if ethylpyruvate would be protective. Treatment of rats with either pyruvate solution or ethylpyruvate solution significantly alleviated the development of intestinal mucosal hyperpermeability during the reperfusion. Treatment with ethyl pyruvate solution also significantly decreased the extent of histological mucosal damage after mesenteric reperfusion. Additional approaches have included hypothermia, prostaglandin E and pharmacological modulation of blood flow by using diltiazem, nitric oxide donors (arginine), or angiotensin-converting enzyme inhibition. Sympathetic and angiotensinergic activation reduce splanchnic oxygen delivery during hypovolemia, which may lead to failure of the intestinal mucosal barrier. Hypovolemia preferentially increased mesentery sympathetic outflow and caused vigorous angiotensinergic activation. Aneman demonstrated that treatment with enalapril prevented the reduction of mesenteric oxygenation and duodenal mucosal alkaline secretion in pig model. Von Ritter has showed the effects of several free radical scavengers and antioxidant enzymes on neutrophil-mediated changes in mucosal permeability. Manganese-loaded desferrioxamine (a superoxide dismutase mimetic), PZS1 (a glutathione peroxidase analogue), desferrioxamine (an iron chelator), or dimethylsulfoxide (a hydroxyl radical scavenger) significantly attenuated mucosal damage. The results of the study indicated that neutrophilic oxidants are responsible for a major portion of the mucosal permeability changes. Xia has studied superoxide dismutase (a free-oxygen radical scavenger), leupeptin (a protease inhibitor) and verapamil to evaluate their efficacy in maintaining cellular integrity in the gut of thermally burned rats whose fluid resuscitation had been delayed. Data indicated that intestinal reperfusion injury in burned rats could be effectively modulated with superoxide dismutase or leupeptin therapy. Intravenous administration of a total parenteral nutrition (TPN) solution results in small intestinal gut-associated lymphoid tissue (GALT) atrophy, lowers small intestinal immunoglobulin A (IgA) levels, and impairs upper respiratory tract secretory IgA-mediated mucosal immunity. Kudsk demonstrated that addition of 2% glutamine, a specific lymphocyte fuel, prevents deleterious effects of TPN on gut-associated lymphoid tissue and IgA while preserving IgA-mediated upper respiratory immunity to influenza virus and preserves respiratory immunity and improves survival to a Pseudomonas pneumonia.

**Intraluminal route**

Intraluminal treatments also have shown promise. These approaches have several advantages including delivery of the active agent directly to the mucosal cells. Maintenance of gut barrier function and integrity is essential in preventing the translocation of bacteria and endotoxin into the portal circulation and mesenteric lymphatics. In addition, intraluminal therapy may be delivered at concentration higher than that tolerated in the circulation with fewer systemic side effects. Intraluminal sodium pyruvate decreased mucosal injury. Schleiffer has proved that intraluminal L-arginine decreased reperfusion injury and this phenomenon was explained by increasing blood flow through a nitric oxide-mediated mechanism. Multiple human and experimental studies emphasized the importance of enteral feeding in treating the effects of ischemic gut injury including different specialised formulas of immunomodulation enteral diet. Marik and Zaloga in their meta-analysis con-
firmed that EEN was associated with a significantly lower incidence of infections and a reduced length of hospital stay. There were no significant differences in mortality or non-infectious complications between the two groups of patients. Caparros demonstrated that critically ill patients fed a high-protein diet enriched with arginine, fibre, and antioxidants had a significantly lower catheter-related sepsis rate than patients fed a standard high-protein diet. There were no differences in mortality or ICU and hospital length of stay.

Monitoring of enteral nutrition

Introduction of feeding protocol is cost-effective and improves nutritional parameters as well as outcome. Tolerance of EN should be monitored and the most often method is measurement of gastric aspirate volume. A gastric aspirate volume of 150 ml after 6 hours is considered to be safe. No evidence – based recommendations can be made on which prokinetic agent is to be preferred. Cisapride, metoclopramide, and erythromycin are all effective in promoting gastric emptying in critically ill. Postpyloric feeding should be considered in cases of intragastric intolerance despite prokinetic agents. Endoscopic placement is most reliable. NOBN is an unusual complication in ICU patients. Most of cases occurred in patients where enteral nutrition was started in a delayed fashion, and full-dose EN was tolerated for several days prior to the development of NOBN. The type of enteral formula could play a role. Mostly patients with NOBN received a polymeric diet. Some as a safer alternative in these patients has proposed TPN.

Conclusion

Present evidence strongly suggests that, in ICU patients, enteral nutrition should be preferred to parenteral nutrition whenever possible, due to its favourable trophic effects on the intestinal mucosa, reduced rate of complications and lower costs. Data is slowly accumulating that in some patients a reduced rate of complications and length of hospital stay can result from the use of immunomodulating enteral formulas, but further studies into this promising development should be performed before their widespread can be recommended. But EN generates complications either related to mechanical or to metabolic effects. Abdominal pain, nausea, vomiting and diarrhoea following enteral feeds infusion may occur, especially when infusion rate is greater than 50 ml/hour. There is necessary to stress the fact, that early enteral nutrition can have also complications. The most serious complication is nonocclusive bowel necrosis. The onset occurs in the second week in high-acuity patients who have had a period of EN tolerance. Clinical findings resemble bacterial sepsis with tachycardia, fever, and leukocytosis. Gastrointestinal specific signs are not consistent or occur late.

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References

CONTINUOUS HEMOFILTRATION AS A TOOL FOR CONTROL OF HOMEOSTASIS: RENAL SUPPORT OR RENAL REPLACEMENT?

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No abstract available.

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CATHETER RELATED SEPSIS AND METABOLIC COMPLICATIONS IN TPN PATIENTS

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No abstract available.

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EFFECTS OF EARLY POSTPYLORIC ENTERAL NUTRITION ON HEPATOSPLANCHNIC HEMODYNAMICS AND METABOLISM IN SEVERE SEPSIS


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Introduction

The administration of enteral nutrition (EN) during states of acute stress and/or circulatory compromise is controversial due to the possible onset of the imbalance between the hepatosplanchnic oxygen and/or energy demand and supply. Recently, the "adequate" central and splanchnic hemodynamic responses to isonenergetic EN have been demonstrated in post-cardiac surgery patients requiring inotropes and/or vasopressors [1]. However, there are no such data in critically ill septic patients. Therefore, we studied the effects of early EN on hepatosplanchnic hemodynamics and metabolism in patients with severe sepsis.

Methods

Eight mechanically ventilated medical ICU patients (mean age 64 ± 10 years) fulfilling the following criteria were studied: (1) severe sepsis or septic shock (2) no enteral feeding before the study. Data were collected at the fasting state (BL1; 90 min of stable hemodynamics), after 120 min of postpyloric EN (EN; 40 ml bolus, then 40 ml/h continuously; Survimed®), and 120 min after EN-cessation (BL2). In addition to systemic hemodynamics (arterial and PA catheters), arterial and hepatic venous (HV) blood gases, lactate (L), pyruvate (P) and glucose levels were measured. Hepatosplanchnic blood flow (HSBF, steady state indocyanine green technique) was estimated using hepatic vein catheter. Gastric mucosal PCO₂ (PgCO₂) was determined by air tonometry (Tonocap) and gastric mucosal to arterial PCO₂ difference (PCO₂ gap) was calculated.

Results

All patients remained stable over the study with no change in norepinephrine dose (6 patients, mean dose 0.2 ± 0.4 μg/kg/min). Data are median, 25th and 75th percentiles (RM ANOVA on ranks, Dunn's test, p < 0.05, *EN vs BL1, *BL2 vs EN).
Conclusion

Our data show that the administration of low dose postpyloric enteral nutrition in medical ICU patients with severe sepsis and/or septic shock leads to the parallel increase of systemic and hepatosplanchnic blood flow. In addition, neither total hepatosplanchnic nor gastric mucosal energy balance deteriorated during enteral feeding. These results suggest that the initiation of low dose postpyloric enteral nutrition may not be harmful even in septic patients requiring norepinephrine.

References


Acknowledgement

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MONITORING OF THE RESIDUAL RENAL FUNCTIONS DURING CONTINUOUS RENAL REPLACEMENT THERAPY – THE APPLICATION OF THE ANALYSIS OF CYSTATIN C AND NATRIURETIC PEPTIDES

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Introduction

The reason for the decrease of urine output (Vu) following the start of continuous venovenous hemodiafiltration (CVVHDF) has not been clarified yet. The renoprotective properties of atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) were described. The sensitive marker of glomerular filtration is cystatin C (cysC).

Methods

ANP levels (normal < 14 pmol/l) and BNP levels (normal < 5.3 pmol/l) were analysed in 13 and cysC levels (normal < 0.99 mg/l) were analysed in 16 ventilated patients, all treated with CVVHDF (blood flow 120 ml/min, dialysis 1000 ml/h, hemofiltration 500 ml/h). Creatinine clearance (Ccr) was monitored before therapy. Samples were drawn before and after 24 h and 48 h of CVVHDF both from the ports proximal and distal to the filter. Arteriovenous concentration differences (A-Vdiff.) reflecting sieving, adsorption or both were calculated. Furosemide was reduced to 1 mg/kg.day after commencing of CVVHDF. Left ventricular dysfunction (LVD) was defined as LV ejection fraction below 40%. Patients were divided according to the Vu after 48h of treatment into the groups with Vu < 3000 ml/24 h and groups which retained Vu > 3000 ml/24 h.

Results

The levels of ANP were significantly higher in the group with decreasing diuresis (48.66–26.83 pmol/l, n = 5, Vu 930+/–1245 ml/24h) than in the group with increasing diuresis (13.79–8.96 pmol/l, n=8, Vu 4998.8+/–1260 ml/24 h, p < 0.004). Similar difference was found for BNP: (267.86–356.22 vs 111.0–100.85, p<0.01). Levels of both peptides were grossly elevated in comparison to controls (n=10, p<0.0001). The significant correlations were revealed for ANP and Vu (r=–0.40, p<0.02) and for BNP and Vu (r=–0.43, p<0.007). Ccr measured before the therapy was not different between the groups. Average AVdiff (%) of ANP was –3.68+/–48.72 and of BNP was –4.04+/–23.68. The differences between cardiac and non-cardiac patients did not reach significance either for ANP or for BNP. The levels of both peptides predicted survival (BNP 114.24+/–143.81 vs 278.47+/–287.18 (p<0.005) of non-survivors, ANP 11.34+/–16.34 vs 29.57+/–19.90 (p<0.0002) of non-survivors). There were 7 patients with increasing diuresis (average 4857.1+/–1460 ml/24h) in the cysC study, in 9 patients the volume of urine decreased (average 546.7+/–945 ml/24h). Ccr taken before treatment was not different between the groups. Average AVdiff (%) of cysC was +5.73+/–15.57. Significant correlation between cysC and Vu was found in particular for the cysC levels below 4.0 mg/l (r=–0.76, p<0.002). cysC levels were significantly higher in nonsurvivors (3.67+/–1.29 vs 2.77+/–1.10, p < 0.002).

Conclusions

The elimination of cysC, ANP and BNP by the CVVHDF is negligible. The levels of cysC and natriuretic peptides are inversely related to Vu. Whether cysC could be used as an indicator of succesful weaning from CVVHDF needs to be confirmed by further study. The levels of cysC, ANP and BNP levels predict survival of patients treated with CVVHDF. ANP and BNP levels did not correlate with LVD which may be caused by their elevation due to renal failure.
Background

Acute renal failure (ARF) requiring renal replacement therapy (RRT) occurs in the postoperative period and is an important risk factor for an early mortality. The purpose of this study was to assess the incidence of ARF, to determine whether there is an association of ARF with the type of surgery and to give some characteristics of the patients requiring RRT after cardiac surgery.

Patients and methods

One thousand patients who underwent coronary artery bypass grafting (CABG) or valve surgery with or without bypass grafting from May 2000 to December 2001 were evaluated to determine the association between ARF sufficient to require RRT and operative mortality, with and without adjustment for comorbidity – preoperative renal function, presence of diabetes.

Results

A total of 823 of the 1000 patients underwent isolated CABG surgery, the remaining 177 patients underwent valve surgery with or without bypass grafting from May 2000 to December 2001 were evaluated to determine the association between ARF sufficient to require RRT and operative mortality, with and without adjustment for comorbidity – preoperative renal function, presence of diabetes.

Conclusion

The development of ARF requiring RRT is associated with a high mortality following cardiac surgery. We have described perioperative variables, which may be useful in stratifying risk for the development of ARF and mortality.

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LOW URINE OUTPUT IN ACUTE RENAL DYSFUNCTION DIAGNOSIS IN LONG TERM ICU PATIENTS

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Introduction

Low urine output (UO) has been recently suggested to define acute renal dysfunction/failure (ARI/ARFS) in addition to urea/creatinine levels. We tested how inclusion of UO would change the incidence of ARI/ARFS in long term ICU patients.

Methods

Medical records of long term ICU patients (> 3 days) hospitalised in 2000 were analysed for UO and urea/creatinine levels on daily basis for the whole ICU stay. Furosemide medication was also recorded. Values given as means ± SD (range).

Results

Out of 189 admissions in 2000, 90 patients (62 males, 28 females) were hospitalised > 3 days. Medical records of 84 patients were available for analysis (age of 59 years (16–85), APACHE II on admission 25.4 ± 7.7). Altogether 1196 ICU days were analysed. Thirty nine ICU days when 7 patients required renal replacement therapies were recorded. Out of remaining 1157 ICU days complete data set (i. e. urine output, urea and creatinine levels) was obtained in 340 cases because creatinine was not performed on daily basis. Based on renal metabolites, ARI/ARFS was present on 62 ICU days (18.2%). Inclusion of UO led to 14 additional ICU days of ARI/ARFS. In all but one patient an episode with low UO was recorded when no furosemide was given.

Conclusion

When diuretics are not given, inclusion of low urine output into an acute renal dysfunction definition increases the number of ARI/ARFS patients.

Reference

HAEMORRHAGIC HYPOVOLEMIA AND SOME OF ITS MARKERS IN EXPERIMENTAL AND CLINICAL MEDICINE

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The most expressive clinical signs of the first phase of haemorrhagic hypovolaemia are: hypotension, tachycardia, tachypnoe and rapid re-organisation of the energy-producing metabolic system. Clinical useful markers for assessing the quantity of blood and state of patient are still and widely discussed. The aim of this study was to define some clinically useful markers of the phase of blood loss by comparing some variables immediately after experimental blood loss at experimental animals in patients with haemorrhagic shock at the Department of anaesthesiology and intensive medicine.

Methods

The acute experiments were performed on 20 cats, anaesthetized by pentobarbital, applied intraperitoneally (40 mg/kg). Haemorrhagic hypovolaemia was induced by removal of 20–30 % of the blood volume. The clinical group consisted of 12 patients in the intensive care unit, mostly some hours after bleeding and therapy. We assess such variables as blood pressure, heart rate, breathing, arterial and venous blood gases, arterial lactate concentration, some haematological variables and blood glucose level. In patients the parameters of internal environment were analysed from capillary blood samples.

Results

In experimental animals immediately after the blood loss (up to 30 %) there was paradox of metabolic acidosis with hypoxemia in venous blood and signs of respiratory alkalasia in arterial blood together with significant increasing of number of erythrocytes, leucocytes, haematocrit ratio, concentration of haemoglobin, lactate and glucose level. There were nearly normal blood pressure with tachycardia, in capillary blood signs of metabolic acidosis, signs of haemodilution and significant increasing of number of leucocytes and concentration of blood glucose in patients few hours after the bleeding and therapy.

Conclusion

Our findings in experimental animals compared with those in patients account for the fact that in the first phase of haemorrhagic hypovolaemia venous blood most accurately reflects the acid base state, and as the markers could be better to use arterio-venous differences of pH, pO2, pCO2, lactate concentration as well as leukocyte count and blood glucose concentration.

References


FLUID AND ELECTROLYTE DISTURBANCE RESULTING IN TONIC-CLONIC SEIZURES, RESPIRATORY AND RENAL FAILURE (A CASE REPORT)

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The case of a man aged 31 is reported, who was admitted to hospital, having lost consciousness after a few days’ history of coughing, having temperature, hicups and vomiting. After admission two grand mal type epileptic seizures had been observed, and he lapsed into a coma. Investigations concerning his physical and neurological status, the laboratory analysis of the cerebrospinal fluid, the chest x-ray and abdominal ultrason scan did not reveal any abnormality. According to the CT scan, a slight cerebral oedema was present. His blood tests showed considerable hyponatraemia, hypochloraemia, hypokalaemia and azotaemia. The blood gas analysis indicated a marked metabolic alkalosis, hypercapnia and hypoxaemia. In his longer-term history a sutured duodenal perforation was known. Following admission to the ICU the patient was intubated, mechanical ventilation was commenced and he received sodium and potassium supplementation and antibiotic. An excessive amount of gastric contents drained through the gastric tube. After 24 hours of treatment the serum Na+, K+ and Cl– concentrations returned to the normal range, he gradually regained consciousness and was extubated, subsequently receiving oxygen through a face mask, although the metabolic alkalosis and hypercapnia still persisted until the end of the third day. Urine output improved, the azotaemia gradually ceased. On the third day the clinical and radiological symptoms of pneumonia appeared on the left side, which responded to the treatment employed within a week. The gastroscopy performed on the fourth day showed a deformed, oedematous, eroded bulbus duodeni with a constricted lumen, it stated stenosis duodeni and suggested that it required surgical intervention later.

We considered this case worthy to be reported because of the severe fluid and electrolyte disturbance leading to a derangement of consciousness, seizures, respiratory and renal failure.
THE DIAGNOSIS AND THERAPY OF HEPARIN INDUCED THROMBOTIC THROMBOCYTOPENIA SYNDROME IN A CZECH GENERAL ICU

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Objective

HITTS is a allergic drug reaction with consequent thrombocytopenia and thrombosis. Up to 2.7–3.0% of patients receiving unfractionated heparin (UFH) develop HITTS. Thrombocytopenia is severe in type II, disease often associates with DIC, thrombosis or embolisations.

Methods

The laboratory diagnosis can be made by the antigen assays (ELISA). Functional assays exploit the ability of HIT-Ig to activate platelets. The results of serotonin release assay (SRA) may confirm or exclude the initial diagnosis made by the antigen assays. We developed method to measure radioactive serotonin release in HITTS sera by high performance liquid chromatography (HPLC) – fluorimetric detection. Patients who developed thrombocytopenia during UFH therapy were tested for antigen ELISA assay and functional SRA with HPLC detection.

Results

The authors present two case studies:

Case I: Patient was admitted for multiple trauma including thoracic, spinal and pelvic trauma. CVVHDF with heparin anticoagulation was initiated on the 4th day, there was gradual trombocyte drop, repeated transfusion requirements, perirenal hematoma progression, repeated GIT bleeding. The epoprostenol anticoagulation was started, and later the patient was switched to citrate anticoagulation. All the tests for HITTS were highly positive. On the 34th day the antiagregation with aspirin was started. The patient was weaned from ventilator and on 50th day transferred to nephrology dept. for nonheparin IHD.

Case II: Patient suffered multiple trauma in Bayern quickly developing bronchopneumonia, sepsis, renal insufficiency and thrombocytopenia. The heparin antibodies were detected. The fall of trombocyte count stopped on hirudin. On the 4th day the patient was moved to our ICU. For sings of septic activation of coagulation and impossibility of hirudin administration the refugium ultimum therapy with reviparin was initiated. Trombocyte level gradually raised to 200th/uL on the 8th day. Patient was extubated and discharged on the 20th day.

Discussion

The only choice of treatment in Czech Republic up to now was to try LMWH or antiaggregation therapy with aspirin which puts a patient at risk of bleeding. Recently lepirudin (Refludan) was registered, another choice would be danaparoid. One patient was succesfully treated with reviparin and the question is thus the validity of the used diagnostic testing for HITTS. The anticoagulation of choice for the patients indicated to CRRRT seems to be citrate. Prostacyclin (epoprostenol) may be used safely but it has not been registered in Czech Republic yet.
ARGININE VASOPRESSIN IN VASODILATORY SHOCK
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We report on physiological and pharmacological aspects of arginine vasopressin (AVP), and summarize current clinical knowledge with a continuous AVP infusion in critically ill patients suffering from catecholamine-resistant vasodilatory shock of different etiologies. During the last years, several investigations impressively demonstrated that AVP can successfully stabilize hemodynamics even in advanced vasodilatory shock. In view of presented experimental evidence and current clinical experience, a continuous AVP infusion (1–4 Uxh–1) can be considered as a supplement to vasopressor catecholamines in order to preserve cardiocirculatory homeostasis in advanced vasodilatory shock. Because data on adverse side effects are still limited, AVP should be reserved for patients in whom adequate hemodynamic stabilization cannot be achieved with conventional vasopressor therapy, or obvious side effects of catecholamines promote further significant hemodynamic deterioration. For the same reasons, AVP should not be used as a single, alternative vasopressor agent instead of catecholamine vasopressors. Future prospective studies will be necessary to define the exact role of AVP in the therapy of vasodilatory shock.

HEMODYNAMIC GOALS IN SEPTIC SHOCK
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Introduction
Septic shock is characterized by hypotension, usually accompanied by signs of altered tissue perfusion as an oliguria, reduced capillary refill and altered consciousness. During sepsis, organ perfusion should be restored as a first and most important goal of any therapeutic approach.

Major goals of therapy
- Restoring organ perfusion, normalization of cellular metabolism and therefore reversal organ dysfunction
- Adequate cardiac filling

Fluids
Key points
- Septic shock is associated with hypovolemia (absolute and relative)
- Fluids should be the first step in restoring organ perfusion
- Giving fluids should be titrated to the clinical and hemodynamic endpoints
- There is a ongoing controversy regarding the choice of “best fluid strategy”
- Colloids and crystalloids are equal in restoring tissue perfusion, however the larger amount of crystalloids (approx. twice to four times) is required compared to colloids
- Colloids may be preferred due to more rapid effect on restoring or increasing plasma volume.
- There is ongoing debate about usefulness of using albumin in this setting

Vasopressor and inotropic support
Key points
- Vasopressor therapy should be employed whenever fluids are inadequate in restoring organ perfusion and targeted blood pressure
- Vasopressor therapy should be always given after volume replacement, however in life life-threatening hypotension maintaining perfusion pressure is essential even in presence of hypovolemia, which must be corrected as fast as possible
- Norepinephrine is a preferred agent in restoring blood pressure
- Dobutamin is preferred agent for inotropic support

Criteria for effectiveness
- Restoring organ perfusion (increase of urine output, adequate skin perfusion, increased capillary refill)
- Increase of cardiac output
- Increase of blood pressure
- Increase of SvO₂
- Decrease of blood lactate level

MYOCARDIAL DYSFUNCTION IN SEPSIS AND MOF
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No abstract available.
A series of clinical trials on the use of corticosteroids for the treatment of sepsis gave negative results. Two meta-analyses led to the conclusion that glucocorticoids for sepsis do not improve survival and may even be harmful. Trials with high doses of glucocorticoids showed adverse effects with a trend to increased overall mortality, with an increased mortality due to secondary infections and with adverse effects on respiratory, hepatic and renal function. Although the precise mechanisms are not completely understood, the dose and the duration of the intervention may account for the negative results of the glucocorticoid trials in sepsis.

Glucocorticoids interact with the host response at virtually all levels exerting suppressive and permissive effects on the immune response. In a dose dependent manner, corticosteroids inhibit the synthesis of many pro-inflammatory mediators such as cytokines, phospholipase A2 and cyclooxygenase. At physiological concentrations of glucocorticoids, the synthesis of anti-inflammatory mediators such as the interleukins 4 and 10 or the interleukin-1-receptor antagonist is not altered or even increased. There is evidence that pharmacological doses of glucocorticoids exert suppressive effects on immune reactions thus threatening an effective host defense. Although immunological data are lacking, the adverse effects observed in the negative glucocorticoid trials were attributed to a prolonged and nonspecific immunosuppressive effect of high doses of corticosteroids when given in the first 24 hours after onset of sepsis or ARDS.

The role of the endogenous glucocorticoid hydrocortisone has been completely neglected in designing the high-dose steroid trials. Cortisol acts as a conductor in the orchestra of various immune reactions. In response to infections cortisol induces suppressive as well as permissive effects on the immune response thus counteracting overshooting immune reactions. There is a body of evidence that the adrenocortical function is impaired and that this impairment appears to correlate with the degree of systemic inflammation. The diagnosis of relative adrenocortical insufficiency is still a source of an ongoing debate and research. The short corticotropin stimulation test is widely used for its assessment. However, the appropriate cutoff value for the diagnosis of relative adrenocortical insufficiency is difficult to determine. Using the different cutoff values proposed in literature, Bouachour found an incidence of relative adrenocortical insufficiency ranging from 6.25 to 75% in one study group of septic shock patients. A recent study of Annane in a large group of patients with septic shock concluded that a cortisol increment of less than 9 µg/dL may be indicative for an inappropriate adrenocortical function. Combined with a basal cortisol level of more than 34 µg/dL a blunted cortisol response is indicative for a high 28-day mortality rate (81%) (ref.8).


The project, which is supported by the European Commission, will further clarify the role of stress doses of hydrocortisone in the treatment of septic shock. The high-dose steroid trials, undertaken more than 10 years ago, may have failed because of inappropriate dosage regimen and target populations.

References

NON-INVASIVE HAEMODYNAMIC MONITORING IN INTENSIVE CARE AND ANESTHESIA

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No abstract available.

INFLUENCE OF THE DEGREE OF TRICUSPID REGURGITATION ON CARDIAC OUTPUT MEASUREMENTS BY THERMODILUTION

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Introduction

The authors were studying the influence of different grade of tricuspid regurgitation (TR) on accuracy of cardiac output (CO) measurement by thermodilution.

Methods

27 patients were separated into three groups. All patients were initially investigated by transesophageal echocardiography (TEE) (multiplanar probe, Omniplane, Hewlett-Packard) and later the pulmonary artery catheter (PAC) was inserted for continuing haemodynamic instability. All patients with higher than the 1st degree of aortic regurgitation were excluded. There were 8 patients with no or the 1st degree of TR graded according to color doppler criteria, the second group consisted of 9 patients with the 2nd degree of TR. The third group included 10 patients with the 3rd degree of TR. All patients were measured twice simultaneously by TEE and PAC for cardiac output. At least three pulsions were measured using continuous doppler for velocity-time integral (VTI) at the level of aortic valve and at least six VTI were averaged in case of stroke volume (SV) variation in atrial fibrilation. Aortic valve area (AVA) was measured by planimetry twice and results were averaged. SV was calculated multiplying VTI with AVA and heart rate. Simultaneous PAC measurement was carried out applying three 10 ccm boluses of iced saline.

Results

The mean difference between TEE measurement and PAC measurement was 514.1+/–541.3 ml/min in the first group of patients (r = 0.96 p < 0.0001). The mean difference of 837.8+/–976.1 ml/min was found in the second group of patients (r = 0.92 p < 0.0001). The difference between the two modes of CO measurement was 1893.0+/–1143.9 ml/min in the third group (r = 0.69 p < 0.001).

Conclusion

The difference in the third group is probably caused by inadequately low values of CO measured by thermomulion. The inaccuracy of CO measurement in the group of patients with the 3rd degree of TR can be misleading for further therapy. It can cause more significant inaccuracy in another calculated parameters like pulmonary and systemic vascular resistances and stroke work indexes of left and right ventricle.

Reference


PAPILLARY MUSCLE RUPTURE WITH SEVERE ACUTE MITRAL REGURGITATION – RARE COMPLICATION OF ACUTE MYOCARDIAL INFARCTION. OUR EXPERIENCE WITH THREE CONSECUTIVE PATIENTS

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The mortality of patients with cardiogenic shock (CS) following acute myocardial infarction (AMI) remains frustratingly high, despite modern pharmacological and interventional therapeutical approaches. The progressive hemodynamic deterioration in patients suffering from AMI is usually caused by severe left ventricular systolic dysfunction as a consequence of large regions affected by necrosis or ischaemia. These patients account for about 10 % of all admitted for AMI and their mortality is as high as 60–80 %. The special subset of CS patients comprises patients presenting with mechanical complications of AMI, mainly the severe acute mitral regurgitation (SAMR), ventricular septal rupture and ventricular free wall rupture or tamponade (8 %, 6 % and 2.7 %, respectively, of all CS patients). Papillary muscle rupture causing severe acute mitral regurgitation paradoxically occurs frequently in patients with relatively small areas of affected myocardium and well preserved systolic function of the left ventricle. There have been 3 small series of patients suffering from SAMR comprising 22–33 patients during the period of 10 to 22 years published in recent literature. We report on 3 consecutive patients who were treated in our institution during the last 9 months. All of them survived. We stress aggressive therapeutical approach with the need of initial stabilization, organ support (mechanical ventilation, intraaortic balloon counterpulsation, eventually continuous renal replacement therapy) and early surgical intervention. Successfull initial management offers excellent long-term prognosis for early survivors.
RELATIONSHIPS BETWEEN CONVENTIONAL HEMODYNAMIC AND BLOOD VOLUME MONITORING DURING AND AFTER ORTHOTOPIC LIVER TRANSPLANTATION

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Purpose

Liver transplantation program started at Semmelweis University in 1995. Our purpose was to evaluate the standard hemodynamic and the newer blood volume monitoring technique in patients undergone orthotopic liver transplantation (OLTx), especially to analyse the correlations among different pressure, volume and flow parameters.

Methods

The relationships among intravascular filling pressures, preload volume and flow parameters (n=130) and their changes (n=110) were analysed in 8 liver transplanted patients underwent conventional and volumetric hemodynamic monitoring. The conventional hemodynamic monitoring consisted of Swan-Ganz catheterization to assess filling pressures (CVP, PCWP) and cardiac index (CI). The blood volume monitoring technique consisted of a fiberoptic catheter for therm-o-dye dilution (COLD System, Pulsion Medizintechnik) to assess the intrathoracic and global enddiastolic volume (ITBVI, GEDVI) and CI. All patients had received the same surgical and anaesthesiological technique. Measurements were obtained during anaesthesia and in the first five postoperative days. Statistical analysis was performed with Statview program.

Results

Preload pressure values showed significant correlation (CVP-PCWP, r=0.78); but the correlation between the intravascular pressure and volume parameters were poor (PCWP-GEDVI, ITBVI, r=0.02). The correlation coefficient between the intrathoracic volume parameters was very high (GEDVI-ITBVI, r=0.97). The relationships between the changes of CI and volumetric preload parameters were more significant (GEDVI-Δ CIa, r=0.61; ITBVI-Δ CIa, r=0.64) then between the changes of preload pressure parameters and CI, (Δ PCWP-Δ CIa, r=0.25; Δ CVP-Δ CIa, r=0.28). Doing multiple regression analysis to evaluate influencing factors of CI, the multiple correlation coefficients was higher using COLD system (r=0.92) compared to the parameters measured by Swan-Ganz catheter (r=0.57).

Conclusion

We found that COLD system gives more adequate information from the hemodynamic status of the patient, than the more invasive Swan-Ganz catheterization. Volumetric preload parameters correlated significantly better with the changes of CI, than the conventional pressure preload parameters.

DIAGNOSIS OF SHOCK DUE TO MASSIVE PULMONARY EMBOLISM

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Study objective

To evaluate the value of transesophageal echocardiography (TEE) as an initial diagnostic method in patients with unexplained shock.

Setting

Medical ICU in 800-bed hospital.

Patients and methods

Forty consecutive shocked patients with congested jugular veins without clinical signs of pulmonary congestion. Both ventricles, atrial septum, main pulmonary artery (MPA), right pulmonary artery (RPA) and left pulmonary artery (LPA) were examined by single plane (24 patients) and multiplane TEE (16 patients).

Measurement and results

Twenty-seven patients had isolated right ventricular dilatation. Global right ventricular hypokinesis was present in 26 and segmental akinesia in one patient. Nineteen thrombemboli were visualized in RPA, 6 in LPA and 3 in MPA. Ten patients had predominant left ventricular dysfunction and 3 had cardiac tamponade. According to pulmonary scintigraphy or autopsy, sensitivity of TEE for diagnosis of massive pulmonary embolism (MPE) in patients with right ventricular dilatation and shock was 90 % and specificity was 100 %.

Conclusion

In contrast to transthoracic echocardiography, TEE is an accurate and definite bedside diagnostic tool in patients with unexplained nonhypovolemic shock and can directly visualize central thrombemboli in shocked patients with MPE.
SECTION: SYSTEMIC INFLAMMATION AND SEPSIS

GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK: DOES IT EXIST?

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No abstract available.

SEPSIS, SEPTIC SHOCK AND MULTIPLE ORGAN DYSFUNCTION: NEW THINKING ABOUT THEIR PATHOPHYSIOLOGY

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Key words: Sepsis / Septic shock / Multiple organ dysfunction / Nitric oxide / Peroxynitrite / PARS / Endothelial dysfunction / Coagulation / Fibrinolysis

Sepsis is a highly complex pathophysiological state representing a major challenge to physicians. The most common cause of death in patients with sepsis/septic shock is deterioration of the function of multiple organs, termed multiple organ dysfunction syndrome (MODS). This brief review addresses the recent important issues concerning the downstream and relatively late effectors of acute inflammation. Among these, a complex interplay of nitric oxide, oxidative stress and PARS pathway is emerging as one of key mechanisms involved in the development of organ dysfunction in various acute pathological conditions including septic shock. In addition, since the endothelium represents both mechanism and target in the pathogenesis of septic shock and multorgan dysfunction, the basic aspects of the microvascular endothelial response to inflammatory and hemostatic stress are also discussed.

Introduction

Recent 1998 data from the Centers for Disease Control show that sepsis is the 11th leading cause of death overall. In addition, Angus and colleagues' projected the incidence of sepsis to increase 1.5% per annum due to growth in predisposed segments of the population. The most common cause of death in patients with sepsis/septic shock is deterioration of the function of multiple organs, termed multiple organ dysfunction syndrome (MODS). Unfortunately, therapy of these syndromes still remains largely supportive. Consequently, the implication of an understanding of the complex pathophysiology of septic shock and organ dysfunction are critical to the development of mechanism-based therapeutic strategies. Clinical trials, however, using so-called "immunotherapy" failed to produce a significant improvement in the treatment of sepsis over the past 20 years. This failure suggest either that multiple mediators must be targeted or that the morbidity of sepsis results from the downstream consequences of cytokine activity. This brief review addresses the recent important issues concerning these downstream and relatively late effectors of acute inflammation. Among these, a complex interplay of nitric oxide, oxidative stress and PARS pathway is emerging as one of key mechanisms involved in the development of organ dysfunction in various acute pathological conditions including septic shock. In addition, since the endothelium represents both mechanism and target in the pathogenesis of septic shock and multorgan dysfunction, the basic aspects of the microvascular endothelial response to inflammatory and hemostatic stress are also discussed.

Cardiovascular failure in septic shock

The circulatory failure associated with septic shock is characterized by severe hypotension as a result of low peripheral vascular resistance, hyporeactivity of the vasculature to vasconstrictor agents (vasoplegia), myocardial dysfunction, maldistribution of microcirculatory blood flow, and reduced tissue oxygen extraction. Previous explanation for this hemodynamic pattern in septic shock included down-regulation of adrenoreceptors, metabolic acidosis, injury to vascular cells due to severe hypotension or effects of many different circulating mediators such as prostaglandins. Although the underlying mechanism of sepsis-induced hypotension seems to be very complex and not yet completely understood, the present evidence suggest that three probably closely interacting major pathways are involved in this loss of peripheral vascular tone.

1. The role of nitric oxide (NO) and reactive nitrogen/oxygen species (RNOS)

Several lines of evidence support the view that the overproduction of NO by inducible nitric oxide synthase (iNOS) contributes significantly to the circulatory failure in septic shock. First, pharmacologic inhibition of iNOS have been documented to improve or reverse hypotension both in rodents and larger mammals models of endotoxemia or sepsis. Second, mice in which iNOS gene has been inactivated by gene targeting (iNOS-knockout mice) exhibited only a minor fall in blood pressure when challenged with endotoxin. Finally, the inhibition of NO production maintained blood pressure and enabled a reduction of vasopressor support in human studies. However, a randomized, placebo-controlled, multicentre phase III trial was recently halted because of significantly worse survival among patients receiving non-selective NOS inhibitor; the mechanisms of this adverse effect remain to be elucidated. Hence, non-selective NOS inhibition — although increasing blood pressure — seems unlikely to find a role in the management of human septic shock. By contrast, results from preclinical studies with selective iNOS inhibitors are promising and require further evaluation. Several possible mechanisms account for NO-mediated hypotension. Not only NO itself (via cGMP-mediated smooth muscle relaxation), but also its downstream biological effects may play a pathophysiologic role in sepsis-induced vasodilatation. Growing body of evidence suggests that peroxynitrite (ONOO⁻), a highly toxic reactive species formed from NO and superoxide (O₂⁻), is capable of inducing endothelial dysfunction and vascular hyporeactivity. Recently, Takakura...
et al. proposed that cardiovascular hyporeactivity to catecholamines in septic shock may be due in part to ONOO−-induced inactivation of alpha-adrenoreceptors. The potential important role of RNOs in the pathophysiology of circulatory failure in septic shock was also recently demonstrated by Macarthur et al.13. They showed that superoxide can deactivate catecholamines resulting in loss of their activity. Moreover, administration of superoxide dismutase mimetic to a rat model of endotoxic shock restored the vasopressor response to norepinephrine13. Finally, NO may also exert ist vasodilatatory effects by activation of potassium channels (see below) in the plasma membrane of vascular smooth muscle cells14, underscoring the complexity of NO-mediated vascular effects.

2. The role of activation of ATP-Sensitive Potassium Channels

The key role in the regulation of vascular tone plays the membrane potential of vascular smooth muscle cells. Hyperpolarization closes calcium channels thereby decreasing the cytosolic calcium concentration resulting in relaxation. ATP-sensitive potassium channels (KATP channels) markedly influence the membrane potential of vascular smooth muscle cells. The opening of KATP channels, triggered by decreased cellular ATP content or increased intracellular concentrations of lactate or hydrogen ion, promotes vasodilatation by hyperpolarizing the membrane and preventing the influx of calcium into the vascular cells15–17. Inhibition of these KATP channels using antidiabetic drug sulfonylurea reversed hypotension in rodent models of endotoxic shock16. As mentioned above, apart from metabolic causes, KATP channels might also be activated by NO14.

3. The role of vasopressin

Vasopressin, a peptide hormone, is an essential component of cardiovascular homeostasis. During the initial phase of septic shock the levels of vasopressin are increased. However, later in the course of septic shock, the plasma levels of vasopressin are inappropriately low14. This deficiency of vasopressin seems to be another crucial player in the pathogenesis of vasodilatatory shock. Indeed, in patients with septic shock infusion of low doses of exogenous vasopressin (to only restore pathogenesis of vasodilatatory shock. Indeed, in patients with septic deficiency of vasopressin seems to be another crucial player in the synthesis of iNOS20.

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cules46. In sepsis/septic shock, however, the exposure of endothelium to cytokines and their downstream effectors described above results in profound alterations in many of physiological endothelial function (endothelial dysfunction)47, 50. These changes encompass altered balance between endothelial vasoactive compounds (i.e., NO, carbon monoxide, endothelins, prostacyclin) resulting in loss of vascular tone and microvascular perfusion heterogeneity, expression of adhesion molecules, production of cytokines and RNOS, and imbalance between pro- and antiocoagulant mechanisms46.

The latter mechanism has recently gained particular importance41, 42. The excessive inflammation and associated endothelial dysfunction lead to release of tissue factor (from endothelial cells and mononuclear), a key mediator linking inflammation and coagulation, which in turn triggers the extrinsic coagulation cascade and accelerates the production of thrombin43. This procoagulant state is normally balanced by the production of endogenous anticoagulant factors, such as antithrombin III, activated protein C and tissue factor pathway inhibitor. However, these modulators are consumed in sepsis and their levels become deficient44. In this context, a critical point in the loss of pro-antiocoagulant balance is ascribed to the endothelial suface proteins thrombomodulin and endothelial protein C receptor (EPCR). These proteins, under normal conditions, activate the protein C possessing antithrombotic, profibrinolytic and anti-inflammatory properties41. If the endothelial injury is present, the functions of these regulating proteins are impaired45, 46. Furthermore, studies have shown that pro-inflammatory mediators causing endothelial dysfunction not only produce the pro-coagulant properties of endothelial cells, but also suppress the fibrinolytic capacity of the endothelium, resulting in marked imbalance between coagulation and fibrinolysis41, 45. Suppressed fibrinolysis means that the capacity of fibrinolytic system to remove formed microthrombi and maintain microvascular blood flow is impaired. The reasons for the diminished fibrinolysis in sepsis include a decrease in tissue-type plasminogen activator (t-PA, produced by endothelial cells), increased activity of plasminogen activator inhibitor (PAI-1, produced by endothelial cells and platelets) and thrombin activatable fibrinolysis inhibitor (TAFI), and formation of plasmin-antiplasmin (PAP) complexes47. Hence, the inflammation-induced shift of endothelial cell phenotype to a prothrombotic state may promote the widespread formation of microvascular thrombi, resulting in microcirculatory failure and tissue hypoxia48. This apparent cross-talk between the inflammation network and coagulation pathway suggest that activation of coagulation may amplify the uncontrolled inflammatory response, ultimately leading to multiorgan dysfunction. The clinical significance of this new paradigm on the pathophysiology of sepsis and organ dysfunction continue to be delineated. Results of recently completed phase III study with activated protein C are promising.

Conclusion

There are many diseases in the medicine that require multiple agents for successful treatment. They include, for example, combined immunosuppression for transplanted organs; diuretics, iontophores and vasodilators for patients with heart failure; multiple antibiotics for polymicrobial infection or combined chemotherapy for cancer treatment. Because of enormous complexity of the pathophysiology of sepsis and related multiorgan dysfunction, it is likely that similar combined and sequential targeting of several principal mechanisms may be needed to yield clinical success when treating sepsis and multiple organ dysfunction. In this context, every effort made to identify a single pathophysiological pathway may help to put together the final picture of “sepsis puzzle”.

Acknowledgement

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References

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GASTROINTESTINAL TRACT RESUSCITATION IN CRITICALLY ILL PATIENTS

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Particular research interest has focused on the resuscitation on the gastrointestinal tract in the recent past: on the one hand, this organ system is regarded to be the "motor of multiple organ failure" representing both a mechanism and a target. On the other hand the gut has been attributed the role of the "canary of the body" i.e. a sentinel organ which is particularly susceptible to derangements of blood flow and/or oxygen and substrate supply due to its particular microcirculatory anatomy, and may therefore promote a vicious circle resulting from the translocation of endotoxin and/or live bacteria and ultimately leading to organ dysfunction. The gastrointestinal tract is characterized by a number of particular features which interfere with every resuscitative measure:

1. The blood supply is unique in the body, inasmuch it comprises both a serial and a parallel vascular bed providing for blood flow to the most important organ, the liver. This vascular bed belongs both to the high pressure as well as to the low pressure vascular net. Since in general access to the portal vein is prohibited for obvious anatomical reasons oxygen and/or substrate kinetics can only yield net balances for the whole hepatoplastic region i.e. gut and liver taken together. Therefore discrimination between these organs is normally impossible.

2. Liver blood flow of which about 75–80 % is supplied by the portal vein and only 20–25 % by the common hepatic artery has an independent regulation, inasmuch changes in the portal venous blood flow are compensated for by compensatory variations in hepatic arterial perfusion in order to maintain total blood flow. This phenomenon is known as the hepatic arterial buffer response.

3. The total blood flow to the hepato-splanchic region accounts for about 20–25 % of cardiac output, while the oxygen uptake in this region contributes approximately 25–30 % to the whole body oxygen consumption. Consequently the regional oxygen extraction is normally higher than the systemic one resulting in the well-known hepatic venous-mixed venous hemoglobin oxygen saturation gradient of 5 in normal healthy volunteers.

4. Because of the central synthetic role of the liver functional changes cannot only be described by blood flow and oxygen exchange rates but have to take into account the numerous organ specific metabolic pathways, some of which are highly oxygen dependent (gluconeogenesis, protein synthesis) (ref.1). This phenomenon is further underscored by the intrahepatic metabolic compartmentation resulting from the different localization of metabolic activity within the perportal and perivenous region.

The strategies primarily aim at the augmentation of blood flow and oxygen/substrate supply by using fluids, vasoactive drugs or epidural anesthesia, but nutritional and metabolic support are considered as well as the role of antioxidant supplementation.

Regional Blood Flow

Augmentation of blood flow to the hepato-splanchic system certainly is the primary aspect in the resuscitation of the gastrointestinal tract. It should be noted that depending on the underlying physiologic status
Hypovolemia

It is trivial that the redistribution of cardiac output to the vital organs brain and heart during hypovolemia – such as changing from the recumbent to the erect position – induces a substantial fall in the blood flow to the hepato-splanchnic organs resulting from increased regional vascular resistance. It should be kept in mind, however, that this splanchnic vasoconstriction does not resume after hypovolemia is corrected. By contrast, optimizing the intravascular filling by peroperative plasma volume expansion was associated with reduced incidence of gastric mucosal acidosis and postoperative morbidity and complications in patients undergoing cardiac surgery. Covert hypovolemia probably is also responsible for the drop in hepato-splanchnic blood flow associated with epidural anesthesia, because when appropriately used epidural anesthesia not only increased colonic mucosal blood flow but also improved the gastric mucosal-arterial PCO2 gap and the small bowel motility and degree of dilatation as determined by ultrasound techniques in patients with peritonitis.

Mechanical Ventilation

Intermittent positive pressure ventilation, in particular with a PEEP, increases mean intrathoracic pressure and, consequently, the “downstream”-pressure of the hepatic circulation due to the rise of the (nontransmural) right atrial pressure. Therefore the hepato-splanchnic blood flow declines, in particular in the portal vein. It must be underscored, however, that hepato-splanchnic blood flow is not affected or even increases when the PEEP level is titrated to the lung pressure-volume curve, i.e. respecting the lower inflection point of the static compliance curve. Finally, ventilation in the prone position, a routine maneuver to improve pulmonary gas exchange may also jeopardize gastrointestinal energy balance: of 12 patients ventilated in the prone position for acute lung injury and who developed increased intraabdominal pressure, 9 ones showed an increased gastric mucosal-arterial PCO2 gap. Those patients in whom the intraabdominal pressure remained unchanged, however, the PCO2 gap was unaffected confirming data reported by Sugrue et al. on the relation between intraabdominal pressure and mucosal acidosis. Inappropriate weaning from mechanical ventilation, however, may also compromise the gastrointestinal perfusion: It is well-known that exercise is associated with an increase of cardiac output at the expense of the perfusion in the gastrointestinal tract. “Breathing as an exercise” may mimic this situation and thus lead to a reduced gastric mucosal perfusion such as demonstrated in patients who could not be weaned from the respirator using Laser Doppler flowmetry.

Vasoactive Drugs

Catecholamines are most commonly used to increase cardiac output and regional blood flow, and in fact, infusing adrenaline or noradrenaline increased hepato-splanchnic blood flow in volunteers in a dose-dependent manner as a function of their β-adrenergic receptor agonist properties. Nevertheless, it must be underscored that “not all catecholamines are created equal”. Adrenaline not only impaired hepato-splanchnic blood flow and oxygen exchange when compared to a combination of noradrenaline and dobutamine, but also compromised hepato-splanchnic lactate clearance, which may be of particular importance since hyperlactatemia in the critically ill is primarily caused by impaired lactate removal in the liver. Moreover, in contrast to this catecholamine combination adrenaline also increased the lactate/pyruvate ratios indicating at least transiently aggravated cytosolic redox state. Finally, adding dobutamine to noradrenaline in septic shock improved gastric mucosal perfusion as assessed with Laser Doppler flowmetry as well as intramural acidosis when compared to noradrenaline or adrenaline alone. Dobutamine alone also improved favorably in this respect with dopamine, and unlike dopexamine lowered the lactate/pyruvate ratios in noradrenaline-dependent patients with septic shock. In fact, the beneficial effects of dopexamine on the gastrointestinal tract remain controversial: although this substance has been reported to “protect the hepato-splanchnic organs”, in part due to increased regional microcirculatory blood flow, this effect has been questioned in the recent past: Kiefer et al. could not confirm the preferential rise of the hepato-splanchnic blood flow attributed to dopexamine when it was added in noradrenaline-dependent patients with septic shock, and no beneficial effect on any parameter of regional metabolism and energy balance was found either. Furthermore, the gastric mucosal-arterial PCO2 gap even worsened despite increased regional blood flow when incremental infusion rates of dopexamine were administered in patients treated with continuous i.v. dobutamine. Nevertheless, the exogenous β-adrenergic receptor stimulation seems to be pivotal in inotrope-dependent patients with septic shock: replacing noradrenaline by the pure α-agonist phenylephrine considerably reduced the regional blood flow and thereby impaired the hepato-splanchnic metabolic performance although no change in systemic hemodynamics or gas exchange had occurred. Interestingly, a “splanchnic-directed”, i.e. pH-guided therapy in trauma patients had already previously suggested the potential importance of β-mimetics for the resuscitation of the gastrointestinal tract: combining folate and mannitol with the infusion of low-dose isoproterenol significantly reduced the number of organ failures and subsequently ICU and hospital length of stay.

In addition to catecholamines non-adrenergic compounds may also be considered to improve the blood flow to the hepato-splanchnic organs, the most studied being prostacyclin (or its stable analogue iloprost) and N-acetylcysteine. Prostacyclin, a vasodilator prostaglandin with platelet-aggregation inhibiting and cytoprotective properties is well-known to increase hepatic blood flow in healthy volunteers, and we could confirm this effect infusing iloprost in noradrenaline-dependent patients with septic shock. It is noteworthy that beyond increasing blood flow prostacyclin or iloprost also seem to beneficially influence gut and liver energy balance and metabolic performance: Lehmann et al. recently reported that 1 ng kg⁻¹ min⁻¹ improved plasma indocyanine-green clearance as measured using thermal-dye double-indicator dilution in a comparable group of patients without any detectable effect on systemic hemodynamics. N-acetylcysteine has become the treatment of choice for paracetamol intoxication-related liver failure due to its glutathione replenishing and, hence, antioxidant effects, as well as to its vasodilator properties as a sulfhydryl donor regenerating the Endothelial Derived Relaxing Factor, in particular during episodes of hyperoxic ventilation. In patients with septic shock requiring vasoressors to maintain adequate blood pressure it increased hepato-splanchnic blood flow and improved both the gastric mucosal-arterial PCO2 gap and the conversion of lidocaine to monoethylglycinexylidide, a parameter of the cytochrome P450 system located in the perivenous hepatocytes.
Nutritional And Metabolic Support

Nutritional and metabolic support for the gastrointestinal tract comprises several aspects, i.e. the supplementation of glutamine, arginine as the precursor molecule of nitric oxide, ω-3 polyunsaturated fatty acids, trace elements and antioxidants, all of which probably being most efficient when used in combination. Clearly, preferring the enteral over the parenteral route is of utmost importance in this context, in part certainly as a result of the increase in regional blood flow affiliated with the enteral administration of calories. It has to be kept in mind, however, that this increased blood flow is the physiologic adaptive response to the rise in oxygen demands associated with enteral intake, and up to now no bedside monitoring is available to discriminate between the supportive and stressful effects of enteral nutrition. While the beneficial role of enteral nutrition per se seems to be unequivocal this issue is not definitely settled for the “key nutrient” supplementation. Two recent meta-analyses reviewing 23 clinical trials including a total of 2,491 patients concluded that this nutritional strategy reduces overall hospital stay of critically ill patients, in particular after surgical interventions, but does not influence mortality. Moreover, enteral feeding supplemented with antioxidants and fish-oil lipids improved pulmonary gas exchange and thereby reduced the duration of mechanical ventilation and ICU stay in patients with acute respiratory failure, possibly due to the anti-inflammatory properties of the ω-3-fatty acids. Finally, an antioxidant-supplemented enteral nutrition comprising vitamin C and E, selenium and N-acetylcysteine reduced both infectious complications and organ failure in trauma patients similar to the effects of trace element supplementation in burn patients. Glutamine supplementation, however, only exerted significant beneficial effects when administered parenterally: Powell-Tuck et al. could not confirm the improved hospital outcome described previously, and length of hospital stay was significantly reduced in the surgical patients only. By contrast, in patients receiving enteral glutamine supplementation mortality was strictly the same as in those given a standard feed.

Conclusions

A variety of therapeutic strategies has been investigated for the resuscitation of the gastrointestinal tract. Among the different approaches volume expansion and vasoactive drugs, either catecholamines or non-adrenergic substances, primarily aim at the augmentation of blood flow and oxygenation and thereby energy balance but may also allow to improve the metabolic performance. Moreover, the potentially profound effects of clinical routine measures in day-to-day ICU practice such as mechanical ventilation and weaning from the respirator need to be taken into account for their impact on the hepato-splanchnic system. Finally, integrating nutritional and metabolic support by combining different substrates and antioxidants adds to the therapeutic orchestra aimed at this organ system.

References


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**GENETICS BEHIND SEPSIS**

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Clinical conditions of patients with sepsis vary dramatically. With similar infections some patients recover uneventfully whereas others develop septic shock and die. This variation may be ascribed to different degree of inflammatory response to infections, e. g. levels of TNF-alfa. However, a great variations in the TNF-alfa was noted despite the fact that the infection focus and the causative bacteria were similar. Genetic factors may determine host sensitivity to endotoxin by modulating the production of TNF and other cytokines. The results of human genome projects has moved genetics into the medical mainstream and shifted emphasis from relatively rare single-gene disorders to common disorders of multifactorial causation, like sepsis. Stuber et all. demonstrated that the genomic polymorphism within the TNF locus influenced plasma TNF-alfa concentrations and the outcome of patients with severe sepsis. Tang and all. have shown that ICU patients with TNF2 allele do not have a higher chance of developing septic shock nor do they have higher baseline TNF-alfa levels after severe infections, but once septic shock develops, those patients are more likely to have higher plasma TNF-alfa levels and usually sustain a poor outcome. This suggest that subjects carrying the TNF2 allele are more likely in need of intensive care after surgical infection. The failure of recent clinical trials with anti-TNF antibodies may be related to the failure to identify the subgroup of patients who might benefit from such therapy (e. g. patients with TNF locus polymorphism). Another candidates for genetic determination of sepsis course are intron 2 for IL-1 receptor antagonist and gene for intracellular heat shock proteins that are responsible for protection against cellular stress. The genes involved in inflammation are numerous as are genomic variations within most of these genes. Not only genes encoding proteins such as TNF, but all genes involved in signal transduction of inflammatory processes are important candidate genes for determining the extent of the individual's response to stress. Analysis and evaluation of these candidate genes will take enormous effort since new state-of-the-art tools of genetic epidemiology are difficult to apply. Critical care investigators have to integrate the stable, interconnected influence of thousands of gene polymorphism with acute changes in gene expression and translation induced by series of often unpredictable insults using the methods of functional genomics. But understanding of genetic determination of the inflammatory process will allow us to develop valuable diagnostic tools and new therapeutic approaches in severe sepsis. Genomic markers will allow us to stratify the risk of septic patients to develop multiorgan failure. Future trials will be more successful if inclusion criteria will include genetics parameters. Genetics moves into the medical mainstream.

**References**


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**DIFFERENTIATION BETWEEN LOCAL AND SYSTEMIC BACTERIAL INFECTION: THE VALUE OF PROCALCITONIN**

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**Introduction**

Bacterial infections with or without systemic inflammatory response represent common problem in critically ill patients. The presence of
systemic response should be assessed correctly and early in the course of infection because of its impact on prognosis and treatment. Procalcitonin (PCT) is a newer marker of bacterial infection with better diagnostic validity, monitoring and prognostic estimation of severe infection and sepsis.

**Methods and patients**

Twenty six patients with microbiologically proven infection were included in prospective study in a 11 – bed medical intensive care unit. PCT, CRP, leukocyte count, SR and body temperature were determined at least two times during hospitalisation. Patients with local infection had clinical signs of infection with positive microbiological finding in any culture without bacteremia. Patients with local infections and positive blood culture represent the group with systemic infection.

**Results**

In patients with positive blood cultures PCT concentrations were significantly higher than in group with negative blood cultures (p = 0.019). The leukocyte count was significantly lower in the group with systemic infection compared to patients with negative blood culture (p = 0.0017). Other markers did not differ significantly between both groups.

**Conclusions**

Patients with bacterial infection and positive blood cultures had significantly higher PCT levels and lower leukocyte count. Other conventional markers of inflammation could not differentiate patients with local and systemic infection. Considering low leukocyte count non-specific for bacterial infection, determination of PCT is helpful for assessment of extension of bacterial infection in critically ill patients.

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**THE SYSTEMIC AND REGIONAL PROCALCITONIN SERUM LEVEL CHANGES DURING AND AFTER LIVER TRANSPLANTATION**

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**Purpose**

Elevated procalcitonin (PCT) serum levels were observed in the early phase after liver transplantation (OLTx). The aim of this study was to analyse the systemic and regional changes of PCT serum level from the time of organ harvesting until the early postoperative phase of OLTx and to evaluate the prognostic value of the early postoperative PCT level changes in liver transplantation.

**Methods**

The relationship among the changes of the inflammatory response parameters (especially PCT, measured by LUMItest, BRAHMS) and the APACHE II, SAPS II scores, liver function tests, renal function tests, cultures were studied in 62 patients who underwent liver transplantation. The systemic measurements were done during surgery: induction of anaesthesia, hepatectomy, anhepatic phase, after reperfusion, end of surgery (n = 40), and in the first five postoperative days (n = 62). The patients were divided in two groups: Group A (n = 32) without and Group B (n = 29) with major postoperative complications (hepatic artery thrombosis, renal or respiratory failure, severe coagulopathy). The regional measurements were done at the end of the anhepatic phase from the portal vein and during the hepatic reperfusion with own blood from the hepatic vein (n = 28). Statistical analysis was performed with Wilcoxon signed rank test, paired t test and chi square test.

**Results**

During organ preservation, hepatectomy and in the anhepatic phase the PCT levels were in normal range. There were no differences between the systemic and portal vein PCT levels. In 11/28 patients the hepatic vein PCT levels were higher than the systemic levels (1.27 vs. 0.16 ng/ml, p < 0.02). Systemic elevations of PCT had begun 20 minutes after graft reperfusion (0.27 vs 1.04 ng/ml, p < 0.01). The PCT level was elevated in both groups but, in Group B the level was significantly higher then in Group A (Group B: 30.6 vs. Group A: 4.8 ng/ml, p < 0.001). There were also significant differences in the postoperative phase between the two groups in APACHE II and SAPS II scores (p = 0.05) and ALAT, ASAT, LDH, serum bilirubin levels (p = 0.05).

**Conclusion**

The elevated hepatic vein PCT level suggests that the PCT may originate from the liver itself. The systemic elevation of PCT had begun immediately after the graft reperfusion without any signs of systemic infection. The postoperative changes of PCT may have prognostic value in the development of multiple organ failure.

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**LUTEINIZING HORMONE, PROLACTIN AND TESTOSTERONE PLASMA LEVELS IN PATIENTS WITH SEPTIC SHOCK**

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**Purpose of the study**

Many researches show important disturbances in hormonal balance in patients with severe sepsis. There are a lot of factors, which are involved in that process but the role of sex steroid hormones is unknown, specially, the role of testosterone, which is a one of the most important anabolic hormone. We hope that sex steroid hormones mechanism of action recognition in the septic shock could help in treatment such patients.

**Material and Methods**

We studied plasma level of luteinizing hormone (LH), testosterone (TE) and prolactin (PRL) in patients with septic shock (group I; n = 20)
and in a control group (group II; n = 20). The group I was divided into two subgroups: survivors (group IA, n = 10) and nonsurvivors (group IB, n = 10). Material for laboratory tests was taken at the moment of recognition of septic shock and in the 1st, 2nd, 5th and 10th day.

Results

We noticed significant decreased in testosterone and LH plasma levels in the group I vs the group II and correlation between TE and LH plasma levels and survival. There were no significant changes in prolactin plasma level in the group I vs the group II and prolactin did not correlate with survival. Acute lung injury (ALI) was associated with higher PRL plasma level and was independent from the LH and TE plasma level. We also noticed incorrect pituitary down-regulation of the testosterone secretion.

Conclusion

Our study showed that sex steroid hormones could be good prognostic factors of survival and complications of the septic shock. It could also give an impulse for supplementary treatment using exogenous hormones, especially testosterone.

References


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HYPERMYOGLOBINEMIA IN CRITICALLY ILL PATIENTS: WHAT DOES IT MEAN?

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Introduction

Myoglobin is released from skeletal muscles in different quantities during various traumatic and non-traumatic conditions. Myoglobin is used in the clinical practice most often as a marker of acute myocardial damage. So far, there is no study describing the incidence and consequences of hypermyoglobinemia among medical critically ill patients. The aim of our prospective study was to assess hypermyoglobinemia incidence and to evaluate its relationship to severity of illness and the risk of acute renal failure as a part of multiple organ dysfunction syndrome (MODS).

Methods

All consecutive patients admitted in the medical ICU (n = 310) during 2001 were enrolled into the study. Admission myoglobin plasma level (immunoturbidimetry) was measured and collected in the integrated ICU database MIRO®. Values are medians (MED) and 95 % confidence interval (CI); statistics: Mann-Whitney test, Spearman’s coefficient of rank correlation, two-sample proportion test, and p < 0.05.

Results

Patients characteristics: age 58 years, CI 55 to 61, female 127/male 183, APACHE II MED = 21, CI 20 to 22, 153 (47.7 %) pts were admitted with diagnosis severe sepsis/septic shock. Hypermyoglobinemia (MED 152, CI 102 to 1052) incidence was 68.5 %. Admission SOFA score correlated with myoglobinemia (r = 0.464, CI 0.374 to 0.546, p < 0.0001). Admission myoglobin concentrations were significantly different between survivors and non-survivors in the whole group (MED 121 vs. 352, p < 0.001) and also in the septic subgroup (MED 157 vs. 414, p < 0.001). Acute renal dysfunction treated by renal replacement technique (RRT) developed in 81 pts (25.2 %) with significantly higher myoglobin compared to the rest of the whole group (MED 445 vs. 116, p < 0.001).

Conclusion

Hypermyoglobinemia occurs very frequently in medical ICU patients without signs of acute myocardial ischemia. In our group of ICU patients was incidence 68.5 %. Admission myoglobin concentrations differ significantly between ICU survivors and nonsurvivors and correlate with the severity of critical illness. Hypermyoglobinemia signals potential risk of acute renal dysfunction and evolution of MODS. Its pathophysiological relevance remains to be further elucidated.

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SERUM INTERLEUKIN-10 IN PATIENTS WITH ISOLATED ACUTE INTRACRANIAL LESIONS

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Rationale

Cerebral inflammation has been implicated in the development of brain oedema and secondary brain damage after traumatic and non-traumatic injury. This inflammatory response consists of mediators (cytokines, chemokines and adhesion molecules) followed by cells (neutrophils early after the onset of brain injury and then a later monocyte infiltration). IL-10 is considered to be the main anti-inflammatory cytokine, thus it may play a pivotal role in those processes. IL-10 is produced by activated T and B-cells, monocytes, macrophages and other cells. Its main biological activity includes suppression of lymphocyte and monocyte activation and suppression of pro-inflammatory cytokine production.
Aim of the study

1) Determining IL-10 serum level and its pattern in patients with two types of isolated acute brain trauma. 2) Evaluation for possible prognostic value of serum IL-10 in those patients.

Material/methods

Serum IL-10 levels in 29 ICU adult patients (teaching hospital) with traumatic brain injury (TBI, N = 18) and nontraumatic intracranial haemorrhage (SAH, N = 11) were detected using ELISA-technique on day “0”, “1”, “4”, “7” (counted from the day of injury) as well as on ICU admission (“adm”). GCS and SAPS II scores were determined at the same moments. IL-10 levels between survivors (N = 17) and non-survivors (N = 12) were compared.

Results

IL-10 was detectable in sera of all but one of the patients. Mean IL-10 level on ICU admission in all patients was 55.0 (±86.7!) pg/ml. No statistically significant differences in IL-10 on any day between TBI and SAH as well as survivors and non-survivors groups were found (Fig 1). No correlation of IL-10 and GCS or SAPS II was stated. Significant fall of IL-10 from day “0”, “1” and “adm” to day “4” and “7” in all patients was observed.

Conclusions

Serum IL-10 in patients with acute brain injury is detectable independently of the nature of injury. It has a considerable high value deviation and in those patients it seems to have no prognostic values, although this is to be proven on greater number of cases.

THE IMPACT OF OVERSEDATION ON SEPTIC SHOCK SEVERITY

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Introduction

Septic shock is defined as hypotension of septic origin that is non-responsive to adequate volume resuscitation. Nevertheless – on top of vasoparalysis – several additional factors may contribute to hypotension, e.g. oversedation may increase the vasopressor requirements.

Methods

Study was approved by local ethics committee. Volume resuscitated ICU septic patients requiring norepinephrine to maintain adequate mean arterial pressure (MAP) (≥ 70 mmHg in most cases) in whom oversedation (i.e. Ramsey score ≥ 4) during morning rounds was found were studied. When feasible (e.g. no head trauma) continuous analgosedation (sufentanil and midazolam) was decreased to 5–10 mg/hour and 1–2 mg/hour, respectively. Haemodynamics was recorded when Ramsey score reached 3. When MAP was higher than baseline the dose of norepinephrine (NE) was stepwise decreased in 10 minute intervals until baseline MAP was recorded for 10 min. Values are provided as means (range).

Results

We provide results of 5 pilot patients. Baseline MAP was 80 (73–87) mmHg with continuous NE infusion of 5.6 (2.5–13.2) mg/min. In all 5 patients Ramsey score 3 was reached within 80 to 135 minutes with MAP of 105 (95–111) mmHg. This enabled reduction in NE doses by 2.5 and 3.3 mg/min in two and discontinuation of NE in three remaining patients. In 2 of 5 patients analgosedation was increased after completion of the study again due to pain (trauma patient) and ventilator interference (peritonitis patient).

Conclusions

Oversedation leads to overestimation of severity of septic shock. This fact should be considered in septic shock diagnosis/stratification. In some ICU patients sedation at Ramsey score 3 is inadequate but might be if adequate analgesia was given.

Reference

SECTION: ACUTE RESPIRATORY FAILURE

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PATOPHYSIOLOGY OF ALI AND ARDS

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No abstract available.

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RESPIRATORY MECHANICS AT THE BEDSIDE

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ARDS – acute respiratory distress syndrome is the most severe presentation of acute respiratory failure – ALI, characterized by bilateral inflammatory pulmonary oedema. Even though recently published results have shown decreasing mortality of ARDS patients it still remains relatively high 11–43 %. CT studies by Gattinoni et al. have shown that dependent dorsal parts of the lung in supine position are more injured than ventral parts, which are relatively free of interstitial oedema and amenable to ventilation. The lung thus behaves like a sponge, with hydrostatic forces causing dependent parts to be compressed by overlying pulmonary oedema. To ensure adequate oxygenation and normocapnia in mechanically ventilated patients with such grossly injured lung, originally PEEP set according to arterial oxygen saturation and large tidal volumes (10–12 ml/kg) have been advocated. However several animal studies have shown that this type of ventilation leads to alveolar overdistension and macroscopic (pneumothorax etc.) as well as microscopic (alveolar epithelial, endothelial) injury aggravating lung injury or even promoting it by maintaining the vicious cycle of inflammatory mediators production.

Results of Brazilian ARDS study and National Institute of Health ARDS Network Group have shown that so called protective ventilatory strategy in ARDS patients with tidal volumes adjusted to 6–8 ml/kg of body lean mass, higher PEEP of 10–20 cm H₂O and correction of respiratory acidoses with bicarbonate can decrease morbidity and even mortality of ARDS patients by 22 % compared with traditional mechanical ventilation (12 ml/kg). However, even within the NIN ARDS Network, physicians tend to use tidal volumes higher and PEEP levels lower than those recommended. The mean tidal volume chosen by the attending physician being 10.3 ml/kg of predicted body weight or 8.6 ml/kg of measured weight for patients with ARDS (PaO₂/FI/O₂ of less than 200), and being not significantly different for ALI patients with PaO₂/FI/O₂ of 201 to 300. Plateau pressures were > 35 cm H₂O in 26 % of patients and 78 % of patients with ARDS received PEEP of 10 cm H₂O or less. This apparent reluctance to the use of strict protocol comes from the clinician’s point of view as tidal volume reduction is associated with hypercapnia, which is associated with increased endogenous catecholamine production and might lead to increased cardiac output and increased shunt with the resulting decrease in oxygenation. Moreover high PEEP levels lead to increased incidence of barotrauma, extracellular water retention, might decrease gut perfusion and the metabolic capacity of the liver. Last but not least the use of very low tidal volumes leads to an increased need for sedation and/or muscle paralysis due to decreased patient tolerance of such ventilation, which is associated with other serious morbidities.

The measurement of respiratory mechanics enables us to get an insight into the individual patient’s degree of lung and chest wall impairment. From the pathophysiologic point of view, bearing in mind the important results of the Brazilian and NIN ARDS Network trials, individually set ventilation based on respiratory mechanics measurement might be preferable to a strict ventilation protocol. Measurement and display of the dynamic respiratory mechanics provided by most of the current mechanical ventilators is of great value in most cases of acute lung injury. However measurement of static pressure volume (P–V) relationship is considered as the standard, although cumbersome, method for assessment of respiratory mechanics in ARDS patients. Recent trials underlined the importance of static P–V curve measurement for optimal ventilator settings. As there is still a discrepancy in the interpretation of lower inflection point of the P–V curve the importance of avoiding ventilation over the upper inflection (deflection) point of the static P–V curve is widely accepted.

We developed software able to control on breath-by-breath basis the mechanical ventilator (Adult Star™, Infrasonics, San Diego, USA) and to simultaneously read and process volume and pressure data from the ventilator output. This features enable one to deliver in chosen interval randomly selected test tidal volume (1 of 14 volumes in range of 2–14 ml/kg/body weight) under constant flow conditions with computer controlled expiratory and inspiratory holds and record the volume and respective pressure differences for automatic P–V curve construction. We tested the performance of this software after studies using a lung model in four ARDS patients on three different PEEP levels (0, 5, 10 cm H₂O). Data obtained automatically from the ventilator were compared with independent calibrated pressure and volume measuring system consisting of proximal airway and oesophageal pressure transducers, and heated pneumotachograph connected to differential pressure transducer. Data were processed and collected via sensor interface card into the same computer operating the ventilator and analysed using customized laboratory software. There was a good correlation between the two independent measurement systems thus suggesting that ARM software driven ventilator is sufficient to automatically perform static P–V curve measurement without the need of disconnecting the patient from the ventilator, and without the need for additional equipment other than mechanical ventilator and external ARM software controlled end expiratory valve.

Such tools might help us, once validated in a prospective manner, to better ventilate our patients in the future.
OPEN LUNG MANEUVERS – HOW TO PERFORM, HOW TO MONITOR, POSSIBLE SIDE EFFECTS

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No abstract available.

NON-INVASIVE VENTILATION IN ACUTE RESPIRATORY FAILURE

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History

By definition, non-invasive ventilation (NIV) means a ventilatory support avoiding endotracheal intubation (ET). Though historically attempted first and the concept not forgotten completely negative pressure ventilation (e.g. Emerson iron lung) is currently not used in the ICU environment and Positive Pressure Ventilation is applied noninvasively in acute respiratory failure (ARF).

Technical aspects

Modern ICU ventilators can be safely and conveniently used for NIV though usage of special devices – high-flow bilevel positive airway pressure generators and CPAP systems – developed exclusively for NIV is also possible (e.g. Respironics®). Pressure support ventilation (5–15 cm H₂O) with PEEP (4–10 cmH₂O) is the most frequently ventilatory mode used though PEEP alone was proved to be also efficient (and sometimes event superior) in several studies (cardiac patients) and pressure controlled ventilation is sometimes used when mask leaks cannot be avoided. Other ventilatory modes are used less frequently.

Probably the most important for NIV to be successful is a soft and gently fitting face mask. (nasal masks are less convenient in critically ill patients).

Indications

Two criteria may be used for NIV list of indications:

1. timing during ARF (ET prevention, ET alternative, Weaning and ET reintubation prevention)
2. primary diagnosis leading to ARF

A. basic:
- Hypercapnic ARF – COPD
- Hypoxemic ARF – ALI/ARDS
- Cardiogenic Pulmonary Oedema (CPE)

B. specific:
- Pneumonia
- Thorax trauma
- Immunocompromised patients
- Obesity hypoventilation syndrome (OHS)

1. Hypercapnic ARF – COPD:
   This was the original patients’ population in whom NIV was applied (Wysocki) and still remains the one with best results achieved. NIV is considered a new standard of care in COPD patients (Brochard).

2. Hypoxemic ARF – ALI/ARDS:
   The profit is not so clear. Probably NIV should be attempted when no contraindication is present but if treatment goals are not reached within 60–120 minutes, ET should not be delayed (Antonelli).

3. Cardiogenic Pulmonary Oedema (CPE):
   NIV is a good option with high success rate but should not be attempted in unstable patients due to increased risk of acute myocardial infarction.

Success rate (i.e. avoiding ET) in pneumonia remains to be limited (50 %) in contrast to thorax trauma where NIV is a very good option (20 % failure). Immunocompromised patients seem to profit from NIV substantially. This profit is maximal when NIV is applied soon in the course of ARF (“preventively”).

Contraindications of NIV

- Cardiac or respiratory arrest
- Hemodynamic instability (AIM, unstable cardiac arrhythmia)
- Significantly impaired consciousness
- Upper airway obstruction
- Facial problems (surgery, trauma, deformity…)
- Severe upper GI bleeding
- Mental problems (claustrophobia…)

Specific problems

Sedation:
- best sedation is personnel at the bedside
- drugs not contraindicated – often necessary
- drugs used depend on ICU experience

Feeding:
- intermittent per os (monitor gastric distension)
- fine bore tube to avoid air leak of face mask
- special face masks with opening for gastric tube
- nasal masks – no major problem with feeding

Bronchial secretions:
- pulmonary rehabilitation
- cough when NIV disconnected
- mirtchaeostomy?

Face bruise and other local problems:
- change different face masks
- face mask applied firmly but not tightly
- avoid position of face mask over eyes
- cushioning materials (over nasal bridge)
- eye irritation
Conclusion

Current practice in the European ICU with regards to the use of NIV differs vastly. NIV is still used seldom mainly in hypoxemic ARF (attempted in 16% patients before ET in a study covering France, Switzerland and Spain). About 50% of ICUs in UK do not have equipment. This should be changed right now as profits for especially some groups of ARF patients are well documented and workload for ICU personnel connected with NIV is acceptable.

Reference


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MUSCLE FATIGUE AND RESPIRATORY FAILURE

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No abstract available.

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THE INFLUENCE OF CO-MORBIDITY ON THE OUTCOME OF NON-INVASIVE VENTILATORY SUPPORT IN PATIENTS WITH ACUTE RESPIRATORY FAILURE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Introduction

Non-invasive positive pressure ventilation (NPPV) has been commonly used for treating acute respiratory failure (ARE), especially in acute exacerbation of chronic obstructive pulmonary disease (COPD) patients1. As yet, however, no unequivocal evidence exists on whether the success of NPPV depends on the patients’ respiratory parameters or on their co-morbidity.

Aim

To verify the importance of NPPV and to clarify the influence of co-morbidity on the success of NPPV in COPD patients with ARF.

Methods

Thirty-six patients with COPD (24 men, 12 women) hospitalized on the ICU because of ARP were evaluated retrospectively. The patients received NPPV (BiPAP ST, Respironics Inc.) via face mask. Their mean age was 62 ± 9.1 years. Their baseline parameters were as follows: pH 7.28 ± 0.07; PO2 9.7 ± 2.7kPa; pCO2 9.2 ± 2.4 kPa; breathing frequency (BF) 27 ± 7.9; heart rate (HR) 115.2 ± 24.8; APACHE III score 40.8 ± 11.6; body mass index (BMI) 27.7 ± 7.8. The initial and final values of pH, PO2, pCO2, BF, HR, and the presence of concomitant diseases were compared. The concomitant diseases were classified as heart disease (H), neuromuscular (NM), vascular (V), metabolic (M), gastrointestinal (GI), cancer (C), psychiatric (P), renal (R), liver (L). Obstructive sleep apnea (OSA), the need for long-term oxygen treatment (LTOT), and the occurrence of other diseases than those mentioned above were also noted. The duration of ventilation, ventilatory parameters, the stay on ICU, the numbers of the intubations and deaths were followed up. The occurrence of adverse effects was evaluated. The reasons for intubation, causes of death, and factors influencing NPPV were also evaluated. Ventilatory parameters, co-morbidity, APACHE III, BMI, and ventilatory parameters following 4-h ventilation were compared in patients treated successfully (S) vs patients in need on intubation, considered as treatment failures (F).

Results

Significant improvements in pH (p = 0.001), pCO2 (p = 0.001), BF (p < 0.001), and HR (p = 0.04) were recorded. The number of intubated patients was 5 (13.9%), the number of deaths 4 (8.3%). Improvements of ventilatory parameters after NPPV were observed in 33 patients (91.7%). In total, 84 diseases were counted (i. e. 2.33 diseases in one patient). Heart diseases (BI) were present in 40 patients, vascular (V) in 14, neuromuscular (NM) in 2, psychiatric (P) in 6, metabolic (M) in 6, endocrine (E) in 2, gastrointestinal (GI) in 4, cancer (C) in 2, and renal (R) in 1 patient, liver (L) in 5, OSA in 1, TB in 1; 13 patients were using LTOT. The duration of ventilation was 51.5 ± 49 hours, the ICU stay lasted 7.6 ± 5.5 hours. The inspiratory pressure was 13.3 ± 3 mm H2O, the expiratory pressure was 5.3 ± 1.2 mm H2O. The patients with intubation (ID) had the same ventilatory support, mean age, initial pH, pO2, pCO2, BF and the same improvement over 4 hours compared with the success group (S). The F group had a significantly higher APACHE III (p = 0.049), more concomitant diseases (p = 0.001). There were significant improvements after 4 hours MPPV in BE (p = 0.024).

The reasons for intubation were worsening of acidosis, hypercapnia within 4 hours in two patients; heart failure with hypotension in 2 patients; hypercapnia and coma in one. All patients died of heart failure. Among adverse effects, stomach inflation was observed in one case (relieved by introduction of nasogastric probe), ileus was noted in 1 case, face lesions due to the mask in none.

Discussion

The results are indicative of a certain trend, but their power is limited by the unbalanced sample and its small size. However, in certain parameters the trends are substantial. Further research, based on a larger group of patients, is needed to confirm our results. Careful observation of patients is necessary to avoid delays of intubation.

Conclusion

We have observed beneficial effects, including improvements of respiratory parameters, in COPD patients with ARP if hospitalized on the...
The success of NPPV was less obvious in patients with polymorbidity, APACHE III score, low BMI, and high HR. Adverse events were not of serious nature, only one patient had to be transferred to surgical department because of ileus.

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POSTINTUBATION TRACHEAL LESIONS WITH ACUTE RESPIRATORY FAILURE – SERIOUS PROBLEM OF THE INTENSIVE CARE TODAY

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Tracheal injury (stenosis or tracheo-esophageal fistula) with acute respiratory failure is usually urgent, life-threatening complication of long-term tracheal intubation. Tracheal resection and the reconstruction of airways is the treatment of choice, but it is often risk procedure for patients after polytrauma, sepsis, severe inflammatory diseases, multiple organs failure and other serious cases. The authors presents in three cases reports serious problem of intensive care today and own outcomes of the treatment for last five years.

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STENT INSERTION IN BENIGN STENOSES OF CENTRAL AIRWAYS

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Incidence of tracheal stenoses due to long lasting intubation and/or tracheostomy is increasing probably because of better postoperative intensive care and improved survival of critically ill patients. Value of endotracheal-bronchial stent was evaluated. Series of 53 stent insertions in 38 patients is present. Stents were inserted in 26 males and 12 females, mean age was 52.2 years. Dumon plastic stents and Streeker metallic stents were used. Strategy of indication, application and extraction of stents is discussed in context with other therapeutic methods (tracheal resection or tracheostomy). Stent was inserted definitively in 24 and temporally in 14 pts. Restenosis appeared in 50 % of them. Migration, bacterial colonisation, mucus stagnation, bleeding and granulation overgrowth were the most frequent complications. There was no life threatening complication. Median time of follow-up after stenting was 42.5 months. Tracheostomy or resection were done in cases of stent dysfunction, on the contrary stent was inserted in 2 cases with restenosis after surgical resection. Present results show that stent is one of potent tools in definitive or temporal treatment of central airway stenoses, but there are many problems in individual decision of therapeutic strategy.

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CRITERIA FOR PREDICTION OF HFOV TREATMENT EFFICIENCY IN ADULT PATIENTS WITH ARDS

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Introduction

The study evaluates suitability of criteria describing ARDS severity for prediction of HFOV treatment efficiency.

Methods

A group of 15 adults with ARDS ventilated on HFO ventilator (Sensor-Medics 3100B) after conventional ventilation (CV) failure. PaO₂, PaCO₂, FIO₂, MAP, PIP, PEEP, V̇, Ṙ, ĊO₂, PaO₂/FIO₂ and LIS were determined before conversion to HFOV. HFOV protocol: f = 5 Hz, Ti/T = 0.5, initial CDP = MAP + 5 cmH₂O, FIO₂ HFOV = FIO₂, DP and V̇ according to arterial gases, bias flow = 40–60 l/min, PaO₂ HFOV and PaCO₂ HFOV measured continuously. The group was retrospectively split into two subgroups: 1. Increase in PaO₂ HFOV/FIO₂ HFOV by >10 % (n = 10). 2. Increase in PaO₂ HFOV/FIO₂ HFOV by <10 % or decrease (n = 5). MAP, PEEP, PaO₂/FIO₂, Ṙ, ĊO₂ and LIS recorded during CV were compared between the created groups.

Results

The CV parameters evaluated for both groups are displayed in table:

Conclusion

The most specific parameters for HFOV efficiency prediction are LIS and ĊO₂.

Acknowledgement

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ARDS DUE TO FAT EMBOLISM – A CASE WITH A PROLONGED COURSE

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Case report

A 38 year old patient was admitted to surgical department after a car accident. On admission diagnosis of cerebral commotion, contusion of the right shoulder and fracture of the left femur was established. The patient was stable, no fat embolism prevention was given and operation was scheduled for the next morning. On arrival to the OR the patient was in mild respiratory distress (SpO2 90% while breathing air), chest X ray showed raised diaphragm on both sides. Intramedular osteosynthesis was done in general anaesthesia. After operation the patient was admitted to the ICU and extubated after several hours. Oxygenation while breathing air remained marginal, the patient was co-operative and was transferred to the high dependency surgical unit (HDU) next morning when chest X-ray revealed raised diaphragm and otherwise clear lung parenchyma. In the HDU the patient deteriorated after 48 hours, severe respiratory distress developed and was transferred back to general ICU. Blood gas analysis (BGA) and chest X-ray revealed severe form of ARDS (OI 100). Due to the history of femur fracture and mild thrombocytopenia connected with agitation fat embolism was considered to be the most probable cause of ARDS. On the next morning oxygenation remained critical, pulmonary artery catheter was inserted revealing severe pulmonary hypertension (pre-capillary as judged from PAOP tracing). Due to this fact and because prone positioning was considered to be contraindicated due to huge oedema of the left trunk and leg, inhaled NO (10 ppm, synchronised with inspiration) was used. On Day 10 the patient was transferred to HDU and then home.

Conclusion

In our case we stress the importance of a complex approach to the ARDS patient. OLA are often successful in non-pulmonary ARDS, might be effective not only during the first days of ARDS and oxygenation response to them might be monitored by pulse oximetry. The oxygenation response to inhaled NO might be tested in severe ARDS cases especially when prone positioning is considered risky but effect is unpredictable even in cases of predominant pre-capillary hypertension. Non-invasive ventilation is an attractive method during weaning and may lead to lung recruitment at lower pressure compared to mechanical ventilation.

DIFFUSE ALVEOlar HEMORRHAGE – UNUSUAL COMPLICATION OF COMBINED ANTIAGREGATION THERAPY FOR ACUTE MYOCARDIAL INFARCTION

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Combined antiagregation and anticoagulation therapy for acute coronary syndromes including administration of glycoprotein IIb/IIIa (GP IIb/IIIa) inhibitors has been commonly used. Complications include major bleeding, but diffuse alveolar hemorrhage (DAH) has been reported very rarely. We refer the case of 71 years old man with acute myocardial infarction of the inferior wall. He was treated by direct percutaneous transluminal coronary angioplasty and standard concomitant medication including eptifibatide was administered. In several hours, DAH developed, presenting typical clinical signs (hemoptysis, pulmonary rales as in pulmonary edema, acute respiratory insufficiency and X-ray scan pattern). Antiagregation and anticoagulant medication has been discontinued and complex therapy was started. In a few days, pulmonary hemorrhage extincted and the patient was dimited. Six month later is doing well. Diffuse alveolar hemorrhage is an unusual complication of therapy for acute myocardial infarction with GP IIb/IIIa inhibitors. There is a very few reports in the literature and its appearance in association with eptifibatide administration have not been published yet.

THE PRONE POSITION AS A PART OF THE RESPIRATORY MANAGEMENT IN TETRAPLEGIC PATIENTS

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In patients with acute high spinal cord injury, the essential ventilation changes occur in dependence on the level of lesion. The patient with complete transverse spinal cord injury above C4 is permanently dependent on the ventilator (eventually the permanent stimulation of phrenic nerv can be performed). In our report we discuss the role of the prone position in patients with transverse spinal cord injury distally to C4. In healthy individual, the ventilation is ensured by normal function of the diaphragma and the respiratory muscles. The ventilation also depends on elastic forces of thorax and lungs. For optimal gas exchange process, the right function of ciliary epithelium and adequate bronchial secretion are necessary. The parameters such static and dynamic lung volumes, ventilation/perfusion relationship, WOB and blood-gas values fluctuate within physiological limits.
In case of the acute high spinal cord injury—under C4—with tetraplegia, following changes occur:
1. the ventilation is ensured mainly by diaphragma and partly by accessory respiratory muscles, reason is the “denervation” of the intercostal and abdominal muscles
2. the distribution of perfusion is changed by adrenergic denervation
3. the mucociliary transport is impaired

It results in:
1. Static lungs volumes (VC, TLC, IRV, ERV) are decreased, RV is affected less than the other volumes
2. FEV1, FEV1 % and PEFR are decreased
3. compliance is decreased (dynamic compliance more than static) and resistance is increased, so that WOB is increasing and it, finally, results in higher oxygen consumption
4. various degree of hypoxemia – its is caused by V/Q disproportion, partly by hypventilation – especially in the dependent parts of the lungs, partly by redistribution of perfusion – due to “sympathetomy” within the acute spinal cord injury
5. stagnation of the bronchial fluid – under normal conditions VC at least 15ml/kg b. w. is necessary – otherwise the effective cough is not possible
6. the character of normal bronchial fluid is changed and the function of mucociliary systems is also negatively affected

The respiratory complications, resulting from mechanisms mentioned above, can be potentially fatal for the tetraplegic patients:
1. collapse of alveoli
2. development and progression of atelectasis
3. hypoxia
4. pneumonia

The goals of the prone position are:
1. to improve ventilation in the dependent parts of lungs
2. to improve ventilation/perfusion relationship
3. to ensure the effective drainage of the bronchial fluid
4. to shorten the weaning from ventilator

The prone position can be performed within:
1. artificial ventilation (ASV Galileo)
2. CPAP
3. spontaneous ventilation

For practical performance the special device – Stryker’s bed is usually used.
The patient is placed in the prone position and after 60 min the blood gas analysis is checked:
1. if hypoxemia and/or hypercapnia occurs/worsens, then the patient is placed back to the supine position – this patient is not “respondent”.
The next attempt with prone position is performed after 2 days – the patient can become “respondent”:
2. if the blood gas values are improved (it means the patient is “respondent”) then the patient is left in the prone position for 4–6 hours.

Advantages of the prone position:
1. reduces the necessity of the flexible fiberoptic bronchoscopy, risk of infection complications and traumatism of the bronchial tree is reduced
2. it makes the weaning from ventilator easier – longlasting ALV further deteriorates muscular force of the auxiliary muscles, that increase probability of the insufficient spontaneous ventilation

Possible complications of the prone position:
1. worse tolerance by patient if ALV is performed – in 30 % of cases the analgosedation and muscle relaxation is necessary
2. excorations of the skin, swelling of the forehead anf face
3. bradycardia – in 15% of cases

Conclusion

The prone position is the necessary part of ventilatory strategy and management in tetraplegic patients. This method decreased number of respiratory complications and accelerates the transition to the spontaneous ventilation. By this way it shortens the stay of the patients in ICU and improves possibilities for further rehabilitation.

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RESPIRATORY MANAGEMENT OF PATIENTS WITH SPINAL CORD INJURIES (SCI)

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Pulmonary complications are a major cause of morbidity and mortality after acute SCI. Dysfunction of respiratory muscles and of auxiliary respiratory muscles depends on the level of injury. Damage of the sfunal cord above C4 involves the phrenic nerve nuclei, and therefore voluntary diaphragmatic respiration mediated by the phrenic nerve is not possible.

Changes of ventilation in SCI patients
– changes of the resistance of the airway
– reduction of the lung elasticity
– reduction of vital capacity (VC) – C4–7 by 30–40 %
– reduction of functional residual capacity (FRC) – C4–7 by 10–25 %
– increase of breathing effort
– increase of secretive viscosity in airways – lesion of the autonomic nervous system
– reduction of maximal oesophageal pressure during forced expiratory vital capacity and coughing manoeuvres
– reduction of movement of the ciliary epithelium
– predisposition to retention of secretions with associated pneumonia and atelectasis

Therapy
– aggressive physiotherapeutic technique
– aerosol inhalation therapy with mucolytics agents, vibrational massage, frequent repositioning including prone position on the Stryker bed
– fiberoptic bronchoscopic toilet – by the means of endotracheal intubation or tracheostomy
– in case of long term ventilation early tracheostomy
+ classical surgical method but only after 14 days following healing wound (complete) – in case of spinal cord operation
+ puncture tracheostomy technique under bronchoscopic supervision. This can be performed between 7th to 10th day.
– non invasive artificial lung ventilation
During this ventilation spontaneous breathing activity is maintained. We use support ventilation. We have a very good experience with ASV – Adaptive Support Ventilation, Hamilton Veolar, Galileo. When cardiovascular stability has been achieved we can use PEEP + 5 cm H₂O.

- maximum inspiratory force +20 cm H₂O
- maximum expiratory force +20 cm H₂O
- vital capacity 1000 ml
- expiratory flow 10 L/s (level dependent)
- \( P_{\text{a}} \text{O}_2/\text{FiO}_2 \) 250
- \( V_{\text{ac}} / V_{\text{T}} \) 55
- lung thorax compliance 30 ml/cm H₂O

Extrusion Criteria
- frequency of breathing 35/min
- \( V_{\text{t}} \) 5 ml/kg
- FVC 10 ml/kg
- NIF 15–25 cm H₂O
- \( P_{\text{a}} \text{O}_2 (\text{FiO}_2 0.4) \) 60 mmHg

When haemodynamically stable, patients can be placed in a vertical position. Concurrently artificial lung ventilation must be closely controlled. After we discontinue ventilatory support, we continue with intensive physiotherapy. We have a very good experience with non-invasive lung ventilation CPAP in 3–4 h intervals. This treatment lasts 15 to 30 min depending on patients tolerance. We administer on daily hours only. At night patient is rested for the period of 8 h. CPAP currently represents prophylaxis of alveolar collapse (Harvey, Ellis 1993).

When the above principles are followed, we can reach satisfactory spontaneous breathing in tetraplegic patients with injury below C4 in 14 days.

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AUTOMATIC CONTROL OF NEOUROMUSCULAR BLOCKER DELIVERY DURING GENERAL ANAESTHESIA DATEX-OHMEDA WORKSHOP

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Modern general anaesthesia (“balanced anaesthesia”) is based on adequate providing of its three fundamental parts (hypnosis, analgesia and muscle relaxation). Older anaesthetic techniques (using single drug only, e. g. ether) covered these components just by increasing the dose of agent, or by concomitant exessive regional anaesthesia. On the contrary, balanced anaesthesia uses several drugs that more or less selectively affect their relevant target areas. The doses can be reduced to influence just the modality, which is insufficient at that moment. This action, though logical and rational, may be potentially risky. It is possible to induce light general anaesthesia without adequate analgesia, or we can unintentionally have relaxed patient who is conscious. Accurate information on the level of every part of general anaesthesia is very important.

Data from our study (Adamus, 2000) confirm that only minority of Czech anaesthetic departments have equipment for neuromuscular blockade monitoring. No anaesthetic department in our country uses NMT monitoring as a routine in everyday practice and the degree of neuromuscular block is usually estimated just from clinical signs during general anaesthesia.

During neuromuscular blockade monitoring the muscle response to motor nerve stimulation is quantified. Following administration of muscle relaxant, which acts on neuromuscular plate, the transmission through this synapse is impaired. This results in weakening of strength of muscle contraction. There are various stimulation patterns useful for different degrees of neuromuscular block (single twitch [TW], tetanic stimulation [TET], train-of-four stimulation [TOF], double burst stimulation [DBS], post-tetanic count [PTC]). Quantification of relevant muscle response can be based on different principles (mechanomyography [MMG], electromyography [EMG], accelerometry [ACC], phonomyography [PhMG]).

The degree of neuromuscular block can be monitored by observing the muscle response to nerve stimulation, commonly the ulnar nerve. Bolus doses of neuromuscular blocker are usually administered intermittently based on this response. However, this method inevitably leads to fluctuations in the degree of neuromuscular block, particularly with recently introduced short-acting agents. To reduce this effect, continuous infusions of neuromuscular blocker may be used, but differences in pharmacodynamics and pharmacokinetics between patients make it difficult to choose the correct infusion rate to maintain the desired level of neuromuscular block.

Closed-loop control offers the ability to provide a stable level of neuromuscular block allowing for variation in individual’s response to the drug. This benefits the patient in that the minimum quantity of drug is administered and the clinical workload is reduced, allowing more time to be spent on other aspects of anaesthesia. The reliability of neuromuscular block monitoring with electromyography permits a precise control strategy to be implemented.

In our department (Dept. of Anaesthesia, University Hospital, Olomouc, Czech Republic) we have developed and introduced into clinical practice a system for automatic delivery of neuromuscular blocker (RelaxA) during general anaesthesia. Fundamental part of the system is a computer interfaced with a NMT monitor Datex AS/3™ and an infusion pump. The monitor is used to determine neuromuscular transmission every 20 seconds. Data are collected and sent to the computer that is programmed to instruct the pump to administer muscle relaxant infusion to maintain stable neuromuscular block. The degree of neuromuscular block is compared to the target level (reference set point). The difference between them (error signal) acts as input information for feedback controller. The controller software automatically exerts those arrangements that return the error signal to zero. If the relaxation is more profound than required the system slows down the infusion pump speed and consequently less neuromuscular blocker is administered. If the blockade is insufficient the pump is instructed to infuse the required.

Bolus doses of neuromuscular blocker may be used, but differences in pharmacodynamics and pharmacokinetics between patients make it difficult to choose the correct infusion rate to maintain the desired level of neuromuscular block.

The muscle response to nerve stimulation, commonly the ulnar nerve, is continuously monitored. When haemodynamically stable, patients can be placed in a vertical position. Concurrently artificial lung ventilation must be closely controlled. We have a very good experience with non-invasive lung ventilation CPAP in 3–4 h intervals. This treatment lasts 15 to 30 min depending on patients tolerance.

We administer on daily hours only. At night patient is rested for the period of 8 h. CPAP currently represents prophylaxis of alveolar collapse.
ACTIVATED PROTEIN C –
A NOVEL AGENT FOR SEVERE SEPSIS
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Sepsis remains a major cause of death in hospitalised patients and the leading cause in non-coronary intensive care units. Despite a massive research effort over the past two decades to identify the innovative therapy for sepsis, current treatment consists primarily of organ support techniques and anti-infective therapies. Activated Protein C (APC), an endogenous protein that inhibits thrombosis and inflammation, while promoting fibrinolysis, plays an important role in the pathogenesis of sepsis. Recombinant APC (drotrecogin alpha), when compared to placebo in randomised study, decreased a relative risk of death at 28 days by 19.4% (Confidence interval 6.6–30.5), although there was a trend for serious bleeding with its use. APC seems to be the first “anti-sepsis” drug, found to have a mortality benefit and was recently approved by the FDA for the reduction of mortality in adult patients with severe sepsis.

A thorough assessment of bleeding risk should be completed for all potential APC candidates. The use of APC is contraindicated in patients with: bleeding, recent hemorrhagic stroke, recent intracranial or intraspinal surgery, severe head trauma, trauma with an increased risk of life threatening bleeding, an epidural catheters, intracranial neoplasm or mass lesion, or evidence of herniation. The presence for other risk factors bleeding (e.g. thrombocytopenia, concurrent therapy with antithrombotic agents) will require clinicians to make a careful risk/benefit decision regarding the initiation of APC therapy.

Although the price of APC is greater than the cost of many innovative therapies, its beneficial effects on patient mortality coupled with the lack of detrimental effects on patient morbidity may in fact make its using as cost effective intervention. A cost-effectiveness analysis was completed and brings encouraging data in this regard. A new trial aiming to prove efficacy of APC in patients with severe sepsis and low risk of death is on the way.

There is a prescribing guideline in Czech Republic developed by Czech Society of Anaesthesiology and Intensive Care to optimise APC therapy.

TRANSFUSION-ALTERNATIVE STRATEGIES
Simple – Safe – Effective

This video program is the first to consider transfusion alternatives from a multi-disciplinary perspective. In all, 18 physicians internationally renowned for their progressive work in the field of transfusion alternatives share their observations and experience. Transfusion-Alternative Strategies reviews recent scientific evidence pointing to the benefits of avoiding donor blood and outlines three pillars of transfusion alternative strategies: appropriate tolerance of anemia, optimizing red blood cell mass, and minimizing blood loss. Surgical and anesthesiological techniques to limit blood loss and pharmaceutical agents to increase blood production are explored for application in preoperative, intraoperative and postoperative settings, as well as application to trauma management.

The program has been endorsed by a prestigious committee of academicians for its scientific accuracy. Total running time: 28 minutes.

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