DOCTORAL THESIS
ASSESSMENT OF PULMONARY DYSFUNCTION AT LARGE BURNT
(SUMMARY)

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Assessment of pulmonary dysfunction at large burnt

Key words: burn, inhalation injury, mechanical ventilation, nosocomial pneumonia, Adult Respiratory Distress Syndrome, free radicals, Swan-Ganz monitoring.

Respiratory tract infection is the most common complication in patients with burn injury. Inhalation injury predisposes the burn patient to the development of pneumonia and ARDS. The lung is the first organ to undergo failure in dying burn patients.

Purpose and objectives:
In this study, I have proposed evaluating the suffering pulmonary dynamics of burning and when the time until healing or death. The synthesis of individualized objectives:

1. Pathophysiological and clinical forms of pulmonary complications that occur in different moments in the evolution of large burned (inflammatory lesions by smoke, ARDS, nosocomial pneumonia, pleurisy and pulmonary embolism).
2. The role of oxygen free radicals in pulmonary complications.
3. Correlation with hemodynamic disturbances, pulmonary dysfunction.

Material and method
The study was conducted on a sample of 466 patients with severe burns admitted to Clinic Hospital of Plastic Surgery Repairers and Burns Bucharest, over 06. 2005 - 09.2008. To study pulmonary complications were selected patients with burns ≥ 20% grade III, grade II ≥ 30%, grade II-III ≥10% associated with upper airway burns caused by flame, cervicofacial and circular chest burns. We monitored: blood pressure, pulse, oxygen saturation of arterial blood (SaO2), number of breaths / min, arterial blood gases, ionograma blood, blood pH, base excess, base deficit, lactate, proteinemia, urea, creatinina, diuresis, transaminases, glucose, bilirubin, number of red blood cells, leukocytes and platelets. PaO2 and blood PaCO2 were determined by harvesting blood from the radial artery. In patients with suspected inhalation trauma and pulmonary dysfunction, we performed bronchoscopy and pulmonary radiographs when the patient's general condition allowed.

- For diagnosis of nosocomial pneumonia we used the simplified clinical score of pulmonary infection (SCIP)
I used to diagnose ARDS diagnostic criteria accepted American-European Consensus Conference (1988) and LISS (1994).

Determination of blood level of antioxidant enzymes (65 cases) was performed in the laboratory of the Department of Pathophysiology of UMF Carol Davila, of the Hospital Bagdazar on venous blood collected from patients hospitalized with severe burns in the Hospital of Plastic Surgery and Burns Bucharest.

Hemodynamically unstable patients with ARDS and IP> 200 (10 cases) were monitored with invasive Swan-Ganz probe in the ICU section of Plastic Surgery and Burns Hospital Bucharest.

Criterion development led to the selection of severe patients who installed Swan-Ganz catheter allowed accurate assessment of central hemodynamic disturbances. Thus, a total of 10 patients, aged between 39 and 67 years whose general condition was very serious need to install the Swan-Ganz catheter in pulmonary artery, the hemodynamic monitoring of critical state since that evolutionary and in therapy.

The study of injuries on internal organs of patients who died because of the burn, we performed the necropsy protocol from the analysis of the observation sheets.

Rezults

A.Injury by smoke inhalation

From the lot of 466 patients, 73% suffered flame burns in an enclosed space. By smoke inhalation injuries were detected in 51.47% of patients who suffered burns in the flame. In burns associated with inhalation injury is found: acidosis, hypoxia, PaCO2 in excess, base excess and deficiency, compared with burns without inhalation. Overall mortality of patients with inhalation injuries was 24.11%. Mortality in patients with inhalation injuries was 69.90% against 6.45% among patients without inhalation lesions. Of 82 deth from the group of 340 severe burns caused by flame, 87.80% are caused by inhalation combustion products. All patients over 60 years with inhalation injury died. These statistics show that inhalation injury and age are factors in predicting mortality of severe burns. Blood gas concentration, pH and base deficit are a good indicator of early diagnosis in inhalation injuries.
B. Nosocomial Pneumonia

For diagnosis of nosocomial pneumonia we calculated SCIP as patients suspected of pneumonia and was found ≥6 to 13.51% patients in group of 466 patients with severe burns. Frequency of nosocomial pneumonia was 27.42% in case of skin burns associated with the inhalation injuries and 2.83% for skin burns without inhalation injury. Nosocomial pneumonia mortality rate in case of severe burns was 51%.

The average age of patients with inhalation lesions was 48 ± 20 years old. The average of the total burned area was 37 ± 10%. In patients with inhalation injury, pneumonia developed after 7.6 ± 3.8 days. In patients with burns over 20% and inhalation injuries, pneumonia rate was 60% versus 21% in patients with burns less than 20%

Duration of hospitalization in patients with inhalation injury and pneumonia was 42 ± 35 days signified an extension of hospitalization compared to patients without pneumonia. The combination of pneumonia to the inhalation injuries increased the mortality rate (19% vs. 9%). In patients with ≥20% area burned, pneumonia has an impact on mortality. In the group patients with burns over 20%, inhalation injury and pneumonia mortality was 42% (13/30), which is significantly higher than mortality of 6.7% in patients with inhalation injury and no pneumonia. The primary endogenous pneumonia was diagnosed in 4 days from the hospitalization. There were detected 59% cases of nosocomial pneumonia primary endogenous, 34% secondary endogenous pneumonia and 7% primary exogenous pneumonia. Aetiology of primary endogenous pneumonia diagnosed by culture of tracheal vacuuming was: Staphylococcus aureus, Streptococcus pneumonia, Acinetobacter and H.influenzae. Secondary endogenous pneumonia etiology was represented by: P.aeruginosa and MRSA. Primary pneumonia was caused by exogenous: MRSA and P.aeruginosa. SCIP was measured 3 days preceding the onset of pneumonia P-3, the onset of pneumonia P0 and on days 3,5,7 (P +3, P +5, P +7) after confirmation of diagnosis. SCIP increase from P-3 to P0 and then gradually decreases when properly treated pneumonia is a significant decrease in 31 survivors, but decreased to 32 dead. The individual components of SCIP, only PaO2/FiO2 distinguished between survivors and deceased, in three days from the onset pneumonia. In patients who received appropriate therapy, SCIP decreased and PaO2/FiO2 increased significantly in the third day from the beginning of pneumonia, and patients with inadequate treatment were
PaO2/FiO2 ratio <200 and SCIP> 6. The report PaO2/FiO2 improving in pneumonia during the survivors, but not dead. Data analysis shows that the SCIP, the report PaO2/FiO2 and pulmonary infiltrate were different in survivors and deceased. We examined the evolution PaO2/FiO2 patients with appropriate antibiotics and inadequate. I noticed that the report gets worse when the beginning of pneumonia and is improving with the appropriate antibiotics and is worse in those with inadequate antibiotic therapy.

C. Adult Respiratory Distress Syndrome:

Of 466 patients selected for the study of pulmonary dysfunction, 91 patients were intubated and ventilated. ARDS diagnostic criteria were fulfilled by 40 patients intubated and ventilated. The total burn surface was about 38 ± 25%, the surface of third degree burn was 29% and the age of patient who developed ARDS was 50 ± 16 years. The report PaO2/FiO2 the onset of ARDS was 117. Patients with ARDS were ventilated for 12 days compared to 6 days as they have been ventilated patients in the control group. We calculated MODS in 91 patients and we found no correlation between ARDS and MODS. Although not statistically significant inhalation injuries were more common in patients who developed ARDS. The average duration of occurrence of ARDS was 6.5 days. More than half 70% of ARDS occurring within 5 days from the occurrence of burns, and 30% occurred after 20 days after the burns. We did not find differences between early ARDS and late ARDS. Forty patients (8.58% of the studied group and 43.95% of intubated patients) developed ARDS according to the criteria AEC and LISS. Percentage of intubated patients who developed ARDS and were diagnosed according to two criteria AEC and LISS was insignificant in burned statistic. MODS which developed ARDS compared to those which did not develop ARDS is not statistically significant. Mortality for intubated patients was de37%. The difference in mortality between the two groups is not statistically significant.

C.1. Antioxidative enzymes and lipoperoxizilor level of patients with severe burns

For the study we used lipoperoxide, antioxidant enzymes and corresponding arithmetic mean values of patient, the prognostic index groups because more patients were admitted to the same surface in different periods. The obtained values from the patients belonging to the study group must be reported to the control value established for each day of reporting.
1. Superoxide –dismutase (SOD)

- all patients with prognostic index greater than 200 have very high levels of superoxide -dismutase in first three days of the burn, but then evolution SOD activity varies according to prognostic index and pulmonary complications occurred. The SOD in the first three days is 49-61U/mgHb, compared to march 42.57 U / mgHb
- patients with prognostic index between 200 and 300 and which evolves without pulmonary or septic complications is found moderate declines (35U/mgHb) of SOD activity after dosing performed between days 6-9, and the dosages taken at the end of the third week evolution SOD activity values tend to normalize (38U/mgHb)
- patients with prognostic index between 200-300, who develop pulmonary complications, dosage made between 6.9 days shows marked decrease of SOD (25U/mgHb) and not normalized after 15 days
- patients with prognostic index over 300 and that evolves with pulmonary complications, dosage performed between days 6.9 shows marked decrease of SOD (22U/mgHb), values that keep down and later complications if the patient survived

2. Glutathione –Peroxidase

Evolution of glutathione-peroxidase is similar to that of SOD. In the first three days to register values between (52-81 U / mgHb) compared to control value of 43.77 U / mgHb
In patients with prognostic index exceeds 300, the glutathione peroxidase decreases during days 6-9, 9 - 12 in values between (27-32U/mgHb) due consumption and decrease synthesis and hemodilution. In patients with septic complications, the decrease is greater (25U/mgHb). Variation of glutathione peroxidase is similar to that of SOD.

3. Catalase

The catalase evolution level is different from the glutathion–peroxidase and superoxide-dismutase evolution.
Persistence of increased levels of catalase (400-700U/mg.Hb) compared to the control of (370U/mgHb) and lipoperoïdes associated with low level of SOD and glutathione
peroxidase signals. Persistent high levels of ROS especially increased risk of tissue damage

4 Transferrin and ceruloplasmin
Analysis of plasma transferrin and ceruloplasmin highlights the following issues:
-the first effectuated dosage, all the patients with severe burns showed normal levels of transferrin.
-the following determinations:
  a) patients with PI <200 were moderate decreases transferrin (210mg/dl) and ceruloplasmin (20mg/dl) compared to blank values tend to normalize in the third week.
  b) patients with PI >200 have low values of transferring (190mg/dl) and ceruloplasmina (5mg%) compared to the blank, the lowest values occurred in patients with ARDS(3mg/dl)

5 Lipoperoxides
In the first three days of the production increase lipoperoxides burns to all burned patients investigated, the increase being directly proportional to the area burned. Keeping value increased lipoperoxides after 72 hours meet burned patients with PI than 200 septic and pulmonary complications. Value lipoperoxides reach 5.21-6.80 nmol / ml compared to the average value of 2.2 ml witnesses.

C2. Monitoring the hemodynamic disorders
Development of severe criterion resulted in the selection of 10 patients who installed Swan- Ganz catheter allowed accurate assessment of central hemodynamic disturbances. In 8 patients monitor PCWP value was between 14-18mmHgl. PCWP value of 20mmHg was recorded in one case and allowed differential diagnosis between EPA hemodynamic and pulmonary edema lesion. In a case of bronchopneumonia with unstable hemodynamics value PCWP was 10mmHg

Discussion
Inhalation injury was recorded at 51.47% patients who suffered flame burns in closed space. The death rate for patients with inhalation injuries was 69.90% compared to 6.45% in patients without inhalation injury, emphasizing that inhalation injury is a predictive factor in mortality of burns. Of the 82 deaths were due to 87.80% inhaling combustion
products. Blood gas concentration, pH and base deficit is a good indicator of early diagnosis in inhalation injuries, which increase the rate of mortality in burns. Incidence of pneumonia in patients with inhalation injuries was 27%. Rates of pneumonia in skin burns> 20% associated with inhalation injuries was 60% . This pneumonia in patients with lesions inhaled increases and doubles the mortality rate during hospitalization (19% vs. 9%). SCIP has worsened in surviving and deceased at the onset of pneumonia. The development of SCIP has improved on 3rd and 5th at the survivors, but not to dead. Contribution of various components of the SCIP has become uneven in the study of evolution pneumonia. The report is PaO2/FiO2 improve after pneumonia in the third and the fifth day, the survivors and decline (worse) to the deceased. In addition, PaO2/FiO2 reach> 250 to survivors and this improvement takes place before other components of the SCIP (leukocytes, fever, secretions and chest x-ray). Impact of adequate therapy was important for PaO2/FiO2, with improvement after three days of appropriate antibiotic therapy and worsening in patients with inadequate therapy. If the report PaO2/FiO2 did not improve, the antibiotic therapy was inadequate. Overall incidence of ARDS in our study was 8.58% in patients with thermal burns and 43.95% of patients intubated. Inhalation injuries were more common in patients who developed ARDS. The death rate for intubated patients was 37%. The level of SOD and glutathione-peroxidase activity increases proportionally with the intensity of oxidative processes and the rate of oxygen intake and decreased by direct consumption as well as because of the presence of inhibitors or fall in its synthesis by liver cells affected by after injury hypoxia. In the first 3 days of evolution, increasing SOD is proportional to increasing levels of oxygen radicals after the sharp rise in terms of ROS, SOD levels begins to decrease. Septic complications cause fall in SOD by direct consumption because of the increased ROS generation. There are other factors that influence the activity of SOD. Trivalent iron increases the cytotoxic effect of oxidizing agents both by its oxidizing ability as well as by decreasing the biosynthesis of SOD. In the first three days of evolution of enzymes is the real value of the needs of buffering free radicals by enzymatic oxigen. Enzyme dosages in patients who died showed very high levels of catalase. Lipoperoxides increase can be considered both a marker of cellular damage, as well as a sign of further aggravation of injuries.
Conclusions:

- Injury from smoke inhalation were found in 51.47% of patients who suffered burns in the flame. In burns associated with inhalation injury is found: acidosis, hypoxia, PaCO2 excess and base deficit compared with burns without inhalation injury from smoke. Overall mortality of burns associated with inhalation injuries was 24.11%. Inhalative products combustion products cause 87.80% of death by flame. All patients over 60 years died. Lesions inhalation and age are a factor in predicting mortality of burns.
- Incidence of nosocomial pneumonia in skin burns associated with inhalation injuries was 27.42% and 2.83% in skin burns without inhalation trauma.
- When occurrence of nosocomial pneumonia, SCIP is ≥6 so the deceased as well as the survivors
- SCIP has a different pattern from the dead and survivors. The dead rise SCIP and the survivors fall
- SCIP evolution (improvement or worsening) correlated with mortality rate of measurement is a method of monitoring SCIP pneumonia nosocomiale.
- Incidence of ARDS in our study was de8, 58%. ARDS occurs in 70% of cases after 5 days from the occurrence of burns. Mortality in post-combustion ARDS was 42%. ARDS late, came after the 5th day, was caused by sepsis and early ARDS was caused by smoke inhalation injuries compounded by ventilation and sepsis.
- The determinations of SOD and glutathione peroxidase enzyme, carried out between days 6-9, in patients who developed complications (especially lung that require respiratory assistance) emphasizes the low values, which maintain and further dosing.
- The persistence of high levels of catalase associated with high levels of persistence points lipoxygenases high levels of oxygen free radicals and particularly increases the risk of tissue damage.
- PCWP measurement is used to differentiate pulmonary edema lesion where PCWP is normal, compared with hemodynamic edema, where PCWP is increased.
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