

## PLASMA EXCHANGE AND CYTOKINES IN FULMINANT MENINGOCOCCAL SEPSIS (FMS)

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Mortality in patients with meningococcal infections and shock or hypotension varies from 20 to 60%. It has been suggested that plasma exchange or whole blood exchange (PEBE) improves survival. Since 1989 we performed PEBE in all patients with acute meningococcal infections and hypotension (n=14). The outcome was compared with the expected mortality (Niklasson prognostic score) and a historical control group admitted from 1984-89. The expected mortality in both groups was respectively 60% and 73%. However, the observed mortality was 14% (2/14) in the PEBE group and 60% (6/10) in the control group (p=0.054). Both fatal cases died within 1 hour after arrival at our ICU before PEBE could be started.

Endotoxin (ET) and ET-induced cytokines play a pivotal role in the genesis of FMS. Therefore, we measured in 9 patients (group A) the concentrations of ET and TNF, IL-1 $\beta$ , IL-6, IL-8 and IL-1 receptor antagonist, and studied the influence of PEBE on these concentrations. For comparison, the same cytokines were measured in 10 patients with meningococcal meningitis without hemodynamic complications who were not treated with PEBE (group B). The concentration at admission of ET, TNF, IL-6, IL-8 and IL-1ra correlated with the severity of disease. The median values of ET and these cytokines in group A were respectively 335 pg/ml (range 90-3400), <100 pg/ml (<100-1190), 27000 pg/ml (600-120800), 2250 pg/ml (325->6000) and 9480 pg/ml (4390->15000). ET disappeared with a t $\frac{1}{2}$  ( $\pm$ SEM) of 180  $\pm$  18 min. This t $\frac{1}{2}$  is similar to values in the literature from patients not treated with PEBE. IL-1 $\beta$  was not increased at admission. IL-6 declined with a t $\frac{1}{2}$  of  $\pm$  5 hours, the IL-8 and IL-1ra pattern more or less paralleled IL-6. PEBE did not influence these patterns. The cytokine pattern in group B showed the same pattern although the median admission values were lower. We tentatively conclude that PEBE might improve survival in FMS, but the beneficial mechanism is not an increased elimination of ET, TNF, IL-1 $\beta$ , IL-6 or IL-8, nor induces PEBE the anti-inflammatory IL-1ra.

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## Cerebral blood flow II

## ROLE OF SJ02 IN MONITORING BRAIN ISCHEMIA IN HEAD-INJURED PATIENTS.

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Cerebral ischemia is a complicating factor increasing mortality rate making neurological recovery poorer, when it's present after head injury. Recently, SJ02 monitoring has become an index of brain oxygenation in clinical practice. The aim of the study was to determine the sensibility and specificity of SJ02 monitoring, in detecting brain ischemia after severe head injury.

Patients and methods.

In forty patients, 32 men and 8 women, aged 34.2 $\pm$ 6.4 yrs, with Glasgow  $\leq$  8 and a CT-scan showing a diffuse brain injury, the physiological variables, CPP, ICP, AVDO2, AVDL, LOI and SJ02, were monitored. All patients were treated by a standard protocol which included hyperventilation, sedation, relaxation, mannitol, fenilephrine and if necessary, barbiturates. Cranial CT-scans were obtained when clinically indicated.

Results.

Eleven patients showed LOI  $\geq$  0.08 at first 24h, which tended to normal values by days 3-5 postinjury. Not only SJ02 in this group did not identify cerebral lactate production in any case, but also CPP, ICP, AVDL and AVDO2. The CT-scan showed cerebral infarction. In the other 39 patients, LOI was < 0.08, and AVDO2 values ranged 0.9-4.1  $\mu$ mol/ml. When AVDO2 was < 1.3  $\mu$ mol/ml, 15 patients, group B, SJ02 values were higher 74.8 $\pm$ 12.4 mmHg when compared with obtained when AVDO2 was >3.0  $\mu$ mol/ml, 54.3 $\pm$ 15.6 mmHg, 24 patients, group C. In this, AVDL was higher, but lower than in the cerebral infarction group. In group B, CPP were lower than in group C, requiring vasoactive treatment only 4 patients. In group B in order to reduce ICP, hyperventilation was used in 13 patients, being the mean $\pm$ SD PCO2 obtained 27.3 $\pm$ 4.2 mmHg. In group C, the vasoactive drug was used in 20 patients, with pCO2 values 34.7 $\pm$ 3.6 mmHg. The initial ICP values in group C were significantly lower, 14.5 $\pm$ 6.4 vs 26.5 $\pm$ 4.7 mmHg.

Conclusions.

- 1- When LOI  $\geq$  0.08, SJ02 does not identify cerebral infarction.
- 2- SJ02 allows to adequate therapeutic protocol at patients cerebral oxygenation requirements
- 3- SJ02 monitoring could improve mortality and neurological recovery by the identification of reversible situations.

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## IS IT POSSIBLE TO PREDICT INFECTION OF CENTRAL VENOUS CATHETER? B Guidet, I Nicola\*, F Staikowsky, V Barakett\*, JC Petit\*, G Offenstadt .

It would be very useful to be able to predict if a central venous catheter (CVC) is infected or not. This could minimize unnecessary catheter removal. **Patients and methods:** The results of a quantitative broth dilution quantitative tip culture of 50 CVC were prospectively compared to cultures of the interior of the hub and of the skin around the insertion point. Blood cultures were obtained from CVC and from a peripheral vein and were processed following routine methods and with a quantitative estimation of colonies (Dupont Isolator). CVC was considered infected when the tip culture was above 500 CFU / ml.

**Results:** CVC were removed because they were unnecessary (group 1; n = 30) or because there was a suspicion of infection (group 2; n=20: unexplained fever n=11; positive blood culture of unknown origin n=5; local signs n=5). In group 1, 2 CVC were infected: 1 polymicrobien (S. epi, S. aureus) with skin positive but with negative blood culture; 1 with S. aureus infection with concomitant infections of skin, hub, blood cultures. In group 2, 6 CVC were infected (32%). The same microorganisms were cultured from tip and skin: 2 S. epi, 2 S. aureus, 1 acinetobacter, 1 candida albicans. Evaluation of the interest of skin and hub culture was appreciated among the 19 patients with suspicion of CVC-related infection.

	sensitivity	specificity	predictive value -
skin (> 15 CFU/ml)	100%	54%	100%
skin (> 100 CFU/ml)	66%	69%	82%
hub (> 15 CFU/ml)	33%	54%	64%
skin+hub(>15CFU/ml)	33%	77%	71%

The skin culture was always above 15 CFU/ml when the tip was infected. In no case, skin culture was negative while CVC was infected. The increase of the threshold of the skin culture to 100 CFU/ml has little effect on specificity but decreases sensitivity. A ratio of quantitative blood cultures obtained from CVC and peripheral vein above 5 has been described as indicative of CVC-related infection. We were unable to confirm this in our study.

**Conclusion:** The culture of skin is easy to perform and if negative can rule out a CVC infection. Hub and quantitative blood cultures were useless in predicting CVC infection.

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## JUGULAR BULB OXIMETRY AND JUGULAR LACTATE DETERMINATIONS IN SEVERE HEAD INJURY C.S. De Deyne, J.I. Poelaert, T. Vandekerckhove, F.A. Colardyn

Recently, combined use of jugular bulb oxygen saturation (Sj02) and jugular lactate determinations has been introduced in ICU practice as a possible monitor of adequate brain perfusion. We analyzed the results of this new method of brain monitoring in severe head injury. Thirty patients suffering from severe head injury (GCS<8) were selected. Jugular bulb oximetry was started within 24 h after trauma and further on every 6 h arterial and jugular bulb blood samples were collected to determine the difference in lactate concentration (AVJDL in mg/dl) and in oxygen content (AVJDO2 in vol %). Out of these values the lactate Oxygen Index (LOI = AVJDL/AVJDO2) was calculated, which is an indicator of developing brain ischaemia. Obtaining these data, we were able to detect the presence of ischaemia (LOI>0.4), compensated hypoperfusion (LOI<0.4 and Sj02<55%) and hyperemia (LOI<0.4 and Sj02>80%).

The admission data indicated that 10 patients were ischemic and that 7 patients suffered from cerebral (compensated) hypoperfusion. During the following days, more than 50% of the patients developed brain ischaemia, while only few (4 patients on day 3) had a cerebral hyperemia. A surprisingly high number of patients suffered from brain ischaemia, although the 6 months-outcome of this group of 30 patients was similar to the expected outcome-value. The most important question remains now the possible therapeutic use of this additional information in the management of patients with severe head injuries.

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CONTINUOUS MEASUREMENT OF YUGULAR O<sub>2</sub> SATURATION IN HEAD INJURY

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With the aim of improving the monitorization of head injury patients, we performed a study evaluating continuously the yugular O<sub>2</sub> saturation with a fiberoptic catheter introduced in the yugular bulb.

**MATERIAL AND METHOD:** It is a preliminary prospective study with 22 head injury patients out of 113 with multiple trauma attended in our Intensive Care Unit from January 1990 through March 1992. The 22 patients carried a fiberoptic catheter to measure yugular O<sub>2</sub> saturation.

**RESULTS:** We encountered the GCS on admission, the highest ICP and the classification of brain damage by CT scan (following Marshall et al.) as the best prognostic indicators.

The patients who died had an ICP maximal peak of 77 mm Hg (7 patients) and continuous yugular oxygen saturation (CYO<sub>2</sub>S) peaks of 96% (9 patients) and minimum of 52% (9 patients).

In the patients who stayed in vegetative coma the highest ICP was 9 mm Hg (5 cases) with CYO<sub>2</sub>S peaks of 78% (5 cases) the highest and 33% (5 cases) the lowest.

The patients that were discharged from ICU without sequelae or more or less disabled, had an ICP high of 18 mm Hg (6 cases) and CYO<sub>2</sub>S peaks of 94% (8 cases) and 49% (8 cases).

**CONCLUSIONS:** The CYO<sub>2</sub>S should be a good parameter for the follow up of the head injury patient. It can improve the continuous cerebral monitorization, helping in the decision of further diagnostic or therapeutic work.

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## INDOMETHACIN/PLACEBOS EFFECTS ON CBF IN HEALTHY YOUNG VOLUNTEERS.

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In experimental and in clinical studies, Indomethacin, like hypocapnia, causes reduction of cerebral blood flow (CBF), whereas cerebral metabolism remains unchanged. A pilot study on 5 patients with severe head injury had suggested a possible role of Indomethacin in the treatment of patients with otherwise uncontrolled ICP. We enrolled 28 persons in a randomised study, with 7 in 4 groups. Group 1 having Indomethacin for 6 hours, group 2 Indomethacin and hypoxia, group 3 Indomethacin and hypercapnia and group 4 placebo. Indomethacin was given in bolus doses of 0.4 mg/kg followed by infusion with 0.4 mg/kg/hour. CBF were measured with CORTEXPLORER 16 and i.v. Xe-133 method.

We found a mean reduction in CBF with 35% (21-44) lasting for the 6 hours of infusion, no obvious rebound phenomenon was recorded. During hypoxia and hypercapnia there was a elevation in CBF returning to the reduced flow after. We found the normal variation in the placebo group. No serious sideeffects was registered.

Indomethacin reduced CBF by 35% (21%-44%) suggesting that Indomethacin might be a new approach in the treatment of patients with severe head injury and intracranial hypertension.

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## CEREBRAL VENOUS OXYGEN SATURATION IN HEAD INJURED PATIENTS

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## Introduction:

One of the aims of neurosurgical treatment is to restore normal cerebral blood flow (CBF), intracranial tension (ICP) and cerebral metabolism, so as to create an optimal milieu for the recovery of damage after severe head injury. Continuous measurement of cerebral venous oxygen saturation S(c)O<sub>2</sub> in the Bulbus venae jugularis with a fiberoptic catheter seems to be an adequate method for detecting the vulnerable period beside the monitoring of ICP as the most relevant parameter for the therapy after head injury.

## Patients and Methods:

20 patients admitted to ICU after a severe head injury (GCS≤5), SAB (H&H IV-V) or ICH (Fisher 3-4) had continuous and simultaneous monitoring of S(c)O<sub>2</sub>, intracranial pressure (ICP), cerebral perfusion pressure (CPP) and arterial oxygen saturation. Arterial, venous and jugular blood gas levels were measured in vitro routinely. S(c)O<sub>2</sub> values obtained by fiberoptic system and measurements with a blood gas analyser in vitro were compared.

## Results:

S(c)O<sub>2</sub> values obtained by fiberoptic system and measurements in vitro showed a good correlation after an initial in vivo calibration when there was adequate light intensity at the catheter tip. Four characteristic constellations were found between S(c)O<sub>2</sub> and CPP/ICP and correlated to the following clinical situations:

- (A) CPP (low) / ICP (high), S(c)O<sub>2</sub> (below 60%) - vulnerable period of the traumatized brain
- (B) CPP (high) / ICP (low), S(c)O<sub>2</sub> (below 60%) - higher oxygen consumption of the brain
- (C) CPP (high) / ICP (low), S(c)O<sub>2</sub> (over 60%) - supposed to be due to greater inactive brain areas
- (D) CPP (low) / ICP (high), S(c)O<sub>2</sub> (over 70%) - start of a deleterious phase

## Conclusion:

The changes of cerebral venous oxygen saturation found in this study suggest that continuous monitoring of S(c)O<sub>2</sub> is of clinical relevance in patients with head injuries

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RELATIONSHIP OF CBF AND CMRO<sub>2</sub> TO OUTCOME IN SEVERELY HEAD INJURED PATIENTS

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Several different factors such as cerebral primary injury, age, ICP value and trend, extracerebral parameters have been described as affecting outcome of the brain injured patients. The relationship between Cerebral Blood Flow (CBF), Cerebral Metabolic Rate in Oxygen (CMRO<sub>2</sub>), ArterioJugular Venous Oxygen Differences (AJDO<sub>2</sub>), Glasgow Coma Scale score (GCS) on admission and outcome at 6 months using the Glasgow Outcome Scale (1) were studied.

20 head injured comatose patients (GCS <7), all mechanically ventilated, admitted to our general Intensive Care, were studied in the first 48 hrs after the trauma. Regional CBF measurements were performed by 133Xenon DSPET using CERTO 96, a brain dedicated tomograph with Xenon administered via a properly adapted mechanical ventilator. Intracranial pressure was monitored in all patients by means of an intraventricular or subdural catheter. A catheter was inserted in the jugular bulb for O<sub>2</sub> content, AJDO<sub>2</sub>, glucose and lactate determinations; CMRO<sub>2</sub> was calculated by the Fick equation. PaCO<sub>2</sub> was maintained between 30 and 35 mmHg and CBF value was corrected to a PaCO<sub>2</sub> of 34 mmHg (± 3% CBF every mmHg of PaCO<sub>2</sub>). The AJDO<sub>2</sub> values were calculated dividing CMRO<sub>2</sub> by the corresponding CO<sub>2</sub>-corrected CBF. Statistical analysis was performed with Spearman's rank test for ordinal scale data.

Results: patients were divided in two groups based on GOS at 6 months (Group 1=GOS I-II, Group 2=GOS III-V). In the Group I (10 pts) mean CBF was 36.0 ± 13.3 ml/100g/m, mean CMRO<sub>2</sub> was 1.1 ± 0.5 ml/100g/m. In the Group II (10 pts) mean CBF was 41.45 ± 6.56 ml/100g/m, mean CMRO<sub>2</sub> was 1.69 ± 0.63 ml/100g/m. A statistically significant difference was obtained only for CMRO<sub>2</sub> values (p=0.015, t = -2.69) while CBF difference did not reach any statistical significance (p=0.26). GCS on admission and CMRO<sub>2</sub> (r = 0.784, p < 0.001; r = 0.548, p < 0.02 respectively) were the most significantly related parameters with outcome.

On the basis of these results, we may attribute a role to CMRO<sub>2</sub> for determination of prognosis in the head injured patients, while determination of CBF by itself, as previously reported (2-3) is of limited value.

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