

Effect of Cerebral Oxygenation Monitoring As an Additional Variable on the Outcome in Severe Traumatic Brain Injury

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ABSTRACT

Aim: To investigate the importance of cerebral oxygenation parameters, estimated from the jugular venous oxygen saturation (SjO_2) and cerebral arteriovenous oxygen difference ($AVDO_2$), as a supportive monitoring and management variable to intracranial pressure (ICP) and cerebral perfusion pressure (CPP), and its impact on the final outcome in patients with severe traumatic brain injury. **Method:** The study included 43 patients of cohort successive cases with severe traumatic brain injury admitted between December 2006 and April 2008, with a post-stabilisation Glasgow Coma Score (GCS) ≤ 8 . These were divided into two groups; one group in which the patients were treated with ICP/CPP management alone (ICP/CPP-guided group) and the other group in which the SjO_2 and $AVDO_2$ were measured in addition to the ICP/CPP and managed accordingly (Jugular bulb variables-guided group). **Results:** The jugular bulb variables-guided group had a slightly better outcome (44% good outcome), as compared to the ICP/CPP-guided group (33% good outcome), and a worse outcome (67% poor outcome) was observed in the ICP/CPP-guided group as compared to the other group (56% poor outcome). **Conclusion:** Outcome from severe TBI is better in patients undergoing management based on monitoring and management of both cerebral oxygenation and ICP/CPP, than in patients subjected to monitoring and management of ICP and CPP alone. Integration of monitored variables allows cross-validation and artefact rejection, better understanding of pathophysiology, and the potential to target therapy. Newer methods for detecting regional areas of ischemia are also important in the management of severe traumatic brain injury patients.

Abbreviations

SjO_2 =jugular venous oxygen saturation, $AVDO_2$ =cerebral arteriovenous oxygen difference, ICP=intracranial pressure, CPP=cerebral perfusion pressure, $CMRO_2$ =cerebral metabolic rate of oxygen, CBF=cerebral blood flow, GCS=Glasgow Coma Score, GOS=Glasgow Outcome Score, MAP=mean arterial pressure

INTRODUCTION

Intracranial pressure (ICP) is probably the most commonly monitored brain parameter in neurocritical care. The majority of the bedside monitors display the mean intracranial pressure (ICP) numerically

or its pulse waveform. However, determination of cerebral perfusion pressure (CPP) is regarded as vital in monitoring patients with severe traumatic brain injury. Several studies have established the relation between low CPP and poor outcome⁽¹⁾. However, despite maintaining a cerebral perfusion pressure of > 70 mm

Hg, cerebral ischemia and hypoxia may still occur, worsening the patient's chances of a satisfactory outcome. Cerebral hypoxia caused by cerebral ischemia-through impaired autoregulation, systemic hypotension, hypoxia, and intracranial hypertension-has been identified as a principal cause of secondary brain damage⁽⁴⁾.

Jugular venous oxygen saturation (SjO_2) reflects the balance between cerebral oxygen delivery and the cerebral metabolic rate of oxygen ($CMRO_2$), if arterial oxyhemoglobin saturation, hemoglobin concentration, and the hemoglobin dissociation curve remain constant. Any disturbance that increases $CMRO_2$ or decreases oxygen delivery may decrease SjO_2 . Conversely, a disorder that decreases $CMRO_2$ or increases oxygen delivery may increase SjO_2 . Thus, a low SjO_2 indicates cerebral hypoperfusion or ischemia. Whereas, an elevated SjO_2 interpretation may not be as simple, it basically indicates either an oxygen extraction problem or focal cerebral ischemia if the involved area of the brain is small or if the reduced oxygen saturation from the ischemic brain is offset by a high oxygen saturation from surrounding hyperemic brain⁽³⁾.

Since the cerebral arteriovenous oxygen difference ($AVDO_2$) equals $CMRO_2/CBF$, the $AVDO_2$, has been proposed as a measure of the adequacy of CBF to support brain metabolism⁽¹¹⁾. A normal $AVDO_2$, (5 to 7.5 vol%) would suggest that cerebral blood flow (CBF) is normally coupled to $CMRO_2$; a decreased $AVDO_2$ (<5 vol%) would indicate that CBF is excessive for cerebral metabolic requirements (relative hyperemia); and an elevated $AVDO_2$ (>7.5vol%) would indicate inadequate CBF (relative ischemia) but may also mean increased oxygen extraction⁽²⁾. If this concept is valid,

$AVDO_2$ and SjO_2 would be valuable in the treatment of comatose head injured patients in whom on-going ischemia may not be evident from neurological signs or ICP monitoring.

MATERIALS & METHODS

Patient characteristics

This is prospective double-blind study included 43 patients of cohort successive cases with severe traumatic brain injury admitted between December 2006 and April 2008, with a post-stabilisation Glasgow Coma Score (GCS) ≤ 8 . All patients were submitted to CT scan after being intubated and ventilated. The patients were allocated alternatively into the two studied groups.

The exclusion criteria included: abnormal arterial oxygen saturation (<90% in room air), anaemia (Hb less than 10g%), haemodynamic instability, convulsions on admission or brain death.

This study was approved by the ethical and research committees of the hospital with informed consent of the patients' guardian.

Setting

Level 1 intensive care unit.

Physiological parameters

Four monitoring parameters were recorded: jugular bulb venous oxygen saturation (SjO_2); cerebral arteriovenous difference ($AVDO_2$)= $Hb \times 1.34(PaO_2$ (percent arterial Hb saturation)- SjO_2); intracranial pressure (ICP); cerebral perfusion pressure (CPP). The SjO_2 and $AVDO_2$ were referred to as the *jugular bulb variables*.

Technique

The SjO_2 was measured by inserting a retrograde catheter placed preferentially into the right superior

jugular bulb, by ultrasound-guided technique (Toshiba PowerVision 8000, Toshiba, Japan) (Figure 1). Additional confirmation of the position was done by plain x-ray (lateral view). The catheter was placed on the side of the worst injury or on the right side if the injury was diffuse. Paired arterial and jugular venous samples were collected every 4 hours and blood gases measured using Blood Gas Analyzer (ABL 77 series, Radiometer, Copenhagen). This was in addition to samples taken during the episodes of increased ICP.

The AVDO₂ was calculated by obtaining an arterial blood sample from a radial artery catheter and a simultaneous sample from the jugular bulb, as described above, and were also recorded every 4 hours. For advanced multiparameter neuromonitoring intracranial pressure catheters were inserted (Camino MPM-1, Integra Neurosciences, USA). The catheters were inserted into the brain as soon as possible after the trauma—that is, in the ICU after admission or during emergency craniotomy for haematoma evacuation. They were usually placed intraparenchymally (OLM*ICP monitoring kit Model 110-4B) in the frontal region of the more severely injured side. An intraventricular monitoring catheter (Microventricular bolt pressure monitoring kit Model 110-4HM) was placed in 3 patients to drain CSF in cases which developed hydrocephalus. In case of a diffuse injury, the right frontal region was chosen. Patients were monitored until normalisation of ICP for 48 hours. The maximum number of monitoring days was 5 days. The mean CPP was calculated as follows: mean arterial blood pressure (MAP) – ICP.

The patient outcome was assessed 3 months after injury, using the

Glasgow outcome scale (GOS) ⁽⁸⁾. A good outcome was GOS 4-5 and a poor outcome was GOS 2-3.

Monitoring and treatment protocol

To evaluate the effects of a therapeutic regimen using the calculated jugular bulb variables (SjO₂ 55-75 vol% and AVDO₂ 5-7.5 vol%) as an additional therapeutic target, two separate groups were studied.

ICP/ CPP-guided group: For the first group of patients (21), treatment was aimed at keeping intracranial pressure (ICP) below 20 mm Hg and cerebral perfusion pressure (CPP) above 70 mm Hg, with the following options. All patients were sedated, intubated, and ventilated to maintain PaO₂ at 100 to 120 mm Hg and PaCO₂ 35-40 mmHg. Mannitol, volume expansion, and vasopressors were given to keep intracranial pressure under 20 mm Hg and cerebral perfusion pressure above 70 mm Hg. In selected cases non-aggressive hyperventilation (PaCO₂ 30-35 mmHg) was used as per *Brain Trauma Foundation protocol*. The FiO₂ was maintained between 38% and 50% so as to maintain the sPaO₂ between 97% and 99%. Surgical options in the treatment protocol included the evacuation of haematomas and decompressive craniotomy in case of operable intracerebral lesion.

Jugular bulb variables-guided group: For the second group of patients (22), the treatment targets were the same as those for the ICP/ CPP guided group but in addition, the avoidance of critical SjO₂/AVDO₂ values, which was accomplished by increasing vasopressors and fluid intake.

Data collection

All patients had initial measurements recorded and for each patient, the initial values of ICP, CPP,

SjO₂ and AVDO₂ were recorded. This was in addition to, the critical events involving periods of abnormality: (1) critical SjO₂/AVDO₂ episode (SjO₂ ≤ 55% or ≥ 75%; AVDO₂ < 5 vol% or > 7.5 vol%) or (2) critical ICP/ CPP episode (ICP ≥ 20mmHg or CPP <

70mmHg for more than 30 minutes) were noted and the incidence of their occurrence recorded. In addition to this, for each patient, the initial values of ICP, CPP, SjO₂ and AVDO₂ were recorded.

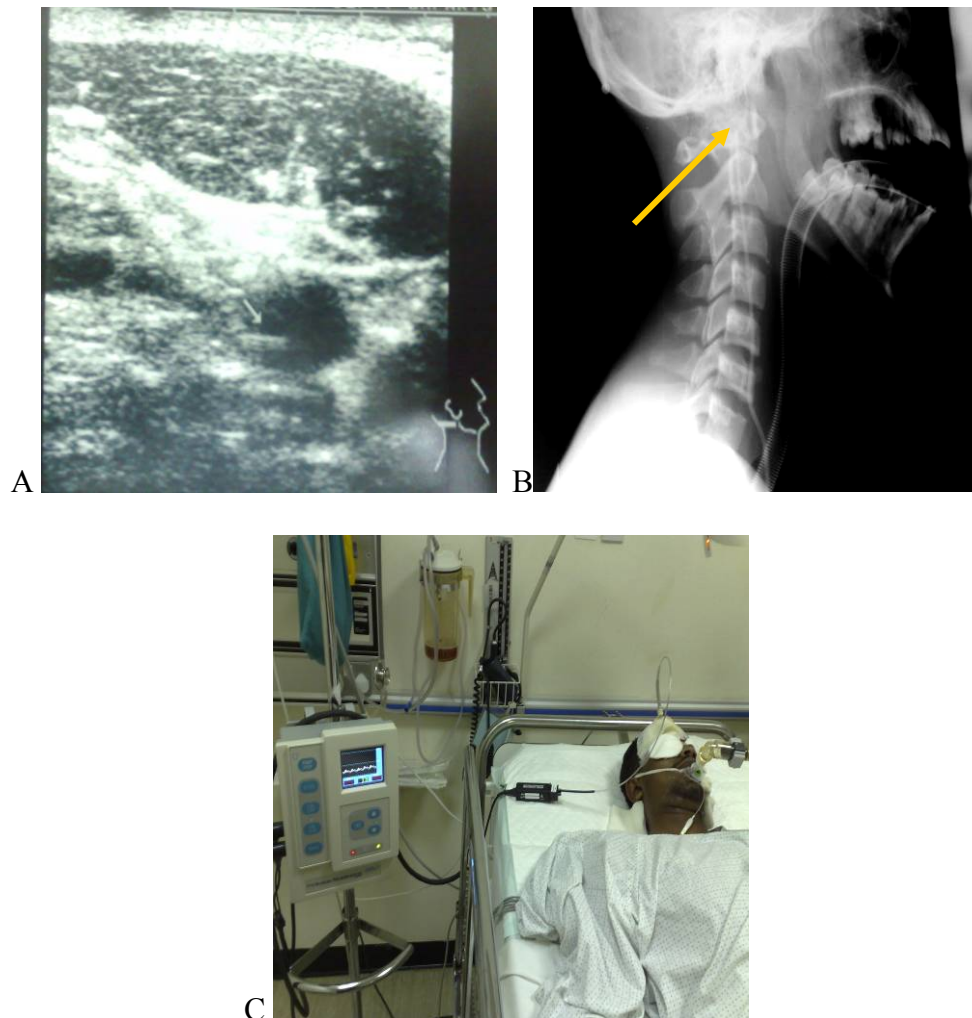


Figure 1. A. U/S-guided placement of jugular bulb catheter (white arrow), B. PXR confirmation (white arrow), C. intraparenchymal monitor placed into the frontal region.

Table 1. Demographic characteristics, initially measured parameters, occurrence of critical episodes and mean values throughout monitoring period
NM (not measured)

	ICP/ CPP-guided group	Jugular bulb variables-guided group
Age	31±10 years	31±8 years
Sex		
Male	11	13
Female	5	1
Initial GCS (mean)	5±1	6±1
Initial ICP		
Mean (mmHg)	18±6	16±8
High	9 (75%)	12 (67%)
Normal	3 (25%)	6 (33%)
Initial CPP		
Mean (mmHg)	72±10	69±14
Low	5 (42%)	8 (44%)
Normal	7 (58%)	10 (56%)
Initial SjO₂ (mean)	NM	61±18
Initial AVDO₂ (mean)	NM	6±3
Initial abnormal SjO₂/AVDO₂	NM	13 (72%)
Initial normal SjO₂/AVDO₂	NM	5 (28%)
No. of patients with critical ICP/ CPP episodes	5	12
No. of episodes of critical ICP/ CPP	8	16
No. of patients with critical jugular bulb variable episodes	NM	12
No. of episodes of critical jugular bulb variables	NM	19
Mean ICP	17±6	15±4
Mean CPP	78±8	82±11
Mean SjO₂	NM	67±10
Mean AVDO₂	NM	5±3

RESULTS

From the initial 43 patients included in this study the following patients were excluded because factors other than cerebral trauma: 6 patients developed sepsis, 2 had a re-bleed and 5 died during the monitoring period due to causes unrelated to the initial

cerebral trauma. From the remaining 30 patients, 12 patients were included in the ICP/ CPP-guided group, and the other 18 patients in the jugular bulb variables-guided group.

The study included 6 females and 24 males. Eleven patients underwent surgery for intracranial mass lesions (7 subdural hematomas-one extradural

hematoma-one intracerebral hematoma-one cerebral contusion). Seven (39%) of these patients were in the jugular variables group and 4 (33%) in the ICP/CP group. Among the remaining patients only 3 had intracranial lesions which did not require surgical intervention. All patients included in the study had to have a GCS ≤ 8 , to have an ICP monitor inserted, according to our protocol. Thus, GCS could not be included as a factor affecting outcome.

The two groups of patients were matched with regard to age, GCS scores and acute surgical traumatic intracranial lesions, and no significant differences could be found. Also the initial levels of intracranial pressure, cerebral perfusion pressure and jugular bulb variables (before management) were measured for each group. Table 1 summarizes the demographic characteristics, initial values and frequency of critical ICP/CP and jugular bulb variables episodes. All patients suffering critical episodes had $SjO_2 \leq 55\%$ and $AVDO_2 > 7.5 \text{ vol}\%$, except one patient who had one episode ($SjO_2 > 75\%$). Most of the patients in both groups had initially high ICP (9 (75%), 12(67%) respectively) while the CPP was initially low in 5 (42%) and 8 (44%) patients respectively. The majority of patients in which the jugular variables were measured had initially abnormal $SjO_2/AVDO_2$ values (13 (72%)). A major difference was found between both groups regarding the frequency of critical ICP/CP episodes, occurring more often in the jugular bulb variables-guided group, however, the majority of the episodes were increases in the ICP with maintenance of the CPP (91%). Twelve patients (67%) among the jugular variables group had critical $SjO_2/AVDO_2$ episodes (the

majority (9) were single episodes). Seventeen (57%) had critical ICP/CP episodes (5 (29%) in ICP/CP group and 12 (71%) in jugular variables group).

The relationships between the initially measured values and the critical episodes were made. Patients with initially abnormal ICP/CP values in both groups, were more prone to critical ICP/CP episodes ($p < 0.0001$ and 0.003 , respectively), as illustrated in Figure 2 and 3. They were also prone to critical $SjO_2/AVDO_2$ episodes ($p = 0.14$ and 0.21 , respectively), measured only in the jugular bulb variable-guided group (Figure 3).

Regarding the outcome of both groups, the jugular bulb variables-guided group had a slightly better outcome (44% good outcome), as compared to the ICP/CP-guided group (33% good outcome), and a worse outcome (67% poor outcome) was observed in the ICP/CP-guided group as compared to the other group (56% poor outcome) (Table 2), however no statistical significance could be demonstrated ($p = 0.71$). Then the relationships between the initial values, critical episodes and the final outcome were investigated (Table 3 & 4). Poor outcome was associated with initial abnormal ICP ($p = 0.42$), CPP ($p = 0.03$) and $SjO_2/AVDO_2$ ($p = 0.02$) values (Table 3), as well as the frequency of critical episodes, and combinations of these factors (Table 4). Poor outcome was also associated with the frequency of critical jugular bulb episodes with a high statistical significance ($p = 0.005$). Among the patients that underwent surgery for intracranial mass lesions, a good outcome was recorded in 4 (36%), which was equally divided between both groups.

Table 2. Final outcome of both groups

	ICP/ CPP-guided group	Jugular bulb variable-guided group
Good outcome	4 (33%)	8 (44%)
Poor outcome	8 (67%)	10 (56%)

Table 3. Final outcome in relation to initially measured parameters NM (not measured)

	ICP/ CPP-guided group		Jugular bulb variables-guided group		p-value
	Good outcome	Poor outcome	Good outcome	Poor outcome	
No. of patients with high initial ICP	2 (22%)	7 (78%)	5 (42%)	7 (58%)	0.42
No. of patients with normal initial ICP	2 (67%)	1 (33%)	3 (50%)	3 (50%)	
No. of patients with low initial CPP	0	5	2 (25%)	6 (75%)	0.03
No. of patients with normal initial CPP	4 (57%)	3 (43%)	6 (60%)	4 (40%)	
No. of patients with low initial S_jO₂	NM	NM	1 (11%)	8 (89%)	0.02
No. of patients with normal initial S_jO₂	NM	NM	7 (78%)	2 (22%)	

Table 4. Final outcome in relation to critical episodes and initially measured parameters

	ICP/ CPP-guided group		Jugular bulb variables-guided group		<i>p</i> -value
	Good outcome	Poor outcome	Good outcome	Poor outcome	
No. of patients with critical jugular episodes			5 (33%)	10 (67%)	0.005
No. of patients with critical ICP/ CPP episodes	2 (40%)	3 (60%)	7 (58%)	5 (42%)	<0.0001
No. of patients with critical ICP/ CPP episodes & high initial ICP	1 (20%)	4 (80%)	2 (29%)	5 (71%)	0.5
No. of patients with critical ICP/ CPP episodes & normal initial ICP	0	0	2 (67%)	1 (33%)	
No. of patients with critical ICP/ CPP episodes & low initial CPP	0	3	2 (29%)	5 (71%)	0.1
No. of patients with critical ICP/ CPP episodes & normal initial CPP	1 (50%)	1 (50%)	5 (83%)	1 (17%)	
No. of patients with critical jugular episodes & high initial ICP			4 (40%)	6 (60%)	0.14
No. of patients with critical jugular episodes & normal initial ICP			3 (60%)	2 (40%)	
No. of patients with critical jugular episodes & low initial CPP			3 (38%)	5 (62%)	0.55
No. of patients with critical jugular episodes & normal initial CPP			3 (75%)	1 (25%)	

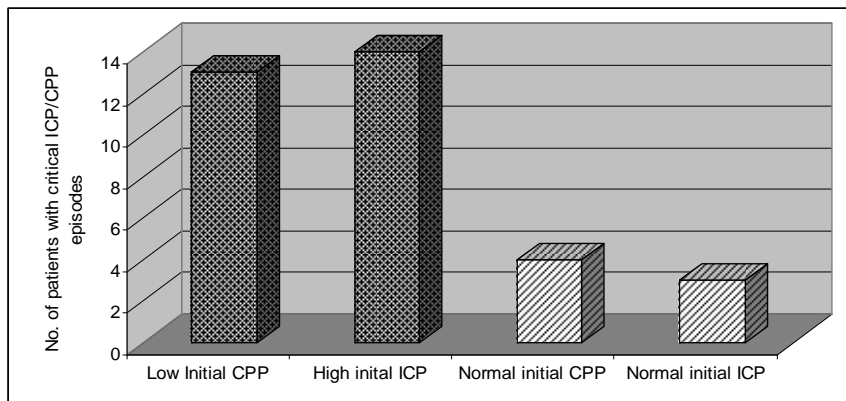


Figure 2. Relationships between critical ICP/CPP episodes and initially measured parameters

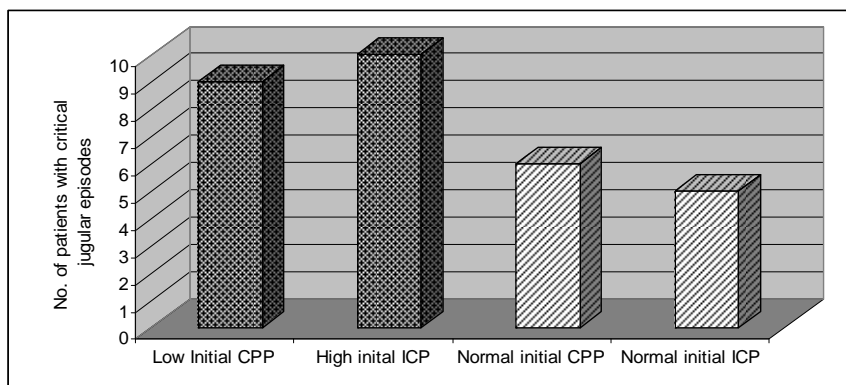


Figure 3. Relationships between critical jugular episodes and initially measured parameter

DISCUSSION

It has been demonstrated that decreased CPP values associate with levels of jugular venous oxygen saturation that correlate with unfavorable outcomes, and that raising the CPP above 60 mm Hg may avoid cerebral oxygen desaturation⁽¹⁰⁾.

Relationship between critical ICP/CPP episodes and critical jugular bulb variables episodes

The patients that experienced critical ICP/CPP (of which 91% were increases in ICP) were markedly greater in the jugular bulb group. An explanation for this would be that the treatment protocol in that group

depended on increasing the CPP to high values to correct the jugular desaturation episodes which may have consequently increased the ICP. This probably would not have affected the outcome as, *Howells et al.*⁽⁷⁾ found that patients with intact pressure autoregulation would have tolerated high ICP without a change in outcome.

Our results show that patients with high initial ICP and low CPP were more liable to develop critical jugular episodes. These findings were clearly depicted in the current study as seen in Figure 2. Data documenting the occurrence of brain ischemia early after injury demonstrated the occurrence of reduced CPP and jugular

venous desaturation due to increased ICP⁽¹⁵⁾.

Value of AVDO₂

SjO₂ values alone may not provide the best critical threshold indicator of prognosis. In our study the initial mean AVDO₂ throughout the monitoring period was 5 vol%, measured in the jugular bulb group, in which the outcome was better. In another study of 229 comatose TBI patients, arteriovenous difference of oxygen content (AVDO₂) in addition to SjO₂ was obtained every 12 h, and the measurements correlated with 6-month outcome. Higher mean AVDO₂ (4.3 vol%) was found to be associated with a good outcome and it was an independent predictor of outcome. It was postulated that a low SjO₂ may indicate low oxygen delivery but AVDO₂ represents oxygen extraction by the brain⁽¹²⁾. This is the reason for including both variables in our management protocol and evaluation of outcome. The difference of our results from the mentioned study may be explained by smaller number patients counterbalanced by the more frequent measurements of our study.

Difference in outcome between both groups

In this study we were investigating the target of basic intensive care management in severe traumatic brain injury, in the area of cerebral oxygenation and metabolism. It was found that there was better outcome when SjO₂ and AVDO₂ were monitored and managed together with ICP/ CPP management. These findings were consistent with *Struchen et al*⁽¹³⁾ who conducted a study of 184 patients severe TBI who received continuous monitoring of ICP, MAP, CPP, and jugular venous saturation (SjO₂). Primary outcomes were GOS and Disability Rating Scale (DRS).

Analysis included evaluating effect of physiologic variables on outcome. ICP > 25 mm Hg, MAP < 80 mm Hg, CPP < 60 mmHg, and SjO₂ < 50% were associated with worse outcomes.

Relationship between initial values and outcome

The value of the jugular bulb-guided management could be demonstrated when both groups were compared in relation to initial abnormal values, as better outcome was associated with that group (22% and 0 in ICP/ CPP group compared to 42% and 25% in jugular bulb group).

In concordance with other studies initially abnormal values were associated with worse outcome. A study found that good outcome was significantly higher when initial CPP was more than 80 mmHg⁽⁹⁾. *van den Brink et al*⁽¹⁴⁾, found worse outcome related to initially low brain oxygenation. So our results may be partly explained by the more frequent occurrence of critical ICP/ CPP and jugular bulb episodes when the patient had initially abnormal values as demonstrated in Figures 1 & 2.

Relationship between critical jugular bulb variables episodes and outcome

The occurrence of jugular venous desaturation has been shown to be associated with poor neurological outcome⁽⁶⁾. *Fandino et al*⁽⁵⁾, demonstrated that the percentage of patients who presented desaturation episodes was higher in patients who died (71%) than in patients who had GOS 2–3 (56%) or GOS 4–5 (48%). In addition, the percentage of patients with favourable outcomes who had no or one desaturation episode was significantly higher than among those who had multiple episodes. This is consistent with our study 67% of the patients who experienced critical jugular episodes had a poor outcome.

This is consistent with Gopinath et al⁽⁶⁾ & Fandino et al⁽⁵⁾ studies. However, the global results in our study showed that in jugular bulb group there was a better outcome (44%) than in ICP/ CPP group (33%) and this can be explained by the higher frequency of management interference & adjustment in the jugular bulb group than the other group. Also in ICP/ CPP group many critical jugular bulb episodes could have occurred but not detected as our management was only directed at correcting the ICP/ CPP episodes. These observations highlight the importance of assessing the global cerebral oxygen supply and demand as an outcome predictor.

CONCLUSION

Outcome from severe TBI is better in patients undergoing management based on monitoring and management of both cerebral oxygenation and ICP/ CPP, than in patients subjected to monitoring and management of ICP and CPP alone. However, both conventional monitoring methods and newer techniques are limited by the fact that they detect either globally averaged or highly localized abnormalities in cerebral physiology and may be unable to detect regional abnormalities in the metabolically heterogeneous injured brain. Although individual monitoring techniques provide information regarding specific aspects of cerebral function, the correlation of data from several modalities has several advantages in the management of head injury. Integration of monitored variables allows cross-validation and artefact rejection, better understanding of pathophysiology, and the potential to target therapy.

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