Increased jugular bulb saturation is associated with poor outcome in traumatic brain injury


Abstract
The objective was to compare secondary insults, particularly decreases in jugular bulb oxyhaemoglobin saturation (SjO₂), during intensive care in patients with “poor” and “good” outcomes 12 months after traumatic brain injury.

A prospective observational study of patients’ physiological data collected each minute from multimodality monitoring was carried out. Patients had duration of physiological insults quantified as a percentage of their validated monitoring time (once invalid data due to technical reasons were removed). Treatment protocols were designed to minimise secondary insults by maintaining intracranial pressure (ICP) less than 20 mm Hg, and cerebral perfusion pressure (CPP) greater than 70 mm Hg, with prompt correction of hypoxia and pyrexia. Twelve months after injury patients’ neurological function was assessed using the Glasgow outcome scale (GOS). A poor outcome was defined as GOS 1 to 3 (group 1) and a good outcome as GOS 4 and 5 (group 2). Seventy five patients (64 male), median age of 34 years (range 15 to 70), were studied. At 12 months 33 patients had a poor outcome (group 1), and 42 a good outcome (group 2). Group 1 spent proportionately more time with SjO₂ below 54% (p<0.05), and more time with SjO₂ greater than 75% compared with group 2 (p<0.05), and more time with SjO₂ below 54% (p<0.04). Group 1 patients also spent proportionately more time with CPP less than 70 mm Hg than group 2 (p<0.04). Patients in group 1 were older (p<0.04) and had a lower postresuscitation Glasgow coma score (p<0.002). There was no difference between the groups for ICP, injury severity score, peripheral pulse saturation, and pyrexia.

This study confirms that secondary insults, including an increased SjO₂, occur significantly more in patients with poor outcomes. More research into strategies to reduce the impact of secondary insults, including management of increased SjO₂, is required.

Keywords: head injury; jugular bulb venous oxygen saturation; cerebral oxygenation

Traumatic brain injury has devastating consequences including severe brain damage and death, and affects predominantly young adults aged 15 to 35 years.¹ No pharmaceutical progress has been made to improve the outcome for these patients. In the absence of a “magic bullet” current best practice recommendations aim to reduce secondary insults to the brain.² Secondary brain injury from physiological insult is common after traumatic brain injury³ and is caused by hypoxia and hypotension, both of which are associated with poor outcomes.⁴ There is evidence to suggest that high intracranial pressure (ICP),⁵ low cerebral perfusion pressure (CPP) and low jugular bulb oxyhaemoglobin saturation (SjO₂)⁶ are also associated with a poor prognosis.

Evidence suggestive of ischaemic brain damage is commonly found in patients who die from traumatic brain injury; thus, ischaemia may be the final common pathway of secondary insults in patients with fatal injuries. The SjO₂ is a measure of global brain oxygen extraction (SjO₂ varies directly with cerebral blood flow and indirectly with the cerebral metabolic rate for oxygen (CMRO₂)). Over the past 15 years continuous measurement of SjO₂ has become part of routine monitoring in many neurointensive care units.

This study reports on multimodality monitoring data, in particular SjO₂, and their relation with neurological outcome in a cohort of patients with traumatic brain injury, and identifies where additional effort to reduce secondary insults may be appropriate.

Patients and methods

PATIENTS
Local ethics committee approval was obtained before the start of the study. Between June 1990 and May 1995 75 patients were recruited on the basis of requiring mechanical ventilation in the neurointensive care unit for management of traumatic brain injury. Patients were studied consecutively except where the number of patients concurrently in the unit exceeded the number of computers available to collect data.

Patients were managed using a protocol to minimise secondary insults. It included paralysis (as clinically indicated), mild hyperventilation to Pa CO₂ of 4.5±0.5 kPa, sedation and analgesia using benzodiazepine and alfentanil, and ICP below 20 mm Hg using furosemide,
mannitol, and more aggressive hyperventilation (keeping SjO2 within normal limits of 54% to 75%) as necessary. The CPP was maintained above 70 mm Hg with fluid and vasopressors (norepinephrine+dobutamine). The jugular bulb was cannulated using a well described technique; a compliance test was performed to determine the jugular bulb which had the largest vascular territory, but if the compliance test was equitable (similar ICP reading for each side) the right jugular bulb was chosen. Catheter tip position was verified by lateral neck radiography (to lie above the disc space of C1 and C2) and the catheter marked externally so that the position could be checked regularly, including calibrations which were done every 12 hours. Inspired oxygen concentration, which influences SjO2, was kept to the minimum required to obtain a PaO2 of 10 mm Hg (and SpO2 of 94%) according to arterial blood gas sampling, which was done at least three times a day; all patients were therefore treated equally. Values for SjO2 outside normal limits were verified by first confirming the catheter tip position, then measuring a jugular bulb blood sample by oximetry (ILS Co-Oximeter 282). If SjO2 was confirmed to be less than 54% mechanical ventilation was manipulated causing Pa CO2 to increase, and CPP was optimised. No specific treatment protocol was instituted for SjO2 values exceeding 75% unless ICP was greater than 30 mm Hg or CPP less than 70 mm Hg for 5 minutes as described above.

CONTINUOUS PHYSIOLOGICAL MEASUREMENTS
Minute by minute physiological data were collated and analysed using purpose written software—the Edinburgh Monitor and Edinburgh Browser. Data included arterial blood pressure, central venous pressure (CVP), ICP, and CPP (mean arterial pressure minus ICP); SjO2, peripheral pulse oximetry, and core temperature. Physiological insults outside normal values have previously been documented and included ICP less than 20 mm Hg, CPP less than 70 mm Hg, SjO2 less than 54% or greater than 75%, peripheral pulse saturation less than 92%, and pyrexia greater than 38°C. An insult was registered when the measurement was continuously outside normal limits for a minimum of 5 minutes. Conversely, the termination of an insult was registered when the measurement was continuously within normal limits for 5 minutes. Data collection began at the time of first set of tests), or when there was no longer a clinical requirement for each particular monitor. The ICP was measured with a Camino fibreoptic monitor (Camino, San Diego, CA, USA) placed in the brain parenchyma. The SjO2 was measured continuously with a 40 cm Shaw Opticath and Oximetrix 3 computer with the Oximetrix 3 system (Abbott Critical Care Systems, Chicago, IL, USA). The system and placement technique for the SjO2 catheter has previously been described.

The physiological data were validated by an experienced clinical researcher who eliminated erroneous measurements—for example, arterial pressure recorded during line sampling and SjO2 values recorded during poor signal quality. The Oximetrix 3 system lends itself particularly well to this validation process as it can be assessed objectively off line using the hard copy signal quality indicator that it produces. Data remaining (56%) were deemed “validated monitoring time” data. To make statistical comparisons between patient outcome groups the total duration of insults was expressed as a percentage of validated monitoring time for each variable, for each patient.

ASSESSMENT OF NEUROLOGICAL OUTCOME
Information was gathered 12 months after injury from hospital notes and questionnaire responses of relatives and the patient’s general practitioner. A blinded researcher then determined the quality of outcome according to the Glasgow outcome scale (GOS). Those judged to have a “poor” outcome with GOS 1 to 3 (group 1), were dead, vegetative, or severely disabled. Those with a “good” outcome, GOS 4 and 5 (group 2), were moderately disabled or had made a good recovery.

STATISTICAL METHODS
Mann-Whitney U tests were used to compare data (all non-gaussian) from both patient groups using computer software (Minitab Inc Release 11, State College, PA 16801–3008, USA). Significance was assumed at p<0.05.

Results
Seventy five patients (65 male) were studied. Follow up at 12 months showed that 33 had poor outcomes (group 1), including 16 deaths, and 42 had good outcomes (group 2). Their median age was 34 (range 15–70) years, group 1 being older (38 (range 15–69)) than group 2 (31 (range 16–70); p=0.04). After initial resuscitation the median Glasgow coma scale (GCS) was 4 (range 3–11) in group 1 and 7 (range 3–12) in group 2 (p<0.002) associated with a median injury severity score in group 1 of 21 (range 13–54) and in group 2 of 22 (range 9–34) (p=0.4). The causes of traumatic brain injury are shown in the table.

The total duration of validated monitoring time of SjO2 in group 1 was 123 135 minutes (median 2698 (range 49 to 19 158)) and in group 2 it was 141 620 minutes (2262 (range 681–11 300)) (p>0.05). Physiological secondary insults, as a proportion of validated monitoring time, differed significantly between the groups. A larger proportion of patients in group 1 had a duration of SjO2 greater than 75% (p<0.05) and SjO2 less than 54% (p=0.04). The causes of traumatic brain injury are shown in the table.

<table>
<thead>
<tr>
<th>Causes of traumatic brain injury</th>
<th>GOS 1 to 3</th>
<th>GOS 4 or 5</th>
</tr>
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<tbody>
<tr>
<td>RTA</td>
<td>4</td>
<td>13</td>
</tr>
<tr>
<td>Pedestrian or cyclist</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Falls, assault, or blow to the head</td>
<td>17</td>
<td>9</td>
</tr>
<tr>
<td>Sport</td>
<td>2</td>
<td>7</td>
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<tr>
<td>Other</td>
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GOS=Glasgow outcome scale; RTA=road traffic accident.
Monitoring of \( \text{SjO}_2 \) was discontinued either at the time that asystole occurred, or after the first set of brain stem tests (four patients). Low \( \text{SjO}_2 \) in those who died gives credence to pathological findings of brain ischaemia but death (including brain stem death) did not influence increased \( \text{SjO}_2 \) in group 1 as there was no difference between the dead and the survivors. In previous traumatic brain injury studies admission GCS has been used to categorise patients, but this serves little purpose in practical terms for patients admitted to neurointensive care units, who all require intensive care. The GCS is obscured by necessary emergency treatment out of hospital (intubation and ventilation), and in addition it has been shown to be of low prognostic power in relation to outcome. This study therefore included patients with both severe and moderate traumatic brain injury, all of whom required ventilation, and in whom the ISS was no different between patients with poor and good outcomes.

Validated insult data expressed as a percentage of validated monitoring time allows statistical comparison between patients. It reflects the duration of insult perhaps more appropriately than other studies where a single insult was registered when the \( \text{SjO}_2 \) was outside normal values for a designated period of time, but with no consideration given to the duration of insult. In addition, the \( \text{SjO}_2 \) equipment used in this study allowed objective validation because of the signal quality indicator.

Normal values for \( \text{SjO}_2 \) have been deduced from clinical observation of patients with traumatic brain injury, and derived values from healthy volunteers in the 1940s by Kety and Schmidt. In their landmark paper on determination of cerebral oxygenation during carotid surgery, and clinical evidence of cerebral dysfuncion, cerebral arteriovenous oxygen content. From these data normal values were deduced for \( \text{SjO}_2 \) and have subsequently been used by other groups to assess physiological derangement.

Different methods for defining normality have caused controversy as to the exact lower limit of normal \( \text{SjO}_2 \). Some authors assuming \( 50\% \) and others \( 54\% \). In fact, neither are incorrect as shown in a recent paper comparing \( \text{SjO}_2 \) monitoring with brain tissue oxygenation (\( \text{PbO}_2 \)) where \( \text{PbO}_2 \) values of about 8.5 to 11 mm Hg (but with a large standard deviation).

A recent retrospective study by Cormio et al., concurs with this report. They divided patients into groups with increased, normal, or decreased \( \text{SjO}_2 \) determined by each patient’s average \( \text{SjO}_2 \) (sampled intermittently). They demonstrated GOS 1 to 3 at 6 months in about 75% (n=260) of patients who had predominantly increased \( \text{SjO}_2 \) values. Although this study may be criticised for using intermittent sampling (at least every 24 hours), it provided evidence that increased \( \text{SjO}_2 \) was associated with variable cerebral blood flow (6.7–195 ml/100 g/m). They also found that increased \( \text{SjO}_2 \) was associated with CPP greater than 70

**Discussion**

This study suggests that prolonged high \( \text{SjO}_2 \) is also associated with a bleak long term prognosis. Furthermore, it confirms the association between poor neurological outcome after traumatic brain injury and other secondary physiological insults.

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**Cumulative histograms of \( \text{SjO}_2 \) values monitored in patients with traumatic brain injury in a neurointensive care unit.** The y-axis represents the percentage of good monitoring time and the x-axis \( \text{SjO}_2 \) values from 20%–100%. (A) 33 patients with 12 month Glasgow outcome scale (GOS) values 1 to 3; total good monitoring time was 141 620 minutes (median 2698). (B) 43 patients with 12 month GOS 4 or 5; total good monitoring time was 12 3135 minutes (median 2698). Comparing \( \text{SjO}_2 \) values outside normal limits, patients with GOS 1–3 had more proportional validated monitoring time at low (<54%) (p<0.03) and high (>75%) (p<0.04) \( \text{SjO}_2 \) values.

**Proportional monitoring time (%)**

**Jugular bulb blood saturation (%)**

(A) 33 patients with 12 month Glasgow outcome scale (GOS) values 1 to 3; total good monitoring time was 141 620 minutes (median 2698). (B) 43 patients with 12 month GOS 4 or 5; total good monitoring time was 12 3135 minutes (median 2698). Comparing \( \text{SjO}_2 \) values outside normal limits, patients with GOS 1–3 had more proportional validated monitoring time at low (<54%) (p<0.03) and high (>75%) (p<0.04) \( \text{SjO}_2 \) values.
mm Hg, and a low cerebral metabolic rate for oxygen (CMRO₂). Heterogeneous physiology associated with increased SjO₂ has also been shown in a study of 50 patients with traumatic brain injury where 49 had increased SjO₂, at least once during admission and 25% of the desaturation episodes (decreased SjO₂) could not be explained by increased PaCO₂, ICP, or decreased CPP. There were no outcome data published for these patients.

Our study population was similar in age and severity of injury to other reports, but the mortality was lower (21% at 12 months and 36% and 31% at 3 months). Monitoring time for SjO₂ also compared favourably, the mean duration of validated monitoring time was 3628 minutes, equivalent to 2.4 days/patient (or about 4.4 days of total monitoring time as only 56% of data were valid). A prerequisite for an insult to be registered was a minimum of 5 minutes, less than in other work where 10 to 15 minutes was required. A 5 minute threshold may be more sensitive at recording significant injury as it has been shown in animal studies that multiple short episodes of ischaemic conditions cause more brain injury than longer periods with the same total ischaemic duration.

There are several plausible explanations for our findings. Inflammation may reduce the ability of neurons to utilise oxygen. McKeating and Andrews found intrinsic brain inflammation with a net production of interleukin-6 by the brain after traumatic brain injury. Also, microvascular shunting (exacerbated by neutropil plugging due to adhesion) as a consequence of inflammatory processes may be occurring in the brain. These hypotheses would explain the low CMRO₂ described by Cormio et al. Hyperaemia is an alternative explanation although the associated rise in ICP was treated according to our protocol—that is, initially by hyperventilation—which would result in a reduced cerebral blood flow. Cormio et al. showed that reduced cerebral blood flow was more commonly associated with increased SjO₂.

SjO₂ gives warning of global cerebral hypoperfusion (SjO₂ <54%), cerebral hyperaemia, or non-utilisation of oxygen by brain tissue (SjO₂ >75%), and allows therapeutic interventions to be assessed. Continuous monitoring of SjO₂ has been possible for several years with the introduction and validation of fiberoptic catheters and is superior to intermittent sampling, which can miss discrete events. The physiology of traumatic brain injury is complex and incompletely understood and no single intervention would seem to be a panacea for high SjO₂ given that the cerebral blood flow may be high, low, or normal and CMRO₂ variable. But given that aggressive attempts to normalise physiology (and therefore minimise presumed secondary insults) is the mainstay of current therapy for traumatic brain injury, more effort should be made to elucidate the pathophysiology of high SjO₂. Only then will rational therapy be applied.