SHORT REPORT

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

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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 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.

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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 injury⁷; 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,

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mannitol, and more aggressive hyperventilation (keeping SjO_2 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 technique⁸; 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 SjO_2 , was kept to the minimum required to obtain a PaO_2 of 10 mm Hg (and SpO_2 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 SjO_2 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 SjO_2 was confirmed to be less than 54% mechanical ventilation was manipulated causing Pa CO_2 to increase, and CPP was optimised. No specific treatment protocol was instituted for SjO_2 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 collected and analysed using purpose written software—the Edinburgh Monitor and Edinburgh Browser.⁹ Data included arterial blood pressure, central venous pressure (CVP), ICP, and CPP (mean arterial pressure minus ICP), SjO_2 , peripheral pulse oximetry, and core temperature. Physiological insults outside normal values have previously been documented³ and included ICP less than 20 mm Hg, CPP less than 70 mm Hg, SjO_2 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 admission to the neurointensive care unit (or as soon as practically possible within 24 hours) and ended either at death (determined in the four patients who were brain stem dead as 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 SjO_2 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 SjO_2 catheter has previously been described.⁸

The physiological data were validated by an experienced clinical researcher who eliminated erroneous measurements³—for example, arterial pressures recorded during line sampling and SjO_2 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).¹⁰ 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 SjO_2 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 SjO_2 greater than 75% ($p < 0.05$) and SjO_2 less than 54%

Causes of traumatic brain injury

	GOS 1 to 3	GOS 4 or 5
RTA	4	13
Pedestrian or cyclist	9	2
Falls, assault, or blow to the head	17	19
Sport	2	7
Other	1	1

GOS=Glasgow outcome scale; RTA=road traffic accident.

Cumulative histograms of 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 SjO_2 values from 20%–100%. (A) 33 patients with 12 month Glasgow outcome scores (GOS) 1 to 3; total good monitoring time was 12 3135 minutes (median 2698). (B) 43 patients with 12 month GOS 4 or 5; total good monitoring time was 141 620 minutes (median 2262) ($p>0.05$). Comparing 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 ($>75\%$) ($p<0.04$) SjO_2 values.

($p<0.04$) (figure). When actual validated time (in minutes) spent at insult values was analysed the difference between the groups for increased and decreased SjO_2 became even more significant. There was no difference in the proportion of those patients with increased SjO_2 in group 1 between those who died (GOS 1) and those surviving with poor outcomes (GOS 2 and 3), but those who died had a greater proportion of decreased SjO_2 ($p<0.003$). Group 1 had a greater proportion of validated monitoring time with CPP less than 70 mm Hg compared with group 2 ($p<0.04$). There were no significant differences between the two groups for ICP greater than 20 mm Hg, pulse oximetry less than 92%, or temperature greater than 38 °C (two patients in each group did not have core temperature recorded).

Discussion

This study suggests that prolonged high 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.

Monitoring of SjO_2 was discontinued either at the time that asystole occurred, or after the first set of brain stem tests (four patients). Low SjO_2 in those who died gives credence to pathological findings of brain ischaemia⁷ but death (including brain stem death) did not influence increased 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.² 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 SjO_2 was outside normal values for a designated period of time, but with no consideration given to the duration of insult.^{6 11–14} In addition, the SjO_2 equipment used in this study allowed objective validation because of the signal quality indicator.

Normal values for SjO_2 have been deduced from clinical observation of patients with traumatic brain injury,^{6 11 15} clinical evidence of cerebral dysfunction during carotid surgery,¹⁶ and derived values from healthy volunteers in the 1940s by Kety and Schmidt.¹⁷ In their landmark paper on determination of cerebral blood flow they included measurements of difference in cerebral arteriovenous oxygen content. From these data normal values were deduced for SjO_2 and have subsequently been used by other groups to assess physiological derangement.¹⁸ Different methods for defining normality have caused controversy as to the exact lower limit of normal SjO_2 with some authors assuming 50%^{6 11} and others 54%.^{3 12 13 15} In fact, neither are incorrect as shown in a recent paper comparing SjO_2 monitoring with brain tissue oxygenation (PtiO_2)¹⁹ where SjO_2 values of 50%–54% correspond to PtiO_2 values of about 8.5 to 11 mm Hg (but with a large standard deviation).

A recent retrospective study by Cormio *et al*¹³ concurs with this report. They divided patients into groups with increased, normal, or decreased SjO_2 determined by each patient's average SjO_2 (sampled intermittently). They demonstrated GOS 1 to 3 at 6 months in about 75% ($n=260$) of patients who had predominantly increased SjO_2 values. Although this study may be criticised for using intermittent sampling (at least every 24 hours), it provided evidence that increased SjO_2 was associated with variable cerebral blood flow (6.7–195 ml/100 g/m). They also found that increased SjO_2 was associated with CPP greater than 70

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 injury¹⁴ 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,^{6 11 13 20} but the mortality was lower (21% at 12 months *v* 36%¹¹ and 31%⁶ 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 valid³). A prerequisite for an insult to be registered was a minimum of 5 minutes, less than in other work where 10^{6 12} to 15¹¹ 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^{21–23}.

There are several plausible explanations for our findings. Inflammation may reduce the ability of neurons to utilise oxygen. McKeating and Andrews²⁴ found intrinsic brain inflammation with a net production of interleukin-6 by the brain after traumatic brain injury. Also, microvascular shunting (exacerbated by neotropil plugging due to adhesion²⁵ as a consequence of inflammatory processes) may be occurring in the brain. These hypotheses would explain the low CMRO₂ described by Cormio *et al.*¹³ 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 blood flow and SjO₂. Cormio *et al.*¹³ 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 fibreoptic catheters^{8 11 26–28} 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 normal¹³ 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.

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- Andrews PJD, Statham PF. Nervous system trauma. Critical care neurology. In: Bolton CF, Young GB, eds. *Baillier's clinical neurology*. London: Baillier Tindall, 1997;5:497–514.
- Maas AI, Dearden M, Teasdale GM, *et al.* EBIC-guidelines for management of severe head injury in adults. European Brain Injury Consortium. *Acta Neurochir (Wien)* 1997;139:286–94.
- Jones PA, Andrews PJ, Midgley S, *et al.* Measuring the burden of secondary insults in head-injured patients during intensive care. *J Neurosurg Anesthesiol* 1994;6:4–14.
- Gentleman D, Jennett B. Audit of transfer of unconscious head-injured patients to a neurosurgical unit. *Lancet* 1990;335:330–4.
- Miller JD, Becker DP, Ward JD, *et al.* Significance of intracranial hypertension in severe head injury. *J Neurosurg* 1977;47:503–16.
- Gopinath SP, Robertson CS, Contant CF, *et al.* Jugular venous desaturation and outcome after head injury. *J Neurol Neurosurg Psychiatry* 1994;57:717–23.
- Graham DI, Adams JH, Doyle D. Ischaemic brain damage in fatal non-missile head injuries. *J Neurol Sci* 1978;39:213–34.
- Andrews PJ, Dearden NM, Miller JD. Jugular bulb cannulation: description of a cannulation technique and validation of a new continuous monitor. *Br J Anaesthesia* 1991;67:553–8.
- Howells TP, Jones PA, Piper IR, *et al.* Design of a research database for the study of secondary insults following head injury. *J Neurotrauma* 1995;12:471.
- Jennett B, Teasdale G, Knill-Jones R. Prognosis after severe head injury. *Ciba Foundation Symposium* 1975:309–24.
- Sheinberg M, Kanter MJ, Robertson CS, *et al.* Continuous monitoring of jugular venous oxygen saturation in head injured patients. *J Neurosurg* 1992;76:212–7.
- Lewis SB, Myburgh JA, Reilly PL. Detection of cerebral venous desaturation by continuous jugular bulb oximetry following acute neurotrauma. *Anaesth Intensive Care* 1995;23:307–14.
- Cormio M, Valadka AB, Robertson CS. Elevated jugular venous oxygen saturation after severe head injury. *J Neurosurgery* 1999;90:9–15.
- De Deyne C, Decruyenaere J, Calle P, *et al.* Analysis of very early jugular bulb oximetry data after severe head injury: implications for the emergency management? *Eur J Emerg Med* 1996;3:69–72.
- Cruz J. Continuous versus serial global cerebral hemometabolic monitoring: applications in acute brain trauma. *Acta Neurochir Suppl* 1988;42:35–9.
- Lyons C, Clark Jr LC, McDowell H, *et al.* Cerebral venous oxygen content during carotid thrombectomy. *Ann Surg* 1964;160:561–7.
- Kety SS, Schmidt CF. The nitrous oxide method for the quantitative determination of cerebral blood flow in man. *J Clin Invest* 1948;27:476–83.
- De Deyne C, Decruyenaere J, Colardyn F. How to interpret jugular bulb oximetry. In: Vincent JL, ed. *Year book of intensive care and emergency medicine*. Berlin: Springer 1996:731–41.
- Kiening KL, Unterberg AW, Bardt TF, *et al.* Monitoring of cerebral oxygenation in patients with severe head injuries: brain tissue Po₂ versus jugular vein oxygen saturation. *J Neurosurg* 1996;85:751–7.
- Cruz J. On-line monitoring of global cerebral hypoxia in acute brain injury. Relationship to intracranial hypertension. *J Neurosurg* 1993;79:228–33.
- Pluta R, Tomida S, Ikeda J, *et al.* Cerebral vascular volume after repeated ischemic insults in the gerbil: comparison with changes in CBF and brain edema. *J Cereb Blood Flow Metab* 1989;9:163–70.
- Vass K, Tomida S, Hossmann KA, *et al.* Microvascular disturbances and edema formation after repetitive ischemia of gerbil brain. *Acta Neuropathol (Berl)* 1988;75:288–94.
- Tomida S, Nowak TSJ, Vass K, *et al.* Experimental model for repetitive ischemic attacks in the gerbil: the cumulative effect of repeated ischemic insults. *J Cereb Blood Flow Metab* 1987;7:773–82.
- McKeating EG, Andrews PJ, Signorini DF, *et al.* Transcranial cytokine gradients in patients requiring intensive care after acute brain injury. *Br J Anaesthesia* 1997;78:520–3.
- McKeating EG, Andrews PJ, Mascia L. The relationship of soluble adhesion molecule concentrations in systemic and jugular venous serum to injury severity and outcome after traumatic brain injury. *Anesth Analg* 1998;86:759–65.
- Souter MJ, Andrews PD. Validation of the Edslab dual lumen oximetry catheter for continuous monitoring of jugular bulb oxygen saturation after severe head injury. *Br J Anaesthesia* 1996;76:744–6.
- Ritter AM, Gopinath SP, Contant C, *et al.* Evaluation of a regional oxygen saturation catheter for monitoring SjvO₂ in head injured patients. *Journal of Clinical Monitoring* 1996;12:285–91.
- Gunn HC, Matta BF, Lam AM, *et al.* Accuracy of continuous jugular bulb venous oximetry during intracranial surgery. *J Neurosurg Anesthesiol* 1995;7:174–7.