On-line monitoring of global cerebral hypoxia in acute brain injury

Relationship to intracranial hypertension

JULIO CRUZ, M.D.

Division of Neurosurgery and Head Injury Center, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

Studies have suggested that early secondary brain insults such as cerebral hypoxia are deleterious in acute brain trauma. This important report did not involve measurements of cerebral venous oxygenation, and thus could not prove that cerebral hypoxia did in fact occur. Threshold values at which neurological deterioration develops in comatose patients have been documented using continuous monitoring of jugular oxyhemoglobin saturation. The present work evaluates the interrelationships of global cerebral hypoxia, intracranial hypertension, and neurological outcome.

Clinical Material and Methods

Sixty-nine adults (median age 31 years) with acute severe closed brain trauma were prospectively evaluated for the period from 1983 to 1992. All patients fulfilled the following five criteria: 1) Glasgow Coma Scale (GCS) scores in the range of 4 to 7 (mean 5.8) on admission to the intensive care unit (ICU) and for at least 12 hours thereafter; 2) admission computerized tomography scans revealing reduced cerebrospinal fluid (CSF) spaces, predominantly due to diffuse brain swelling and contusions (59 cases) or acute subdural hematomas with brain swelling (10 cases); 3) intracranial pressure (ICP) monitoring as the patient reached the ICU (postoperatively in the 10 cases of acute subdural hematomas); 4) visual confirmation of pulsation and re-expansion of the underlying brain in the surgical patients; and 5) global cerebral oxygenation monitoring to supplement ICP monitoring.

Once in the ICU, all patients were maintained at an approximate 30° head tilt and underwent continuous monitoring of electrocardiogram, rectal temperature, systemic arterial pressure (SAP), ICP, expired CO₂ tension, and arterial and right jugular bulb oxyhemoglobin saturation. The jugular bulb catheter was positioned as previously described. The multivariate monitoring system has also been previously described, and has been modified by replacing intra-arterial femoral fiberoptic monitoring of the oxyhemoglobin saturation with monitoring using a pulse oximeter.
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The ICP was monitored from the subarachnoid space in 61 patients (88.4%) and from the intraventricular space in the remaining eight, because of the size of the lateral ventricles. The cerebral perfusion pressure (CPP) was calculated as the difference between mean SAP and ICP values. Global cerebral hypoxia was graded according to whether the jugular oxyhemoglobin saturation fell to the ranges of 50% to 54% (Grade I), 45% to 49% (Grade II), or lower than 45% (Grade III) [11]. Correlation between conventional laboratory oximetry and continuously monitored jugular oxyhemoglobin saturation values was also assessed, with intermittent blood sampling.

Maintenance of ICP below 20 mm Hg involved the following nine cumulative steps: 1) sedation; 2) paralysis; 3) optimized hyperventilation, avoiding jugular oxyhemoglobin saturation values below Grade I [1,3,5,7,9,11]; 4) fast delivery of 25% mannitol intravenous boluses of 25 to 50 gm, up to a serum osmolality of 315 mOsm/liter; 5) CSF drainage; 6) barbiturate therapy (Nembutal); 7) hypothermia; 8) delivery of mannitol boluses regardless of serum osmolality; and 9) decompressive craniotomy. Due to basic ICP requirements, the first four modalities were routinely combined, while the latter five were less frequently required and/or feasible. Cerebrospinal fluid drainage was feasible in only four patients (5.8%).

Arterial oxygenation was managed based on the detection of abnormal decreases in arterial oxyhemoglobin saturation (with the alarm set at 90%). The first step was to increase the fraction of inspired oxygen (FIO2), except when it was already at the maximum. The second step was to increase the positive end-expiratory pressure and/or to clear the airway using endotracheal suctioning, bronchoscopy, and aspiration. When indicated, chest tubes were placed to manage associated pneumothorax. If tests were positive for pulmonary infection, the appropriate antibiotic agents were administered.

All patients underwent placement of a central venous line with the aim of normovolemic. In cases requiring more careful systemic hemodynamic monitoring, the central venous line was replaced by a Swan-Ganz catheter. Management of CPP primarily involved therapeutic control of elevated ICP. This was because most patients tended to be normo- or hypertensive, and vasoactive drugs were rarely required for CPP control.

Episodes of global cerebral hypoxia associated with arterial desaturation (despite prompt treatment) were evaluated for duration and magnitude during the first 72 hours (early episodes) and thereafter (late episodes). Simultaneously, sustained ICP elevations of longer than 10 minutes at levels of 20 mm Hg or higher (despite prompt treatment) were also evaluated. Glasgow Coma Scale scores assessed prior to these episodes were designated as initial scores, and at 2 weeks postinjury as final scores.

Differences in initial and final GCS scores were assessed in patients who sustained brief or prolonged (> 10 minutes) desaturation and in those who did not. The magnitude of desaturation and the maximum sustained ICP elevations of longer than 10 minutes were also evaluated in relation to the GCS scores. Eight patients who died because of unmanageable intracranial hypertension (four cases, 5.8%) or refractory septic hemodynamic failure (four cases, 5.8%) were excluded from this analysis. In an additional four patients, the initial GCS scores were assessed prior to the start of barbiturate therapy, but they were also suitable for assessment of final GCS scores at 2 weeks. Thus, the 2-week outcome figures comprised the 61 patients who survived (88.4%).

Linear regression, chi-squared test, Fisher's exact test, and Student's t-test were used for statistical analysis, and a p value of less than 0.05 was considered significant. Data are presented as means ± standard deviation. Institutional Review Board approval was waived.

Results

Correlation of Conventional and Fiberoptic Oximetry

Overall, the correlation between conventional and fiberoptic oximetry values was strong (496 values, r = 0.86, p < 0.00001). By excluding artifactual values (identified by sudden drifts and/or poor light-intensity tracings) from analysis, an even stronger correlation was found (454 values, r = 0.92, p < 0.00001). The incidence of unreliable recordings was 8.5%. Artifactual recordings were almost invariably associated with inadequate positioning of the patient's head, neck, or shoulders, which precluded anatomical positioning of the fiberoptic catheter. Adequate anatomical repositioning restored reliable recordings in all but three of the artificial events.

Intracranial Hypertension and Cerebral Hypoxia

Sixty patients had initial (opening) ICP values above 25 mm Hg (mean 36 mm Hg), despite moderate hypocapnia. The remaining nine patients had opening ICP values close to 20 mm Hg under the same circumstances. The ICP response to the cumulative treatment protocol was initially satisfactory in all but one case.

Out of a total of 10,072 multivariate monitoring hours (an average of 6 days per patient), excluding the four patients who developed sustained and unmanageable intracranial hypertension, the length of time manageable sustained ICP elevations were above 20 mm Hg for longer than 10 minutes totaled 532 hours (5.3% of the total monitoring time).

Eighteen patients (26%) developed at least one episode of arterial desaturation, which was prolonged (> 10 minutes) at least once in 12 of these (17.4%). In total, 121 episodes of arterial and jugular desaturation were documented; 89 were brief, rapidly responding to management (Fig. 1), and 32 were prolonged, not rapidly responding to management (Fig. 2). The brief episodes lasted 3.3 ± 1.4 minutes and the prolonged ones lasted 25.4 ± 10.6 minutes.

Arterial Desaturation

Four types of arterial desaturation were found: neurogenic desaturation, triggered by sudden ICP spikes.
corresponding prolonged lative the 230rogenic, 33 reported. After yield normal results. was 33 recalibration (C2). Auscultation pressure. After yield was discernible (five episodes) found to apparent causes, early and late arterial desaturation differed significantly (p < 0.0005). In the initial 72 hours, 64 episodes of arterial desaturation were detected in nine patients. Of these, one was accidental, 33 were idiopathic, and 30 were radiologically supported. After 72 hours, 57 episodes were detected in 16 patients. Of these, six were accidental, five were neurogenic, and 46 were pulmonary; there were no idiopathic episodes.

Of the short-lasting desaturation episodes, 54 were Grade III, 21 were Grade II, and 14 were Grade I. Of the prolonged episodes, 21 were Grade III, 10 were Grade II, and only one was Grade I. The total cumulative duration of prolonged desaturation episodes was 13.5 hours, corresponding to only 0.13% of the total 10,072 multivariate monitoring hours.

Desaturation, ICP, and Neurological Changes

The maximum reversible sustained ICP increase in patients who developed prolonged desaturation was 33 ± 8 mm Hg, while in patients who did not develop prolonged desaturation it was 30 ± 7 mm Hg. The corresponding CPP values were 66 ± 8 mm Hg and 68 ± 9 mm Hg. These differences were not statistically significant.

While the cumulative sustained ICP elevation period was 5.3% of the total monitoring time, the cumulative desaturation time corresponded to only 0.13% of the total time. These differences were statistically significant (p < 0.0001). In addition, of the 51 patients free of episodes of desaturation, only three presented with decreased GCS scores at 2 weeks, in contrast to nine of the 12 patients who sustained prolonged desaturation (Table 1). These differences were statistically significant.

None of the patients who sustained brief but profound desaturation deteriorated neurologically after these episodes, despite maximum sustained ICP values in the above-described range. In addition, of the 12 patients who sustained prolonged and profound desaturation, one of the four who were undergoing barbiturate therapy when desaturation occurred suffered neurological deterioration, compared with all eight who were not receiving barbiturate therapy (Table 2).

The lowest jugular oxyhemoglobin saturation recorded in prolonged desaturation was 32% ± 9%, in contrast to 59% ± 6% in patients who did not sustain...
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![Image](https://example.com/image.png)

Fig. 3. Jugular bulb oxyhemoglobin saturation (SjO₂, in %, upper) and arterial oxyhemoglobin saturation (SaO₂, in %, lower) recorded against minutes (M) in a patient who did not deteriorate neurologically. Recordings were made later than 72 hours posttrauma. While the intracranial pressure (ICP) and SjO₂ were normalized by optimized hyperventilation, the patient was routinely turned onto his back. A large ICP spike to 70 mm Hg triggered a sudden, brief, and selflimited fall in SjO₂ (curved arrow). This was immediately followed by a fall in SaO₂ and linearly followed by a fall in SjO₂ (short arrows). This episode was self-limited, lasting approximately 5 minutes. Immediately afterward, as the ICP leveled off at 37 mm Hg, large amounts of 25% manitol were given to bring the ICP down to 17 mm Hg, which took 10 minutes. Long arrows each indicate a fast intravenous injection of 12.5 gm (50 ml) of 25% manitol. The ICP and SjO₂ responses to administration of manitol boluses were as expected.¹¹

These differences were statistically significant (p < 0.0005).

While the initial GCS scores prior to prolonged ICP and/or desaturation problems were 6.8 ± 1.1 and 6.5 ± 1.3 for hypoxemic and nonhypoxemic patients, respectively (difference not statistically significant), the final GCS scores at 2 weeks were 3.8 ± 0.7 and 10.6 ± 2.2 for prolonged hypoxemic and nonhypoxemic patients, respectively. This difference was statistically significant (p < 0.0001) and is an important finding.

Discussion

Saturation Monitoring

Since the first report on continuous monitoring of jugular oxyhemoglobin saturation,¹ the influence of artifactual recordings has been stressed. The initial 19.2% incidence of artifactual false jugular desaturation in the first 16 cases¹ has been reduced to acceptable rates of false desaturation in the present series.

As described above, artificial false desaturation was almost invariably due to inadequate positioning, which plays a major role in this type of monitoring. This was easily identified in the preliminary phase of this work and improved with experience with the monitoring system. Others, however, have recently reported a much higher, clinically unacceptable rate of false desaturation, with a poorer correlation between fiberoptic and conventional oximetry (r = 0.60).¹¹ This probably could have been minimized by adequate nursing, since the monitoring system is otherwise very stable.

<p>| TABLE 1 |
| Association of global cerebral hypoxia and neurological deterioration* |</p>
<table>
<thead>
<tr>
<th>Presence of Hypoxia</th>
<th>Deterioration</th>
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<th>No</th>
</tr>
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<tbody>
<tr>
<td>no global cerebral hypoxia</td>
<td>3</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>prolonged global cerebral hypoxia</td>
<td>9</td>
<td>3</td>
<td></td>
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</table>

* Distribution of the patients who sustained prolonged and profound global cerebral hypoxia and those who did not, in relation to neurological deterioration. The difference was statistically significant (p < 0.00002, Fisher's exact test).

<p>| TABLE 2 |
| Barbiturate therapy and neurological deterioration in 12 patients with prolonged and profound desaturation* |</p>
<table>
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<td>3</td>
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<tr>
<td>no</td>
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* The difference was statistically significant (p < 0.02, Fisher's exact test).

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Intracranial Hypertension and Cerebral Hypoxia

The importance of posttraumatic intracranial hypertension has been well documented. However, the present results disclosed that elevated ICP, while responsive to aggressive treatment, was associated with significantly less neurological deterioration than prolonged and profound cerebrovenous desaturation, even though cumulatively the latter lasted significantly less time than the sustained ICP elevations. Most of the ICP problems developed with the CPP at acceptable values (CPP usually > 60 to 70 mm Hg). Most of the patients were normo- to hypertensive throughout the acute phase; exceptions were one patient in the very acute phase who had transient hypovolemia and six patients at a later phase due to barbiturate administration and/or sepsis. Nevertheless, volume expansion and vasodilator drugs allowed adequate blood pressures and CPP's in these patients for most of the monitoring phase (Figs. 2 and 4).

This report on detailed monitoring of global cerebral hypoxia in relation to intracranial hypertension in acute brain trauma demonstrates that manageable ICP problems free of global cerebral hypoxia are far more benign than when complicated by prolonged and profound cerebrovenous desaturation. A recent study has shown that cerebrovenous desaturation due to hypocapnia may significantly compromise neurological outcome. In the vast majority of patients, however, such episodes are expected to be short because increasing the pCO₂ and/or the fast administration of mannitol boluses are very effective in rapidly reversing oligemic cerebral hypoxia. Exceptions are found when jugular desaturation is not detected (usually because of errors in resetting the monitor alarm).

The ease with which oligemic cerebral hypoxia can be reversed suggests that hypoxemic cerebral hypoxia deserves further investigation. However, the present results should not be interpreted as reflecting the overall incidence of severe hypoxemic brain insults, since approximately 85% of the prolonged episodes were documented in the first 27 patients during two epidemic periods of severe Gram-negative pneumonia in the intensive care unit. In fact, in the most recent 30 patients, only seven episodes were documented, and only one of them was prolonged and profound. This is in agreement with a marked reduction in the incidence of severe pulmonary infection in recent years.

A relevant finding was the occurrence of arterial and cerebrovenous desaturation with no apparent cause (Fig. 1). All but two of these episodes responded immediately to increasing the FiO₂. Even though auscultation and chest x-ray films were unremarkable, we could not rule out the possibility of transient pulmonary hemodynamic and diffusional abnormalities causing such sudden episodes. Additional monitoring, including early placement of Swan-Ganz catheters for monitoring the pulmonary artery pressure, might have clarified these occurrences. From a clinical standpoint, such episodes are almost invariably benign if rapidly detected and managed, and respond promptly to FiO₂ modulation.

The above findings were not noted in a previous report on continuous jugular oxyhemoglobin saturation monitoring in acutely comatose patients, which used a different technique from ours. The main difference was that arterial oxygenation and CO₂ tension were not monitored. We believe that this monitoring is important in explaining the causes of jugular desaturation.

Clinical Implications

In acute traumatic coma, the present findings are clinically relevant because the global cerebral metabolic rate of oxygen consumption is abnormally low. This might lead to the erroneous impression that low oxygen delivery to the acutely comatose brain is adequate, but the present results strongly indicate otherwise.

In the nontraumatized cat brain, thresholds for brain energy failure (virtually brain death) were reported as being associated with cerebral venous oxygen content levels of only 2 vol% (normal mean value 12.5 vol%). This finding had been proposed as a safety parameter in clinical practice for therapies aimed at reducing cerebral blood flow. Given the present results, however, threshold values for neurological deterioration in the severely injured human brain were found at jugular oxyhemoglobin saturation levels of approximately 30%, confirming previous findings. Since most of these episodes occurred when the total hemoglobin content was in the 8.5 to 11 gm/dl range, the corresponding jugular oxygen content levels would range from 3.5 to 4.5 vol%, which is well above the proposed safety parameter of 2 vol% in the noninjured cat brain. Therefore, caution should be exercised in extrapolating findings from the normal animal brain to human brain injury.

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Address reprint requests to: Julio Cruz, M.D., Division of Neurosurgery, Hospital of the University of Pennsylvania, 3400 Spruce Street, Philadelphia, Pennsylvania 19104.