Comparisons of Hemodynamic and Respiratory Parameters, and Outcomes between High and Low Cerebral Perfusion Pressure Groups in a Severe Head Injury

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ABSTRACT A secondary hypoxic brain injury is one of the most important determinants of a neurological outcome after a head injury. In the absence of a specific therapy to normalize cerebral blood flow (CBF), some advocators decided that one approach toward preventing cerebral ischemia was to monitor and maintain the cerebral perfusion pressure (CPP). To date, there is no evidence to support which level of CPP is needed to keep an adequate CBF in the management of severe head injuries. Furthermore, some studies suggested that side effects like acute respiratory distress syndrome (ARDS) or a respiratory complication with intentional CPP management therapy affected the patient's outcome. To examine the relationship between CPP and CBF, we analyzed CBF using the Ketty-Schmidt N₂O technique, and studied the patient's outcome and respiratory complications. We studied forty patients with severe head injuries (Glasgow Coma Scale < 8), who were treated at the Musashino Red Cross Hospital between years 1999 to 2001. We divided the patients into the “high-CPP group (group-H),” in which CPP was kept above 70 mmHg as a threshold of CBF, and the “low-CPP group (group-L),” in which CPP was kept from 50 to 70 mmHg. We analyzed the patients’ CBFs and their outcomes, and examined their cardiac indices (CI) and pulmonary arterial diastolic pressures with a thermo-dilution catheter. We also calculated the patients’ cerebral vascular resistances (CVR) and compared the results in the two groups. There was no statistical significance concerning CBF, neurological outcomes, pulmonary hemodynamics, or the existence rate of pulmonary complications. The mean CVR in group-H was higher than that of group-L, and we considered that the CBF would be affected by both CVR and CPP. We concluded that the threshold of CPP at 70 mmHg is not always appropriate for patients. CPP is affected by certain factors, such as the degree of pressure autoregulation. We should consider both CPP and CVR in the treatments of head injury patients. CPP management is one of the optional therapies that should be chosen with sufficient consideration.

Keywords: cerebral blood flow, cerebral perfusion pressure, cerebral vascular resistance, nitrous oxide saturation technique, severe head injuries
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INTRODUCTION

Previous studies have reported that cerebral autoregulation becomes impaired after a traumatic brain injury¹⁴. Some studies have demonstrated that abnormalities of cerebral blood flow (CBF) regulation might cause patients with head injuries to be unusually susceptible to secondary ischemic insults, such as hypotension, intracranial hypertension, and hypoxia. The secondary ischemic insult can increase the incidence of neurological damage⁵⁻⁸. These studies have also revealed a relationship between the incidence of a secondary ischemic insult and a poor neurological outcome⁵⁻⁸.

Without a specific therapy to normalize CBF regulation, several doctors have advocated that one approach to preventing cerebral ischemia is to monitor and maintain the cerebral perfusion pressure (CPP)⁹,¹⁰. The CPP is defined as the mean arterial blood pressure (MABP) minus the intracranial pressure (ICP). Several clinical studies have
Suggested that 70 mmHg to 80 mmHg of CPP may be the critical threshold\(^9,10\). Rosner et al. managed patients with head injuries by keeping their CPPs above 70 mmHg, and reported good outcomes\(^9\). However, Cruz et al. demonstrated that the CBF does not change in correlation with the CPP in severe brain trauma with a CBF measurement found by the Xenon technique\(^11\). They concluded that in severe acute brain trauma, cerebral hemodynamics and the oxygen metabolic variable are not necessarily correlated with normal or even high levels of CPP. Under this circumstance, they determined that cerebral vascular resistance (CVR) is more closely correlated with CBF. Furthermore, Robertson et al. conducted a prospectively controlled randomized trial of 189 adult patients with severe head injuries (closed and gun shot wounds)\(^12\). The patients were randomized into “ICP-targeted protocol,” where their CPPs were kept above 50 mmHg, or into “CBF-targeted protocol,” where their CPPs were kept above 70 mmHg. No significant differences were found in a 3- or 6-month GOS (Glasgow Outcome Scale) or in the ICPs. However, there was a significant increase in the incidence of acute respiratory distress syndrome (ARDS) in the “CBF-targeted” group. Therefore, it remains unclear which level of CPP is needed in order to maintain an adequate CBF.

The following problems were examined in this study: a) Whether or not the CBFs of the higher CPP group are higher than that of the lower CPP group, b) Whether the pulmonary hemodynamics are abnormal in the higher CPP group, c) Whether the incidence of pulmonary complications is higher in the higher CPP group than in the lower group, and d) Whether or not a higher CPP group resulted in a better long-term outcome.

MATERIALS AND METHODS

Patients

From January 1999 to December 2001, 833 patients with head injuries were admitted into the Musashino Red Cross Hospital. Among them, 40 patients with severe head injuries (Glasgow Coma Scale [GCS] less than\(^12\)) and without any other major injuries to the trunk or extremities were retrospectively selected for this study. They were treated without induced hypothermia therapy.

Definition of the classification with CPP values

In the present study, the CBFs were measured using a nitrous oxide saturation technique (Kety-Schmidt technique) in the 40 patients with severe head injuries\(^13\). We divided these 40 patients into the “high-CPP group” (group-H), in which the CPPs were spontaneously above 70 mmHg, and the “low-CPP group” (group-L), in which the CPPs ranged from 50 mmHg to 70 mmHg spontaneously at the time of CBF measurement. However, it was difficult to maintain the CPP completely above or below 70 mmHg in the duration of ICU hospitalization. We therefore calculated the percentage of time that the CPPs were maintained above 70 mmHg in the entire ICU management period and statistically verified the significant difference between the two CPP groups. We analyzed all of the patients’ CPPs and CBFs, and compared their outcomes between the two groups.

Nitrous oxide saturation technique (Kety-Schmidt technique)

The modified blood sampling protocol of the original Kety-Schmidt method was used to measure the global CBF\(^13-14\). A 16-gauge venous catheter was percutaneously inserted into the dominant internal jugular vein, and its tip was positioned into the transverse sinus to prevent the contamination of the blood from the external jugular vein. This was performed under a diaphanoscopy. A 22-gauge arterial catheter was inserted into a peripheral artery, and 6 ml of venous blood were sampled as a control. 15% \(\text{N}_2\text{O} \) gas was then mixed with 21% oxygen and 64% nitrogen, and the mixture was administered by inhalation for 10 minutes. Blood samples (1 ml) were collected in heparinized syringes from the peripheral artery and the jugular vein catheter every minute. The nitrous oxide content of each blood sample was determined using a gas chromatography analyzer (Perkin Elmer; Boston, USA). Letting \( C_a \) and \( C_v \) be the arterial and cerebral venous concentrations, respectively, the global CBF value (ml/100g/min) can be calculated using the following equation:

\[
\text{CBF (ml/100g/min)} = \frac{(C_v)_{10}}{\int_0^{10} (C_a - C_v) dt} (1)
\]

where \((C_v)_{10}\) is the venous blood concentration of \(\text{N}_2\text{O}\) 10 minutes after measurement, and the partition coefficient of \(\text{N}_2\text{O}\) between the blood and brain was assumed to be 1.

Correction of CBF value

CBF measurements using the Kety-Schmidt method were performed 1 to 7 days after the injuries. All patients were treated with mechanical ventilation, which was intended to maintain \(\text{PaCO}_2\) between 30 mmHg to 35 mmHg.
However, the CBF measurements were not performed simultaneously, and the cerebral blood flow changed with the level of PaCO₂. We therefore used the following equation to correct all of the obtained CBF values for a PaCO₂ of 34 mmHg (CBF₃₄ in Eq. 2), assuming a 3% change in CBF per mmHg difference in PaCO₂:

\[
CBF₃₄ \ (ml/100g/min) = CBF \ [1 + 0.03 (34 - PaCO₂)] (2)
\]

ICP and CPP measurements

ICP was continuously monitored with an intraparenchymatous or an intraventricular catheter (model-110B Camino, Integra Lifesciences, USA). CPP was calculated as the difference between the mean arterial pressure and the intracranial pressure. In the present series, cerebrospinal fluid drainage was utilized only in a few cases.

The calculation formula for cerebral metabolic rate of oxygen (CMRO₂) and cerebral vascular resistance (CVR)

CMRO₂ was estimated from the product of the arteriovenous oxygen difference (AVDO₂) and the global value of CBF. The calculation formulas are given as:

\[
AVDO₂ \ (ml/dl) = CaO₂ - CjvO₂ (3)
\]

and

\[
CMRO₂ \ (ml/100g/min) = \frac{AVDO₂ \times CBF}{100} (4)
\]

where \( CaO₂ \) is the arterial oxygen content (ml/dl) and \( CjvO₂ \) is the jugular venous oxygen content (ml/dl). The cerebral vascular resistance (CVR) was assessed using the following formula as the ratio of the cerebral perfusion pressure to the mean cerebral blood flow:

\[
CVR \ (mmHg \ ml^{-1} \ min \ 100g) = \frac{CPP}{CBF} (5)
\]

Systemic and pulmonary hemodynamic measurements

Systemic and pulmonary hemodynamic measurements were recorded using No. 8 French thermo-dilution catheters (Edwards Lifesciences; California, USA) applied for diagnostic and therapeutic purposes. The cardiac indices (CI) were calculated using the thermo-dilution technique with a computed analyzer (Baxter; California, USA). The pulmonary arterial pressure (systolic/mean/diastolic) was measured using a bedside monitoring system. The zero reference was placed at the midchest level. An incidence of pulmonary complication, such as ARDS or severe pneumonia, was prescribed by a chest roentgenogram and the PaO₂ / FiO₂ (P/F) ratio.

Hemodynamic and Respiratory Parameters in a Head Injury

<table>
<thead>
<tr>
<th>Table 1. Patient characteristics.</th>
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<tbody>
<tr>
<td>No. of cases</td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
</tr>
<tr>
<td>Initial GCS (mean ± SD)</td>
</tr>
<tr>
<td>Diagnosis (cases)</td>
</tr>
<tr>
<td>ASDH</td>
</tr>
<tr>
<td>AEDH</td>
</tr>
<tr>
<td>DAI</td>
</tr>
<tr>
<td>Cerebral contusion</td>
</tr>
<tr>
<td>Days of CBF measurement after injury (mean ± SD)</td>
</tr>
</tbody>
</table>

GCS: Glasgow coma scale, ASDH; acute subdural hemorrhage, AEDH; acute epidural hemorrhage, DAI; diffuse axonal injury

Neurological outcome

The neurological outcome in 6 months after the injury was determined by the GOS. We divided the patients’ outcomes into “favorable outcome” (good outcome and moderate disability in GOS) or “unfavorable outcome” (severe disability, persistent vegetative state, and death in GOS).

Statistical analysis

In normally distributed data, each variable was represented by the mean ± SD. Differences in the means of continuous measurements were tested by the Student’s paired t-test. The neurological outcomes in the two groups were compared using the chi-square test (without the Yates’ correction). A p value less than 0.05 was considered to be statistically significant. All statistical analyses were conducted using the statistical program Statview, Version 4.5 (Abacus, Concepts, Berkley; CA, USA).

RESULTS

The patients’ ages ranged from 15 to 75 years old, with a mean ± SD of 45.8 ± 18.4 years. Initial diagnoses with computed tomography (CT) findings were acute subdural hemorrhages in 15 cases, acute epidural hemorrhages in 9 cases, diffuse axonal injuries in 15 cases, and cerebral contusions in one case. CBF measurements were performed 3.6 ± 1.9 (mean ± SD) days after they were injured (Table 1).

Difference in two groups divided from CPP value

In each group, there was no patient with a hypotention status (<90 mmHg). The patients were all stable in CBF.
Table 2. Each result of patients divided into high CPP group and low CPP group.

<table>
<thead>
<tr>
<th></th>
<th>Group-L 50mmHg&lt;CPP≤70mmHg</th>
<th>Group-H 70mmHg&lt;CPP</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean CPP (mmHg)</td>
<td>61.1 ± 5.8</td>
<td>82.2 ± 7.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CPP % (&gt;70mmHg)</td>
<td>51.1 ± 26.6</td>
<td>83.7 ± 20.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CBFs4 (ml/100g/min)</td>
<td>57.9 ± 16.4</td>
<td>50.9 ± 16.4</td>
<td>0.201</td>
</tr>
<tr>
<td>AVDO2; (ml/100ml blood)</td>
<td>5.01 ± 1.27</td>
<td>4.85 ± 1.62</td>
<td>0.634</td>
</tr>
<tr>
<td>CMRO2; (ml/100g/min)</td>
<td>2.77 ± 0.64</td>
<td>2.72 ± 0.76</td>
<td>0.846</td>
</tr>
<tr>
<td>CI (L/min/m²)</td>
<td>4.0 ± 0.3</td>
<td>4.5 ± 0.7</td>
<td>0.126</td>
</tr>
<tr>
<td>PA-diastric (mmHg)</td>
<td>11.3 ± 2.1</td>
<td>11.172 ± 6.4</td>
<td>0.881</td>
</tr>
<tr>
<td>P/F ratio</td>
<td>379.0 ± 102.6</td>
<td>356.0 ± 84.8</td>
<td>0.612</td>
</tr>
<tr>
<td>PaCO2</td>
<td>37.3 ± 3.9</td>
<td>34.5 ± 4.8</td>
<td>0.054</td>
</tr>
<tr>
<td>CVR (mmHg ml⁻¹ min 100g)</td>
<td>1.14 ± 0.35</td>
<td>1.77 ± 0.55</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CPP: cerebral perfusion pressure, CBF: cerebral blood flow, AVDO2: arterial venous oxygen difference, CMRO2: cerebral metabolic rate of oxygen, CI: cardiac index, PA-diastric: pulmonary artery diastolic pressure, P/F ratio: arterial partial pressure of oxygen / fractional inspired oxygen ratio, CVR: cerebral vascular resistance

Table 3. Age and GCS on admission in the two groups.

<table>
<thead>
<tr>
<th></th>
<th>Group-L 50mmHg&lt;CPP≤70mmHg</th>
<th>Group-H 70mmHg&lt;CPP</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>15</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Age (y/o)</td>
<td>45.6 ± 23.1</td>
<td>45.9 ± 15.4</td>
<td>0.967</td>
</tr>
<tr>
<td>Initial GCS</td>
<td>6.3 ± 1.6</td>
<td>6.6 ± 2.3</td>
<td>0.667</td>
</tr>
<tr>
<td>Time of measurement (days)</td>
<td>3.4 ± 2.1</td>
<td>3.7 ± 1.8</td>
<td>0.623</td>
</tr>
</tbody>
</table>

The mean CBFs4 values in the two groups were 50.9 ± 16.4 ml/100g brain/min in group-H and 57.9 ± 16.4 ml/100g brain/min in group-L, respectively, and they were not statistically significant difference (p=0.201) (Table 2). Furthermore, there was no statistical significance between the two groups in the AVDO2 and CMRO2 values (Table 3).

CBF, AVDO2, CMRO2, and CVR values

The mean CPPs of these two groups were 82.2 ± 7.7 mmHg in group-H and 61.1 ± 5.8 mmHg in group-L at the time of CBF measurement, and there was a statistically significant difference between these two groups (p<0.001) (Table 2). Moreover, the percentages of time that the CPPs were maintained above 70 mmHg in the entire ICU management period were 83.7 ± 20.7% in group-H and 51.1 ± 26.6% in group-L, respectively (p<0.001) (Table 2). Between these two groups, there was no statistically significant difference in age, initial GCS values, or days that the CBFs were measured after the injuries (Table 3).

The mean CVR values in the two groups were 1.77 ± 0.55 in group-H and 1.14 ± 0.35 mmHg ml⁻¹ min 100g in group-L, respectively, and there was a statistically significant difference (p<0.001) (Table 2).

The values of CO, CI, and pulmonary artery pressure in the two groups

Continuous measurement of the cardiac index (CI) and pulmonary arterial (PA) pressure was performed with the thermo-dilution catheter. We obtained these data from only 19 patients. Eleven of them belonged to group-H and eight were from group-L. The mean values of the CI and PA diastolic pressure had no statistical difference in the two groups (Table 2). However, we could not obtain the continuous data from the other 21 patients. Several of them had high fevers that were thought to be caused by the thermo-dilution catheters, and we had to terminate the measurements. Furthermore, there was no incidence of pulmonary complication like ARDS or severe pneumonia, and there was no significant difference in these two groups concerning the P/F ratio (p=0.612) (Table 2).
### Hemodynamic and Respiratory Parameters in a Head Injury

**Fig. 1.** Outcomes six months after the patients suffered head injuries.

The outcomes described using the Glasgow Outcome Scale (GOS) of the Group-H were: good recovery (GR) in 7 cases, moderate disability (MD) in 6 cases, severe disability (SD) in 9 cases, persistent vegetable state (PVS) in 2 cases, and dead (D) in one case. In Group-L, the outcomes were GR in 2 cases, MD in 5 cases, SD in 5 cases, PVS in 2 cases, and D in one case. GR and SD belong to the good outcome group. MD, PVS, and D are members of the poor outcome group. There were no statistically significant data between the two groups (p=0.774). The outcomes in the two groups were compared using the chi-square test (without the Yates correction).

<table>
<thead>
<tr>
<th>Group</th>
<th>Good Outcome</th>
<th>Poor Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group-H</td>
<td>7 (47%)</td>
<td>8 (53%)</td>
</tr>
<tr>
<td>Group-L</td>
<td>13 (52%)</td>
<td>12 (48%)</td>
</tr>
</tbody>
</table>

### Neurological Outcome

Six months after their injuries, it was found that the ratios of the favorable outcomes (GR or MD) were 52.0% in group-H (13 out of 25 patients) and 46.7% in group-L (7 out of 15 patients), respectively (Fig. 1). There was no significant difference in these two groups (p=0.744).

### DISCUSSION

**The relationships among CPP, CBF, and Cerebral vascular resistance (CVR)**

Our study indicates that an adequate CBF value is induced in spite of a CPP value less than 70 mmHg. We also found that a CPP threshold at 70 mmHg is not always correct for patients.

In previous studies, the level at which the CPP should be maintained is not clearly specified. Several clinical studies have suggested that 70 mmHg to 80 mmHg may be the clinical threshold.[10] Rosner et al had the largest prospective cohort series of patients that were managed with the intention of keeping the CPP above 70 mmHg.[10] They documented the outcomes of 158 patients in whom the CPPs were kept to at least 70 mmHg. Outcomes 10.5 months after the injuries were a mortality percentage of 29%, a moderate disability of 20%, and a good recovery percentage of 39%. Rosner et al also found an 80% favorable recovery rate in 71% of their surviving patients and suggested that these results compared quite favorably with those of the Traumatic Coma Data Bank (TCDB).[10]

McGraw developed a model to relate the outcomes with the CPP.[17] When the CPP was greater than 80 mmHg, it was found that the mortality was between 35% and 40%. When the CPP was decreased below this level, the mortality progressively increased by 20% for each 10-mmHg epoch. Therefore, when the CPP was less than 60 mmHg, the mortality was about 80%. Morbidity and neurologic deterioration were reliably (p<0.02) associated with a decrementing CPP.

However, in the above studies, it was unclear whether or not an adequate CBF level was provided with the management of an adequate CPP in each patient. Our study suggested that a CPP threshold lower than 70 mmHg could provide adequate CBF levels. Indeed, there were no statistically significant differences in the two groups divided by a threshold of 70 mmHg. Interestingly, the average CBF in group-H was not higher than that of group-L. Therefore, we can conclude that CPP is not the only factor determining the patient’s CBF.

One important factor is the autoregulation of cerebral vessels. Lang et al suggested the pressure autoregulation theory, and they advocated that it was the brain’s intrinsic ability to maintain a stable CBF over a wide range of perfusion pressures by varying the degree of vasoconstriction or vasodilation.[18] When the pressure autoregulation was completely disrupted, the CBF proportionally increased with the CPP because of the vasoparalysis of the cerebral vessels. In normal autoregulation, when the CPP increased within the range of 50 mmHg to 150 mmHg, progressive vasoconstriction served to maintain the CBF at a constant level. In a partial disruption situation, the
breakpoint of the CPP-CBF curve was shifted to 80 mmHg, and the system became pressure-passive up to the reset breakpoint of 80 mmHg. Pressure autoregulation occurs between 80 mmHg and 150 mmHg. In our study, there was no difference found between the two groups divided at the 70 mmHg point in CBF. We suspected that the patients’ cerebral autoregulations in our study may have been kept more comparatively than in those of Rosner’s study. Our results indicate the possibility that the CPP threshold, which is adequate for enough CBF, is at least over 50 mmHg in the patients with severe head injuries.

CBF is determined by CPP and intracranial vessel resistance. However, when the CPP is maintained steadily, the CBF amount can change with various resistance degrees.

Cruz et al suggested that CBF does not change in correlation with CPP in severe brain trauma with a CBF measurement found by Xenon technique. They concluded that hemodynamics and the oxygen metabolic variable are not necessarily correlated with normal or even high levels of CPP. Under this circumstance, they advocated that CVR is more closely correlated with CBF.

In our study, we measured the CBF value using the Kety-Schmidt N2O technique. The mean CVR in group-H was higher than that of group-L, and there was no statistically significant difference between the mean CBFs in the two CPP groups. This indicates that CBF would be affected by both CVR and CPP. We should therefore consider both CPP and CVR in the treatment of patients with head injuries. With consideration of this fact, we should understand the pathogenesis of each patient and make an individual strategy for each patient.

The time of CBF measurement after suffered injury
Cerebral ischemia is an early event after severe head injury. The initial or the first day management frequently decides the prognosis in most severe brain trauma patients. In our study, the CBF measurements were performed 1 to 7 days after the injuries, and the mean time was 3.6 ± 1.9 days after the injury. From the comparisons of spontaneous CBFs and patients’ outcomes, it might be too late.

In Robertson’s study, the global CBF measurements were performed every 1 to 7 days, and the results were compared to their average values. The average global CBF was significantly higher in the CBF-targeted group, where the CPPs were kept above 70 mmHg, than in the ICP targeted group, where the CPPs were kept between 50 mmHg and 70 mmHg. These averages were 66.4 ± 2.2 ml/100 g/min and 56.4 ± 1.6 ml/100 g/min, respectively.

Pulmonary hemodynamics and existence rate of pulmonary complication
A Traumatic Coma Data Bank (TCDB) study suggested that the development of acute lung injury was associated with a three-fold increase in the risk of death from a head injury. Robertson et al reported that there was a significant increase in the incidence of ARDS in the “CBF-targeted” group. They reported that the incidence rate of ARDS was nearly five times higher in the “CBF-targeted” group than in the “ICP-targeted” group. They concluded that the incidence rate of ARDS might have affected the long-term outcome results. They claimed that the reasons for the higher incidence of ARDS in the “CBF-targeted” group might have been because of the treatment-related variables, such as fluid intake, use of pressure agents, and the physiologic variables that reflected these treatment differences, such as pulmonary arterial pressure.

In our study, the mean values of CI and PA diastolic pressure were not significantly different in the two groups. One reason for this inconsistency with the incidence of pulmonary complication may have been because of the intensive CPP management. There was no intensive manipulation to manage the CPPs, and the patients were naturally observed in this study.

Relationship of the CPP value and the neurological outcome
Outcomes have been reported for prospective traumatic brain injury studies in which the CPP was actively maintained at about 70 mmHg. When morbidity was considered, the percentage of good recovery and moderate disabilities in these studies was about 54%, higher than the 37% in the TCDB database. In the current study, the favorable outcome rate in the higher CPP group was 52%, and that of the lower CPP group was 46.7%. Thus, there did not appear to be any adverse clinical outcomes when the CPP was maintained. Further studies and analyses with large populations are needed.

Considerations of patients’ ages and outcomes
The mean age of the patients was 45.6 ± 23.1 years old in the lower CPP group, and it was 45.9 ± 15.4 years old in the higher CPP group. We therefore consider that the patients’ ages have little influence on the spontaneous CPP levels in the two groups. Generally, the patient’s age affects the outcome. Vollmer et al studied 661 patients and investigated the relationship between ages and outcomes.
following traumatic comas. In their study, eighty percent of the patients older than 55 years died within 6 months postinjury, and none showed a good recovery. They claimed that there were age-dependent variables, such as significant premorbid diseases, and these variables might affect the patients’ clinical outcomes.

In our study, 10% of the good outcome patients and 50% of poor outcomes were over 55 years old. The mean ages of the good and poor prognoses were 38.1 ± 15.1 years and 53.6 ± 18.6 years, respectively (p=0.0063). We therefore believe that the outcomes of severe head injury were not solely affected by hemodynamic parameters, but also affected by patients’ ages.

Regrettably, we could not obtain the 40 patients’ past illness histories, and hence, could not analyze the influence of their premorbid diseases on their outcomes. Further extensive studies on the relationship between premorbid diseases and outcomes in large populations are definitely needed.

Practical consideration and future implication

It has been commonly believed that an adequate CPP was above 70 mmHg in patients with severe head injuries. However, this study indicates that the adequate threshold of CPP can be lower than that.

Some authors have suggested the new Lund concept, which is intended to maintain a lower CPP in order to avoid ICP elevation. These authors advocate that a high CPP may have the adverse effect of triggering the development of a vasogenic brain edema through forces striving toward the classical Starling fluid equilibrium, and hence, may cause an increase in ICP. Their treatment protocol includes the followings: a) preservation of a normal colloidal-absorbing force; b) a reduction in intracapillary pressure through a reduction in systemic blood pressure by antihypertensive therapy (a β1-antagonist, metoprolol, combined with an α2-agonist, clonidine); and c) a simultaneous, moderate constriction of precapillary resistance vessels with low-dose thiopental and dihydroergotamine. These authors advocate that a CPP of 60 mmHg to 70 mmHg is considered optimal. However, if it is necessary to control ICP, the CPP values of 50 mmHg for adults and 40 mmHg for children are acceptable. They reported that nearly 80% of patients with severe head injuries had favorable outcomes with this treatment.

In order to confirm the adequate CPP value, we should analyze the CBF in each patient with an initially lower CPP, and intentionally raise the CPP over 70 mmHg. We must examine the correlation of the entire body blood pressure and CPP, and find whether or not the intentional elevation of the body blood pressure elevates the CPP. Further extensive study on each type of head injury in a large population is definitely needed.

CONCLUSION

We conclude that the CPP threshold at 70 mmHg is not always necessary to manage patients with severe head injuries. We consider that CPP management therapy is one of many therapeutic options that may improve morbidity. We should choose a therapeutic method, including CPP management therapy, for each individual patient with sufficient consideration. We should also consider both CPP and CVR in the treatment of a patient with a head injury. In any case, more investigations will be needed with large populations.

REFERENCES

Shoji Yokobori, et al


重症頭部外傷における脳灌流圧、血行動態、呼吸機能および予後の検討

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要旨 頭部外傷受傷後に脳虚血により起こる二次的脳損傷は、神経学的予後を決定する重要な因子の一つである。脳血流cerebral blood flow (CBF)を適正化させる特異的な治療がないことから、頭蓋内圧intracranial pressure (ICP)さらには脳灌流圧cerebral perfusion pressure (CPP)をモニタリングし維持する、いわゆる CPP oriented therapyが提唱されている。しかしながら重症頭部外傷急性期管理においてCPPをいかほどに維持すべきか明確なエビデンスはない。また、CPPを意図的に高値に維持する際には、カテコラミンあるいは輸液を投与することで成人呼吸窮迫症候群（ARDS）など呼吸器合併症の発生率が高まりとなるとの報告もある。われわれは笑気法（Kety-Schmidt method）を用い、CBFを測定し、CPP および呼吸器合併症および予後について検討した。対象は1999年1月から2001年12月までに、武蔵野赤十字病院に搬送されたGlasgow Coma Scaleが8点未満の重傷頭部外傷のうち脳低温療法を施行例40例である。それらを CPPの治療目標とする70mmHgを境として、L群（50≤CPP≤70mmHg）とH群（70mmHg<CPP）の2群に分け、2群間でCBFおよび予後を比較した。また肺動脈カテーテルを用い、心係数cardiac index (CI)，また輸液負荷の指標となる肺動脈拡張期圧pulmonary artery diastolic pressure (PAD)を測定し、2群間での比較を行った。各種パラメーターから脳血管抵抗cerebral vascular resistance (CVR)を計算し比較検討した。CPP=70mmHgを境とした2群間では、CBF、神経学的予後、肺動脈圧に有意な差を認めなかった。また呼吸器合併症についても差がみられなかった。H群でのCVRはL群よりも有意に高く、CBFはCPPだけでなくCVRにも影響を受けることが推測された。以上のことから、CPP=70mmHgという値は必ずしも適切でないことが明らかとなった。CBFは脳血管のpressure autoregulation（自動調節能）に影響を受けるため、CPPのみならずCVRをともに考慮した上で重傷頭部外傷の急性期管理を行うべきであると考える。

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