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Early Metabolic Suppression Therapy for Severely Increased Intracranial Pressure after Emergency Brain Decompression

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---- Abstract

Objective: Patients suffering from severe traumatic brain injury or cerebral hemorrhage need to be closely monitored and be intensively managed in order to prevent irreversible neurological damage. However, progressive neurological deterioration may occur despite the rapid physiologic resuscitation after emergency brain decompression. In this study, the clinical outcome of the early metabolic suppression treatment was evaluated in patients suffering from severe cases of refractory increased intracranial pressure following emergency brain decompression.

Methods: We retrospectively reviewed the charts of all patients who received early metabolic suppression therapy after emergency brain decompression between January 1, 2002 and January 1, 2007.

Result: A total of 42 patients were included in this study. Twelve (29%) of these have survived. Six (50%) of the survivors showed favorable outcomes (i.e., good recovery and moderate disability) at 1 year after hospital discharge. Cerebral perfusion pressure was higher in the survivors than in the non-survivors.

Conclusion: Early aggressive metabolic suppression therapy with barbiturates may be used to effectively control the intracranial pressure in a substantial number of patients with severely increased intracranial pressure even after emergency brain decompression, without adversely affecting the cerebral perfusion pressure in these patients.

Key words: Metabolic suppression therapy · Barbiturate · Cerebral perfusion pressure · Increased intracranial pressure

Introduction

For the past three decades, the most commonly used therapies for the reduction of intracranial pressure (ICP) have included hyperventilation, ventricular drainage of cerebrospinal fluid (CSF), osmotherapy with mannitol, and metabolic suppression therapy. Metabolic suppression therapy remains controversial, and it is usually considered as a last resort measure to reduce increased ICP.

In this study, we evaluated the clinical outcome of patients who were treated with high doses of barbiturates, as a metabolic suppression therapy, during the immediately postoperative period following emergency brain decompression in order to validate its effectiveness in combination with the proper maintenance of cerebral

교신저자 : Jung-Yul Park Add : Department of Neurosurgery, Korea University Ansan Hospital, 516 Gojan-1-dong Danwon-gu Ansan 425-707, Korea Tel : +82-031-412-5050 Fax : +82- 031-412-5054 E-mail : jypark@kumc.or.kr perfusion pressure in the early and aggressive management of patients with severely increased ICP.

Materials and methods

Metabolic suppression therapy was attempted in all patients with persistent, severely increased intracranial pressure following emergency craniectomy. We obtained valid informed consent from the patients' family members or relatives in all cases.

We retrospectively reviewed the charts of all patients (n=42) who received early metabolic suppression therapy after emergency brain decompression between January 1, 2002 and January 1, 2007. We excluded the patients who suffered from other vital organ dysfunctions at the time of admission.

In all patients, we obtained information regarding their demographic data, medical history, diagnosis at admission, and neurologic status according to the Glasgow Coma Scale (GCS). The treatment protocol for patients who continued to experience persistent, increased intracranial pressure even after emergency brain decompression was outlined according to the following standard protocol. After securing the airway and providing respiratory support, the patients werehyperventilated in order to maintain their PaCO₂ level between 25 and 35 mmHg. CSF drainage and mannitol osmotherapy were initiated simultaneously. Once emergency decompressive surgery had been completed, early metabolic suppression was induced with thiopental at a dose of 3 to 5 mg/kg over 10 minutes, followed by the continuous infusion of thiopental at a dose of 3 to 5 mg/kg/hr. The dose was adopted in order to obtain an areflexive coma (i.e., in which the patient was unresponsive to stimuli). The barbiturate levels were assessed 2 or 3 times a day, and the plasma concentration of barbiturates was kept below 40 g/mL.

From the patients' medical records, we obtained detailed information regarding the duration of metabolic suppression therapy, complications that occurred in the ICU, causes of death, and the patients' neurologic status at the time of discharge according to the Glasgow Outcome Scale (GOS) rating. The five categories on the GOS are: 1) death; 2) persistent vegetative state; 3) severe disability (conscious but disabled); 4) moderate disability (disabled but independent); and 5) good recovery (resumption of normal life, though minimal neurologic and psychologic deficits may persist).

The results are presented as the mean \pm standard deviation distributed) (when normally or median with minimum-maximum values (when not normally distributed). The ages and GCS scores of the survivors and non-survivors were compared. A Student's T-test was used to compare the CPP between the survivors and non-survivors. P-values less than 0.05 were considered statistically significant.

Results

The patients' demographic data and GCS score on admission are presented in Table 1. The study population

included 42 patients: 20 with head trauma, 21 with vascular accidents, and 1 with an abscess. The vascular accidents includedsubarachnoid hemorrhage and cerebral hemorrhage. Twelve (28%) of these patients survived and were discharged from the hospital (Fig. 1).

Table	1.	Demographic	data.
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	Number of	Sex	Age GCS		Number of Survivors (%)	
	Patients (%)	M / F	(years)	on admission	Hospital	At 1 year
Head trauma	20(47.6)	18/2	40 ± 17.0	6.4 ± 1.63	7(16.7)	7(16.7)
Vascualr accident	21(50.0)	18/3	$49~\pm~13.5$	7.2 ± 1.44	5(11.9)	5(11.9)
Abscess	1 (2.4)	0/1	51	5	0(0.0)	0(0.00)
Total	42(100)	36 / 6	45 ±15.6	$6.7~\pm~1.58$	12(28.6)	12(28.6)

GCS: Glasgow coma scale, M: male, F: female



Fig. 1. The results of metabolic suppression therapy.

Barbiturates were administered for a median duration of 5.5 days and for up to 9 days. The barbiturates were discontinued in some patients due to brain death, uncontrollable ICP despite adequate serum levels, and intolerable side effects (i.e., hypotensionnot responsive to cardiac inotropes, peripheral vasopressors or progressive pulmonary dysfunction). The barbiturate therapy was continued when the following conditions were well maintained: ICP below 25 mmHg, cerebral perfusion pressure (CPP) above 70 mmHg, and a burst suppression pattern on EEG.

The causes of death included brain death due to increased ICP in 25 patients, pneumonia in 4 patients, and acute renal failure in 1 patient (Fig. 2). The 12 survivors were younger than the non-survivors (Fig. 3). None of the survivors had a GCS score lower than 8 at the time of admission (Fig. 4).



Fig. 2. The causes of death among non-survivors.



Fig. 3. The distribution of survivors and non-survivors according to age.



Fig. 4. The distribution of patients according to GCS score on admission



Fig. 5. The distribution of Glasgow Outcome Scale among the survivors at 1 year after discharge.

Five of the seven trauma survivors showed good recovery at hospital discharge, while one patient was severely disabled and one was in a vegetative state. Of the five survivors of vascular accidents, one patient was moderately disabled at hospital discharge, while three were severely disabled and one was in a vegetative state. The long-term neurologic outcome at one-year follow-up was the same as at hospital discharge (Fig. 5).

A Student's T-test was used to compare the CPP between the survivors and non-survivors (Fig. 6). P-values less than 0.01 were considered statistically significant. A CPP greater than 60 mmHg was achieved in all survivors. The CPP failed to rise above 60 mmHg in the non-survivors.



Fig. 6. The comparison of CPP between survivors and non-survivors by Student's T-test. A CPP above 60 mmHg is associated with the survivors.

preMST-CPP:CPP before metabolic suppression therapy immediately after decompressive brain surgery, MST-CPP-01: CPP on the first day after metabolic suppression therapy, MST-CPP-mid: CPP at the mid-point of metabolic suppression therapy, MST-CPP-final: CPP on the final day of metabolic suppression therapy.

Discussion

Increased intracranial pressure is a relatively common problem when treating critically ill patients. It is a leading cause of death in patients with intracranial pathologies. The basic pathophysiologic and clinical principles of increased intracranial pressure should be considered in the management of increased ICP. The major treatment options for increased ICP include hyperventilation, ventricular drainage of CSF, osmotherapy with mannitol, maintenance of an adequate CPP, and metabolic suppression therapy. The traditional approach to the management of traumatic brain injuries has been to control the ICP using a step-wise approach, adding or subtracting therapies as needed.1-4) However, in recent years, several groups have advocated for different overall approaches to the management of traumatic brain injuries.⁵⁻¹³⁾ These approaches are based on the understanding of certain aspects of the pathophysiology of traumatic brain injuries as well as on the favorable

clinical experiences with these approaches. However, there is no evidence in the literature to strongly support the superiority of these approaches over the others.

Shapiro et al.¹⁴⁾ introduced metabolic suppression therapy in

1974 to initiate hypothermia in patients with intractable intracranial hypertension. Since then, investigators in numerous studies have addressed the benefits and side effects of high-dose barbiturate therapy on patients with severe head injuries.¹⁵⁻¹⁸⁾ However, the effects of metabolic suppression therapy remain controversial.

High-dose barbiturates are known to reduce ICP, but their side effects have limited their use in patients to first-line therapies.¹⁹⁻²¹⁾Barbiturates appear to exert their ICP-lowering effects through two distinct mechanisms: the suppression of metabolism and the induction of changes in vascular tone. 22-24) Barbiturates can lower the resting cerebral metabolic rate for oxygen by 50%.²⁴⁾ Barbiturates are also decreased when cerebral blood flow and cerebral blood volume are coupled to regional metabolic rate. This mechanism mediates the observed beneficial effects of barbiturates on ICP and cerebral perfusion pressure. However, Cruz²⁵⁾ reported that some patients treated for intractable ICP with barbiturate metabolic therapyshowed jugular venous oxygen saturation levels of less than 45%, which was associated with a significantly worse outcome when compared with patients with higher jugular venous oxygen saturations. This suggested that barbiturate coma induced oligemic hypoxia in some patients. The use of jugular venous oxygen saturation monitoring allows for safer use of hyperventilation therapy and blood pressure changes by monitoring for treatment-induced global ischemia.²⁶⁾ Barbiturates confer additional direct neuroprotective effects independent of their ICP-lowering properties, such as the inhibition of free radical-mediated lipid peroxidation or membrane stabilization.²⁴⁾

In recent years, the maintenance of an adequate CPP, via so-called CPP therapy as described by Rosner and colleagues,^{27, 28)}has also been used as a means of improving or stabilizing ICP. Over the past 5 years, cerebral perfusion pressure (CPP) management has become the standard in the treatment of severe head injuries.²⁹⁾ The guidelines published in 2000 suggest that CPP should be maintained at least 70mmHg; however, the optimal CPP is still a matter of debate.³⁰⁾

Three important conclusions can be drawn from the findings of this study. First, patient age and admission GCS

score were important factors in the survival of patients who underwent emergency brain decompression. Second, a the survivors were associated with a CPP above 60 mmHg. Third, favorable outcomes (i.e., GOS 4 or 5) were achieved in 50% of the survivors.

We acknowledge that our conclusions are limited by the retrospective nature of this study, though our protocol did not alter during the course of the study and followed current guidelines. In addition, because the present study was uncontrolled, we could not evaluate the usefulness of the metabolic suppression therapy as an aggressive first-line treatment for the patients who underwent emergency brain decompression.

Conclusion

Early aggressive management with barbiturate metabolic therapy can be used to effectively control intracranial pressure in a substantial number of patients who show persistent, severely increased intracranial pressure following emergency brain decompression, without adversely affecting the cerebral perfusion pressure in these patients.

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