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The influence of mild hypothermia on ICP, CPP and outcome in patients with primary and secondary brain injury

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Summary

Aim of this study was to examine the hypothesis that only a subgroup of patients with lesser primary brain damage after severe head injury may benefit from therapeutic hypothermia.

We prospectively analysed 72 patients with severe head injury, randomized into groups with (n = 37) and without (n = 35) hypothermia of 34 °C maintained for 72 hours. The influence of hypothermia on ICP, CPP and neurological outcome was analysed in the context of the extent of primary brain damage.

Patients with normothermia and primary lesions (n = 17) – values: GCS on admission 5 (median), ICP 18.9 (mean), CPP 73 (mean), GOS 4 (median). Patients with normothermia and extracerebral hematomas (n = 20): GCS 4, ICP 16, CPP 71, GOS 3. Patients with hypothermia and primary lesions (n = 21): GCS 4,62, ICP 10,81, CPP 78,1, GOS 4. Patients with hypothermia and extracerebral hematomas (n = 14): GCS 5, ICP 13.2, CPP 78, GOS 5.

Hypothermia decreased ICP and increased CPP regardless of the type of brain injury. Hypothermia was not able to improve outcome in patients with primary brain lesions but this pilot study suggests that it significantly improves outcome in patients with extracerebral hematomas.

Keywords: Severe head injury; primary and secondary brain damage; mild hypothermia.

Introduction

Severe head injuries (Glasgow Coma Scale – GCS $\leq$ 8) generally have a very serious prognosis. About 30% of patients have a good result, but 25% are severely disabled, 5% end up in a vegetative state and about 40% of patients die [6]. Most important for the final result is the extent of primary brain damage and the development of secondary ischemic brain damage. Modern methods of the management of patients after severe head injury are therefore based on the principle of maintaining an adequate cerebral perfusion pressure (CPP) above 60 mmHg (see European and American guidelines) [3, 4]. Despite all effort, secondary ischemic changes may continue to evolve in many patients after severe head injury. It seems that neither the early evacuation of the hematoma, nor the correct management on the intensive care unit is able to protect many patients from secondary ischemic brain damage. One option to improve the results is the use of mild hypothermia. Hypothermia is not a new neuroprotective method, it has been in use already for several decades. Contemporary technology, however, has improved. Hypothermia now is used in accordance with modern knowledge of the pathophysiology of brain injury. In the clinical setting it is necessary to use hypothermia together with multimodal monitoring of the brain physiology, which was not available previously.

The laboratory results after application of mild hypothermia (30–34 °C) confirm less neuronal damage, decreased release of neurotransmitters and a prevention of blood-brain barrier breakdown as a consequence of ischemic insult, which is the most frequent cause of secondary brain damage [2].

Not all experimental and clinical studies, however, confirm a positive effect of hypothermia. Despite the fact that hypothermia influences physiological variables important for the patient s prognosis (intracranial pressure – ICP and cerebral perfusion pressure – CPP), the results of clinical studies are often controversial [1, 5].

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Material and method

We studied 72 patients after severe head injury (GCS $\leq$ 8) treated in our hospital during the years 2001–2003. Their mean age was 41 years and there were 51 males and 21 females. Patients older 60 years of age and those with severe primary brain damage with no possibility to survive (bilateral mydriasis, no reflexes above C1) were excluded.

Patients with significant hematomas were urgently operated on. The intraparenchymal probe for ICP monitoring (Codman, Lelocle, Switzerland), jugular bulb oxymetry probe (Edwards Lifesciences LLC, Irvine, USA) and invasive blood pressure monitoring (a.radialis) were instituted. The patients were randomized into two groups: with hypothermia (n = 35) and without hypothermia (n = 37). There were no statistical age or sex differences between the groups. In those randomized for hypothermia, mild hypothermia (34 °C) was started as soon as possible for a period of 72 hours by means of surface cooling (Blanketrol II, Cincinnati, USA). Central body temperature was measured in the urinary bladder. After 72 hours the patients were passively warmed-up to reach normothermia. All patients were cooled down within 15 hours after injury and we were able to reach the desired temperature within 3 hours after initiation of cooling. Intensive care for these patients was otherwise performed according to the international standards for severe head injuries [2, 3].

The observer who had access only to the CT scans divided this group into those with dominant primary brain injury (diffuse injury, contusions) (n = 38) and with dominant extracerebral hematoma (21 patients with subdural and 13 patients with epidural hematoma) (n = 34). Finally we evaluated the influence of mild hypothermia on ICP, CPP and $SvjO_2$ (jugular bulb oxygen saturation) and Glasgow Outcome Scale (GOS) 6 months after trauma taking into account the dominant type of injury (primary lesions versus extracerebral hematomas). The results are expressed as mean and standard deviation. We tested the conformity of scatters by F-test and we used an unpaired t-test to compare the differences between the groups.

Results

The results are presented in Tables 1–4.

Discussion

Our study differed from many studies using controlled hypothermia in severe head injuries by the fact that we used a milder degree of hypothermia (34 °C) for a relatively longer time (72 hours). This temperature is more easily reached in the clinical setting and is accompanied by no or minimal side effects with a similar influence on ICP and CPP. With the use of multimodal monitoring, this method can also be safely used in patients with multiple trauma.

Jugular bulb oximetry monitoring, in particular, is advantageous during therapeutic hypothermia because it can give a warning regarding a global decrease of cerebral metabolism.

Hypothermia did not influence the systemic blood pressure. We observed only 2 episodes of bradycardia below 40/min which reacted well to atropine. The occurrence of pneumonia did not differ significantly between the groups.

Mild hypothermia of 34 °C was able to decrease ICP and improve CPP in hypothermia patients (although

Table 1. *Results of all patients after severe head injury (hypothermia of 34 °C for 72 hours versus normothermia)*

	Normothermia (n = 37)	Hypothermia (n = 35)	
MABP (mmHg)	123.11 ± 5	123.45 ± 4	p = 0.9013
CPP (mmHg)	72.16 ± 4	78.23 ± 6	p < 0.0001
ICP (mmHg)	17.65 ± 7	11.77 ± 5	p < 0.0001
$SvjO_2$ (%)	71.12 ± 4	69.05 ± 4	p = 0.2436
GCS	4.27 ± 1.24	4.57 ± 1.27	p = 0.3115
GOS	3.16 ± 1.69	4.09 ± 1.36	p = 0.0131

MABP Mean arterial blood pressure; *CPP* cerebral perfusion pressure; *ICP* intracranial pressure; *$SvjO_2$* jugular bulb oxygen saturation; *GCS* Glasgow Coma Scale; *GOS* Glasgow Outcome Score.

Table 2. *Results of patients with primary brain injury*

	Normothermia (n = 17)	Hypothermia (n = 21)	
MABP (mmHg)	129.83 ± 10	123.44 ± 14	p = 0.3692
CPP (mmHg)	73.71 ± 5	78.10 ± 6	p = 0.0240
ICP (mmHg)	18.88 ± 6	10.81 ± 5	p < 0.0001
GCS	4.59 ± 1.37	4.62 ± 1.24	p = 0.9426
GOS	3.47 ± 1.74	3.71 ± 1.62	p = 0.4470

Table 3. *Results of patients with brain compression through extracerebral hematoma*

	Normothermia (n = 20)	Hypothermia (n = 14)	
MABP (mmHg)	118.67 ± 11	123.33 ± 11	p = 0.4402
CPP (mmHg)	70.85 ± 2	78.43 ± 6	p < 0.0001
ICP (mmHg)	16.60 ± 7	13.21 ± 5	p = 0.1077
GCS	4.00 ± 1.08	4.50 ± 1.34	p = 0.2377
GOS	2.90 ± 1.65	4.64 ± 0.50	p = 0.0006

Table 4. *Morbidity and mortality of patients according to GOS (mean 6 months after injury)*

GOS	Normothermia (n = 37)	Hypothermia (n = 35)	Total (n = 72)
5 (good)	13 (35%)	18 (51%)	31 (43%)
4 (moderate disability)	5 (13.5%)	12 (34%)	17 (24%)
3 (severe disability)	5 (13.5%)	0	5 (7%)
2 (vegetative state)	3 (8%)	0	3 (4%)
1 (death)	11 (30%)	5 (15%)	16 (22%)

the decrease of ICP in the extracerebral hematoma group was not significant) which correlates with previous studies [1, 5]. The outcome (GOS) was significantly better in the hypothermic group of patients with extracerebral hematomas but did not differ in patients with primary brain injury.

Hypothermia has basically three important roles in influencing brain physiology. First it lowers ICP, second it improves CPP, and third it has a direct neuroprotective effect on cerebral neurons. We consider the use of hypothermia in patients with brain compression as very well-founded since these patients are threatened by the development of a secondary ischemic brain damage. Hypothermia may help these patients not only by its effect on ICP and CPP but also by its neuroprotective effect. This might be why there were better results in patients with extracerebral hematomas. The very good results in this group were the reason why the hypothermia group had better results even when evaluated regardless of the type of injury. In patients with primary brain injury, hypothermia may affect mainly ICP and CPP. Brain ischemia does not play such an important role in this type of injury (with some exceptions) and therefore the neuroprotective effect of hypothermia in primary injuries does not influence pathophysiology that much.

This does not mean, however, that hypothermia in primary head injury is useless and should be neglected. We think that in these patients, hypothermia should be used in cases with otherwise intractable intracranial hypertension.

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