

THE IMPACT OF MILD HYPOTHERMIA ON VASOSPASMS IN PATIENTS AFTER SEVERE SUBARACHNOID HAEMORRHAGE

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Abstract

Vasospasms occur in 30% of patients after subarachnoid haemorrhage (SAH). The most severe spasms are in patients with Hunt and Hess IV and V, who have usually much blood in the basal cisterns. According to some reports, hypothermia could decrease the incidence and severity of vasospasms in these patients.

We have analysed 15 patients (HH IV and V) after SAH from a ruptured intracranial aneurysm. In 8 patients the aneurysm was embolised during the first 4 days, 3 patients were operated on because of intraparenchymal haematoma and their aneurysm was clipped, the other 4 patients were initially treated conservatively. In all patients mild hypothermia (34 °C for 72 hours) had been started immediately after their admission by means of cooling blankets. Monitoring of ICP (intraventricular), CPP and jugular bulb oxymetry was instituted and everyday TCD examination was performed.

Results – ICP, CPP and jugular bulb oxymetry were maintained in the normal range in all patients. In 11 patients, however, severe vasospasms with infarctions on the CT scan occurred (during days 5 and 16 after SAH). TCD showed increased velocities only in 6 of these patients. Ten patients with vasospasms died within 6 months after SAH. One patient remained vegetative, 1 severely disabled, and 3 had a good outcome (2 of them had intraparenchymal haematoma).

Hypothermia applied immediately after SAH does not seem to decrease either the incidence or the severity of vasospasms in HH IV and V patients after SAH.

Key words

Subarachnoid haemorrhage, Vasospasms, Hypothermia

Abbreviations used

SAH, subarachnoid haemorrhage; HH, Hunt and Hess scale; CT, computed tomography; ICP, intracranial pressure; CPP, cerebral perfusion pressure; TCD, transcranial Doppler; GOS, Glasgow Outcome Score

INTRODUCTION

Subarachnoid haemorrhage (SAH) from a ruptured aneurysm occurs in the Czech Republic with the incidence of 10/100 000 inhabitants per year. Approximately 50 % of these patients will die within the period of 24 hours, the rest may benefit from a specialised treatment. We have been treating about 50–60 patients with this serious disease annually in our department. About 30 % of these patients are Hunt and Hess grade 4 or 5 on admission and mortality and severe morbidity of this subgroup highly exceeds 50 %. In the majority of the cases the reasons are refractory vasospasms and the subsequent fatal brain ischaemia.

The treatment of a subarachnoid haemorrhage from a ruptured aneurysm is still a challenge for the neurosurgeon. Several pathophysiological mechanisms may influence the prognosis of the patient and they themselves represent medical problems. In the acute phase after the aneurysm rupture they involve a steep increase of intracranial pressure (ICP), a mass effect of the intracerebral haematoma or an acute hydrocephalus. Although it is basically a haemorrhagic stroke, the patients are paradoxically threatened very often by ischaemic complications. As many as 30 % of the patients will encounter the development of vascular spasms and the so-called delayed ischaemic neurological deficit (1). As many as 30 % of the patients die due to this complication (2). The most endangered by this complication are patients in a severe clinical condition, 4 and 5 according to the Hunt and Hess scale. Their mortality may be as high as 80 %.

Hypothermia still does not belong among the standard treatment methods and has been the subject of research in both experimental and clinical studies. On the other hand, hypothermia is considered to be the most effective of all neuroprotective methods currently available.

Hypothermia is not a new neuroprotective method. Its use was tried already many decades ago. The current technology is on a much higher level and, above all, hypothermia has now been used in the context with modern knowledge of the pathophysiology of brain damage. Moreover, in clinical practice it is necessary to use hypothermia together with a multimodal monitoring of brain functions, which was not available earlier, either.

There have been several clinical studies published whose results show lower mortality and a better quality of life after the use of mild hypothermia as part of the therapeutic protocol in patients after severe brain injury (3, 4). According to international and our own experience, controlled hypothermia decreases significantly intracranial pressure (ICP) and increases significantly cerebral perfusion pressure (CPP) in patients with a severe head injury (5–8).

There is much less experience with the use of hypothermia in patients after severe subarachnoid haemorrhage than in patients after severe head injury, but it does exist. Experimental (9, 10) and infrequent clinical studies show that hypothermia could be effective not only through its neuroprotective effect on the ongoing

ischaemia but it could even have a prophylactic effect and thus lower the incidence of vasospasms (11).

There has been no experience with the use of mild hypothermia in patients after subarachnoid haemorrhage in the Czech Republic so far. The aim of this study was to improve the otherwise bad results of treatment of patients after a severe subarachnoid haemorrhage, who are often jeopardised by the development of ischaemic complications as a result of vascular spasms. We used a mild hypothermia of 34 °C for this purpose. A secondary aim was to evaluate the influence of mild hypothermia on the incidence of vasospasms, on intracranial and cerebral perfusion pressures, and on the brain oxygen metabolism (jugular bulb oxymetry - SvjO₂).

MATERIALS AND METHODS

We studied 15 patients admitted to our department in Hunt and Hess grade 4 or 5 after a severe subarachnoid haemorrhage (i.e., patients with no reaction or reaction to painful stimuli were enrolled for this study). We excluded patients with bilateral dilated pupils and patients older than 70 years. There were 11 females and 4 males; their mean age was 55 years.

There were 8 patients embolised by coils within 4 days after SAH (6 anterior communicating artery aneurysms, 2 posterior communicating artery aneurysms), 3 patients were operated on urgently because of their large temporal lobe haematoma (2 patients with middle cerebral artery aneurysm and 1 patient with carotid bifurcation aneurysm), and 4 patients had initial conservative treatment due to their severe medical and neurological condition (all grade V).

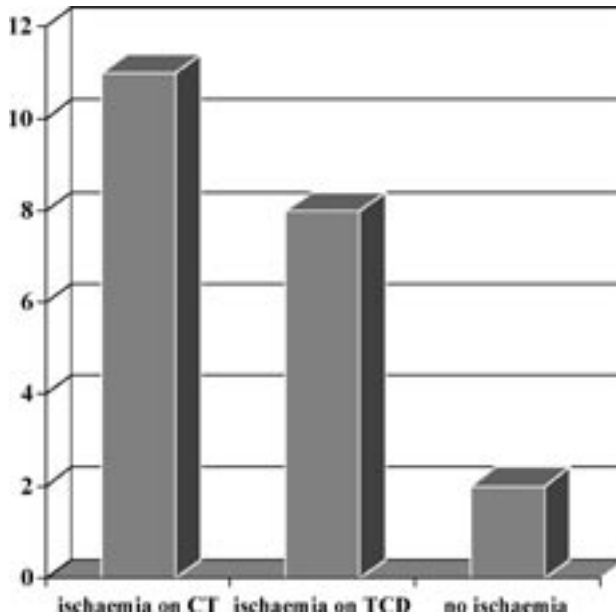


Fig. 1

The number of patients with signs of ischaemia on CT or TCD (n=15)

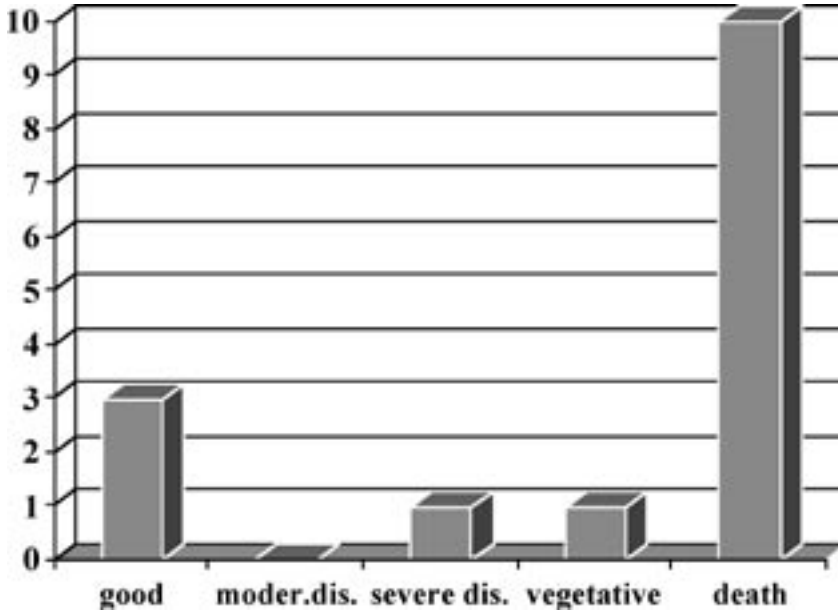


Fig. 2

Results - GOS (6 months' follow-up) (n=15)

Table 1a

The number of patients with normal or pathological (one hour or more) monitored values during the period of hypothermia (first 3 days after SAH)

	normal	pathol.
ICP	15	0
CPP	13	2
SvjO ₂	15	0

Table 1b

The number of patients with normal or pathological (one hour or more) monitored values after a hypothermia period (from day 4 after SAH)

	normal	pathol.
ICP	6	9
CPP	4	11
SvjO ₂	5	10

The circulating water cooling mattress was placed below and above the patient. The surface cooling of these patients was started as soon as possible after the admission with the device for controlled hypothermia HYPO-1 (Czech Space Research Centre, Ltd., Czech Republic) to reach a central body temperature of 34 °C, which was maintained for 72 hours. Then the cooling was switched off and the patients were passively warmed up to the level of normothermia, which was maintained for the rest of the patient's stay at the intensive care unit. The central body temperature was monitored continuously from the urinary bladder (urinary catheter Kendall).

An external ventricular drainage was introduced to all patients and used for ICP and CPP monitoring as well as for cerebrospinal fluid (CSF) removal. All patients had a jugular bulb oxymetry monitoring (Edwards) and blood pressure was monitored invasively from the radial artery. All patients were monitored two times a day using transcranial doppler sonography (TCD) to detect vasospasms. The occurrence of cerebral infarctions was evaluated on the basis of repeated CT scan examinations.

We have analysed the intracranial and cerebral perfusion pressures as well as the levels of jugular bulb oxymetry during and after the period of hypothermia. We also evaluated the incidence of vasospasms (TCD) and cerebral infarctions (CT). The treatment results were evaluated using the Glasgow Outcome Score (GOS).

RESULTS

A mild hypothermia of 34 °C was achieved quite easily by means of circulating water mattresses within 3 hours from the start of cooling. Five patients developed pneumonia and one patient had a bradycardia below 40/min which reacted well to atropine. Generally, hypothermia was very well tolerated and we have not observed any influence on blood count, biochemistry or coagulation.

The amount of CSF drained from the external ventricular drainage varied from 30 to 250 ml per day. During the period of hypothermia we were able to maintain normal ICP and SvjO₂ in all patients and CPP in all but two patients (*Table 1a*). During the period without hypothermia the levels of ICP, CPP, and SvjO₂ were frequently pathological (*Table 1b*).

Ischaemia or infarction developed between days 5–16 after SAH in 13 patients. We found signs of vasospasms detected on TCD in 8 patients. Six of them died, one was severely disabled, and one had a good outcome. All the 6 patients with TCD vasospasms who died had CT scan infarction as well. There were 11 patients with CT scan infarction, out of them 10 died and one ended up in the vegetative state. There were 2 patients without any signs of TCD vasospasms or CT scan infarction. Both had a good outcome (*Fig. 1*).

The outcome (mean follow-up 6 months) was as follows: 3 patients had a good outcome, one was severely disabled, one became vegetative, and 10 patients died (*Fig. 2*).

DISCUSSION

The cause of vasospasms is not yet known. According to the current hypothesis, oxyhaemoglobin released from the disintegrated erythrocytes in the subarachnoid space activates the gene for endothelin-1, which is one of the most potent known vasoconstrictors. At the same time oxyhaemoglobin is bound on the molecules of nitric oxide (NO), and thus decreases the amount of NO in the vessel wall and by

this mechanism enables the initiation of vasospasms (12, 13, 14). Vasospasms are most frequent between days 4 and 14 after the initial bleeding and are more frequent in patients with disturbed consciousness (grades 3, 4 and 5 according to Hunt and Hess scale), who have a large amount of blood in the subarachnoid space or haemorrhage (15). Standard treatment with HHH therapy (hypertension, haemodilution, hypervolaemia), nimodipine or with neuroradiological intervention is not effective in many cases (16, 17).

Some hope is placed in the intrathecal administration of sodium nitroprusside as a source of exogenous NO. This treatment, however, requires first of all to exclude the aneurysm from the circulation, no matter if by microsurgery or coiling (18). In patients of grades 4 and 5 according to Hunt and Hess, however, acute intervention is not always indicated just for their severe clinical condition. The use of mild controlled hypothermia could be the life-saving procedure for these patients. The laboratory results with the use of mild hypothermia (33–34 °C) confirm the decreased neuronal damage, a lower release of neurotransmitters, and a prevention of the blood-brain barrier damage as a result of the ischaemic insult, which is the most common cause of secondary brain damage (19).

Clinical studies show that the lowest safe body temperature that has no cardiovascular, haematological, metabolic or neurological toxicity is 32–33 °C. The decreased release of excitatory amino acids as a result of ischaemia was noted even during mild hypothermia (34 °C), which is reached more easily in the operating room or intensive care unit setting (3).

It may not be safe to use hypothermia during the whole period of time when the patient is in the intensive care unit, and this approach is not used in practice. In this project we used mild controlled hypothermia applied prophylactically right from the time of admission of the patient to our department and maintained for 3 days. The use of such algorithm was safe. We encountered an adequate number of pneumonias (30%) and only one case of deep but pharmacologically reversible bradycardia.

We hypothesised that besides the possible influence on the incidence of later vasospasms we reach an improvement of ICP and CPP in the acute phase after the stroke. This finding was confirmed; we were able to maintain normal ICP, CPP and brain oxygenation during the first 3–4 days. Of course, there was an important role of external ventricular drainage of the CSF which helped to normalise ICP. In the later course with the ongoing ischaemic changes and oedema evolution, ICP, CPP and SvjO₂ became more frequently pathological.

The incidence of vasospasms on TCD in our group of patients (53%) is not lower compared to other series. The number of patients who suffered a delayed ischaemic neurological deficit with CT scan infarction (73%) is also high. Finally 12 patients (80%) with unfavourable result including 66% mortality does not really mean any improvement in the outcome.

Two out of three patients with a good outcome had a temporal intracerebral haematoma from an aneurysm located on the middle cerebral artery. The reason

for their good outcome was an urgent evacuation of the haematoma, young age, and no or only mild vasospasms.

Using hypothermia in the very acute phase after SAH we are probably missing the most dangerous phase when the vasospasms really occur and brain perfusion is insufficient. The positive influence of hypothermia on acute intracranial hypertension is not enough to improve the outcome of these patients. On the other hand, we still consider hypothermia as a promising neuroprotective tool. It has to be used not prophylactically but to really cover the period when the patient is threatened by decreased brain perfusion.

There are basically two options: first, to start with hypothermia on day 4 after SAH and keep it for a relatively long period of time (4–6 days). Second, to monitor closely the cerebral blood flow (CBF)(TCD, tissue oxymetry – ptO_2 , laser-Doppler velocimetry, etc.) and start with hypothermia with the first signs of CBF disturbances.

CONCLUSION

A mild hypothermia of 34 °C used prophylactically during the first 3 days after SAH has not influenced the incidence or severity of vasospasms in Hunt and Hess IV and V patients and has not improved the outcome of these patients. A different algorithm of hypothermia employment has to be considered to maximise its neuroprotective effect.

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Smrčka M., Juráň V., Jura R., Gál R., Smrčka V.

VLIV MÍRNÉ HYPOTERMIE NA VAZOSPASY U PACIENTŮ PO TĚŽKÉM SUBARACHNOIDÁLNÍM KRVÁCENÍ

Souhrn

Vazospasmy se objevují asi u 30 % pacientů po subarachnoidálním krvácení (SAK). Nejtěžší spasmy jsou u pacientů Hunt-Hess IV a V, u kterých je obvykle velké množství krve v subarachnoidálních prostorách. Podle některých zpráv by mohla hypotermie snížit incidenci a závažnost vazospasmů u těchto pacientů.

Analyzovali jsme 15 pacientů (HH IV a V) po SAK z prasklého intrakraniálního aneuryzmatu. U 8 pacientů bylo aneuryzma embolizováno v průběhu prvních 4 dnů, 3 pacienti byli operováni kvůli odstranění intracerebrálního hematomu a jejich aneuryzma bylo zasvorkováno, další 4 pacienti byli zpočátku léčeni konzervativně. U všech pacientů byla ihned po přijetí zahájena mírná řízená hypotermie (34 °C na 72 hodin) pomocí povrchového chlazení. Byl zahájen monitoring ICP, CPP a jugulární oxymetrie a denně byl monitorován TCD.

Výsledky: ICP, CPP a jugulární oxymetrie byly zpočátku udržovány v normálních mezích u všech pacientů. U 10 pacientů však došlo k rozvoji těžkých vazospasmů s infarkty na CT (mezi 5. a 16. dnem

po SAK). TCD ukázalo zrychlené toky pouze u 6 těchto pacientů. 10 pacientů s vazospasmy zemřelo do 6 měsíců po SAK, 1 pacient zůstal ve vegetativním stavu, 1 těžce postižen a 3 měli dobrý výsledek léčby (2 z nich měli intracerebrální hematom).

Závěrem lze konstatovat, že hypotermie aplikovaná ihned po SAK pravděpodobně nesnižuje ani incidenci ani závažnost vazospasmů u pacientů HH IV a V.

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