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CLINICAL STUDY

Neuroprotective use of mild hypothermia in patients with severe vasospasms after subarachnoid haemorrhage

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Abstract: *Background:* The authors describe two cases of patients with a severe subarachnoid haemorrhage, where mild hypothermia was successfully applied as a part of comprehensive neuroprotective therapy.
Patients: A 56-year-old patient was admitted to an intensive care unit with the diagnosis of subarachnoid haemorrhage, with a consciousness dysfunction requiring artificial ventilation. Angiography failed to establish the cause of the haemorrhage, even after repeated examinations. Furthermore, the authors describe the case of a 28-year-old woman with negative anamnesis and without long-term pharmacological medication, who was admitted to the hospital with a severe headache and a qualitative consciousness dysfunction. Angiography showed an aneurysm appearing closely above the left internal carotid artery bifurcation. After detecting vasospasms, mild hypothermia was repeatedly used in both patients, keeping the temperature of the body core between 34–34.5 °C.
Results: The total length of the introduced therapeutic hypothermia was 12 days in the first case and 6 days in the second case. The method used was non-invasive all-body cooling by means of blankets with circulating cooling liquid (Blanketrol II, Cinncinnati Sub Zero). In both cases the computed tomography findings and the clinical conditions gradually improved and the patients were released from the intensive care unit on the 22nd and 30th day, respectively, following the disorder detection.
Discussion: Mild hypothermia is a clinically attainable neuroprotective method, which – in combination with other therapeutic measures – led to minimising the neurological deficit in patients with severe subarachnoid haemorrhage *(Ref. 11)*. Full Text (Free, PDF) *www.bmj.sk.*
Key words: subarachnoid haemorrhage, intensive care management, mild hypothermia.

Subarachnoid haemorrhage (SAH) from brain arteries represents a serious problem affecting the whole society. It usually afflicts social groups in productive age, with global incidence reported at 10.5/100 000 (1). The consequences of this disorder tend to be serious and often permanent; the social fulfilment of the patient is also considerably impaired. The economic losses for society are caused both by a necessity of long-term treatment as well as by the patients loss of the working ability. Each improvement regarding the number of surviving patients with brain artery disorders and the quality of their lives is of great importance. Unlike in most published studies dealing with the clinical application of controlled hypothermia, a milder stage of hypothermia was used in our department (34–35 °C). Our observations have shown that this temperature is more easily attainable in clinical conditions and the accompanying undesirable side effects are minimised (2, 3).

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Case 1

A 56-year-old man with negative anamnesis and without long-term pharmacological medication was urgently admitted to the University Hospital Brno with an acute severe headache complicated by nausea and hypertension; the initial Glasgow Coma Score reached 15. As the computed tomography (CT) examination indicated SAH in the area of basal cisterns, the patient was transferred to the Neurosurgery Ward to deal with a suspected aneurysm. However, neither the following angiography nor the magnetic resonance examination detected the source of the haemorrhage. Within the next 24 hours, the patient gradually lost consciousness, finally reaching the level of GCS 7. Therefore external ventricular drainage was introduced and the patient was transferred to the intensive care unit; the patient was sedated and intubated with maintaining artificial ventilation and stable blood circulation. An external ventricular drainage released slightly sanguinolent cerebrospinal fluid. Complex intensive care was fully applied, including intracranial pressure (ICP) monitoring and repeated CT checks, without any progression in the findings. The treatment also included monitoring the body core temperature and keeping the temperature strictly within the set boundaries. On the 5th day after the SAH occurred, vasospasms were detected during regular checks of blood flow by means of trans-

cranial examinations using Doppler's ultrasound (TCD, twice daily). The neuroprotective treatment was at once extended to include mild controlled hypothermia, using the method of non-invasive whole-body cooling by means of blankets with circulating cooling liquid (Blanketrol II, Cincinnati Sub Zero). The body core temperature (checked continually in the urinary bladder, Kendall) was kept at between 34–34.5 °C. The ultrasound checks indicated that vasospasms subsided on the 12th day, when the patient was warmed back to a normal temperature. The CT of the brain taken on the 12th day showed that the SAH had already been absorbed; a small haemocefalus still remained in the side chambers; the conditions were normal in the posterior fossa and the position of the ventricular drainage was stable. On the 14th day TCD again indicated the occurrence of vasospasms and therefore the therapy was extended again to include controlled hypothermia. The final decline of vasospasms occurred on the 19th day, when hypothermia was also discontinued. The total length of time when hypothermia was applied was 7+5 days. Angiography repeated on the 15th day failed to establish the source of the haemorrhage. After the intra-cranial flows were brought back to normal on the 20th day, the analgo-sedation was stopped and on the 22nd day the patient was extubated. The next day, during standard ICP monitoring, the ventricular drainage was also discontinued.

The final brain CT showed no subarachnoid blood, only slightly more spacious cerebrospinal fluid spaces. The objective neurological findings were dominated by a mixed phatic disorder and a weak quadruparesis accentuated in the lower extremities, which had probably had combined causes (the result of SAH, poly-neuropathy of critically ill patients). The neurological condition of the patient gradually improved; when he was transferred to the intensive care unit of the Neurological Department on the 38th day, the patient was conscious, well-oriented, cooperating, cardio-pulmonary compensated, non-pyretic, with sufficient oral intake; he had just started walking as a part of the rehabilitation process. Six months after the disorder appeared, the patient was able to perform his intellectually and manually demanding profession to the same extent as before the SAH first appeared.

Case 2

This is the case of a 28-year-old woman with negative anamnesis and without any long-term pharmacological medication, who was admitted to the Neurology Ward with a severe headache and qualitative consciousness disorders; her initial GCS was 12. The brain CT indicated subarachnoid haemorrhage in the drainage area of the left internal carotid artery, where the angiography that followed showed an aneurysm close above the bifurcation. Five hours after the patient's admission her consciousness suddenly deteriorated, finally reaching GCS 8; therefore the patient was sedated, intubated and transferred to the intensive care unit. On admission, the patient was sedated, with artificial ventilation applied and with stable blood circulation. The same day, the aneurysm was clipped, a spinal line was inserted to drain the cerebrospinal fluid, and a parenchymal probe was introduced to monitor the ICP and to check the tissue oxygenation (Licox). 8 hours after the surgery was performed, the level of tissue oxygenation dropped sharply, so a TCD was performed, which detected vasospasms predominantly in the drainage area of the left internal carotid artery. Afterwards, this already-introduced neuro-protective therapy was extended to include mild controlled hypothermia (34–34.5 °C). Also in this case the method of non-invasive whole-body cooling by means of blankets with circulating cooling liquid was applied; the temperature was taken continually in the urinary bladder by means of a urinary catheter with a temperature sensor.

TCD checks were done twice daily; the 7th day after the operation the vasospasms disappeared. The patient was gradually taken out of hypothermia. The spinal line for draining the cerebrospinal fluid was exchanged the 8th day after the operation. The brain CT taken on the 11th day after the clipping showed that the SAH had already been absorbed, but some post-ischemic changes appeared on the left frontal and temporal lobes.

Due to a complication caused by ventilator-associated pneumonia, the patient was left under sedation and artificial ventilation until the 14th post-operation day. On the 15th day after the operation, the sedation was gradually reduced, the spinal line, the ICP and Licox probes were taken out (the CT indicated that the width of the chambers was normal, the ICP levels and the values of tissue oxygenation were also within normal levels); on the 16th day the patient was extubed with a GCS of 15. Unfortunately the patient was not capable of sufficient expectoration, so she had to be re-intubated and surgical tracheotomy was performed. The patient was disconnected from the ventilator on the 18th post-operation day, and on the 21st day she was transferred back to the Department of Neurology. On the day of the transfer, the patient was fully conscious, cooperating, with a GCS of 15, according to the neurological examination without lateralization. The brain CT that was done on the 30th day after the operation showed – in addition to stationary post-operation changes – only slight progression of the chambers width, but the infusion test did not indicate a necessity to introduce a shunt. The patient was discharged to continue her treatment at home on the 37th day after the operation; she was fully conscious, well-oriented, without any neurological deficit.

Discussion

Neuro-protective methods are preventive treatment measures, which aim is to improve the neurological result of treating patients with a risk of development of brain ischemia. The primary objective is to prevent the devastating effects of ischemia. The strategy of neuroprotection is based on understanding pathophysiological processes, which occur after hypoxic-ischemic damage. The most important and also most effective neuro-protective methods therefore include keeping sufficient cerebral perfusion pressure and preventing hypoxemia. In addition to these treatments, there are also efforts to apply pharmacological interventions in order to increase the cerebral blood flow in the ischemic area, to inhibit the accumulation of lactates and the activities of

excitatory neurotransmitters, to prevent the influx of calcium ions, to inhibit lipids oxidation and the formation of free radicals.

As a result of biochemical research and experimental studies, a number of pharmacological preparations have been tested to decrease the consequences of brain tissue ischemia; however, in clinical practice they have not proved to be very effective (4). On the other hand, one of the effective methods of decreasing the consequences of brain tissue ischemia is controlled hypothermia. Experimental studies confirm the impact of decreasing the metabolism on maintaining the tissue homeostasis, on decreasing the release of excitatory amino acids and free radicals, as well as on inhibiting cytoskeletary axonal injury (5). Clinical studies have shown the neuroprotective effectiveness of hypothermia on ischemic damage caused by cardiac arrest and in perinatal asphyxia (6, 7). It has also been proved that mild hypothermia improves and mild hyperthermia aggravates the consequences of ischemic neuronal injury (8).

There are several techniques of attaining hypothermia of the system, such as cooling blankets, endovascular cooling systems with a catheter inserted in the lower vena cava, as well as the application of iced intravenous solutions (9). In experiments and in clinical practice some work places also use direct cooling of brain by both invasive and non-invasive methods (10).

The results of studies focusing on the use of system hypothermia in patients with brain trauma and subarachnoid haemorrhage are ambiguous, which is probably caused by considerable heterogeneity of the disorder in the observed population (11, 12).

Non-traumatic subarachnoid haemorrhage still represents a serious diagnosis, with respect to its high mortality rate and the considerable impairment of the quality of life in those who survive. These are the main reasons why a number of therapeutic measures are applied today in clinical practices aiming to improve the neurological output. One of these methods is a mild system hypothermia, which is clinically attainable and in combination with other therapeutic methods can lead to minimising the neurological deficit in patients with vasospasms, who are resistent to other therapeutic steps. However, opinions regarding the timing, the method of application and the depth of hypothermia still vary considerably, therefore further research in this area is necessary.

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