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Novel applications of therapeutic hypothermia: report of three casesKoen J Hartemink¹, Willem Wisselink², Jan A Rauwerda³, Armand RJ Girbes⁴ and Kees H Polderman⁵¹Surgical Resident, Department of Intensive Care and Surgery, VU University Medical Center, Amsterdam, The Netherlands²Senior Consultant in Vascular Surgery, Department of Surgery, VU University Medical Center, Amsterdam, The Netherlands³Chairman of the Vascular Surgery Division, Department of Surgery, VU University Medical Center, Amsterdam, The Netherlands⁴Chairman of the Intensive Care Department, VU University Medical Center, Amsterdam, The Netherlands⁵Senior Consultant in Intensive Care Medicine, Department of Intensive Care, VU University Medical Center, Amsterdam, The NetherlandsCorresponding author: Kees H Polderman, k.polderman@tip.nl

Received: 22 July 2004

Accepted: 26 July 2004

Published: 18 August 2004

Critical Care 2004, **8**:R343-R346 (DOI 10.1186/cc2928)This article is online at: <http://ccforum.com/content/8/5/R343>© 2004 Hartemink *et al.*; licensee BioMed Central Ltd. This is an Open Access article: verbatim copying and redistribution of this article are permitted in all media for any purpose, provided this notice is preserved along with the article's original URL.**Abstract**

Therapeutic hypothermia can provide neuroprotection in various situations where global or focal neurological injury has occurred. Hypothermia has been shown to be effective in a large number of animal experiments. In clinical trials, hypothermia has been used in patients with postanoxic injury following cardiopulmonary resuscitation, in traumatic brain injury with high intracranial pressure, in the perioperative setting during various surgical procedures and for various other indications. There is thus evidence that hypothermia can be effective in various situations of neurological injury, although a number of questions remain unanswered. We describe three patients with unusual causes of neurological injury, whose clinical situation was in fundamental aspects analogous to conditions where hypothermia has been shown to be effective.

Keywords: neurological injury, neuroprotection, outcome, postanoxic injury, spinal cord ischaemia, therapeutic hypothermia

Introduction

Evidence from a large number of animal studies and clinical trials strongly suggests that mild (32-34°C) hypothermia can have neuroprotective effects in various situations of imminent or actual neurological injury [1-12]. Protective effects of therapeutic hypothermia have been clearly demonstrated in patients with postanoxic coma after cardiopulmonary resuscitation (CPR) [1-4]. Other categories of patients that could benefit from therapeutic hypothermia include patients with traumatic brain injury [1,2,5-8], stroke [9,10], subarachnoid haemorrhage [11,12], and fever, in patients with neurological injury [13-15], although the evidence is less clear-cut than for patients with postanoxic injury [1-4]. In addition, there is some evidence from animal and small clinical studies that induced

hypothermia may also have cardioprotective effects after ischaemic cardiac events [16,17].

Hypothermia is also used during various surgical procedures, including major vascular surgery [1,18-20]. Cooling is thought to provide spinal cord protection as well as overall neuroprotection in the latter category of patients. In the present article we describe three exceptional cases of neurological injury. Although each of these three patients had a rare and unusual cause of injury, their clinical situations nevertheless were in many aspects similar to those where therapeutic hypothermia has been shown to be, or is thought to be, effective. We therefore decided to treat these patients with artificial cooling to prevent postischaemic neurological injury.

Patients

Patient A, a 49-year-old man with no significant medical history, was admitted to another hospital after being stabbed in his neck. He was transferred to our centre for emergency surgery, which was started nearly 1 hour following the incident. Surgical exploration showed a dissection of the left internal carotid artery and a complete transection of the left internal jugular vein and vagal nerve. Haemostasis and anastomosis of the artery was achieved by saphenous vein interposition. During the surgical procedure, however, the patient developed dilation of his left pupil. A postoperative computerized tomography (CT) scan revealed a lesion in the left parietal region, suspect for postischaemic injury and developing infarction. The patient was subsequently admitted to the intensive care unit. Artificial cooling (32–34°C) was immediately started and continued for 24 hours.

In the following days the patient's overall condition improved and he was extubated. Eight days after the first scan, a second CT scan was performed; the lesion observed on the first CT scan was still present, but had not increased in diameter. Two smaller lesions, suspect for small infarctions, were also seen. Ten days after admission, the patient left the hospital in good clinical condition. On clinical investigation there was no evidence of neurological impairment, and no signs of hemiparesis were present.

Patient B, a 57-year-old man with a history of hypertension, noninsulin-dependent diabetes mellitus, tonsillectomy and percutaneous transluminal coronary angioplasty, was admitted after elective thoraco-abdominal aneurysm repair for a type Crawford II aneurysm. A thoraco-phrenico laparotomy was performed and a prosthesis was implanted from the left subclavian artery to the aorta-iliacal bifurcation, with implantation of the abdominal and renal arteries in the prosthesis. Perioperative neurological controls including evoked potential measurements to monitor for spinal ischaemia showed no abnormalities. For distal perfusion, a left–left heart bypass was used combined with relative organ perfusion. In addition, spinal cord drainage was performed to keep the spinal fluid pressure ≤ 10 mmHg. Because the evoked potentials remained unchanged during the surgical procedure, no lumbar and/or intercostal arteries were re-implanted.

Following surgery, the patient was admitted to the intensive care unit. One day after surgery sedation was stopped, the patient woke up and was able to move both legs. The following day, however, the patient suddenly became restless and required sedation. It was noticed during his agitation that he had not moved his legs at all. On neurological examination he was unable to move his legs, and his leg reflexes had disappeared. A delayed onset paraplegia was diagnosed. Artificial cooling (32°C) was immediately started and emergency surgery was prepared. Surgery took place 1 hour following the diagnosis, and two intercostal arteries were successfully

implanted in the prosthesis. The procedure took about 2 hours. Hypothermia was maintained during surgery and for 24 hours following surgery. Bleeding was not excessive in spite of the fact that hypothermia was maintained during surgery.

Postoperatively, the patient developed transient respiratory failure and renal failure. The overall course was favourable, however, and after 10 days it was possible to extubate the patient. The spinal reflexes returned 24 hours after surgery, and when the patient awoke he was able to move both legs. His strength returned slowly, and 23 days after his admission the patient was transferred to the ward, where he recovered without any complications. The patient left the hospital walking normally.

Patient C, a 55-year-old construction worker, fell asleep in the space between two large concrete building blocks with a height of 25 cm. His coworkers had not noticed this and a crane put another block on top of the two blocks with the worker in between. The air was pressed out of his lungs and he could not shout or even breathe due to the thoracic compression. After about 15 min his coworkers noticed what had happened and they removed the building block, finding their colleague blue and pulseless. CPR was started, and an ambulance arrived within 2 min (the building site was adjacent to our hospital). Upon admission to our intensive care unit, the heart rhythm had been restored. The patient was comatose with a Glasgow Coma Scale score of 3 and had a dilated pupil on the right side, with no other abnormalities. A cerebral CT scan revealed no abnormalities. A diagnosis of asphyxia and postanoxic encephalopathy was established, and artificial cooling (32°C) was started immediately and maintained for 24 hours.

Two days after admission, the patient was extubated and the following day he was transferred to the ward. His neurological condition steadily improved, and after 6 days he carried out verbal commands. During his stay in the ward, neurological screening revealed loss of strength of both shoulders and arms and sensibility loss of both arms. This was attributed to compression of the shoulders by the concrete blocks. Eight days after admission he was discharged. Neurological evaluation in an outpatient setting revealed proximal bilateral brachial plexus-paresis as a result of the compression trauma. This condition also steadily improved, and at this time the patient's condition is virtually normal in all aspects.

Discussion

The three cases described are exceptional clinical situations in which the effectiveness of artificial cooling will never be tested in a randomized clinical trial. This means that case reports describing the use of therapeutic hypothermia and demonstrating therapeutic results and outcome will probably be the only evidence available apart from observations in similar clinical situations. In our opinion the clinical condition of these

patients, although rare and unique, was in many aspects analogous to, and closely resembled, situations where therapeutic hypothermia has been shown to be effective.

The situation of patient A is comparable with the clinical situation of stroke. There was a localized ischaemic period resulting from the dissection of a cerebral blood vessel. In this situation a central core region, closest to the occluded vessel, becomes necrotic whereas the area around this region, referred to as the penumbra, is hypoperfused and at risk of dying but can still be saved. With time the penumbra becomes core (and thus becomes necrotic) whereas the injured region expands outward and into the surrounding area, which then becomes penumbra. Outward expansion of the penumbra can be prevented by restoring flow; the penumbra can be salvaged with increased perfusion and/or other early interventions. Patient A was at risk for focal brain ischaemia because of the partial absence of brain perfusion as a result of a stab wound in his neck, damaging his internal carotid artery. Several studies have suggested that selected patients with stroke, particularly those with medial cerebral artery occlusion, might benefit from therapeutic hypothermia [9]. As our patient had been stabbed 1 hour before admission we immediately started cooling while preparing for emergency surgery. The aim was to mitigate post-ischaemic neurological injury.

Patient B had a delayed-onset paraplegia after an elective thoracic-abdominal aneurysm repair. Since there is evidence suggesting that intraoperative hypothermia in neurosurgical procedures and major vascular surgery provides spinal cord protection (in addition to its overall neuroprotective effects) [1,16,18-21], we decided to induce hypothermia during surgery and for 24 hours following surgery in this patient. Reflexes had been absent for at least 1 hour before surgery was started and it took another hour before blood flow to the spinal cord could be restored. Our hope was that there would still be some perfusion of the spinal cord during this period, and that induced hypothermia could provide enough neuroprotection to save the spinal cord in this phase. Fortunately, the patient indeed recovered and, although there was a prolonged phase of weakness of the legs, his motor functions were fully restored.

The situation of patient C was comparable with the global ischaemia occurring after a cardiac arrest with return of spontaneous circulation. Favourable effects of cooling have been most clearly demonstrated in specific categories of patients with postanoxic injury following CPR [1-4], although of course the cause of injury in this patient was not related to cardiac disease. In this sense his situation was more favourable because he did not have cardiac disease; however, his period of anoxia was relatively long, because it took 15 min before he was found by his coworkers and CPR was started. We determined that this (neurological) situation was comparable with CPR caused by arrhythmias, and decided to treat this patient with

artificial cooling to prevent postischaemic neurological injury. The patient recovered with virtually no evidence of neurological impairment.

Although we cannot prove that hypothermia was the cause of favourable outcome in these three patients, the extent of neurological injury was much less severe than had been expected on the basis of their initial injury and the duration of hypoxia/ischaemia. Hypothermia can be neuroprotective even after some delay because many of the destructive processes occurring after ischaemia take place over a period of hours, or even days, after injury [1]. These processes include decreases in oxygen and glucose metabolism [22,23], suppression of ischaemia-induced inflammatory reactions [24,25], prevention of reperfusion-related injury [26], improvement of ion homeostasis [24-26] and blocking of free radical production [27,28].

Hypothermia has been shown to be effective in clinical situations analogous to those in our patients. In our opinion, these cases illustrate that hypothermia should at least be considered as a therapeutic option in cases where posthypoxic injury of the brain or spinal cord has occurred, provided the cause of this problem has been removed or can be quickly treated.

In conclusion, these cases suggest that doctors treating patients with various types of postischaemic neurological injury should consider the use of induced hypothermia for neuroprotection. Moreover, in this way additional time may be gained to carry out emergency surgical procedures or other interventions to restore blood flow to the endangered parts of the central nervous system.

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