Brain Hypothermia Relieves Severe Brain Swelling Following Acute Major Cerebral Artery Occlusion

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Abstract

Seven patients were treated with brain hypothermia following acute major cerebral artery occlusion to utilize the suppressive effect against brain swelling. Five patients had internal carotid and two had proximal middle cerebral artery occlusion. Except for the first two cases, hypothermia was introduced early and the temperature reached 35.0°C within 6 hours after the onset. The core temperature finally stabilized between 32°C to 34°C. Hypothermia had a suppressive effect against brain swelling and the temperature showed a significant correlation to intracranial pressure. Recurrence of brain swelling was observed during the rewarming process, but two patients became independent and three patients were moderately disabled in wheelchairs. Only two patients died. Brain hypothermia is an effective treatment for acute major cerebral artery occlusion through the relief of brain swelling. The overall outcome may be improved by combining brain hypothermia with other conventional therapies such as osmotherapy and external decompression implemented with an extended period of rewarming.

Key words: brain edema, brain hypothermia, cerebral ischemia, embolism, internal carotid artery, middle cerebral artery

Introduction

Recent experimental studies under strict brain temperature management have suggested that brain hypothermia is effective for protection of the brain following cerebral ischemia.8,9) The mechanism of brain protection under hypothermia is not fully understood, but may improve the outcome following cerebral ischemia.2) Extensive clinical studies on brain injury following head trauma revealed that hypothermia was associated with a favorable outcome. Hypothermia for severe head trauma had no harmful effects and reduced intracranial pressure (ICP), cerebral blood flow, and oxygen consumption.1,10,16) Experimental studies have also disclosed that hyperthermia following head trauma aggravates the outcome with the increase of both brain contusion volume and mortality.3)

Cerebral ischemia following acute major cerebral artery occlusion, such as internal carotid artery (ICA) and proximal middle cerebral artery (MCA) occlusion, has an extremely poor outcome despite combined treatment with barbiturate coma, osmotherapy, external as well as internal decompression, and thrombolytic therapy. The major cause of this poor outcome is brain swelling over a wide area with or without hemorrhagic change.9,15) Therefore, the effects of lowering the raised ICP and of neuroprotection due to brain hypothermia may improve the outcome.

This study investigated mild brain hypothermia following acute major cerebral artery occlusion as a method to improve the outcome by suppression of brain swelling.

Materials and Methods

Our hospital is prepared to receive emergency patients around the clock. Computed tomography (CT), magnetic resonance (MR) imaging, and digital subtraction angiography (DSA) are performed as is needed. Patients suspected of suffering from cerebral vascular diseases, indicated by sudden onset of consciousness disturbance, hemiparesis, and
speech disturbance, immediately undergo CT or MR imaging to assess the cause of their neurological deficits.

Our criteria for hypothermia induction are presented in Table 1. All selected patients showed consciousness disturbance, aphasia, and moderate hemiparesis or worse, with MR angiography evidence of acute major cerebral artery occlusion such as the ICA or proximal MCA. Patients were excluded if suffering from major systemic complications such as renal failure, respiratory distress, and cardiac failure. Therefore, once a patient is determined as suffering from acute major cerebral artery occlusion, close relatives were informed that the patient has suffered a life-threatening cerebral infarction and that brain hypothermia may be a beneficial procedure. The informed consent procedure also includes explanation of the possibility of complications such as pneumonia, paralytic ileus, coagulofibrinolytic abnormality, cardiac suppression, and immunosuppression.

### Table 1 Criteria for induction of hypothermia

| 1. | Acute major cerebral artery occlusion such as the internal carotid or proximal middle cerebral artery, showing consciousness disturbance, aphasia, and moderate hemiparesis or worse |
| 2. | Younger than 75 years |
| 3. | No major systemic complications such as renal failure, respiratory distress, and cardiac failure |

**I. Induction of brain hypothermia**

Early and rapid induction of hypothermia is basically needed to achieve effective suppression against severe brain swelling. The patient was sedated and intubated, a cooling blanket (Blanketrol II; Baxter Healthcare Corporation, Irvine, Calif., U.S.A.) was placed over the ventral surface of the body, and gastric lavage with cold water started as early as possible. At the same time, a Swan-Ganz continuous cardiac output/oximetry thermodilution catheter (Model 744H 7.5F; Baxter Healthcare Corporation, Irvine, Calif., U.S.A.) was inserted into the pulmonary artery for continuous monitoring of the cardiac output (CCO), saturation with venous oxygen, and the pulmonary arterial temperature. Another catheter (93-631H 5.5F; Baxter Healthcare Corporation) was inserted into the jugular vein for continuous monitoring of the jugular venous temperature and saturation with jugular venous oxygen (Sjvo\(_2\)), as a gross indicator of cerebral blood flow. In some cases, a catheter (110-4BT; Integra NeuroCare, San Diego, Calif., U.S.A.) to monitor brain parenchymal pressure (ICP) and temperature was surgically implanted through a tiny burr hole a few days after the onset. The patient was hospitalized in a restricted area of the intensive care unit with a respirator and covered with temperature-controlled plastic water blankets (Blanketrol II) on both the dorsal and ventral surface of the body as well as the extremities to control the temperature. The brain parenchymal temperature (BT), jugular venous temperature (JT), rectal temperature (RT), and cooling blanket surface temperature (CoT) were continuously monitored. All these parameters such as BT, JT, RT, CoT, arterial blood pressure (ABP), ICP, CCO, Sjvo\(_2\), and endotidal partial pressure of carbon dioxide (Pco\(_2\)) were recorded by a personal computer following an analog/digital conversion every 2 minutes.

The initial temperature was set at 34.0°C following induction. Once RT or JT reached this point, vital signs such as heart rate, urine volume, ABP, CCO, and partial pressure of oxygen (Po\(_2\)) were reevaluated to assess whether the patient was suffering from cardiopulmonary suppression. Absence of suppression allowed the final temperature to be set to between 32.0°C to 33.0°C. The temperature of 34.0°C was sustained if the patient showed any sign of systemic problems. Brain CT was repeated every 2 or 3 days to assess the degree of brain swelling. If minimum brain swelling or cardiopulmonary suppression were observed in the first several days, gradual rewarming was induced over the next few days. Basically, the rewarming process proceeded at less than 1.0°C over a 24-hour period.

**II. Controlling of systemic conditions during hypothermia**

Intravenous midazolam and vecuronium bromide were administered continuously for sedation and immobilization until the patient's RT exceeded 37.0°C for more than 2 days, when the patient had recovered from hypothermia. Cerebral perfusion pressure was maintained at more than 70 mmHg, and CCO was sustained above 4.0 l/min by the continuous administration of dopamine and dobutamine hydrochloride solutions. Serum potassium, usually below normal during hypothermia, was supplied as needed. A long intestinal tube was introduced to buffer the paralytic ileus. Recent patients received a long intestinal tube inserted right before the completion of the hypothermic state, because once paralytic ileus occurred, the tube was very hard to insert, as experienced in our earlier cases.

Routine examinations of hematology and serum biochemistry were performed daily. Some patients showed severe consumption of platelets and received platelet-rich plasma associated with a pro-
teolytic enzyme inhibitor. Analyses of arterial blood gas, electrolytes, and blood sugar level (BS) were performed every 2 hours and the following parameters were maintained within the normal ranges as follows: Pco₂ 35 to 42 mmHg; Po₂ more than 100 mmHg; pH 7.380 to 7.500; serum sodium concentration 135 to 145 mEq/l; serum potassium 3.5 to 4.5 mEq/l; and BS less than 150 mg/dl. Osmotic agents such as glycerol were periodically administered in all patients to relieve brain swelling. Mannitol was administered as needed if ICP increased rapidly or Sjvo₂ decreased.

Results

I. Patient characteristics

Seven patients were treated with hypothermia for acute major cerebral artery occlusion (Table 2). The patients were four males and three females aged from 35 to 74 years. Initial consciousness level varied from 8 to 15 by the Glasgow Coma Scale. The major vessels affected were the intracranial ICA in three cases, cervical ICA in two cases, and proximal MCA in two cases. Angiographical appearance of the ipsilateral anterior cerebral artery was normal or good opacification in four of the five ICA cases, and no flow in the other case. Thus, six patients had wide MCA territory ischemia and the other had a severe hemispheric infarction. Five patients showed continuous atrial fibrillation, one had paroxysmal atrial fibrillation, and the other had a sinus rhythm on electrocardiography. Six patients had cerebral embolism, and the other had a cerebral thrombosis (Case 1). ICP and BT were recorded in two cases.

Associated thrombolytic therapy was performed for three patients using tissue plasminogen activator (TPA) intraarterial injection in one case, urokinase intraarterial administration in one case, and intravenous TPA in one case. Case 1 with ICA occlusion resulting from thrombosis showed no complete recanalization. Case 3 showed partial branch recanalization by urokinase injection during the initial thrombolytic therapy. Case 7 had thrombus migration from the ICA to the MCA as shown by DSA performed the day after onset. Cases 2, 5, and 6 showed partial recanalization which was later confirmed. None of the patients showed hemorrhagic change on CT.

One patient was initially treated by barbiturate administration followed by hypothermia and external decompression because of the presence of anisocoria. No other patient received barbiturate therapy associated with hypothermia.

II. Summary of hypothermia treatment

Hypothermia treatment was introduced on the day of admission in all but one patient (Fig. 1). Hypothermia was initiated from 1 hour 10 minutes to 10 hours 30 minutes (mean 3 hours 45 minutes) after onset in these six cases. The time from induction to reaching the temperature of 35.0°C required 2 hours to 5 hours 20 minutes (mean 3 hours 14 minutes).

The duration of the hypothermia varied from 4 to 19 days depending on the degree of brain swelling and cardiopulmonary suppression. The timing of the severest brain swelling revealed by CT or signs of anisocoria also varied.

The degree of brain swelling on CT was assessed and classified into absent, minimal (only slight shift of midline structures), moderate (shift of midline structures without change in the ipsilateral ventricle), moderately severe (shift of midline structures with slit ipsilateral ventricle), and severe (shift of midline structures with complete absence of ipsilateral ventricle). Figure 2 shows the CT scan at maximum brain swelling in each case.

The relationship between the degree of brain swelling and the daily profiles of the reference temperature could be classified into three groups. Group A was characterized by brain swelling relieved by the hypothermia therapy for the first 4 days with no recurrence of brain swelling during the rewarming period (Case 1). Group B was characterized by later
Table 2  Patients treated with brain hypothermia

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age/Sex</th>
<th>GCS</th>
<th>Occlusion, development of AcomA</th>
<th>Ischemic territory</th>
<th>Rhythm on ECG</th>
<th>ICP monitor</th>
<th>Thrombolysis</th>
<th>Recanalization, confirmed at</th>
<th>Hemorrhagic change</th>
<th>Barbiturate coma</th>
<th>External decompression</th>
<th>Duration of hypothermia (days)</th>
<th>GOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65/M</td>
<td>15</td>
<td>rt ICA (C₁), normal</td>
<td>rt MCA</td>
<td>sinus</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>yes</td>
<td>yes</td>
<td>4 MD</td>
<td>MD</td>
</tr>
<tr>
<td>2</td>
<td>71/M</td>
<td>11</td>
<td>lt ICA (Ce), well</td>
<td>lt MCA</td>
<td>Af</td>
<td>yes</td>
<td>TPA i.a.</td>
<td>part, yes, 5 mos later</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>8 GR</td>
<td>GR</td>
</tr>
<tr>
<td>3</td>
<td>73/F</td>
<td>8</td>
<td>rt M₁</td>
<td>rt MCA</td>
<td>Af</td>
<td>none</td>
<td>urokinase i.a.</td>
<td>part, yes, day 0</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>4 MD</td>
<td>MD</td>
</tr>
<tr>
<td>4</td>
<td>57/M</td>
<td>8</td>
<td>rt ICA (Ce), none</td>
<td>lt hemisphere</td>
<td>Af</td>
<td>none</td>
<td>TPA i.v.</td>
<td>not available</td>
<td>none</td>
<td>none</td>
<td>yes</td>
<td>6 death</td>
<td>death</td>
</tr>
<tr>
<td>5</td>
<td>74/F</td>
<td>9</td>
<td>rt ICA (C₁), well</td>
<td>rt MCA</td>
<td>Af</td>
<td>none</td>
<td>none</td>
<td>part, yes, day 13</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>4 MD</td>
<td>MD</td>
</tr>
<tr>
<td>6</td>
<td>66/F</td>
<td>9</td>
<td>lt M₁</td>
<td>lt MCA</td>
<td>Af</td>
<td>yes</td>
<td>none</td>
<td>part, yes, day 14</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>19 death</td>
<td>death</td>
</tr>
</tbody>
</table>
Fig. 2 Computed tomography scans of each case showing the maximum brain swelling. Case 1 on day 3 (A), Case 2 on day 10 (B), Case 3 on day 16 (C), Case 4 on day 5 (D), Case 5 on day 7 (E), Case 6 on day 9 (F), and Case 7 on day 7 (G).

moderate brain swelling after recovery from hypothermia for 4 days with initial minimal brain swelling (Cases 3, 5, and 7). Group C was characterized by rapid and severe brain swelling in spite of the hypothermia therapy (Cases 2, 4, and 6).

III. Representative cases

Group A: Case 1 had right ICA occlusion. Bar-
Fig. 3 Correlation between brain swelling (—) and hypothermia (——) in Group A in which hypothermia prominently suppressed brain swelling (Case 1). Brain swelling never recurred during the rewarming process. The degree of brain swelling on computed tomography was classified into five stages: absent (0), minimal (1), moderate (2), moderately severe (3), and severe (4).

Fig. 4 Correlation between brain swelling (—) and hypothermia (——) in Group B in which hypothermia initially suppressed brain swelling (upper: Case 3, middle: Case 5, lower: Case 7). Brain swelling became aggravated after the rewarming process. The classification of brain swelling is the same as in Fig. 3.

Biturate coma was started 4 hours after onset. External decompression followed by hypothermia was performed on day 3 because of the presence of anisocoria (Fig. 2A). Brain swelling was rapidly relieved by hypothermia (Fig. 3). During the rewarming process, brain swelling was suppressed. The patient could manage daily tasks in a wheelchair and had no major problems some 19 months later.

**Group B**: Cases 3, 5, and 7 showed no significant brain swelling on CT in the first 4 days, so rewarming was started on the following day (Fig. 4). Brain swelling became prominent after a week or more (Fig. 2C, E, G). However, these instances of brain swelling were not life-threatening and the patients were able to recover after the initiation of wheelchair rehabilitation (Cases 3 and 5) and no major problems (Case 7).

**Group C**: Cases 2, 4, and 6 showed a marked brain swelling during the hypothermia (Fig. 5). In Case 2 (Fig. 5 upper), ICP was controllable until day 6, though the brain swelling gradually became aggravated. Cardiopulmonary suppression forced us to cease hypothermia on day 7, then ICP showed frequent increases. His temperature was lowered to 32.0°C again on day 9. The severest degree of brain swelling was observed on day 10 (Fig. 2B). Thereafter, brain swelling was not aggravated. The patient recovered well and became ambulant with moderate aphasia 12 months after the onset. Case 4 (Fig. 5 middle) showed rapid and aggressive brain swelling (Fig. 2D) which could not be relieved by hypothermia resulting in death on day 5. Case 6 (Fig. 5 lower) exhibited long-term brain swelling (Fig. 2F) even under hypothermia. ICP showed an apparent correlation to brain temperature during the course, but the marked brain swelling finally could not be relieved which resulted in death after a long struggle.

**IV. Complications and outcome**

The major complications experienced are summarized in Table 3. Two patients suffered from severe
Table 3 Systemic complications

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Catecholamine requirement</th>
<th>Oxygenation (maximum FIO2)</th>
<th>Hypokalemia (least serum level, mEq/l)</th>
<th>Paralytic ileus</th>
<th>Thrombocytopenia (lease counts, ×10^3)</th>
<th>Renal failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>minimal</td>
<td>0.45</td>
<td>2.6</td>
<td>minimal</td>
<td>85</td>
<td>none</td>
</tr>
<tr>
<td>2</td>
<td>moderate</td>
<td>0.70</td>
<td>2.8</td>
<td>moderate</td>
<td>48</td>
<td>none</td>
</tr>
<tr>
<td>3</td>
<td>moderate</td>
<td>0.70</td>
<td>2.4</td>
<td>moderate</td>
<td>49</td>
<td>none</td>
</tr>
<tr>
<td>4</td>
<td>great</td>
<td>1.00</td>
<td>2.9</td>
<td>minimal</td>
<td>72</td>
<td>minimal</td>
</tr>
<tr>
<td>5</td>
<td>minimal</td>
<td>0.65</td>
<td>2.7</td>
<td>moderate</td>
<td>80</td>
<td>none</td>
</tr>
<tr>
<td>6</td>
<td>great</td>
<td>1.00</td>
<td>2.7</td>
<td>moderate</td>
<td>39</td>
<td>severe</td>
</tr>
<tr>
<td>7</td>
<td>minimal</td>
<td>0.35</td>
<td>2.7</td>
<td>minimal</td>
<td>84</td>
<td>none</td>
</tr>
</tbody>
</table>

Fig. 5 Correlation between brain swelling (—) and hypothermia (–––) in Group C in which severe brain swelling appeared despite hypothermia (upper: Case 2, middle: Case 4, lower: Case 6). Intracranial pressure (ICP) (–––) had a significant correlation to brain temperature during hypothermia in Cases 2 and 6. The classification of brain swelling is the same as in Fig. 3.

Hypothermia had been induced in only a few cases of major cerebral artery occlusion. Hypothermia definitely reduced ICP and mortality fell to 44% in a series of 25 cases. These cases required 14 hours from the onset to induction of hypothermia. Patients showing a prominent increase of ICP with rewarming over 18 hours tended to have a poor outcome. Our series contained only seven cases but indicated a definite effect to relieve the brain swelling in various degrees and the outcome was more favorable than could be expected based on cases treated with only conventional therapies. Induction of hypothermia needed 2.5 hours and the temperature reached 35.0°C in 3 hours in our most recent five cases. Therefore, hypothermia was completed within 6 hours from the onset achieving more rapid brain cooling than previously reported. This shorter induction time may explain the better results. Induction of hypothermia should be carried out as early as possible and the cooling time should be as short as possible for protection of the brain. However, this does not always hold true in clinical cases. Case 4 took only 2.5 hours from onset to introduction and the temperature reached 35.0°C within 6 hours, but rapid and severe hemispheric brain swelling could not be controlled by hypothermia. In contrast, hypothermia was introduced relatively late after the time of onset in our first and second cases, but brain swelling was suppressed, and the outcome was controlled because the severity was moderate. Thrombocytopenia was also observed in all patients, but only one patient needed platelet-rich plasma transfusion. Two patients had renal failure, one only minimally, but the other suffered from the severest form of failure and needed hemodialysis.

Two patients had a good recovery, three were moderately disabled, and two died, assessed at 2 months to 19 months (mean 8 months) in the five survivors.

Discussion

Hypothermia following Acute Major Cerebral Artery Occlusion
good. Therapeutic windows in experiment studies indicate that hypothermia should be introduced within 30 minutes, and that a longer duration is needed. However, in the clinical setting, this window seems much wider than was first thought, probably depending on the degree of collateral flow. This observation should encourage the introduction of hypothermia in more patients suffering from acute major cerebral artery occlusion.

Hypothermia in Cases 2 and 6 showed a definite effect to reduce ICP and to suppress the brain swelling, and was increased when the temperature was further lowered from 34°C to 32°C. Maximum as well as life-threatening brain swelling usually occurs between days 2 and 5 after the onset. However, we observed the maximum swelling on CT in most cases as long as 2 weeks after the onset. The effect to reduce brain swelling may also prolong the occurrence somehow. This confuses the issue of when to start the rewarming process from hypothermia. Therefore, hypothermia should be continued for 7 days or more.

Re-elevation of ICP during rewarming is a sign of a very poor outcome. Case 6 underwent a far longer period of hypothermia of about 2 weeks. The ICP seemed under control and showed a significant correlation to BT. Even so, re-elevation of ICP was prominent during the gradual rewarming process. Rapid rewarming induces disequilibrium of temperature between the body core and the brain and is also known to cause glutamate surge, nitric oxide production, and increased cerebral metabolic rate of oxygen and cerebral blood flow, which may explain the recurrence of brain swelling. We are not sure whether rewarming for a longer time of several days will prevent the relapse of brain swelling. However, a better outcome is achieved when hypothermia of more than one week is followed by a longer rewarming period of 3 to 4 days, whereas hypothermia of less than one week needs about rewarming for about 24 hours. Furthermore, combined treatments such as external decompression or osmotherapy with hypothermia against brain swelling may be more beneficial to relieve the aggravation of the brain swelling during the rewarming process.

Various moderate systemic complications were experienced, but most had been anticipated and were treatable except for severe renal failure seen in Case 6 during hypothermia for more than 2 weeks. Our small series could not show whether recanalization had any correlation with aggravated brain swelling. MR angiography examination is difficult during hypothermia, so we were not sure exactly when partial recanalization occurred in most cases.

Confirmation was ascertained at a later time. However, no patients showed hemorrhagic changes during the course of treatment. The suppressive effect for brain swelling indicates that hypothermia affects blood-brain barrier stabilization to some degree, and so hypothermia could lower the incidence of hemorrhagic change. This suppressive effect may be helpful during thrombolytic therapy under hypothermia.

The present study indicates that the therapeutic window for hypothermia in cases of major cerebral artery occlusion is wider than expected based on our experimental study. We suggest that more patients should be treated by hypothermia. This study cannot define the absolute indications for this controversial therapy because of the small number of cases. However, a better outcome may be expected when hypothermia is continued for about 7 days with a rather longer duration of rewarming combined with conventional therapies in cases of acute major cerebral artery occlusion without severe systemic complications.

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Hypothermia Following Acute Major Cerebral Artery Occlusion

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The authors report their experience of therapeutic hypothermia in 7 patients with major cerebral artery occlusion. Most experimental studies on ischemic or traumatic brain injury have demonstrated that hypothermia is beneficial only when it is induced within 30 minutes after the onset of insult. In contrast, the authors suggest a much wider therapeutic window in the clinical setting. More interestingly, hypothermia appears to inhibit brain swelling and to reduce ICP, regardless of when the hypothermia is induced after the onset of major cerebral artery occlusion. They further report a temporal correlation between the core temperature and ICP. Such effects of hypothermia have been recognized clinically in patients with head trauma. Little is yet known, however, regarding the brain swelling inhibition and ICP reduction that occur during hypothermia. It is possible that their mechanisms may differ completely from those underlying the neuroprotective effects of hypothermia which have been investigated in most experimental studies. The present paper represents an outstanding example of a clinical investigation which discloses a vital aspect of therapeutic hypothermia. The authors’ approach may also be extremely important for understanding the mechanisms of brain swelling and/or edema occurring in a variety of brain injury processes.

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In this interesting study, the authors accomplished early induction of mild brain hypothermia in patients after major cerebral arterial occlusion to eliminate brain swelling induced by cerebral ischemia. In seven patients treated with mild hypothermia, two had good recovery, three became moderately disabled, and two died. To verify the therapeutic efficacy of hypothermia in eliminating brain swelling, demonstration of a good correlation between brain temperature, intracranial pressure (ICP), and clinical outcome is necessary. However, in this study ICP monitoring was only applied in two patients and the degree of brain swelling was mainly assessed from a rough grading system based on CT scans done every 2–3 days. Lack of continuous ICP monitoring to reflect the precise effect of lowering brain temperature against brain edema after

Commentary

Kurokawa et al. have reported seven patients with acute major cerebral artery occlusion and associated cerebral ischemia who were treated with hypothermia. There is an abundance of experimental data supporting the role of moderate hypothermia in protecting the brain from cerebral ischemia and its consequences. The role of hypothermia in the clinical setting has been investigated primarily for head injury. This study demonstrates the feasibility of rapidly inducing moderate hypothermia in patients with acute cerebral ischemia. Although the data included in this report supports the author’s conclusion that hypothermia reduced brain swelling in their patients, the series is too small to draw any conclusions regarding the precise role of hypothermia in this clinical setting. Although the author’s results are encouraging, the report also underscores the potential complications of induced hypothermia, including electrolyte abnormalities, cardiopulmonary suppression, paralytic ileus and thrombocytopenia. Further studies will be required to determine the precise role of hypothermia in the management of cerebral ischemia.

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ischemia weakens the strength of this study. The two patients with good recovery seem to have less severe involvement of ischemia. One younger patient with good outcome (Case 7) had mild brain swelling, a small area of involvement on CT imaging and was fully conscious at onset, so hypothermia was probably not necessary to be included as a part of his treatment. The other patient with good outcome also received intra-arterial administration of tissue plasminogen activator. These variations in patient selection may affect the results of this study. Systemic complication of cardiopulmonary suppression was noted in two mortality cases in this study. Both patients required large amounts of catecholamine infusion and higher degree of oxygenation to maintain their vital signs. Renal failure, probably a consequence of the large amount of catecholamine administration, occurred in both of these two patients. Unfortunately, the authors did not provide more information and discussion on the complications of this controversial treatment modality. The small size of this study and the lack of a control group preclude a meaningful conclusion of the efficacy of hypothermia in treating massive cerebral ischemia. I hope that the next stage will be a larger scale prospective study including control and comparison between this treatment and other therapeutic modalities for ischemic brain swelling such as decompressive craniectomy and barbiturate coma.

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