Hyperbaric Oxygen Therapy Adjunctive to Mild Hypertensive Hypervolemia for Symptomatic Vasospasm

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Abstract

The efficacy of hyperbaric oxygen (HBO) therapy was evaluated retrospectively in 43 patients who developed symptomatic vasospasm following acute aneurysm surgery. HBO therapy was given as an adjunct to mild hypertensive hypervolemia in 24 patients. Before HBO therapy, 17 patients had no infarct (Group 1), and seven had infarcts (Group 2) caused by vasospasm. A further 19 patients received mild hypertensive hypervolemia alone (Group 3). Cerebral infarcts developed in four Group 1 and 12 Group 3 patients. A good outcome 1 month after surgery was achieved by 13 Group 1 (76%), one Group 2, and seven Group 3 patients (37%). Fifteen of the 24 patients who received HBO therapy responded to HBO exposure, and 12 responding patients (80%) had a good outcome. During HBO exposure, electroencephalographic improvements were all accompanied by neurological improvements. There were no complications related to HBO therapy. HBO therapy adjunctive to mild hypertensive hypervolemia is helpful in preventing cerebral infarction associated with symptomatic vasospasm.

Key words: hyperbaric oxygen, hypertension, hypervolemia, subarachnoid hemorrhage, vasospasm

Introduction

Cerebral vasospasm is probably initiated by extravasation of red blood cells (RBCs), but the pathogenesis is not certain. Various agents may prevent or reverse cerebral vasospasm, but clinical effectiveness has not been proven. The current trends in therapy for symptomatic vasospasm concentrate on protection against associated ischemic brain damage. Induced hypertension and hypervolemic hemodilution are widely used to maintain regional cerebral blood flow (rCBF), but other options should be considered to prevent ischemic damage to the brain.

The beneficial effects of hyperbaric oxygen (HBO) therapy have been demonstrated in the management of cerebral ischemia in humans and in animal experiments. Cerebral vasospasm has been treated with HBO therapy, but the relationship between the effects of HBO therapy and the severity or duration of neurological deficits caused by vasospasm is not clearly understood.

We reviewed the results of HBO therapy as an adjunct to mild hypertensive hypervolemia after aneurysm surgery, and evaluated the clinical effects.

Patients and Methods

111 patients treated surgically for ruptured intracranial aneurysm within 7 days of subarachnoid hemorrhage (SAH) during the 11-year period from June, 1980 through May, 1991 were retrospectively reviewed. Their ages ranged from 19 to 72 years (mean, 56 yrs). Computed tomography (CT) and cerebral angiography (CAG) were performed on admission to our hospital. The aneurysms were clipped and as much subarachnoid blood clot as possible evacuated, followed by irrigation of the subarachnoid space with lactated Ringer's solution. No bilateral craniotomy was performed to remove any clot on the contralateral side. All patients were treated postoperatively with a calcium channel blocker or thromboxane A2 synthetase inhibitor to prevent cerebral vasospasm. Symptomatic vasospasm was diagnosed clinically based on slow onset of confusion and decreased level of consciousness followed by focal cerebral impairment.
Immediately after the diagnosis of symptomatic vasospasm, mild hypervolemic hemodilution was begun if CT revealed no low-density area caused by vasospasm, using colloid agents (fractionate, albumin, low-molecular weight dextran, etc.) in volumes not exceeding 1000 ml/day. Whole blood transfusion was given to anemic patients. The central venous pressure was increased to 7-10 cmH2O, and the hematocrit value reduced and maintained at 35-40%. Simultaneously, the systolic blood pressure was increased slightly using dopamine and/or dobutamine, and maintained at 140-160 mmHg.

Adjunct HBO therapy was given in a multipurpose hyperbaric chamber (P-1000SA; Hanyuda, Tokyo) according to the following schedule: 15 minutes of compression with air, 60 minutes of 100% oxygen inhalation using an oxygen mask at 2.5 atmospheres absolute, and 10 minutes of decompression with oxygen inhalation. HBO therapy was performed once or twice a day for a total of two to 21 cycles (10 cycles on average).

Neurological function was evaluated using the Glasgow Coma Scale before, during, and after each HBO cycle. If neurological function improved more than level during or immediately after an HBO exposure, even if transient, the patient was defined as responding to HBO exposure. The outcome 1 month after surgery was assessed using the modified Glasgow Outcome Scale.* (Table 1).

Electroencephalograms (EEGs) were monitored continuously during the first HBO cycle with a 16-channel recorder and EEG power analysis (EEG Trend Monitor; Nihon-Kohden Ltd., Tokyo) in eight patients. EEG topography was displayed for four patients, the values of % time and amplitude were calculated for each electrode point on the scalp, and compared using the unpaired Student’s t-test.

**Results**

Forty-three (39%) of the 111 patients developed symptomatic vasospasm. Adjunct HBO therapy was given in 24 patients. Before HBO therapy, 17 patients had no infarct (Group 1) and seven had infarcts (Group 2) caused by vasospasm. The other 19 patients received mild hypertensive hypervolemia without HBO therapy (Group 3) (Table 2). Table 3 summarizes the data for individual patients treated with HBO therapy.

Four (24%) of 17 patients in Group 1 had infarcts on CT scans 1 month postoperatively. Thirteen (76%) patients in Group 1 had a good outcome, one had moderate disability, two suffered severe hypernatremia and had poor outcome, and one died from vasospasm. Only one Group 2 patient, who developed small infarcts, achieved a good outcome, five had moderate or severe disability, and one died. Seven (37%) of the 19 patients in Group 3 had no permanent infarcts from vasospasm, and achieved good outcomes. The other 12 patients (63%) all showed evidence of infarcts on CT scans. Eight patients had moderate disability, one was in poor condition, and three died as a result of delayed infarction.

CAG showed severe arterial narrowing in five postoperative patients. N-isopropyl-p-[123I] iodoamphetamine (123I-IMP) single photon emission CT (SPECT) revealed decreased rCBF in the territory of the narrowed arteries. Consequently, HBO therapy was begun to prevent ischemia despite the absence of neurological symptoms. Four patients (Cases 1, 7, 8, and 11) showed transient ischemic symptoms after several days, but recovered without neurological deficits or infarcts. The other patient showed no symptoms due to arterial narrowing.

Table 4 presents the overall outcome. Fourteen (58%) of 24 patients who received adjunct HBO therapy achieved a good neurological outcome.
Fifteen (63%) of the 24 patients receiving HBO therapy demonstrated a response, with some neurological improvement observed during and/or immediately after the initial few exposures (Table 5). Twelve patients demonstrated improvement persisting for several hours. Neurological symptoms returned to the pretreatment level, fluctuated, then improved over the course of HBO therapy, except for two patients with severe hypernatremia. Three responding patients showed permanent neurological improvement after the first or second HBO ex-

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**Table 3** Summary of 24 patients treated with HBO therapy

<table>
<thead>
<tr>
<th>Group</th>
<th>Case No</th>
<th>Age/Sex</th>
<th>Location of aneurysm</th>
<th>Operation (day*)</th>
<th>Consciousness level at onset of spasm**</th>
<th>Interval between onset of spasm and HBO (days)</th>
<th>HBO cycles</th>
<th>Response to HBO</th>
<th>Infarcts from spasm</th>
<th>Outcome at 1 month***</th>
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<td>1</td>
<td>39/M</td>
<td>AComA</td>
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<td>no</td>
<td>good</td>
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<td>2</td>
<td>55/M</td>
<td>rt MCA</td>
<td>1</td>
<td>&lt;1</td>
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<td>3</td>
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<td>no</td>
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<td>III</td>
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<td>no</td>
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</tr>
<tr>
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<td>&lt;1</td>
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<td>yes</td>
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<td>good</td>
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<td>yes</td>
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<td>poor</td>
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<tr>
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<td>&lt;1</td>
<td>IV</td>
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<td>no</td>
<td>yes</td>
<td>death</td>
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<tr>
<td>2</td>
<td>61/M</td>
<td>lt ICA</td>
<td>0</td>
<td>4</td>
<td>III</td>
<td>11</td>
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<td>yes</td>
<td>fair</td>
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<td>fair</td>
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<tr>
<td>21</td>
<td>46/F</td>
<td>lt ICA</td>
<td>0</td>
<td>&lt;1</td>
<td>IV</td>
<td>7</td>
<td>yes</td>
<td>yes</td>
<td>poor</td>
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<td>2</td>
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<td>fair</td>
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<td>24</td>
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<td>1</td>
<td>2</td>
<td>IV</td>
<td>3</td>
<td>no</td>
<td>yes</td>
<td>death</td>
<td></td>
</tr>
</tbody>
</table>

*The day of SAH is defined as day 0. **According to Hunt and Hess grade.*** According to modified Glasgow Outcome Scale. HBO therapy was initiated to prevent vasospasm. AComA: anterior communicating artery, ICA: internal carotid artery, MCA: middle cerebral artery.

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**Table 4** Relationship of infarcts and outcomes to treatments and neurological grade

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Consciousness level at onset of spasm*</th>
<th>No. of cases</th>
<th>Infarcts from spasm</th>
<th>Outcome at 1 month**</th>
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<tr>
<td>1</td>
<td>HH, HBO</td>
<td>III</td>
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<td>2</td>
<td>HH, HBO</td>
<td>III</td>
<td>7</td>
<td>4</td>
<td>Fair</td>
</tr>
<tr>
<td>3</td>
<td>HH</td>
<td>III</td>
<td>4</td>
<td>0</td>
<td>Poor</td>
</tr>
</tbody>
</table>

*According to Hunt and Hess grade. **According to modified Glasgow Outcome Scale. HH: mild hypertensive hypervolemia.

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month after surgery.
Fifteen (63%) of the 24 patients receiving HBO therapy demonstrated a response, with some neurological improvement observed during and/or immediately after the initial few exposures (Table 5). Twelve patients demonstrated improvement persisting for several hours. Neurological symptoms returned to the pretreatment level, fluctuated, then improved over the course of HBO therapy, except for two patients with severe hypernatremia. Three responding patients showed permanent neurological improvement after the first or second HBO ex-

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*K. Kohshi et al.*

Neurol Med Chir (Tokyo) 33, February, 1993
posure, with no subsequent regression.

Twelve of the 15 responding patients achieved a good outcome, all of whom had no infarct before therapy, one had moderate disability, and two were in poor condition. Two of the nine non-responding patients had a good outcome; the others had moderate or severe disabilities or died.

There were no complications related to HBO therapy. However, mild hypertensive hypervolemia induced pulmonary edema in one patient and electrolyte disturbance in two. Arrhythmia was apparent in two patients who were treated with dopamine and/or dobutamine.

EEGs of patients with symptomatic vasospasm showed abnormalities such as slowing of the background activity and increased delta waves. Five of eight patients who underwent continuous EEGs and EEG power analysis during HBO exposure showed an increase in fast components in the background, a decreased and lowered delta activity, or an increase in or appearance of definite alpha activity. EEG improvements were evident in all responding patients.

Representative Cases

Case 3: A 67-year-old female was admitted 20 hours after onset of SAH. CT scans showed a high-density area in the left Sylvian fissure.

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Table 5  Outcomes and response to HBO therapy

<table>
<thead>
<tr>
<th>Group</th>
<th>Infarcts before HBO</th>
<th>Response to HBO</th>
<th>No. of cases</th>
<th>Overall infarcts from spasm</th>
<th>Outcome at 1 month*</th>
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<tbody>
<tr>
<td>1</td>
<td>no</td>
<td>yes</td>
<td>13</td>
<td>2</td>
<td>Good 12 Fair 0 Poor 1 Death 0</td>
</tr>
<tr>
<td>2</td>
<td>yes</td>
<td>yes</td>
<td>2</td>
<td>2</td>
<td>Good 0 Fair 1 Poor 1 Death 0</td>
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<tr>
<td></td>
<td></td>
<td>no</td>
<td>5</td>
<td>5</td>
<td>Good 2 Fair 1 Poor 1 Death 1</td>
</tr>
</tbody>
</table>

*According to modified Glasgow Outcome Scale.110

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Fig. 1  Case 3.  A: CT scans on admission, showing a high-density area in the left Sylvian fissure.  B: Left CAG on day 15, showing severe arterial narrowing.  C: 123I-IMP SPECT scans, showing decreased rCBF in the left frontotemporal region.
Fig. 2 Case 3. *upper:* EEG power analysis, showing an increase in fast components and a decrease in slow components in the occipital leads during HBO exposure. *lower:* EEG topography, showing the % time and amplitude of delta band reduced significantly (p < 0.01). The fast components are maintained immediately after HBO exposure. ATA: atmosphere absolute.

Fig. 2 Case 3. *upper:* EEG power analysis, showing an increase in fast components and a decrease in slow components in the occipital leads during HBO exposure. *lower:* EEG topography, showing the % time and amplitude of delta band reduced significantly (p < 0.01). The fast components are maintained immediately after HBO exposure. ATA: atmosphere absolute.

area in the left Sylvian fissure (Fig. 1A). She was classified as Hunt and Hess grade\(^1\) III on day 1 of SAH. She underwent surgery for a ruptured aneurysm arising from the left internal carotid artery. Postoperatively, she was slightly confused, and consciousness disturbance increased on day 15. CT scans showed no low-density area, but CAG identified arterial narrowing (Fig. 1B), and \(^{123}\)I-IMP SPECT showed reduced rCBF in the left frontotemporal region (Fig. 1C). Mild hypertensive hypervolemia was given, and HBO therapy started on day 16. Consciousness disturbance decreased during and after the first HBO exposure. EEG during HBO therapy showed an increase in fast components in the background and decreased delta activity (Fig. 2). The degree of consciousness disturbance fluctuated for a few days after beginning HBO therapy, but

Fig. 3 Case 14. A: CT scans on admission, showing diffuse SAH. B: Left CAG on day 12, showing severe arterial narrowing.
other neurological functions were normalized.

**Case 14:** A 53-year-old female presented with a ruptured anterior communicating artery aneurysm. CT scans on admission showed diffuse SAH (Fig. 3A) and she was in Hunt and Hess grade III. She underwent surgery on day 2 of SAH. She did well until 10 days after SAH, when she became drowsy and developed motor aphasia and right hemiparesis. CAG showed severe arterial narrowing (Fig. 3B), but CT scans found no low-density area. HBO therapy was given as an adjunct to mild hypertensive hypervolemia on day 13. Consciousness disturbance and right hemiparesis improved during and after the first HBO exposure. During HBO therapy, EEG showed an increase in fast components in the background and decreased delta activity (Fig. 4). The neurological improvement was sustained, and she was discharged without deficits.

**Discussion**

Once symptomatic vasospasm is diagnosed, there are two approaches to improve oxygen delivery to the ischemic brain tissue. The first is to increase the rCBF, previously reduced by vasospasm, by hypervolemic hemodilution and induced hypertension. In fact, reduced rCBF after SAH is increased by induced hypertension with or without hypervolemic hemodilution. The second approach is to deliver oxygen directly, a reasonable strategy for ischemic brain tissue resulting from vasospasm.

The effects of HBO therapy on acute brain damage have been explained by mechanisms such as oxygenation of brain tissue, improvement of glucose utilization, and suppression of brain edema. HBO exposure reduces rCBF, but the cerebral tissue PO2 is increased by increasing the oxygen-carrying capacity of plasma. Ischemic brain tissue resulting from vasospasm may benefit from increased rCBF after mild hypertensive hypervolemia decreases the blood viscosity, if the increased rCBF can transport a higher oxygen concentration under HBO therapy.

SAH increases both coagulability and platelet activity and intracerebral multiple microthrombi occur in autopsy cases with symptomatic vasospasm. Intra-arterial thromboembolism may contribute to the development of ischemic deficits, particularly in smaller arteries. HBO therapy is reported to reduce RBC and platelet agglutination and improve RBC deformability. In our study, three responding patients improved gradually during and after HBO exposure, without regression. If the effect of HBO therapy resulted from simple tissue oxygenation, any neurological improvement would be transient and reversed after HBO exposure ended. Possibly, HBO therapy inhibits the formation of microthrombi and improves microcirculation in symptomatic vasospasm.

Symptomatic vasospasm occurs in over one-third of patients with SAH, and half of these suffer infarction resulting in severe disability or death. Recently, induced hypertension and/or hypervolemic hemodilution have improved the prognosis, but may induce cardiovascular and pulmonary complications. We introduced adjunct HBO therapy to prevent ischemic brain tissue and reduce these complications. Our study shows that the incidence of cerebral infaracts was lower and the outcome was better in patients receiving HBO therapy. In particular, 13 (76%) of 17 patients without infarct before the initiation of HBO therapy could resume normal life 1 month after surgery. However, HBO therapy was not so effective in patients with infarcts before therapy; this result is similar to that of Kawamura et al. HBO therapy caused no complications and seems to be safe and effective in preventing cerebral infarction caused by symptomatic vasospasm, although our series of patients was quite small.

HBO therapy was also used to prevent symptomatic vasospasm in five asymptomatic patients with severe arterial narrowing. All made a complete recovery without infarction, although slight transient neurological symptoms occurred in four patients. HBO therapy can reduce the severity of cerebral vasospasm if initiated before the patient becomes symptomatic.

EEG was used to evaluate brain function under HBO exposure in this study. Clinical improvement is achieved in patients with acute brain damage when EEGs improve during HBO exposure. EEG improvements are associated with neurological improvements in patients with symptomatic vasospasm. EEGs and EEG power analysis are useful in evaluating brain function during HBO exposure.

Our study shows that HBO therapy as an adjunct to hypertensive hypervolemia helps prevent cerebral infarction associated with symptomatic vasospasm, although a further study is required to prove this conclusively.

**Acknowledgments**

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