

Hyperbaric oxygen and steroid therapy for idiopathic sudden sensorineural hearing loss

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Received: 6 November 2006 / Accepted: 31 January 2007 / Published online: 6 March 2007
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Abstract In our controlled retrospective analysis of medical records in tertiary care academic medical center, we aimed to investigate the therapeutic effects of hyperbaric oxygen (HBO) therapy combined with steroid administration for idiopathic sudden sensorineural hearing loss (ISSNHL) in comparison with that of steroid administration alone. Our subjects were 130 consecutive inpatients with ISSNHL (hearing levels ≥ 40 dB; time from the onset of hearing loss to the start of treatment ≤ 30 days). Sixty-seven patients underwent HBO plus steroid therapy (HBO group), and 63 were given steroids alone (steroid group). Hearing recovery was evaluated by grade assessment and by the improvement in hearing compared to that in the unaffected contralateral ear. The cure rate and hearing improvement rate were not statistically different between the two groups; however, the recovery rate was significantly higher in the HBO group than in the steroid group (59.7% vs. 39.7%; $P < 0.05$). With regard to patients with initial hearing levels of ≥ 80 dB, the hearing improvement rate was significantly higher in the HBO group than in the steroid group ($51.1 \pm 7.0\%$ vs. $27.1 \pm 7.8\%$; $P < 0.05$), while in patients whose initial hearing levels were < 80 dB, hearing outcomes were not statistically different between the two groups. In both the HBO and steroid groups, patients with initial hearing levels of < 80 dB showed a better hearing improvement rate than

those with initial hearing levels of ≥ 80 dB. In conclusion HBO therapy shows a significant additional effect in combination with steroid therapy for ISSNHL, particularly in patients with severe hearing loss.

Keywords Idiopathic sudden sensorineural hearing loss · Hyperbaric oxygen · Steroid

Introduction

Idiopathic sudden sensorineural hearing loss (ISSNHL) is not a distinct disease, but rather is thought to be the clinical manifestation of diverse pathologic processes; viral infection, circulatory disorders, labyrinthine membrane rupture and autoimmune reactions have been suggested to be possible causative factors [1]. Because such multifactorial etiopathologies are believed to underlie the disease, many different regimens have been employed as therapy, including vasodilators, anticoagulants, corticosteroids, vitamins, plasma expanders, histamine treatment, antiviral agents, batroxobin, contrast media, stellate ganglion blocks, hyperbaric oxygen (HBO) and carbogen treatment. Although a randomized, double-blind, placebo-controlled study by Wilson et al. [2] demonstrated the efficacy of corticosteroids for the treatment of ISSNHL, the efficacy of the other therapies has not yet been proven by strict clinical trial.

Since the medical application of HBO for the purpose of increasing blood and tissue oxygen was first advocated in 1960 by Boerema et al. [3] it has been employed for the treatment of various diseases such as severe anaerobic infections, carbon monoxide poisoning, decompression sickness, etc. HBO therapy was then introduced for inner ear disorders in the early 1970s [4, 5] and for ISSNHL in

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the late 1970s [6, 7]. The therapeutic usefulness of HBO for ISSNHL has been described by a few authors, but has not yet been widely approved. The present study was performed in an attempt to examine the effect of HBO therapy combined with steroid administration for ISSNHL in comparison with that of steroid administration alone.

Patients and methods

Patients

A total of 130 consecutive inpatients with ISSNHL who visited the Department of Otolaryngology, University of Occupational and Environmental Health Hospital, were enrolled in the study. All patients met the following inclusion criteria: (i) sudden onset of sensorineural hearing loss; (ii) unknown cause of hearing loss; (iii) hearing loss did not fluctuate; (iv) arithmetic mean of hearing levels at 250, 500, 1,000, 2,000 and 4,000 Hz ≥ 40 dB; (v) time from the onset of hearing loss to the start of treatment ≤ 30 days; (vi) no history of severe diabetes mellitus, active peptic ulcer or viral hepatitis. Unless refused by the patient, magnetic resonance imaging of the internal auditory canal/cerebellopontine angle was performed during or after treatment, and acoustic tumors and brainstem lesions were thus ruled out.

Treatment protocols

From 1979 to 1990, 63 patients received steroid therapy (steroid group). They were given 8 mg/day of dexamethasone followed by tapered doses for 12 days, as shown in Table 1. From 2002 to 2005, 67 patients received HBO therapy combined with steroid administration

(HBO group). The patients were treated in a hyperbaric chamber, in which they breathed 100% oxygen at a pressure of 2.5 atm for 60 min, once daily from Monday through Friday for 2 weeks (a total of 10 sessions). During the same period, they were given 400 mg/day of hydrocortisone sodium succinate followed by tapered doses for 14 days (Table 1). Any of the present patients who underwent HBO therapy did not have otitis media before treatment, and was expected to have tolerable Eustachian tube function.

Evaluation of hearing recovery

The arithmetic mean of hearing levels at 250, 500, 1,000, 2,000 and 4,000 Hz was used to evaluate hearing recovery. The hearing level at 1 month after the initiation of treatment was considered to be fixed, and hearing recovery was classified into one of four grades (complete recovery, good recovery, fair recovery and no change/deterioration) according to the criteria proposed by the Ad Hoc Committee of the Japanese Ministry of Health, Labor and Welfare (Table 2) [8]. The cure rate was defined as the proportion of patients with complete recovery, and the recovery rate was defined as the proportion of patients with good or complete recovery. The hearing improvement rate was calculated using the following equation [9]:

Hearing improvement rate

$$= (\text{HL}_{\text{pre}} - \text{HL}_{\text{post}}) / (\text{HL}_{\text{pre}} - \text{HL}_{\text{contra}}) \times 100(\%)$$

where HL_{pre} is the initial hearing level, HL_{post} is the hearing level after treatment (1 month after the initiation of treatment) and $\text{HL}_{\text{contra}}$ is the hearing level of the unaffected contralateral ear.

Table 1 Protocol of steroid administration

| Day | Steroid group (mg div) | HBO group (mg div) |
|-----|------------------------|--|
| 1 | Dexamethasone 8 mg div | Hydrocortisone sodium succinate 400 mg div |
| 2 | Dexamethasone 8 mg div | Hydrocortisone sodium succinate 400 mg div |
| 3 | Dexamethasone 6 mg div | Hydrocortisone sodium succinate 400 mg div |
| 4 | Dexamethasone 6 mg div | Hydrocortisone sodium succinate 200 mg div |
| 5 | Dexamethasone 4 mg div | Hydrocortisone sodium succinate 200 mg div |
| 6 | Dexamethasone 4 mg div | Hydrocortisone sodium succinate 200 mg div |
| 7 | Dexamethasone 2 mg div | Hydrocortisone sodium succinate 100 mg div |
| 8 | Dexamethasone 2 mg div | Hydrocortisone sodium succinate 100 mg div |
| 9 | Dexamethasone 1 mg div | Hydrocortisone sodium succinate 100 mg div |
| 10 | Dexamethasone 1 mg div | Prednisolone 10 mg po |
| 11 | Dexamethasone 1 mg div | Prednisolone 10 mg po |
| 12 | Dexamethasone 1 mg div | Prednisolone 10 mg po |
| 13 | | Prednisolone 5 mg po |
| 14 | | Prednisolone 5 mg po |

div intravenous drip infusion, *po* oral administration

Table 2 Criteria for hearing recovery in idiopathic sudden sensorineural hearing loss

| |
|--|
| Complete recovery |
| Healing level returns within 20 dB at 250, 500, 1,000, 2,000 and 4,000 Hz, or to the equal level of the unaffected contralateral ear |
| Good recovery |
| Improvement in the hearing level ^a is ≥30 dB |
| Fair recovery |
| Improvement in the hearing level ^a is ≥10 dB but <30 dB |
| No change or deterioration |
| Improvement in the hearing level ^a is <10 dB |

As proposed by the Ad Hoc Committee of the Japanese Ministry of Health, Labour and Welfare⁸

^a Arithmetic mean of hearing levels at five frequencies (250–4,000 Hz)

Statistics

Data values are expressed as means ± SEM. Statistical differences of ratios and means were analyzed using the χ^2 test and a two-tailed Student's *t* test, respectively. Differences were considered to be significant when *P* was <0.05.

Results

Profile of patients

Table 3 shows the profiles of the patients in the steroid and HBO groups. There were no significant differences in age, association with vertigo or interval between onset and treatment between the two groups. However, the initial hearing level was significantly higher in the HBO group than in the steroid group (*P* < 0.01).

Therapeutic outcomes

The overall therapeutic outcomes are summarized in Table 4. The cure rates were 25.4% and 17.9% in the steroid

Table 4 Overall therapeutic outcomes

| | Steroid group | HBO group | <i>P</i> |
|---------------------------------------|---------------|---------------|--------------------|
| Cure rate | 16/63 (25.4%) | 12/67 (17.9%) | NS ^a |
| Recovery rate | 25/63 (39.7%) | 40/67 (59.7%) | <0.05 ^a |
| Hearing improvement rate (mean ± SEM) | 56.0 ± 4.6% | 64.4 ± 4.2% | NS ^b |

NS nonsignificant

^a χ^2 test

^b Student's *t* test

and HBO groups, respectively. The recovery rate in the HBO group was 59.7%, which was significantly higher than that in the steroid group (39.7%; *P* < 0.05). The hearing improvement rates were 56.0 ± 4.6% and 64.4 ± 4.2% in the steroid and HBO groups, respectively. We also analyzed variations in therapeutic outcomes with respect to age, vestibular symptoms and time between onset and treatment; however, no significant differences were observed between the two groups (data not shown). With regard to patients with initial hearing levels of ≥80 dB, the hearing improvement rate was significantly higher in the HBO group than in the steroid group (51.1 ± 7.0 vs. 27.1 ± 7.8%; *P* < 0.05), while in patients with initial hearing levels of <80 dB, the hearing improvement rate was not statistically different between the two groups (Table 5). In both groups, patients with initial hearing levels of <80 dB showed a better hearing improvement rate than those with initial hearing levels of ≥80 dB (Table 5).

Side effects

Seventeen (25.4%) of the 67 patients in the HBO group manifested the signs and symptoms of eustachian tube dysfunction. Of these 17 patients, 9 (13.4%) developed otitis media with effusion, myringotomy was required in four cases (6.0%), and one patient (1.5%) underwent tympanostomy tube insertion. No occurrence of sinus

Table 3 Profiles of patients

| | Steroid group | HBO group | <i>P</i> |
|--------------------------------------|---------------|---------------|--------------------|
| No. of patients | 63 | 67 | |
| Age (years) | | | |
| Mean ± SEM | 52.2 ± 1.7 | 53.0 ± 2.1 | NS ^a |
| Range | 11–77 | 13–83 | |
| Vertigo | 11/63 (17.5%) | 10/67 (14.9%) | NS ^b |
| Initial hearing level (dB) | | | |
| Mean ± SEM | 62.8 ± 2.2 | 74.7 ± 2.3 | <0.01 ^a |
| Range | 40–106 | 40–115 | |
| Interval between onset and treatment | | | |
| Mean ± SEM | 6.5 ± 0.7 | 6.3 ± 0.7 | NS ^a |
| Range | 0–30 | 0–30 | |

^a Student's *t* test

^b χ^2 test

Table 5 Initial hearing levels and therapeutic outcomes

| Therapeutic response | Steroid group | HBO group |
|---------------------------------------|---------------|---------------|
| Initial hearing level <80dB | | |
| Cure rate | 16/51 (31.3%) | 11/43 (25.6%) |
| Recovery rate | 22/51 (43.1%) | 26/43 (60.5%) |
| Hearing improvement rate (mean ± SEM) | | |
| | 62.8 ± 4.9% | 71.6 ± 5.0% |
| Initial hearing level ≥80dB | | |
| Cure rate | 0/12 (0%) | 1/24 (4.2%) |
| Recovery rate | 3/12 (25%) | 14/24 (58.3%) |
| Hearing improvement rate (mean ± SEM) | | |
| | 27.1 ± 7.8% | 51.1 ± 7.0% |

NS

**

*

* $p < 0.05$ ** $p < 0.01$

headache, toothache or barotraumatic lesions such as tympanic membrane laceration, inner ear membrane rupture or pneumothorax was noted.

Discussion

The present study found that the overall recovery rate was higher in the HBO group than in the steroid group, and that, in patients with severe hearing loss (initial hearing levels of ≥ 80 dB), the hearing improvement rate was better in the HBO group than in the steroid group. Patients were treated with 8 mg/day of dexamethasone and 400 mg/day of hydrocortisone sodium succinate as initial doses in the steroid and HBO groups, respectively. Because the anti-inflammatory effects of dexamethasone and hydrocortisone are ten times and one-fifth as strong as those of prednisolone [10], respectively, the steroids administered in the two groups correspond to an almost equal dose (80 mg/day) of prednisolone. Our present results indicate that the combination of HBO and steroid therapy, in comparison with steroid administration alone, significantly improves hearing outcome in patients with ISSNHL.

Several researchers have previously studied the clinical efficacy of HBO for ISSNHL. Goto et al. [7] reported that HBO therapy combined with a stellate ganglion block for patients with ISSNHL yields a better hearing outcome compared to conventional medical treatment; however, their study did not discuss the efficacy of HBO alone. Kau

et al. [11] performed HBO therapy as the second choice treatment for patients with cochlear disorders who had not responded to medication, and achieved noticeable improvement in those who had had hearing loss or tinnitus for less than 3 months. Horn et al. [12] performed HBO therapy as the second choice treatment for patients with ISSNHL who did not respond to steroid and antiviral treatment, but their trial did not include control subjects. Likewise, there was no control group in the retrospective analysis of 546 patients with ISSNHL by Nakashima et al. [13]. Controlled retrospective analyses have been described in three papers [14–16]. Racic et al. [14] showed that HBO therapy is more effective than pentoxifylline, and Aslan et al. [15] and Narozny et al. [16] found that HBO therapy exhibits an additional effect in combination with other treatments, including steroid administration. In stricter studies, Fattori et al. [17] and Topuz et al. [18] conducted randomized controlled trials, proving the significant efficacy of HBO for ISSNHL.

A number of authors have suggested that circulatory disorder could be the main etiopathology of ISSNHL. It is known that patients with systemic vascular or hematologic abnormalities such as sickle-cell disease, Buerger disease or polycythemia have a higher risk of contracting sudden sensorineural hearing loss [19]. Chao [20] reported the case of a 46-year-old man with malignant hypertension who manifested sudden sensorineural hearing loss immediately after a rapid reduction in blood pressure, and commented that this case might provide an *in vivo* human model of

ISSNHL caused by ischemia. It has also been reported that anterior inferior cerebellar artery infarction may result in a sudden vestibulocochlear nerve deficit without manifestations of other neurological findings [21]. Furthermore, Patzak et al. [22] suggested that a sudden onset of hearing loss could be a characteristic sign of a vertebrobasilar circulatory disturbance.

In experimental animals, sudden hearing loss induced by artificial ischemia of the inner ear has been studied [23, 24]. Kimura [25] stated that animal models of vascular disorders were a useful tool for achieving a better understanding of ISSNHL: in sudden occlusion of the major vascular supply to the inner ear of guinea pigs, the cochlea was found to be more vulnerable than the vestibular labyrinth; the outer and inner hair cells and stria vascularis were most often affected.

Circulatory disorders of the inner ear cause cochlear ischemia, and thus lead to a decrease in partial oxygen pressure (pO_2) in the perilymph; indeed, Nagahara et al [26] found low pO_2 in the perilymph of patients with ISSNHL. The purpose of HBO in the treatment of ISSNHL is to increase pO_2 in the blood and then, via diffusion, to increase pO_2 in the inner ear fluids, which nourish the sensory and neural elements in the cochlea [27, 28]. HBO inhalation thereby stimulates cell metabolism in the inner ear even under conditions of poor blood supply [17]. Upon inhaling air at 1 atm, only 0.32% of total oxygen is dissolved in blood. If 100% oxygen is inhaled at 1 and 2 atm, the amounts of dissolved oxygen rise to 2.09 and 4.44%, respectively [17]. Lamm et al. [27] found that inhalation of 100% oxygen markedly increased pO_2 in the perilymph of guinea pigs, and the increase multiplied under hyperbaric conditions. Moreover, the elevated level of pO_2 in the perilymph remained significantly high for 60 min after the termination of the HBO treatment [28].

On the other hand, HBO may augment the production of reactive oxygen species and may exert cytotoxic effects. Several detoxification and antioxidant enzymes such as catalase, superoxide dismutase, glutathione peroxidase, glutathione reductase and glutathione S-transferase have been demonstrated in the cochlea [29]. Additionally, Gregorevic et al. [30] found that acute and repeated HBO inhalation modifies the activity of antioxidant enzymes in skeletal muscles. These biochemical processes may cause oxygen toxicity in the airway and central nervous system, including laryngeal pain, cough, dyspnea, or generalized convulsions [31]. However, the cytotoxic effects of oxidants are thought to be negligible in clinical HBO administration under 2–3 atm at sessions of no longer than 1 h [31]. Plafki et al. [32] investigated complications and side effects in a total of 11,376 HBO therapy sessions in 782 patients treated for various indications. In Plafki's study, barotraumatic lesions were verified by visual otological

examination using otomicroscopy in 3.8% of all patients, barotrauma of the paranasal sinuses rarely occurred, and no barotraumatic lesions of the inner ear or lung were noted. Fernau et al. [33] examined 33 patients who underwent HBO therapy, finding that 15 (45%) of them showed evidence of eustachian tube dysfunction: all 15 patients complained of a sensation of ear fullness, 13 (39%) developed otitis media with effusion, and 7 (21%) required tympanostomy tube insertion. Compared with these previous reports, the incidence of middle ear complications was low in our study. The anti-inflammatory effect of hydrocortisone administered together with the HBO therapy may have reduced vascular permeability, edema and the inflammatory responses of constituent cells in the middle ear.

Conclusions

We conducted a controlled retrospective analysis of patients with ISSNHL who underwent HBO plus steroid therapy in comparison with those who received steroid administration alone. Hearing outcome was better in the HBO group than in the steroid group, particularly when the initial hearing level was ≥ 80 dB. We conclude that HBO therapy shows a significant additional effect in combination with steroid therapy for ISSNHL.

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