Eur Arch Otorhinolaryngol (2007) 264:861–866
DOI 10.1007/s00405-007-0272-6

OTOLOGY

Hyperbaric oxygen and steroid therapy for idiopathic sudden sensorineural hearing loss

Takeyuki Fujimura · Hideaki Suzuki · Teruo Shiomori · Tsuyoshi Udaka · Takanori Mori

Received: 6 November 2006 / Accepted: 31 January 2007 / Published online: 6 March 2007

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 ± 7.0% vs. 27.1 ± 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

T. Fujimura · H. Suzuki (✉) · T. Shiomori · T. Udaka · T. Mori
Department of Otorhinolaryngology, School of Medicine, University of Occupational and Environmental Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan
e-mail: suzuhyde@med.uoeh-u.ac.jp

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

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]:

$$\text{Hearing improvement rate} = (HL_{pre} - HL_{post})/(HL_{pre} - HL_{contra}) \times 100(\%)$$

where HL_{pre} is the initial hearing level, HL_{post} is the hearing level after treatment (1 month after the initiation of treatment) and HL_{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 Welfare[8]

[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 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).

Table 4 Overall therapeutic outcomes

	Steroid group	HBO group	*P*
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

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	*P*
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%)
	NS	
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%
	*	

*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 el 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 cytotxic 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.

References

1. Eisenman DJ, Arts HA (2000) Effectiveness of treatment for sudden sensorineural hearing loss. Arch Otolaryngol Head Neck Surg 126:1161–1164
2. Wilson WR, Byl FM, Laird N (1980) The efficacy of steroids in the treatment of idiopathic sudden hearing loss. a double-blind clinical study. Arch Otolaryngol 106:772–776
3. Boerema I, Meyne NG, Brummelkamp WH, Bouma S, Mensch MH, Kamermans F, Stern HM, von Aalderen (1960) Life without blood: a study of the influence of high atmospheric pressure and hypothermia on dilution of the blood. J Cardiovasc Surg 1:133–146
4. Appaix A, Demard F (1970) Hyperbaric oxygenotherapy and sudden perceptive deafness. Rev Laryngol Otol Rhinol (Bord) 91:951–972
5. Lamm H, Kimpel L (1971) Hyperbaric oxygen therapy in internal ear and vestibular disorders. Preliminary report. HNO 19:363–369
6. Vincey P (1978) Application and use of hyperbaric oxygenation in ENT. Rev Laryngol Otol Rhinol (Bord) 99:619–634
7. Goto F, Fujita T, Kitani Y, Kanno M, Kamei T, Ishii H (1979) Hyperbaric oxygen and stellate ganglion blocks for idiopathic sudden hearing loss. Acta Otolaryngol 88:335–342
8. Kanzaki J, Taiji H, Ogawa K (1988) Evaluation of hearing recovery in sudden and efficacy of steroid treatment in sudden deafness. Acta Otolaryngol Suppl 456:31–36
9. Suzuki H, Furukawa M, Kumagai M, Takahashi E, Matsuura K, Katori Y, Shimomura A, Kobayashi T (2003) Defibrinogenation

therapy for idiopathic sudden sensorineural hearing loss in comparison with high-dose steroid therapy. Acta Otolaryngol 123:46–50
10. Melby JC (1974) Systemic corticosteroid therapy: pharmacology and endocrinologic considerations. Ann Intern Med 81:505–512
11. Kau RJ, Sendtner-Gress K, Ganzer U, Arnold W (1997) Effectiveness of hyperbaric oxygen therapy in patients with acute and chronic cochlea disorders. ORL J Otorhinolaryngol Relat Spec 59:79–83
12. Horn CE, Himel HN, Selesnick SH (2005) Hyperbaric oxygen therapy for sudden sensorineural hearing loss: a prospective trial of patients failing steroid and antiviral treatment. Otol Neurotol 26:882–889
13. Nakashima T, Fukuta S, Yanagita N (1998) Hyperbaric oxygen therapy for sudden deafness. Adv Otorhinolaryngol 54:100–109
14. Racic G, Maslovara S, Roje Z, Dogas Z, Tafra R (2003) Hyperbaric oxygen in the treatment of sudden hearing loss. ORL J Otorhinolaryngol Relat Spec 65:317–320
15. Aslan I, Oysu C, Veyseller B, Baserer N (2002) Does the addition of hyperbaric oxygen therapy to the conventional treatment modalities influence the outcome of sudden deafness? Otolaryngol Head Neck Surg 54:121–126
16. Narozny W, Sicko Z, Przewozny T, Stankiewicz C, Kot J, Kuczkowski J (2004) Usefulness of high doses of glucocorticoids and hyperbaric oxygen therapy in sudden sensorineural hearing loss. Otol Neurotol 25:916–923
17. Fattori B, Berrettini S, Casani A, Nacci A, DeVito A, DeIaco G (2001) Sudden hypoacusis treated with hyperbaric oxygen therapy: a controlled study. Ear Nose Throat J 80:655–660
18. Topuz E, Yigit O, Cinar U, Seven H (2004) Should hyperbaric oxygen be added to treatment in idiopathic sudden sensorineural hearing loss? Eur Arch Otorhinolaryngol 261:393–396
19. Schweinfurth JM, Parnes SM, Very M (1996) Current concepts in the diagnosis and treatment of sudden sensorineural hearing loss. Eur Arch Otorhinolaryngol 253:117–121
20. Chao TK (2004) Sudden sensorineural hearing loss after rapid reduction of blood pressure in malignant hypertension. Ann Oto Rhinol Laryngol 113:73–75
21. Lee H, Ahn BH, Baloh RW (2004) Sudden deafness with vertigo as a sole manifestation of anterior inferior cerebellar artery infarction. J Neurol Sci 222:105–107
22. Patzak MJ, Demuth K, Kehl R, Lindner A (2005) Sudden hearing loss as the leading symptom of an infarction of the left anterior inferior cerebellar artery. HNO 53:797–799
23. Asai Y, Umemura K, Kohno Y, Uematsu T, Nakashima M (1993) An animal model for hearing disturbance due to inner ear ischemia: photochemically induced thrombotic occlusion of the rata anterior inferior cerebellar artery. Eur Arch Otorhinolaryngol 250:292–296
24. Schweinfurth JM, Cacace AT (2000) Cochlear ischemia induced by circulating iron particles under magnetic control: an animal model for sudden hearing loss. Am J Otol 21:636–640
25. Kimura RS (1986) Animal models of inner ear vascular disturbances. Am J Otolaryngol 7:130–139
26. Nagahara K, Fisch U, Yagi N (1983) Perilymph oxygenation in sudden and progressive sensorineural hearing loss. Acta Otolaryngol 96:57–68
27. Lamm K, Lamm H, Arnold W (1998) Effect of hyperbaric oxygen therapy in comparison to conventional or placebo therapy or no treatment in idiopathic sudden hearing loss, acoustic trauma, noise-induced hearing loss and tinnitus: a literature survey. Adv Otorhinolaryngol 54:86–89
28. Lamm K, Lamm H, Arnold W (1998) Effect of isobaric oxygen versus hyperbaric oxygen on the normal and noise-damaged hypoxic and ischemic guinea pig inner ear. Adv Otorhinolaryngol 54:59–85
29. El Barbary A, Altschuler RA, Schacht J (1993) Glutathione S-transferases in organ of corti of the rat: enzymatic activity, subunit composition and immunohistochemical localization. Hear Res 71:80–90
30. Gregorevic P, Lynch GS, Williams DA (2001) Hyperbaric oxygen modulates antioxidant enzyme activity in rat skeletal muscles. Eur J Appl Physiol 86:24–27
31. Takahashi H, Kobayashi S (1998) New indications for hyperbaric oxygen therapy and its complication. Adv Otorhinolaryngol 54:1–13
32. Plafki C, Peters P, Almeling M, Welslau W, Busch R (2000) Complications and side effects of hyperbaric oxygen therapy. Aviat Space Environ Med 71:119–124
33. Fernau JL, Hirsch BE, Derkay C, Ramasastry S, Schaefer SE (1992) Hyperbaric oxygen therapy: effect on middle ear and eustachian tube function. Laryngogoscope 102:48–52