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OTOLOGY

Multivariate analysis of prognostic factors for idiopathic sudden sensorineural hearing loss treated with adjuvant hyperbaric oxygen therapy

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Abstract The objective of this study is to evaluate possible prognostic factors of idiopathic sudden sensorineural hearing loss (ISSNHL) treated with adjuvant hyperbaric oxygen therapy (HBOT) using univariate and multivariate analyses. From January 2008 to October 2016, records of 178 ISSNHL patients treated with auxiliary hyperbaric oxygen therapy were reviewed to assess hearing recovery and evaluate associated prognostic factors (gender, age, localization, initial hearing threshold, presence of tinnitus, vertigo, ear fullness, hypertension, diabetes, onset of HBOT, number of HBOT, and audiogram), by using univariate and multivariate analyses. The overall recovery rate was 37.1%, including complete recovery (19.7%) and partial recovery (17.4%). According to multivariate analysis, later onset of HBOT and higher initial hearing threshold were associated with a poor prognosis in ISSNHL patients treated with HBOT. HBOT is a safe and beneficial adjuvant therapy for ISSNHL patients. 20 sessions of HBOT is possibly enough to show its therapeutic effect. Earlier HBOT onset and lower initial hearing threshold is associated with favorable hearing recovery.

Keywords Idiopathic sudden sensorineural hearing loss · Hyperbaric oxygen therapy · Prognostic factors · Multivariate analysis.

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Introduction

Idiopathic sudden sensorineural hearing loss (ISSNHL) is an emergency medical condition which is defined as hearing loss of at least 30 dB in three contiguous frequencies during a maximum of 3 days [1]. ISSNHL is no longer a rare disease with an increasing incidence; some authors have reported an annual incidence of 160 cases per 100,000 [2]. Many theories have been proposed to explain the pathogenesis of this clinical problem, including infectious causes, vascular occlusion, immune-mediated mechanisms, coagulation disorders, and breaks of labyrinthine membrances [3, 4]. The equivocal etiologies lead to a large number of empirical treatment protocols, but the most frequently used therapy is the administration of steroids, which can be administrated intravenously, orally or by intratympanic injections [5, 6].

Hyperbaric oxygen therapy (HBOT) was first used in the treatment of ISSNHL in the late 1970s [7]. This medical therapy can increase perilymph oxygenation when performed by intermittent 100% oxygen administration to an ISSNHL patient in a pressure chamber [8]. During HBOT, oxygen is diffused by various terminal cochlear capillary networks into the perilymph, supplying the oxygen needs of the peripheral neuronal structures of the inner ear and stimulating cell repair [8, 9].

Clinical and experimental studies have reported the additional therapeutic effect of HBOT in ISSNHL patients [8, 10]. In 2012, a latest Cochrane Review confirmed the value of HBOT for ISSNHL [11]. HBOT has been recommended as an optional treatment to ISSNHL patients in Europe since the First European Consensus Conference on Hyperbaric Medicine [12]. Although not applied as a standard treatment in our country, HBOT is frequently used as auxiliary therapy combined with the conventional treatment modalities in ISSNHL. In clinical practices, hearing improvement

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differed among different studies because of various influencing factors, predicting recovery of ISSNHL patients treated with HBOT is becoming a need for otologists and hyperbaric physicians. The aim of this study was to investigate possible prognostic factors of ISSNHL treated with adjuvant HBOT using univariate and multivariate analyses.

Materials and methods

Patients

We retrospectively reviewed the medical records of 178 patients with ISSNHL who received HBOT as adjuvant treatment in our department from January 2008 to October 2016. ISSNHL was diagnosed by pure-tone audiometry and/or speech audiometry. In addition to audiological examination, magnetic resonance imaging of the brain and inner ears was undergone to screen for acoustic neuromas. The inclusion criteria were as follows: (1) age > 10 years, (2) unilateral hearing loss, (3) interval between onset of symptoms and treatment ≤ 30 days, (4) HBOT were performed for more than 2 days or 4 sessions, and (5) the absence of otitis media, neuropsychiatric disease and acoustic trauma, and no previous history of ISSNHL, Meniere's disease, trauma, and exposure to ototoxic medications.

Treatment

HBOT was applied at a pressure of 2.5 atmosphere absolutes (ATA) for 60 min twice a day. The decision of terminating HBOT depended on the referral clinic by evaluating the audiological follow-ups. Medical treatments (steroids, blood flow promoting agents, and vitamin B complex) were started at the beginning of HBOT.

Assessment

Data on gender, age, localization, initial hearing threshold, presence of tinnitus, vertigo, ear fullness, hypertension, diabetes, onset of HBOT, number of HBOT, audiogram were collected to analyze factors associated with prognosis.

Four types of audiogram were classified in relation to the pattern of hearing loss: ascending, descending, flat, and profound [13]. "Ascending" meant that the average threshold of 250 to 500 Hz was 20 dB higher than the median threshold of 4000 to 8000 Hz. The audiogram was described as "descending" when the average threshold of 4000 to 8000 Hz was 20 dB higher than the average threshold of 250 to 500 Hz. The difference in hearing threshold ≤ 20 dB at any frequency, the audiogram was classified as "flat". For the patient with a flat audiogram and hearing threshold more than 90 dB, the audiogram shape was defined as "profound".

All patients underwent pure-tone audiometry on the first day of treatments and after treatment. The pure-tone average of four frequencies (500, 1000, 2000, and 3000 Hz) was employed to determine the initial hearing threshold and assess the treatment outcomes according to Siegel's criteria [13, 14]. Complete recovery meant "final hearing level better than 25dB". More than 15 dB hearing gain and a final hearing level between 25 and 45 dB were "partial recovery". "Slight recovery" meant a final hearing level over 45 dB with hearing gain of ≥ 15 dB. Final hearing level more than 75 dB with hearing gain of ≤ 15 dB was "no recovery". In this study, complete recovery plus partial recovery were defined as "recovery", and the last two were classified as "no recovery".

Statistical analysis

All statistical analysis was performed with SPSS version 19.0 for windows. Student *t* tests were applied to continuous variables; Chi-square tests or Fisher's exact tests were used for categorical variables. Variables that were statistically significant in the univariate analysis were included in the multivariate analysis. Binary logistic regression analysis was performed to confirm the effects of possible prognostic factors. $P < 0.05$ was considered statistically significant.

Results

In total, 178 patients, including 90 men and 88 women with a mean age of 40.6 ± 15.3 years (range 11–75 years). The right ear was involved in 73 (41.0%) cases and the left in 105 (59%) cases. As accompanying symptoms, 155 (87.1%) exhibited tinnitus, 56 (31.5%) exhibited vertigo, and 64 (36.0%) exhibited ear fullness. Of total, 24 (13.5%) patients had hypertension and 12 (6.7%) had diabetes. Mean pure-tone threshold at the initial presentation was 73.8 ± 24.8 dB. The mean interval between the onset of symptoms and HBOT was 7.8 ± 6.8 days (range 1–30 days). The average number of HBOT session was 16.8 ± 6.1 (range 4–34). The audiogram configuration before HBOT was ascending in 6.2%, descending in 6.7%, flat in 39.8% and profound in 47.2% cases (Table 1).

With regard to final recovery according to Siegel's criteria, percentages of patients in complete recovery, partial recovery, slight recovery, and no improvement were 19.7, 17.4, 13.5, and 49.4%. The overall recovery rate (complete + partial) was 37.1% (Table 2).

Based on treatment outcomes, patients were divided into two groups: recovery and no recovery, which was described in the "Materials and methods" section. In univariate analysis, the initial hearing threshold in the recovery group was lower than that in no recovery

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Table 1 Baseline clinical characteristics of patients

Variables	
Number of enrolled patients	178
Gender, male	90 (50.6%)
Age, year	40.6 ± 15.3 (range 11–75)
Localization, right	73 (41.0%)
Initial hearing threshold, dB	73.8 ± 24.8
Accompanying symptoms	
Tinnitus	155 (87.1%)
Vertigo	56 (31.5%)
Ear fullness	64 (36.0%)
Hypertension	24 (13.5%)
Diabetes	12 (6.7%)
Interval between onset of symptoms and HBO therapy, d	7.8 ± 6.8 (range 1–30)
Number of HBO treatments	16.8 ± 6.1 (range 4–34)
Audiogram	
Ascending	11 (6.2%)
Descending	12 (6.7%)
Flat	71 (39.8%)
Profound	84 (47.2%)

HBOT hyperbaric oxygen therapy

group ($P = 0.000$). The mean interval between the onset of symptoms and HBOT was significantly shorter in the recovery group than that in the no recovery group ($P = 0.001$). With regard to the frequency of tinnitus or ear fullness, no statistical difference was found between the two groups, whereas there was a significantly higher incidence of vertigo in the recovery group ($P = 0.001$). The recovery group included more ascending type and flat type audiograms ($P = 0.000$, $P = 0.003$), and less profound type audiograms ($P = 0.000$) (Table 3).

Variables with a P value < 0.05 in the univariate analysis were included in the multivariate analysis. As both profound hearing loss and initial hearing threshold represented hearing level, we chose the latter in the multivariate analysis. Multivariate analysis revealed that later onset of HBOT and higher initial hearing threshold were associated with a poor prognosis in ISSNHL patients treated with HBOT (Table 3).

Discussion

There is still no consensus on the best treatment option of ISSNHL because of an indefinite etiology. Various empirical treatments have been applied to improve blood circulation and to increase oxygen pressure in the inner ear, including corticosteroids, vasodilators, plasma expanders, and anticoagulant agents [12].

Since the first application in ISSNHL in 1970s, the therapeutic usefulness of HBOT has been discussed for about 40 years [8, 15]. There have been many reports of HBOT being used as a primary treatment with different options and durations in ISSNHL with a significant additional therapeutic benefit [8, 15, 16]. HBOT was widely applied as an auxiliary therapy in the treatment of ISSNHL in our country, but the recovery rate was fluctuant with various influencing factors. Therefore, it is particularly difficult for otologists and hyperbaric physicians to predict recovery of ISSNHL patients treated with adjuvant HBOT. In this present study, we tried to collect data (gender, age, localization, initial hearing threshold, presence of tinnitus, vertigo, ear fullness, hypertension, diabetes, onset of HBOT, number of HBOT, and audiogram) to investigate possible prognostic factors using univariate and multivariate analyses.

The initial hearing level is a widely reported prognostic factor for hearing recovery of ISSNHL [13], while in a Japanese study, the authors found no association between initial hearing level and hearing outcome in patients who were treated with HBOT and intravenous steroids [16]. Liu et al. [17] analyzed the hearing improvement of 112 patients treated with HBOT and pharmacologic agents and found that profound cases yielded a higher rate of hearing recovery. In the current study, most patients suffered profound hearing loss (mean initial hearing threshold was 73.8 ± 24.8 dB), the overall recovery rate (37.1%) was lower than previously published results [8, 13]. Our multivariate analyses showed that the initial hearing threshold was a significant prognostic indicator for hearing recovery. It is believed that in cases with profound hearing loss, the extent hair cell injury is more extensive, it is more difficult to get a significant structural and functional recovery, although HBOT is applied in combination with the conventional treatments [18].

This study showed that urgent HBOT following hearing loss increased the chances of hearing recovery in ISSNHL patients. The previous reports agreed that the response to

Table 2 Final treatment outcomes according to Siegel's criteria

Description	*n* (%)
Complete recovery: final hearing level < 25 dB	35 (19.7)
Partial recovery: final hearing level 25–45 dB with hearing gain ≥ 15 dB	31 (17.4)
Slight recovery: final hearing > 45 dB with hearing gain ≥ 15 dB	24 (13.5)
No recovery: final hearing > 75 dB with hearing gain ≤ 15 dB	88 (49.4)

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Table 3 Results of analysis on factors influencing the recovery of SSNHL treated with HBOT

	Recovery	No recovery	Univariate	Multivariate			
	$n=66$	$n=112$	P value	B	SE	Exp (B)	P value
Gender, male	34 (51.5%)	56 (50.0%)	0.878				
Age, year	39.4 ± 14.3	41.4 ± 15.8	0.415				
Localization, right	45 (68.2%)	60 (53.6%)	0.060				
Initial hearing threshold, dB	58.5 ± 22.1	82.8 ± 21.7	**0.000**	− 0.045	0.008	0.971	**0.000**
Accompanying symptoms							
Tinnitus	58 (87.9%)	97 (86.6%)	1.000				
Vertigo	11 (16.7%)	45 (40.2%)	**0.001**	− 0.576	0.444	0.562	0.195
Ear fullness	29 (43.9%)	35 (31.3%)	0.106				
Hypertension	6 (9.1%)	18 (16.1%)	0.257				
Diabetes	2 (3.0%)	10 (8.9%)	0.215				
Onset of HBOT, days	5.6 ± 5.2	9.1 ± 7.3	**0.001**	− 0.095	0.032	0.558	**0.003**
Number of HBOT treatments	14.9 ± 6.1	17.8 ± 5.9	**0.002**	− 0.042	0.032	0.959	0.195
Audiogram							
Ascending	10 (15.2%)	1 (0.9%)	**0.000**	0.757	1.106	0.469	0.494
Descending	7 (10.6%)	5 (4.4%)	0.131				
Flat	36 (54.5%)	35 (28.7%)	**0.003**	0.791	1.033	0.453	0.444
Profound	13 (19.7%)	71 (63.4%)	**0.000**				

Bold text indicates statistical significance ($P<0.05$)

B standardized coefficient, *SE* standard error, *Exp(B)* odds ratio, *SSNHL* sudden sensorineural hearing loss, *HBOT* hyperbaric oxygen therapy

the HBOT was better in the cases with earlier onset of this therapy [8, 16]. Alimoglu et al. [19] suggested that adjuvant HBOT should be administered soon after the onset of ISSNHL as a primary treatment to achieve a good hearing recovery. Nakashima et al. [20] analyzed 1614 cases and found that hearing gain was better when HBOT was added to the conventional therapies in the first week of the disease. Poor prognosis associated with delayed treatment start might be a reflection of the natural history of ISSNHL, and hearing loss lasting more than 2 to 3 months is likely to become permanent [13]. In our study, we only included SSNHL patients who received HBOT and conventional treatments within 30 days after hearing loss to minimize the confounding effect of the natural history of this clinical disease.

Another important aim of this study was to investigate the association between hearing outcomes and the number of HBOT sessions in the treatment of ISSNHL. Körpinar et al. [8] believed that the excessive number of HBOT sessions positively affected the hearing recovery. In a Chinese study, Liu et al. [21] found that 10 sessions of HBOT was enough to show its therapeutic effect, and the excessive courses were unnecessary. In our study, most patients received HBOT about 20 sessions (an average of 16.8 sessions) and completed within 10 days (an average of 8.9 days). According to multivariate analyses, we found that the number of HBOT sessions was not a factor in hearing recovery in ISSNHL patients. It is believed that the therapeutic effect of HBOT and conventional treatments will eventually reach a plateau after a course of standardized treatment, and excessive courses of HBOT will not exercise a decisive influence on hearing recovery [21].

ISSNHL patients always care deeply about the safety and side effects of HBOT before choosing it. HBOT is usually performed at about 2.5 ATA for 60 min twice a day in our country. In general, HBOT is safe when pressures do not exceed 3 ATA and the duration is less than 120 min [22]. In an evidence-based review conducted by Bennett et al. [11], no systematic adverse effects were reported after HBOT. The middle ear barotraumas, sinus barotraumas, and confinement anxiety may occur during HBOT. In our study, 10 patients (5.6%) suffered otalgia during the first session of HBOT. After being taught how to equalize the pressure during compression before receiving HBOT, 7 patients continued the HBOT with any uncomfortableness and 3 patients still complained about otalgia on the second day. These 3 patients refused to continue HBOT when tympanic membrane hyperemia and hydrotympanum were found in their ears during otoscpic examinations. 3 days later, otoscpic examinations showed normal results in these patients.

Conclusions

Our clinical experience and results in this retrospective study suggested that HBOT is a safe and beneficial adjuvant therapy for ISSNHL patients. 20 sessions of HBOT is possibly

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enough to show its therapeutic effect. According to multivariate analyses, we found that the earlier HBOT onset and lower initial hearing threshold is associated with favorable hearing recovery.

Compliance with ethical standards

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Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent For this type of study, formal consent is not required.

References

1. Schreiber BE, Agrup C, Haskard DO et al (2010) Sudden sensorineural hearing loss. The Lancet 375:1203–1211
2. Klemm E, Deutscher A, Mösges R (2009) A present investigation of the epidemiology in idiopathic sudden sensorineural hearing loss. [in German] Laryngorhinootologie 88:524–527
3. Pezzoli M, Magnano M, Maffi L et al (2015) Hyperbaric oxygen therapy as salvage treatment for sudden sensorineural hearing loss: a prospective controlled study. Eur Arch Otorhinolaryngol 272:1659–1666
4. Yin T, Huang F, Ren J et al (2013) Bilateral sudden hearing loss following habitual abortion: a case report and review of literature. Int J Clin Exp Med 6:720–723
5. Qiang Q, Wu X, Yang T et al (2017) A comparison between systemic and intratympanic steroid therapies as initial therapy for idiopathic sudden sensorineural hearing loss: a meta-analysis. Acta Otolaryngol 137:598–605
6. Labus J, Breil J, Stutzer H,et al (2010) Meta-analysis for the effect of medical therapy vs placebo on recovery of idiopathic sudden hearing loss. Laryngoscope 120:1863–1871
7. Goto F, Fujita T, Kitani Y et al (1979) Hyperbaric oxygen and stellate ganglion blocks for idiopathic sudden hearing loss. Acta Otolaryngol 88:335–342
8. Körpinar S, Alkan Z, Yiğit O et al (2011) Factors influencing the outcome of idiopathic sudden sensorineural hearing loss treated with hyperbaric oxygen therapy. Eur Arch Otorhinolaryngol 268:41–47
9. Filipo R, Attanasio G, Viccaro M et al (2012) Hyperbaric oxygen therapy with short duration intratympanic steroid therapy for sudden hearing loss. Acta Otolaryngo 132:475–481
10. Lamm K, Lamm C, 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
11. Bennett MH, Kertesz T, Perleth M et al (2012) Hyperbaric oxygen for idiopathic sudden sensorineural hearing loss and tinnitus. Cochrane Database Syst Rev 10:CD004739
12. Topuz E, Yigit O, Cinar O, Seven H (2004) Should hyperbaric oxygen be added to treatment in idiopathic sudden sensorineural hearing loss? Eur Arch Otorhinolaryngol 261:393–396
13. Chung JH, Cho SH, Jeong JH et al (2015) Multivariate analysis of prognostic factors for idiopathic sudden sensorineural hearing loss in children. Laryngoscope 125:2209–2215
14. Siegel LG (1975) The treatment of idiopathic sudden sensorineural hearing loss. Otolaryngol Clin North Am 8:467–473
15. Fujimura T, Suzuki H, Shiomori T et al (2007) Hyperbaric oxygen and steroid therapy for idiopathic sudden sensorineural hearing loss. Eur Arch Otorhinolaryngol 264:861–866
16. Hosokawa S, Sugiyama K, Takahashi G et al (2017) Prognostic factors for idiopathic sudden sensorineural hearing loss treated with hyperbaric oxygen therapy and intravenous steroids. J Laryngol Otol 131:77–82
17. Liu SC, Kang BH, Lee JC et al (2011) Comparison of therapeutic results in sudden sensorineural hearing loss with/without additional hyperbaric oxygen therapy: a retrospective review of 465 audiologically controlled cases. Clin Otolaryngol 36:121–128
18. Bogaz EA, Maranhão AS, Inoue DP et al (2015) Variables with prognostic value in the onset of idiopathic sudden sensorineural hearing loss. Braz J Otorhinolaryngol 81:520–526
19. Alimoglu Y, Inci E, Edizer DT et al (2011) Efficacy comparison of oral steroid, intratympanic steroid, hyperbaric oxygen and oral steroid + hyperbaric oxygen treatments in idiopathic sudden sensorineural hearing loss cases. Eur Arch Otorhinolaryngol 268:1735–1741
20. Nakashima T, Fukata S, Yanagita N (1998) Hyperbaric oxygen therapy for sudden deafness. Adv Otorhinolaryngol 54:100–109
21. Liu Y, Jiang W, Mao K (2012) Application of hyperbaric oxygen therapy for sudden deafness [in Chinese]. J Otolaryngol Ophthal Shandong Univ 26:70–72
22. Feldmeier JJ (2003) Hyperbaric oxygen: indications and results; the hyperbaric oxygen therapy committee report. Undersea and Hyperbaric Medical Society, Kensington

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