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Comparison of Therapeutic Results of the Starting Time of Hyperbaric Oxygen Therapy in Sudden Sensorineural Hearing Loss

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ABSTRACT

This study aimed to assess the impact of the hyperbaric oxygen (HBO) therapy starting time (early or late) on the treatment of idiopathic sudden sensorineural hearing loss (ISSNHL).

A retrospective analysis examined 203 patients with ISSNHL between January 2014 and June 2018 at Van Training and Research Hospital. We divided the patients into two groups according to the HBO therapy starting time as follows: early HBO (n = 88) and late HBO (n = 115).

The early HBO group demonstrated complete, partial, weak, and no recovery in 21 (23.9%), 15 (17.0%), 17 (19.3%), and 35 (39.8%) patients, respectively. The late HBO group demonstrated complete, partial, weak, and no recovery in 5 (4.3%), 9 (7.8%), 15 (13.0%), and 86 (74.8%) patients, respectively. In addition, 53 (60.2%) and 29 (25.2%) patients in the early and late HBO groups, respectively, responded to treatment, which was statistically significant ($P < 0.05$). Considering patients with severe and profound hearing loss only, we observed a statistically significant difference in response to treatment between the early and late HBO groups ($P < 0.05$).

The study demonstrates that providing HBO therapy during the first 14 days of the treatment period contributed significantly to treatment success. Therefore, patients with severe and profound hearing loss can significantly benefit by starting HBO therapy at an early stage of the disease.

Key Words: Hyperbaric oxygen therapy; Idiopathic sudden sensorineural hearing loss; Salvage treatment

Introduction

Idiopathic sudden sensorineural hearing loss (ISSNHL) is described as an unperceived, unilateral loss of hearing with onset of more than 30 dB within a minimum 72 hours affecting three consecutive frequencies (1). It is an an otological disease that warrants prompt diagnosis and treatment. Although the reported incidence rate of ISSNHL ranges 5–20 cases for every 100,000 individuals per year with a high spontaneous recovery rate, its actual incidence is estimated to be far more (2). Spontaneous remission can be seen in up to 65% of patients with ISSNHL (3). Despite partial understanding of ISSNHL pathogenesis, the most common theories of etiology comprise vascular causes, viral infections, cochlear membrane disorders, and autoimmune disorders. Most reported cases are idiopathic, however there are many factors that explain its etiology (4). Therefore, because of the variability of the etiopathogenetic mechanisms, no single treatment option exists for sudden hearing loss, even though literatures report the use of several medicines and therapies (5).

But yet, the drugs used most widely about management of ISSNHL in many treatment protocols which have been used, are steroids (6).

It is assumed that ISSNHL can arise from hypoxia in the cochlear device. Hyperbaric oxygen therapy is viewed as an acceptable choice. HBO therapy, which has become widespread in clinical practice for the treatment of ISSNHL in recent years, increases pressure of oxygen in the blood partially. After this process, pressure of oxygen is increased partially through diffusion in the inner ear fluids, that feed the sensory and neural elements (7).

The Committee of the Undersea and Hyperbaric Medical Society approved ISSNHL as an indication for HBO therapy (8) so as to advantage of HBO in the treatment of ISSNHL were demonstrated (9), Nevertheless, HBO therapy is still investigated for its efficacy and timing for treating sudden sensorineural hearing loss. Thus, it is aimed to determine whether

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beginning HBO therapy earlier affected ISSNHL treatment and also to compare the recovery rates between early HBO therapy use in combination with steroid in treating sudden hearing loss and late HBO therapy use as salvage therapy in patients who suffer from failed initial oral steroid therapy.

Materials and Methods

Patients: 203 patients with ISSNHL who presented at the Department of Otorhinolaryngology - Head and Neck Surgery were retrospectively reviewed at Van Training - Research Hospital, between January 2014 - June 2018. Inclusion criteria consisted of unilateral sensorineural hearing loss with a minimum 30 dB hearing loss at three adjacent frequencies lasting minimum three days. The exclusion criteria included pediatric patients, pre-existing Meniere's disease, auditory trauma, tumors, retrocochlear disease, barotrauma, bilateral hearing loss, a history of chronic otitis in the same ear, and surgery of the same ear. Besides, we excluded patients with an anidentified cause and bilateral cases and investigated only idiopathic cases. The patients in 5 groups were examined in accordance with guidelines of the American Speech and Hearing Association. Patients were categorized in pursuance of average pure tone thresholds at 500, 1000, 2000 and 4000 Hz. It was evaluated as mild (26-40 dB), moderate (41-55 dB), moderate-severe (56-70 dB), severe (71-90 dB) and deep or total (≥91 dB) hearing loss. The ethics council of university approved this study on 26/10/2017 with decision no: 2017/8.

Treatment Group: Patients were categorized in two groups considering treatment protocol received: early HBO (n = 88) and late HBO (n = 115) groups. All 203 patients were treated according to the protocol for ISSNHL, including administration of oral steroids and oral corticosteroids (oral prednisolone - 2 mg/kg/day for ten days). First 3 days after the high dose, the steroid dose was gradually decreased and stopped. Meanwhile, we also administered gastro protective oral lansoprazole - 30 mg/day and a salt-free diet combination.

In Hyperbaric Oxygen Therapy Center of our hospital, patients in the early HBO therapy group received HBO therapy. First administered once daily for 14 days (ISSNHL) protocol by addition of an oral steroid intake for 90 minutes at 2.5 ATA pressure 100% oxygen treated patients by inhalation (Hiperbot Model 101; Hiperbot Ltd., Istanbul, Turkey). Only other hospital in our city and other clinics outside the city do not have a Hyperbaric Oxygen Therapy Center. Hence, they treat patients according to the ISSNHL protocol with oral steroids. Patients who don't give a respond to the primary therapy are referred to our hospital.

In this study, we divided SSNHL cases into two groups. The first group of patients was given HBO therapy together with steroids in the early period. The second group was evaluated as the group referred to us for the treatment of HBO, who received steroid treatment in the another center. Patients in the late HBO therapy group received HBO therapy as a salvage therapy (Hiperbot Model 101).

Hearing Assessment: The acoustic function was determined by PTA; the mean hearing levels were pointed out as the average of hearing thresholds at 500, 1000, 2000, and 4000 Hz (4-tone average), in compliance with the guidelines of the Committee on Hearing Equilibrium of the American Academy of Otolaryngology-Head and Neck Surgery. We performed acoustic measurements pre-treatment and one month later, according to the Siegel's hearing improvement criteria. According to Siegel criteria, the hearing scores were compared pre- and after the treatment, and the patients were classified into 4 groups considering the success achieved in hearing. Complete recovery; patients with a better hearing level than 25 dB after treatment, regardless what the extent of hearing correction, partial recovery; patients with more than 15 dB hearing gain and after hearing treatment between 25-45 dB, slight improvement; patients with more than 15 dB hearing gain and hearing levels less than 45 dB after treatment, no improvement; patients with less than 15 dB hearing gain. Gender, treatment modalities, audiogram types (up sloping, down sloping, flat, and total deafness) and their relationship with prognosis were evaluated.

Statistical Analysis: The statistical significance level (α) was set to 5%; IBM SPSS Statistics for Windows, version 23, was used for all calculations. Comparisons between the early-late HBO groups were examined by using the Mann Whitney U test, Pearson χ^2 tests for categorical parameter and an independent t-test for constant data (e.g., mean). Descriptive statistics included means, standard deviations, minima, and maxima; categorical variables were expressed as numbers with percentages.

Results

Among 203 patients who enrolled in this study, it wasn't observed any significant differences in patients' median age, sex distribution, affected side, audiogram shape, and initial hearing level between the early and late HBO groups (Table 1). The mean hearing thresholds for each of the four frequencies (500, 1000, 2000, and 4000 Hz) was calculated at beginning

Table 1. Demographic characteristics of groups and Pre-treatment distribution of hearing loss and audiogram shape in Groups

	Early HBO Group	Late HBO Group	p
Sex			
Male	58 (65.9)	85 (73.9)	0.216*
Female	30 (34.1)	30 (26.1)	
Age	44.45±14.96	44.80±15.84	0.876**
Affected Side			
Right ear	45 (51.1)	66 (57.4)	0.375*
Left ear	43 (48.9)	49 (42.6)	
Audiogram Shape			
Flat	33 (37.5)	33 (28.7)	
Downsloping	24 (27.3)	36 (31.3)	0.257*
Upsloping	12 (13.6)	11 (9.6)	
Total deafness	19 (21.6)	35 (30.4)	
Degree of initial hearing loss			
Mild	16 (18.2)	10 (8.7)	
Moderate	18 (20.5)	24 (20.9)	
Moderate-severe	12 (13.6)	25 (21.7)	0.248*
Severe	13 (14.8)	19 (16.5)	
Profound or total	29 (33.0)	37 (32.2)	

p<0.05; *Pearson's Chi-squared test.; ** Independent Samples T Test

Table 2. İnitial hearing gain values at each four frequencies in Groups

	Early HBO Group	Late HBO Group	p*
500 Hz % ± SD	71.19±32.85	71.56±31.89	0.905
1000 Hz % ± SD	71.42±34.71	75.39±31.65	0.358
2000 Hz % ± SD	72.84±34.10	75.78±31.98	0.511
4000 Hz % ± SD	77.39±32.39	84.87±28.93	0.105

p<0.05; * Mann Whitney U Test. SD standard deviation

and end of two therapy methods. No important differences were observed between initial thresholds at all frequencies in these two groups ($P > 0.05$, Mann–Whitney *U*-test; Table 2). Furthermore, no statistically important difference in PTA values was observed by comparing the pretreatment phase between the two groups.

An assessment based on the criteria of Siegel according to their recovery levels revealed that the early HBO group exhibited complete, partial, weak, and no recovery in 21 (23.9%), 15 (17.0%), 17 (19.3%), and 35 (39.8%) patients, respectively. In contrast, the late HBO group demonstrated complete, partial, weak, and no recovery in 5 (4.3%), 9 (7.8%), 15 (13.0%), and 86 (74.8%) patients, respectively. In addition, the early HBO group demonstrated a substantially higher response rate to treatment than the late HBO group ($P < 0.05$; Table 3).

Regarding treatment response rates, 53 (60.2%) and 29 (25.2%) patients in early-/late HBO groups, respectively, responded to treatment. Among the entire patient groups, the response rate was 40.4%. In addition, the early HBO group revealed a substantially higher response rate to treatment than the late HBO group ($P < 0.05$; Table 4). The audiogram curve was flat in 41 (62.1%), down sloping 37 (61.7%), up sloping in 12 (52.2%), and total deafness in 31 (57.4%) patients. No substantial difference was observed in giving a response to treatment according to the types of audiograms ($P > 0.05$), and there wasn't any substantial difference in giving a response to treatment with respect to degree of initial hearing loss ($P > 0.05$; Table 5).

Furthermore, 69.2% and 26.3% of patients who suffer from severe hearing loss in early and late HBO groups, respectively, responded to the treatment. Moreover, 62.1% and 35.1% of patients who suffer

Table 3. The groups' response rates to treatment according to siegel's criteria

	Complete recovery	Partial recovery	Weak recovery	No recovery	Total
Early HBO Group	21 (%23.9)	15 (%17.0)	17 (%19.3)	35 (%39.8)	88
Late HBO Group	5 (%4.3)	9 (%7.8)	15 (%13.0)	86 (%74.8)	115

Table 4. The groups' response to the treatment

	No Response to treatment	Response to treatment	Total
Early HBO Group	35 (%39.8)	53 (%60.2)	88
Late HBO Group	86 (%74.8)	29 (%25.2)	115
Total	121 (%59.6)	82 (%40.4)	203

Table 5. Response to the treatment in patients according to initial hearing loss

	No Response to treatment	Response to treatment	p
Degree of initial hearing loss			
Mild	14 (53.8)	12 (46.2)	0.336*
Moderate	30 (71.4)	12 (28.6)	
Moderate-Severe	24 (64.9)	13 (35.1)	
Severe	18 (56.3)	14 (43.8)	
Profound-or Total	35 (53.0)	31 (47.0)	

$p<0.05$; * Pearson's Chi-squared test

from excessive hearing loss in early - late HBO groups, respectively, responded to the treatment. With respect to patients with severe and excessive use of HBO hearing loss only, we observed statistically an important divergence in giving a response to treatment between the early and late HBO groups ($P < 0.05$; Table 6).

Discussion

During many years, SSNHL remained a contradictive disease in various aspects, including etiology and treatment, also continues to remain debatable even at the present. The level of hearing loss is considered as essential prognostic factor in SSNHL. Filippo et al. (10) reported that a preliminary loss of hearing ≤45 dB yielded a satisfactory prognosis. In contrast, if there is a severer initial hearing loss, the prognosis will be worse. In this study, HBO therapy combined with steroids provided more advantage for patients with SSNHL preliminary presenting with severe and profound hearing loss.

Spontaneous remission of hearing has been identified in the first few weeks from the onset of SSNHL; however, hearing recovery rate after the failure of preliminary therapy remains highly low. At present, steroids are the most commonly used drugs for SSNHL owing to their anti-allergic, anti-inflammatory, and immunosuppressive effects. Moskovitz et al. (11) reported 89% recovery ratio in corticosteroid-administered group and 44% in control group. Nevertheless, additional therapies are required for patients who do not adequately benefit from preliminary systemic steroid treatment.

To date, several studies proved the efficacy of HBO therapy (12, 13) Cvorovic et al. (12) reported that HBO therapies and intratympanic steroids were efficacious in patients who don't give a respond to steroid therapy. Moreover, Yang et al. (13) reported that the combined intratympanic and HBO therapy enabled to better hearing gains as salvage treatment in patients who suffer from ISSNHL after the failed systemic therapy. In the treatment of ISSNHL, extensive research has been conducted on HBO therapy with different timing and durations; however, no consensus has been attained on the routine clinical application and effectiveness with these patients (14). During the last four decades, investigators using HBO therapy as a co-treatment with other medications or as salvage therapy reported different results. However, systemic corticosteroids seemed to be more effective than HBO as the primary treatment, with no combination with other drugs. Hence, the initial treatment option for SSNHL is generally based on systemic corticosteroids. Alimoglu et al. (15) compared oral steroids, HBO + oral steroid, intratympanic steroid, and HBO-alone therapies for their effectiveness in treating ISSNHL and reported

Table 6. Response to the treatment in patients with severe and profound hearing loss

	Group	No Response to treatment	Response to treatment	p
Severe hearing loss	Early HBO	4 (30.8)	9 (69.2)	0.016*
	Late HBO	14 (73.7)	5 (26.3)	
Profound hearing loss	Early HBO	11 (37.9)	18 (62.1)	0.030*
	Late HBO	24 (64.9)	13 (35.1)	

p<0.05; * Pearson's Chi-squared test

higher success rate in oral steroid + HBO group (86.8%), followed by the oral steroid (63%), intratympanic steroid (46.5%), and HBO (43.8%) groups.

Horn et al. (14) performed HBO therapy as the second treatment option for patients who suffer from ISSNHL and didn't give a respond to steroid and antiviral treatment; however, their trial didn't involve in control subjects. Lamm et al. (6) reported a meta-analysis of HBO therapy as salvage therapy and informed a hearing gain (>10 dB) in 86% of patients. HBO therapy is used as preliminary and salvage therapy. The combination of HBO and steroid therapy compared with steroid therapy alone significantly improved hearing outcome. In retrospective chart review of Liu et al. (16), 465 patients with ISSNHL were divided into three different treatment groups: systemic steroid, steroid+dextran, and steroid + dextran + HBO therapy group. The results indicated that patients in the latter group with the initial profound hearing loss (≥91 dB) exhibited better recovery rates than the systemic steroid and steroid + dextran groups ($P < 0.05$).

Topuz et al. (17) added HBO therapy to the other treating in two weeks after the symptoms had seen, and they realized important positive effect of HBO therapy on hearing loss >61 dB at frequencies of 250, 500, 1000, and 4000 Hz in 51 patients and reported HBO therapy as more effective for severer hearing loss. A study found that HBO therapy had a substantial extra effect in combination with a systemic steroid therapy in 43 patients, in comparison with 51 patients treated solely with steroids (18). In patients with preliminary hearing levels of >80 dB, the hearing recovery ratio was substantially higher in the HBO group than in the steroid group. In patients with initial hearing levels of <80 dB, the hearing improvement rate was substantially higher in the HBO group than in the steroid group. The study suggests that patients with profound deafness, treated with HBO and IV therapy, had a better remission ratio compared to those treated with IT steroid and HBO therapy (18). Overall, these findings suggested that HBO plays an important role in treating patients who suffer from ISSNHL with preliminary severe and profound hearing impairments.

In one study (19), patients were distinguished in three groups according to the duration of HBO therapy. HBO treatment was initiated for the first group A within the first 7 days, HBO treatment was started for the second group B within 8-14 days, HBO treatment was started for the third group C between 15-28 days. The mean hearing gains were reported for group A, B, C, were 24, 23, 5 dB. The lowest hearing gain was seen in group C, and the hearing gain in this group was importantly less than in the other two groups.

In this study, recovery ratios were significantly higher in group that HBO therapy was initiated with oral steroid therapy synchronously. It was observed that starting HBO therapy as the first-line therapy with an oral steroid for patients with ISSNHL is substantially more useful than starting it immediately afterwards the failure of the initial oral steroid treatment.

In addition to the steroids, HBO treatment is a potent therapy method for ISSNHL. In this study, healing rates were found better in the groups that started HBO treatment together with steroids in the first 14 days of treatment period than the groups that started HBO treatment after the failure of the first oral steroid treatment. Therefore, beginning HBO treatment at an early phase of the disease enhances the treatment success. It was inferred that combined therapy is more efficacy, especially, in deep hearing loss.

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