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Clinical Research

ENT Updates 2017;7(3):120–125
doi:10.2399/jmu.2017003002

# Therapeutic efficacy of salvage hyperbaric oxygen therapy in sudden sensorineural hearing loss after failure of steroids

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## Abstract

**Objective:** The aim of this study was to evaluate the efficacy of hyperbaric oxygen (HBO) therapy as salvage therapy in patients with idiopathic sudden sensorineural hearing loss (ISSNHL) after failure of systemic therapy.

**Methods:** Forty-eight consecutive patients with refractory ISSNHL were enrolled retrospectively. All patients were given systemic steroid therapy by tapered doses. In addition, forty-one patients received intratympanic dexamethasone injection. Hearing outcomes were determined by recovery rate according to Siegel's criteria and hearing gains in pure-tone average (PTA) measured by audiometry before and after HBO therapy. The effects of prognostic factors on hearing recovery were also evaluated.

**Results:** Thirteen (27%) patients responded to HBO therapy. The remaining 35 (73%) patients did not show any improvement. After HBO therapy, significant improvement was found in mean hearing thresholds at all frequencies. Only the level of initial PTA level and gender were significantly associated with recovery. Patients with severe hearing loss (≥70 dB) had significantly better results.

**Conclusion:** Salvage HBO therapy may be beneficial in patients with ISSNHL who failed to recover by primary combined steroid therapy. Further hearing recovery with salvage HBO therapy can be expected, particularly in patients with PTA greater than 70 dB.

**Keywords:** Hyperbaric oxygen therapy, idiopathic sensorineural hearing loss, salvage therapy.

## *Özet:* Steroidlerin başarısız kalmasından sonraki ani sensörinöral işitme kaybında hiperbarik oksijen kurtarma tedavisinin terapötik etkinliği

**Amaç:** Bu çalışmanın amacı sistemik tedavi başarısızlığından sonra ani idiyopatik sensörinöral işitme kaybı (ISSNHL) olan hastalarda kurtarma tedavisi olarak hiperbarik oksijen (HBO) tedavisinin etkinliğini değerlendirmekti.

**Yöntem:** Dirençli ISSNHL'li 48 ardışık hasta retrospektif çalışmaya dahil edilmiştir. Hastaların hepsine giderek azalan dozlarda sistemik steroid tedavisi, 41 hastaya intratimpanik deksametazon enjeksiyonu verilmiştir. Siegel kriterlerine göre işitme sonuçları iyileşme oranına ve HBO tedavisi öncesi ve sonrasında odyometriyle ölçülen saf ton ortalamasına (PTA) göre işitme kazançları belirlenmiştir. Prognostik faktörlerin işitme duyusundaki iyileşme üzerine etkisi de değerlendirilmiştir.

**Bulgular:** On üç (%27) hasta HBO tedavisine yanıt vermiştir. Geri kalan 35 (%73) hasta herhangi bir iyileşme göstermemiştir. HBO tedavisinden sonra her frekanstaki ortalama işitme eşiğinde anlamlı iyileşme saptanmıştır. Yalnızca başlangıçtaki PTA düzeyi ve cinsiyet iyileşme ile anlamlı derecede iyileşmişti. Ağır işitme kaybı (≥70 dM) olan hastalarda anlamlı derecede daha iyi sonuçlar elde edilmişti.

**Sonuç:** Birincil kombine steroid tedavisinin başarısız olduğu ISSNHL hastalarında kurtarma HBO tedavisi yararlı olabilir. Özellikle PTA'sı 70 dB'den daha yüksek olan hastalarda kurtarma HBO tedavisinin işitme duyusunda daha fazla iyileşme sağlaması beklenebilir.

**Anahtar sözcükler:** İdiyopatik sensörinöral işitme kaybı, hiperbarik oksijen tedavisi, kurtarma tedavisi.

Idiopathic sensorineural hearing loss (ISSNHL) is described as an instant hearing loss of ≥30 dB in at least three consecutive frequencies in the standard pure tone audiogram occurring within 3 days. Sudden sensorineural hearing loss affects 5 to 20 per 100,000 cases.[1] Various conditions including viral infection of the labyrinthine membrane rup-

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**Received:** August 10, 2017; **Accepted:** September 17, 2017

Online available at:
www.entupdates.org
doi:10.2399/jmu.2017003002
QR code:

ture, vascular insult and autoimmune inner ear disease have been proposed to be potential causal factors. The spontaneous recovery in untreated patients characteristically arises within two weeks in 45% to 65% of cases.[2]

Even though spontaneous recovery might develop in some cases, numerous therapeutic regimens including corticosteroids, vasodilators, antiviral drugs, plasma expanders, carbogen and hyperbaric oxygen have been used due to the multifactorial etiopathology of ISSNHL. Among them, systemic steroids are widely used as a standard therapy.[3] However, no matter which procedure is chosen, the hearing outcome is limited. Approximately half of the patients have a poor response to oral or intravenous steroid therapy, and only 61% achieve complete recovery.[4] Therefore, salvage therapy has been common recently for these cases who are refractory to steroid therapy. A current clinical guideline has recommended the use of intratympanic steroid (ITS) when cases have partial recovery after failure of initial treatment.[5] Besides, ITS can be used as combination therapy (ITS+ systemic steroid tapering) for initial management. Recently, data from three randomized controlled studies showed the benefit of combination therapy, especially in patients with mild-to-severe hearing loss.[6–8] In our institution, we have been preferring combination therapy as the initial management for ISSNHL and HBO therapy as salvage or adjuvant therapy after failure of combination therapy since 2013.

Hyperbaric oxygen therapy is used as primary or salvage therapy for ISSNHL. However, the efficacy of salvage HBO therapy is still unclear and varies among studies. The purpose of this study was to determine whether HBO therapy is beneficial as a salvage therapy for ISSNHL after failure of initial combination steroid therapy or not.

## Materials and Methods

### Patients

The medical records of patients who were treated with salvage HBO therapy for ISSNHL after failure of combination therapy between June 2013 and June 2017 in a tertiary care center were reviewed retrospectively. The Institutional Review Board approved this study (23-February 05, 2015). A total of 48 patients who met the following criteria were included: (1) unilateral ISSNHL which was defined as a hearing loss of ≥30 dB in at least 3 contiguous frequencies over a period of ≤3 days; (2) the cause of hearing loss was unknown; (3) time from the onset of hearing loss to the treatment ≤14 days; (4) no fluctuation in hearing loss; (5) no history of ear disease in the affected ear; (6) received salvage HBO therapy. Patients who did not complete the full course HBO therapy were excluded from the study.

### Treatment characteristics

All the patients were hospitalized and treated with a 14-day course of oral steroid (1 mg/kg of oral methylprednisolone and 10 mg tapering for 3 days). Patients were also given proton pump inhibitors for gastrointestinal protection. ITA was also applied during this 14 day course of oral steroid as adjunctive therapy (administration of 0.4 mL of 62.5 mg/mL methylprednisolone once every three days). Patients were referred to HBO therapy after initial therapy if they had failed primary therapy or showed slight recovery.

HBO therapy was performed in a hyperbaric chamber where they breathed 100% oxygen at 2.5 atmospheres pressure for 60 minutes once daily (a total of 20 sessions).

### Evaluation criteria

All patients underwent audiometry just before and 1 month after the HBO therapy. Hearing thresholds at 250, 500, 1000, 2000, 4000 and 8000 Hz were noted. Pure tone average (PTA) calculated as an average of the threshold was measured at 0.5, 1, 2 and 4 kHz.

The hearing recovery was classified according to Siegel's criteria into four grades (complete, partial, slight recovery and no improvement) as follows:

- Complete recovery: final threshold <25 dB
- Partial improvement: gain >15 dB with final hearing threshold of 25–45 dB
- Slight improvement: gain >15 dB with final hearing threshold of ≥45 dB
- No improvement: gain<15 dB with final hearing threshold of >75 dB

### Statistical analysis

All continuous variables were expressed as mean±standard deviation, and categorical variables were expressed as percentage. The data normality test to evaluate the distribution of variables was done with the Kolmogorov-Smirnov test. Paired t test was used for continuous variables with normal distribution, and Mann-Whitney U test was used for continuous variables without normal distribution. The relationship between independent variables (age, gender, initial PTA, PTA before HBO, presence of vertigo, tinnitus and comorbid disease, and neutrophil/lymphocyte ratio) and the clinical outcome after HBO therapy were assessed using chi-square, Fisher's exact and Mann-Whitney U tests. $p<0.05$ value was accepted statistically significant level. For statistical calculations, SPSS statistical software (SPSS for Windows, version 18.0; SPSS Inc., Chicago, IL, USA) was used.

## Results

### Clinical characteristics

A total of 48 patients who completed the full 20 sessions of HBO therapy were included. The patients included 28 males and 20 females with a mean age of 46 (range: 21 to 70) years. The mean days from onset to treatment was 5.1±0.6 (range: 1 to 15 days). Demographic, clinical, and audiological features of the patients including age, gender, initial PTA, audiogram type, presence of vertigo and tinnitus, previous treatment and neutrophil/lymphocyte ratio are presented in Table 1.

**Table 1.** Demographic, clinical and audiological characteristics of the patients.

| Characteristics | n (%) | p-value |
|---|---|---|
| Age (years) | | 1.000* |
| <60 | 43 (90) | |
| ≥60 | 5 (10) | |
| Gender | | 0.0 18† |
| Male | 28 (58) | |
| Female | 20 (42) | |
| Initial PTA level | | 0.03† |
| <70 | 16 (33) | |
| ≥70 | 32 (67) | |
| Days from onset to treatment | | 0.702* |
| <7 | 37 (77) | |
| ≥7 | 11 (23) | |
| Disease side | | |
| Right | 18 (38) | |
| Left | 30 (62) | |
| Audiogram type | | 0.162† |
| Upsloping, low frequency | 9 (19) | |
| Flat | 16 (33) | |
| Downsloping, high frequency | 11 (23) | |
| Total, profound | 12 (25) | |
| Presence of vertigo | | 0.923† |
| No | 29 (60) | |
| Yes | 19 (40) | |
| Presence of tinnitus | | 0.297† |
| No | 20 (42) | |
| Yes | 28 (58) | |
| Presence of comorbid disease | | 0.190* |
| No | 43 (90) | |
| Yes | 5 (10) | |
| Neutrophil/lymphocyte ratio | NA | 0.270‡ |
| Response to HBO therapy | | |
| No | 35 (73) | NA |
| Yes | 13 (27) | |
| Slight recovery | 7 (15) | |
| Partial recovery | 4 (8) | |
| Complete recovery | 2 (4) | |

*Chi-square test; †Fisher-Exact test; ‡Mann-Whitney U test, Fisher's exact test. **HBO:** hyperbaric oxygen; **NA:** not available; **PTA:** pure tone average.

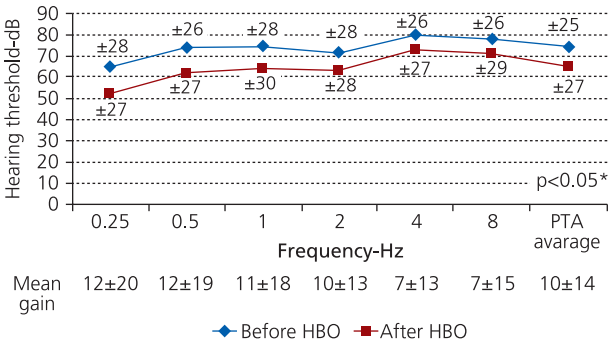


**Fig. 1.** Initial and final hearing thresholds (±SD values) and mean hearing gains (±SD values) at six frequencies and pure tone average. *Paired t-test.

### Hearing improvement

Thirteen (27%) patients responded to HBO therapy. The remaining 35 (73%) patients did not show any improvement. Two patients (%4) achieved complete recovery with mean hearing gains of 24 dB and 45 dB, respectively. Four patients (8%) achieved partial recovery with mean hearing gains of 23 dB, 26 dB, 45 dB, and 50 dB respectively. Seven patients (15%) achieved slight recovery with mean hearing gains of 15, 25, 19, 28, 28, 29, and 31 dB, respectively.

After HBO therapy, significant improvement was found in mean hearing thresholds at all frequencies. Mean hearing levels before and after HBO therapy are shown in Fig. 1.

Hearing improvement was independent of age, days from onset to treatment, audiogram type, neutrophil/lymphocyte ratio, and presence of vertigo, tinnitus and comorbid disease. Only the initial PTA level and gender were significantly associated with recovery. We analyzed the hearing improvement in patients according to the level of initial PTA. Patients were divided in those with severe hearing loss (≥70 dB) and those with moderate hearing loss (<70 dB). Patients with ≥70 dB initial level of PTA showed statistically significant hearing improvement after HBO therapy while patients with <70 dB initial level of PTA did not have any improvement (p=0.022; Tables 2 and 3). Furthermore, there

**Table 2.** Hearing recovery according to the initial PTA levels.

| Initial PTA levels (dB) | n | Hearing improvement after HBO | | p-value |
|---|---|---|---|---|
| | | No | Yes | |
| <70 | 16 | 15 (43%) | 1 (8%) | 0.022 |
| ≥70 | 32 | 20 (57%) | 12 (92%) | |

**dB:** decibel; **HBO:** hyperbaric oxygen; **PTA:** pure tone average.

**Table 3.** Hearing recovery according to initial PTA levels.

| Initial PTA levels (dB) | n | PTA at 500, 1000, 2000, and 4000 Hz | | Mean hearing gain (db) | 95% CI | p-value |
|---|---|---|---|---|---|---|
| | | PTA before HBO | PTA after HBO | | | |
| <70 | 16 | 50.1±13.9 | 45.8±18.6 | 4.3±8.8 | 0.4–9.0 | 0.07 |
| ≥70 | 32 | 88.6±19.6 | 75.7±25.3 | 12.9±16.0 | 7.1–18.7 | 0.00* |

**dB:** decibel; **HBO:** hyperbaric oxygen; **PTA:** pure tone average.

is a linear-by-linear association with initial level of PTA and hearing recovery (p=0.027).

## Discussion

In patients with ISSNHL who failed to recover after steroid therapy, both patient and clinician concern about what can be done else. The most commonly used salvage therapies are ITS and HBO therapy if they are not administered as primary treatment. ITS or HBO therapy applied either as salvage or adjuvant therapy for ISSNHL has shown positive results in terms of hearing improvements.[9] But there is still ongoing controversy about which salvage therapy is better. Furthermore, to the best of our knowledge, there is very limited data regarding the efficacy of HBO therapy following combined steroid (systemic+ITS) treatment.[10] In our study, we found that the addition of HBO therapy after failure of combined steroid treatment led to statistically significant hearing improvement in patients with severe (≥70 dB) hearing loss. HBO therapy showed significant improvement in mean hearing thresholds at all frequencies. The overall recovery rate, including complete recovery, partial recovery and slight recovery was 27%. But complete recovery is very rare (4%).

Perilymphatic oxygen tension decreases significantly in patients with ISSNHL. HBO therapy increase oxygen tension in blood and perilymphatic fluid.[11] A recent Cochrane review indicated a significantly greater chance of a 25% increase in the average PTA level in patients receiving HBO therapy.[12] Although prospective clinical trials of salvage HBO therapy with a control group are limited, result of these studies showed some benefits in hearing improvement.[10,13,14] The results of salvage HBO therapy in previous studies are demonstrated in Table 4.[9,14–18] To date, no reports have been published about the hearing outcomes of salvage HBO therapy after combined steroid treatment. The results of this study indicate that there is still something to do after combined steroid treatment in ISSNHL.

HBO therapy is used either as primary treatment or as salvage therapy in the management of ISSNHL. There is still no universally accepted approach. Similarly, ITS is performed for ISSNHL as salvage therapy or as primary therapy. Although the efficacy of steroids in ISSNHL is still conflicting irrespective of the delivery method, recent previous studies found that combined steroid treatment (systemic steroid+ITS) provides better hearing recovery than systemic steroid alone.[6,7] Suzuki et al. reported that systemic plus intratympanic steroid administration is more effective than systemic steroid plus HBO therapy.[19] It is believed that the diffusion of higher steroid concentration

**Table 4.** Comparison of hearing gains following salvage HBO therapy in previous studies.

| References | Design | n | Previous therapy | PTA gain in salvage group | PTA gain in control group | p-value |
|---|---|---|---|---|---|---|
| Desloovere et al., 2006 | RS | 56 | Various agents+ steroid | 19.7±15 | 2.6±15 | <0.007 |
| Ohno et al., 2010 | RS | 48 | Conventional treatment | 5.2 | 2.0 | 0.09 |
| Körpınar Ş et al., 2011 | RS | 80 | Various agents | 29.5±27.6 | NA | <0.01 |
| Pezzoli M et al., 2015 | RS | 23 | IV steroid | 15.6±15.3 | 5.0±11.4 | 0.013 |
| Alimoğlu Y et al., 2016 | RS | 36 | Oral steroid | 10.5±13.5 | NA | 0.00 |
| Hosokawa S et al., 2017 | RS | 167 | IV steroid | 46%* | 32.5%* | 0.02 |
| Current study | RS | 48 | IV steroid+ITS | 10±14 | NA | 0.00 |

**ITS:** intratympanic steroid; **NA:** not available **PTA:** pure tone average; **RS:** retrospective. *recovery rate.

into cochlear fluids reduces inflammation in the inner ear. Therefore, HBO and ITS may have synergistic role in decreasing edema in the cochlea. In the current study, salvage HBO therapy following systemic plus intratympanic steroid therapy provided additional improvement in patients with severe hearing loss.

Patient age, audiogram type, presence of vertigo and comorbid disease did not affect hearing recovery rates. However, interestingly, gender differences occurred in our study. Female patients showed better recovery rates than males. There is no supporting data in the literature for this condition, but it may be explained by the fact that there are differences in oxygen, nitrogen and carbon dioxide rates of loading and tissue gas tensions between males and females.[20]

Prior reports have revealed the advantage of HBO treatment just among the cases with profound hearing loss (>60, >80 or >90).[5,13] Similarly, we found that only patients with severe hearing loss (cut-off level of initial PTA was at 70 dB) had significant hearing improvement after HBO therapy. Previous studies on salvage HBO therapy reported mostly mean gains of hearing. However, although the improvement in terms of PTA is statistically significant, categorical recovery indicating the clinically improvement is important in these patients when interpreting the results. In our study, overall recovery rate was 27% (4% complete, 7% partial and 15% slight recovery, respectively).

The main limitation of our study is the relatively small sample size and retrospective design of the study without control group which is subject to the omissions and inaccuracies in the medical records. This study represents a single institutional experience. Nevertheless, although the results of our study have to be interpreted cautiously in the light of these preservations, we believe that this preliminary study presents an important data that may be used to design a larger prospective trial.

## Conclusion

According to results of our study, salvage HBO therapy may be beneficial in patients with ISSNHL who failed to recover by primary combined steroid therapy. Further hearing recovery with salvage HBO therapy can be expected, particularly in patients with PTA greater than 70 dB.

**Conflict of Interest:** No conflicts declared.

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*Please cite this article as:* İmre A, Aladağ İ, Pınar E, Aslan H, Duran R, Yazır M. Therapeutic efficacy of salvage hyperbaric oxygen therapy in sudden sensorineural hearing loss after failure of steroids. ENT Updates 2017;7(3):120–125.