Int J Clin Exp Med 2015;8(6):9876-9882
www.ijcem.com /ISSN:1940-5901/IJCEM0008475

Original Article

Comparison of simultaneous systemic steroid and hyperbaric oxygen treatment versus only steroid in idiopathic sudden sensorineural hearing loss

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Received March 26, 2015; Accepted June 4, 2015; Epub June 15, 2015; Published June 30, 2015

Abstract: A retrospective chart review to assess the effectiveness of hyperbaric oxygen treatment in sudden sensorineural hearing loss. 44 patients aged between 17-67 years diagnosed with idiopathic sensorineural hearing loss less than 30 days were admitted to our clinic Patients were treated with systemic steroid alone or systemic steroid plus hyperbaric oxygen therapy. In the comparison of two groups, there was no statistically significant difference of audiometric evaluation (P>0.0028) found in hearing improvement for each frequency on 5th day of the treatment and post treatment. Age (≤45 and >45) and initial hearing level (≤60 dB. And >60 dB.) does not seem to be an influential factor according to the results of the study (P>0.0007). The present study did not show more superior healing effect of hyperbaric oxygen therapy added to systemic steroid therapy than steroid infusion alone. The results are consistent with those of some papers. However there are also conflicting data that support significant effect of hyperbaric oxygen therapy. Routine administration of this therapy seems to be unnecessary in view of these results.

Keywords: Hearing loss, treatment, hyperbaric oxygen

Introduction

The Idiopathic sudden sensorineural hearing loss (ISSNHL) is a loss that is greater than 30 dB in three consecutive pure-tone frequencies and occurs within 3 days and early treatment as soon as possible is warranted. The treatment modalities are dependent upon possible etiologic factors such as viral infections, vascular distruption, labyrinthine membrane rupture and autoimmune inner ear disease [1].

In the treatment of ISSNHL, most popular medication is either systemic or intratympanic steroid administration [2]. Also vasodilators, plasma volume expanders, antiviral agents, vitamins and antioxidants are used as co-treatment regimens [3-5]. However there is no strong evidence that either of these have a stronger effect on outcome.

Hyperbaric oxygen therapy (HBOT) was first employed for treatment of decompression sickness in 1873. HBOT has been used for its possible benefit in several diseases such as systemic and localized vascular disorders during last 50 years [6-8]. In otolaryngology, HBOT has various clinical applications and since 1970, sudden sensorineural hearing loss (SSHL) has been regarded as one of these indications [9-12].

HBOT for sudden sensorineural hearing loss is still examined for its efficacy and timing. In this study our aim is to compare the effectiveness of HBOT combined with steroid in early phase of the idiopatic SSNHL and to find out the characteristics of most treatable patient group.

Material and methods

Study design

The charts of forty-four patients (30 male, 14 female) with idiopatic sudden sensorineural hearing loss aged between 17 and 67 years,

Table 1. Patient demographics between the groups

Variables	SS+HBOT (n=21)	SS (n=23)	*p*-value
Age	43.1±14.8	49.4±12.6	0.139
Sex			0.133
Male	12 (57.1%)	18 (78.3%)	
Female	9 (42.9%)	5 (21.7%)	
Duration of symptoms	3 (1-10)	3 (1-21)	0.862
≤5 days	16 (76.2%)	17 (73.9%)	
>5 days	5 (23.8%)	6 (26.1%)	
Basal hearing level			0.166
<60 dB	13 (61.9%)	19 (82.6%)	
60-80 dB	4 (19%)	1 (4.3%)	
>80 dB	4 (19%)	3 (13%)	

HBOT-hyperbaric oxygen therapy SS-systemic steroids.

Table 2. Distrubituon of hearing improvement for each frequency comparing the 5 day and post treatment to initial day of the treatment

Variables	SS+HBOT (n=21)	SS (n=23)	*p*-value[a]
5 day-İDT*			
250 Hz	10 (-2.5-17.5)	10 (5-30)	0.041
500 Hz	5 (0-17.5)	20 (15-30)	0.007
1000 Hz	5 (0-15)	20 (5-30)	0.021
2000 Hz	10 (0-20)	15 (0-25)	0.166
4000 Hz	10 (0-17.5)	10 (0-15)	0.858
8000 Hz	15 (5-20)	5 (0-10)	0.059
Post treatment-İDT*			
250 Hz	10 (2.5-27.5)	25 (5-40)	0.252
500 Hz	10 (0-27.5)	30 (15-40)	0.028
1000 Hz	10 (0-32.5)	25 (5-35)	0.185
2000 Hz	10 (0-25)	15 (5-35)	0.332
4000 Hz	10 (0-22.5)	10 (0-20)	0.953
8000 Hz	10 (0-22.5)	5 (0-15)	0.381

[a]= Bonferroni adjustement with Mann Whitney U test, results P<0.003 accepted as statistically significant. *= Initial day of the teatment.

who were administered systemic steroids (SS) or systemic steroid plus hyperbaric oxygen treatment (SS + HBOT) in our clinic from June 2009 to October 2011, were reviewed retrospectively. Exclusion criteria were underlying primary etiology, severe diabetes mellitus, coronary artery disease, rhematoid arthritis, systemic lupus erythematosis, hypertension, retrocohlear pathology or fluctuating hearing loss. Patients describing hearing loss for more than 30 days and patients experiencing otitis media with effusion or any other side effects were also excluded. The patients were separated into two groups according to treatment modality. In the systemic steroid group (18 male and 5 female), 1 mg/kg/day iv methylprednisolone was administrated for 10 days, then tapering the dose 20 mg every 3 days within the following 12 days. In the systemic steroid plus HBO group, administration of methylprednisolon was the same and concurrent HBO treatment consisted of breathing 100% oxygen for 90 Minutes at a pressure of 2.5 atm in a hyperbaric chamber during 20 days. When early response was seen during the treatment period with systemic steroid + HBOT group, HBOT was no longer continued.

Audiometric evaluation

All patients had undergone audiogram tests on the first, fifth day of the treatment and post treatment. In audiograms, the mean hearing levels of 250, 500, 1000, 2000, 4000 and 8000 Hz. were calculated for each frequency. Audiograms were divided into 2 groups according to their levels of hearing loss (≤60 dB. And >60 dB).

Statistical analysis

Data analysis was performed by SPSS package program for Windows 11.5 (SPSS Inc. Chicago, IL, United States). It was investigated by Shapiro Wilk test whether continuous variables were distributed normally. Descriptive statistics for continuous variables were shown as mean ± standard deviation or median (interquartile width), and categorical variables were shown as number of cases and percentage. Significance of the difference between the groups in terms of avarages was investigated by Student's T test and significance of the difference in terms of median values was investigated by Mann Whitney U test. Pearson's chi-sguare test was used for the analyis of categorical variables. It was assesed by Wilcoxon signed rank test whether there was a statistically significant difference between groups during follow up, in terms of median

Table 3. Hearing level comparison for different age groups, between SS+ HBOT and SS during follow-up period

Age	≤45	>45	
	SS+HBOT (n=12)	SS (n=9)	SS+HBOT (n=9)
250 Hz			
*IDT**	57.5 (35-73.7)	45 (30-62.5)	40 (27.5-60)
5 day	50 (21.2-78.7)	20 (12.5-50)	40 (17.5-45)
Post treatment	32.5 (11.2-78.7)	15 (10-40)	25 (15-32.5)
500 Hz			
*IDT**	60 (38.7-83.7)	35 (17.5-52.5)	45 (27.5-55)
5 day	47.5 (20-80)	10 (5-25)	35 (17.5-55)
Post treatment	17.5 (11.2-83.7)	5 (5-20)	35 (17.5-50)
1000 Hz			
*IDT**	65 (31.2-90)	30 (20-40)	50 (22.5-57.5)
5 day	52.5 (10-85)	10 (7.5-17.5)	35 (17.5-50)
Post treatment	32.5 (10-81.2)	10 (7.5-15)	25 (12.5-50)
2000 Hz			
*IDT**	62.5 (26.2-78.7)	20 (15-55)	45 (27.5-50)
5 day	35 (15-76.2)	10 (5-15)	40 (17.5-47.5)
Post treatment	27.5 (10-77.5)	10 (5-12.5)	30 (10-45)
4000 Hz			
*IDT**	65 (41.2-83.7)	30 (12.5-52.5)	45 (25-87.5)
5 day	40 (25-68.7)	10 (7.5-45)	50 (20-65)
Post treatment	35 (20-73.7)	10 (7.5-37.5)	50 (17.5-67.5)
8000 Hz			
*IDT**	77.5 (50-90)	30 (22.5-60)	60 (50-97.5)
5 day	47.5 (23.7-81.2)	20 (12.5-50)	50 (35-87.5)
Post treatment	45 (25-76.2)	20 (12.5-50)	55 (40-90)

*= Initial day of the treatment.

hearing level. P<0.05 was considered statistically significant for the results. However in all possible multiple comparisons, the Benferroni adjustment to control Type 1 error was made.

Results

Patient demographics

There were no significant differences with regarding to patient's median age, sex distribution, duration of the symptoms and initial hearing level between HBOT and systemic steroid groups (P>0.05) (**Table 1**).

Improvement in hearing levels

Hearing improvement was evaluated on fifth day and post treatment, by comparing to the values of first day of treatment for each frequency. In systemic steroid + HBOT group significant improvement was noticed on the fifth day in 8000 Hz. and post treatment in 2000 Hz. frequencies compared to the first day (Benforrini adjustment P< 0.0014). In systemic steroid group, on both fifth day and post treatment, there was a significant improvement in all frequencies except 4000 Hz. which only improved on post treatment, compared with the hearing levels of first day (Benforrini adjustment P< 0.0014) (**Table 2**). The recovery rates for each frequencies were not significantly different betweeen two groups due to Bonferroni adjustment (P> 0.0028).

In both groups, different age of patient groups, i.e. P≤45 and >45 were compared according to the hearing variations at each frequency on fifth day and post treatment after baseline. All the subanalysis using Bonferroni adjustment showed no statistically significant difference between age groups (P>0.0007) (**Table 3**).

Table 4 demonstrates comparison of SS + HBOT and SS groups according to the baseline hearing levels (divided into <60 dB and ≥60 dB) and follow-up hearing improvement. In SS + HBOT group there were no significant difference in <60 dB and ≥60 dB initial hearing level, according to Bonferroni correction on follow-up audiometric evaluations (P>0.0007). However in SS group with <60 dB initial hearing level, at 250, 500, 1000, 2000 Hz frequencies there was a statistically significant improvement on both follow-up days (Bonferroni adjustment P<0.0007). The number of patients was not enough to make a statistical comparison for the SS group at ≥60 dB hearing level.

Patients at initial hearing levels <60 dB and ≥60 dB were compared with respect to improvement of audiometric evaluation on fifth days and post treatment in both SS + HBOT and SS groups. Due to Bonferroni adjustment, there

Tablo 4. Distribution of each frequency since initial hearing level (divided two groups as <60 dB. and ≥60 dB.) to 5 day and post treatment controls

	5. - IDT*			Post treatment - IDT*	
	SS+HBOT	SS	*p-value*[a]	SS+HBOT	SS
250 Hz					
<60 dB	10 (0-20)	25 (10-30)	0.084	20 (7.5-27.5)	30 (10-45)
≥60 dB	5 (-20-13.7)	0 (0-18.7)	0.683	7.5 (-13.7-40)	2.5 (0-16.2)
P value[b]	0.238	0.067		0.500	0.044
500 Hz					
<60 dB	15 (0-20)	25 (15-30)	0.014	15 (2.5-22.5)	30 (15-40)
≥60 dB	0 (-3.7-13.7)	7.5 (0-26.2)	0.461	7.5 (-7.5-47.5)	12.5 (0-32.5)
P value[b]	0.238	0.162		0.972	0.162
1000 Hz					
<60 dB	5 (0-20)	20 (10-30)	0.071	10 (0-32.5)	25 (10-35)
≥60 dB	2.5 (0-8.7)	12.5 (0-32.5)	0.683	10 (-3.7-47.5)	17.5 (0-38.7)
P valuei[b]	0.414	0.456		0.916	0.667
2000 Hz					
<60 dB	5 (-2.5-17.5)	15 (5-25)	0.108	10 (0-22.5)	15 (5-25)
≥60 dB	10 (2.5-23.7)	17.5 (0-38.7)	0.933	12.5 (2.5-35)	20 (0-47.5)
P valuei[b]	0.301	0.969		0.595	0.907
4000 Hz					
<60 dB	0 (0-15)	10 (0-15)	0.570	10 (-2.5-22.5)	10 (0-20)
≥60 dB	10 (10-23.7)	5 (0-25)	0.461	12.5 (1.2-22.5)	12.5 (0-25)
P value[b]	0.185	0.845		0.595	0.845
8000 Hz					
<60 dB	15 (2.5-22.5)	5 (0-15)	0.195	10 (0-17.5)	10 (0-15)
≥60 dB	10 (5-20)	0 (0-3.7)	0.073	12.5 (6.2-25)	0 (0-18.7)
P value[b]	0.860	0.097		0.414	0.505

*Initial day of treatment. [a]= Bonferroni adjustment with Mann Whitney U test, comparement between SS+HBOT and SS groups, for P<0.0014 results are accepted as statistically significant, [b]= Bonferroni adjustment, on with Mann Whitney U test, Basal hearing level group comparements, for P<0.0014 results are accepted as statistically significant.

was no significant difference observed in this sub analysis (P>0.0014).

In the evaluation of the duration of the symptoms before treatment, in SS + HBOT group, patients with hearing loss ≤5 days and >5 days were compared. No significant difference in hearing gain was found on the fifth day and post treatment audiometric evaluation compared to initial treatment in any frequencies in SS + HBOT group (Bonferroni adjustment P>0.0007). But in the SS group, in patients with hearing loss ≤5 days on the 500 Hz. Frequency, there was a significant hearing gain both on fifth day and post treatment audiometric evaluation compared to pretreatment level (Bonferroni adjustment P<0.0007) (**Table 5**). In subanalysis of total hearing improvement in patients with hearing loss ≤5 days and >5 days, there was no statistically significant difference at fifth day and post treatment controls between SS + HBOT and SS groups (Bonferroni adjustment P>0.0014).

Hearing improvement was investigated for each frequencies since the initial audiogram to fifth day and post treatment into SS + HBOT and SS groups respectively. In SS + HBOT group, no statistically significant difference was seen, due to Bonferroni adjustment, between frequencies on the fifth day and post treatment (P>0.0007). In SS group, there was significant improvement in hearing level improvement on fifth day and post treatment at frequencies of 500 Hz and 8000 Hz (P<0.0007), and only on fifth day at 1000 Hz and 8000 Hz frequencies compared to baseline levels (P<0.0007).

Table 5. Distrubition of hearing levels for each frequencies during the follow-up period

	≤5 Day	>5 Day	
	SS+HBOT (n=16)	Steroid (n=17)	SS+HBOT (n=5)
250 Hz			
0 Day	52.5 (35-70)	50 (40-67.5)	40 (27.5-65)
5 Day	45 (20-71.2)	20 (10-57.5)	25 (22.5-62.5)
Post-treatment	30 (15-56.2)	20 (10-57.5)	20 (12.5-55)
500 Hz			
0.Day	52.5 (31.2-60)	50 (32.5-67.5)[a,b]	50 (37.5-87.5)
5.Day	47.5 (16.2-63.7)	15 (5-42.5)[a]	35 (22.5-67.5)
Post-treatment	27.5 (15-62.5)	15 (5-42.5)[b]	30 (12.5-67.5)
1000 Hz			
0 Day	55 (23.7-65)	45 (25-65)	45 (27.5-92.5)
5 Day	47.5 (10-68.7)	10 (10-40)	35 (20-70)
Post-treatment	25 (10-67.5)	10 (10-40)	35 (12.5-67.5)
2000 Hz			
0 Day	47.5 (22.5-68.7)	50 (17.5-62.5)	50 (32.5-77.5)
5 Day	35 (15-63.7)	15 (7.5-27.5)	45 (20-67.5)
Post-treatment	22.5 (10-66.2)	15 (7.5-27.5)	45 (10-62.5)
4000 Hz			
0 Day	47.5 (26.2-88.7)	40 (22.5-57.5)	75 (45-77.5)
5 Day	37.5 (17.5-70)	20 (10-57.5)	50 (32.5-62.5)
Post-treatment	35 (12.5-68.7)	20 (10-55)	60 (25-72.5)
8000 Hz			
0 Day	60 (46.2-97.5)	40 (25-70)	85 (52.5-87.5)
5 Day	42.5 (23.7-85)	25 (20-67.5)	50 (42.5-85)
Post-treatment	47.5 (26.2-83.7)	25 (20-62.5)	70 (37.5-82.5)

[a]= Bonferroni adjustment with Wilcoxon rank test, comparement between the 0 and 5 days difference was statistically significant, [b]= Bonferroni adjustment with Wilcoxon rank test, between the 0 days and post- treatment difference was statistically significant (P<0.0007).

Discussion

In the treatment of ISSHL, several researches have been carried out on HBO treatment with different timing and durations but still there is no concensus on routine clinical application and effectiveness with these patients [1, 13, 14].

In 1980 Wilson et al. [15] showed the efficacy of steroids when they became the first line drugs for the treatment of ISSHL. Given etiologic factors in ISSHL such as diminished blood supply of inner ear, the investigators tried to increase oxygenation by several treatment methods including HBO [2-5]. Some experimental studies showed significant response to HBO treatment in ears with acoustic damage to inner ear cells by producing effective PO_2 in perilymph [16, 17].

During the last four decades, investigators using HBO therapy as a co-treatment with other medications or salvage therapy, found different results. Topuz et al. [9]. administrated steroid 2 mg./kg. + rheomacrodex 500 ml/d for 5 days + diazepam p.o. twice daily to one group and the same medication plus HBO therapy to other group and showed significant improvement in hearing of SSNHL when the treatment started within 2 weeks. However they concluded that HBOT was more effective at 250, 500, 1000, 2000 and 4000 Hz frequencies with pretreatment levels less than 60 dB and patient age <50 as well [9].

Dundar et al. [13] found similar results to Topuz et al. [9] regarding the hearing gain between HBOT + medical treatment versus medical treatment in patients with sudden sensorineural hearing loss. In contrast to Topuz et al. [9], in the present study there was no significant difference in patients at ages of ≤45 and >45 in hearing levels at each frequency on fifth and post-treatment days compared to baseline (P>0.0007). We didn't find a significant difference in control audiometric evaluations of patients between two groups in these age distribution (P>0.0014).

HBO treatment was also administrated as co-treatment with medical drugs in the very early stage of the disease by Domachevsky in two cases showing improved hearing levels [18].

Horn et al. [19]. and Muzzi et al. [14]. used HBO therapy mostly as a part of salvage treatment following medical therapy and found it as an effective treatment. However, Muzzi et al. concluded that the teratment was more beneficial

in older age group and in early administration of HBO therapy.

Goto et al. [20] showed 71% improvement in late onset treatment period (2-6 weeks) of seventeen patients treated with stellate ganglion blockage plus HBO and found it significantly better than medical treatment group. Results of the present study revealed that improvement of hearing levels in SS + HBO treatment were similar to that obtained with systsemic steroid per se. This finding seems to be in conflict with the study of Fujimura et al. [1]. which showed significant improvement in hearing levels, especially in the patients with severe hearing loss.

Alimoğlu et al. [21] compared oral steroid, hyperbaric oxygen + oral steroid, intratympanic steroid and hyperbaric oxygen alone therapies for their effectiveness. Higher success was obtained in oral steroid + hyperbaric oxygen group with 86.88%; followed by oral steroid group with 63%, intratympanic steroid group with 46.5%, and hyperbaric oxygen group with 43.85%.

In the retrospective chart review of Liu et al. 465, SSNHL patients were divided into 3 different treatment groups including systemic steroid + dextran, steroid-dextran and steroid + dextran + HBOT group. Results indicated that patients in the latter group with initial profound hearing loss (≥91 dB) have better recovery rates than systemic steroid and steroid + dextran group ($P<0.05$) [22].

In the literature, there are some other studies showing similar effectiveness of HBOT compared to medical treatment. Bennett at al [23] compared the effectiveness of HBOT with SSNHL and found no clinical significance between the groups [7]. These results are consistent with the findings of the present study.

HBO treatment can have side-effects, which have already been reported in the literature. Plafki et al. in their series of 782 patient, stated that 3.8% of subjects experienced barotraumatic changes and Fernau et al found otitis media with effusion in 13 of 33 patients who were treated by HBOT [24, 25]. In our series, two patients were excluded from the study due to otitis media with effusion.

In the present study, the relation between hearing recovery and age distribution of patients in SS + HBOT group was not significantly different from that in SS group as underlined in some papers [9]. Both groups seem to be successful in hearing improvement compared to pretreatment levels. Although we did not note a significant role of HBOT therapy, in the literature it seems to be a useful treatment for SSNHL but also when cost-effectivity is considered a high amount of money should be reserved for this part of treatment.

Further studies are required with larger patient series with double-blind randomization for comparing HBOT with other modalities, in especially profound hearing loss which tends to need additional treatment. It is our suggestion determination of the subgroup of patient who have the maximum gain and standardization of the timing in maximum response level in large case series should be the subject of future project on the issue.

Acknowledgements

The Authors would like to thank statistician Salih Ergöçen for technical support.

Disclosure of conflict of interest

None.

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