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Original Article* / *Çalışma - Araştırma

Efficacy of multimodality approach to sudden hearing loss

Ani işitme kaybında çoklu tedavi yaklaşımın etkinliği

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ABSTRACT

Objectives: This study aims to investigate whether addition of intratympanic steroid (ITS) to systemic steroid and hyperbaric oxygen (HBO) is effective in the treatment of sudden hearing loss (SHL).

Patients and Methods: Between January 2008 and October 2011, 58 patients diagnosed with SHL were enrolled in the study. Twenty patients (11 males, 9 females; mean age 45.3±21 years; range 24 to 66 years) who received systemic steroid and HBO composed group 1, while 38 patients (19 males, 19 females; mean age 41.6±16 years; range 25 to 61 years) who received ITS in addition to systemic steroid and HBO composed group 2.

Results: Post-treatment hearing improvement was statistically significant in both groups in terms of the mean pure tone according to the Siegel's criteria ($p<0.05$). Treatment was successful at 55% of patients in group 1 and 63% in group 2. Despite increased success rate with the addition of ITS, it did not indicate statistical significance ($p>0.05$). However, there was a strong statistically significant difference in terms of profound hearing loss over 90 dB ($p<0.05$). None of six patients (0%) with profound hearing loss in group 1 benefited treatment, while addition of ITS to the treatment yielded success in six of 12 patients with profound hearing loss (50%) in group 2 ($p<0.05$).

Conclusion: Addition of ITS to systemic steroid and HBO treatment may yield better results in patients with SHL. However, ITS injection seems beneficial for patients with profound SHL.

Keywords: Hyperbaric oxygen; intratympanic steroid; sudden sensorineural hearing loss.

ÖZ

Amaç: Bu çalışmada ani işitme kaybının (AİK) tedavisinde sistemik steroid ve hiperbarik oksijene (HBO) ilave olarak intratimpanik steroidin (ITS) etkinliği araştırıldı.

Hastalar ve Yöntemler: Ocak 2008 - Ekim 2011 tarihleri arasında AİK tanısı konulan 58 hasta çalışmaya dahil edildi. Sistemik steroid ve HBO tedavisi uygulanan 20 hasta (11 erkek, 9 kadın; ort. yaş 45.3±21 yıl; dağılım 24-66 yıl) grup 1'i oluştururken; sistemik steroid ve HBO tedavisine ek olarak ITS tedavisi uygulanan 38 hasta (19 erkek, 19 kadın; ort. yaş 41.6±16 yıl; dağılım 25-61 yıl) grup 2'yi oluşturdu.

Bulgular: Tedavi sonrası iyileşme oranları, Siegel kriterlerine göre saf ses ortalamalarında her iki grup arasında istatistiksel olarak anlamlı bulundu ($p<0.05$). Tedavi başarısı grup 1'de %55, Grup 2'de %63 idi. Başarı oranlarında ITS ilave edilmesiyle bir artış olmasına rağmen, bu istatistiksel olarak anlamlı değildi ($p>0.05$). Ancak 90 dB üzeri derin işitme kayıplarında güçlü bir istasitiksel fark vardı ($p<0.05$). Grup 1'de derin işitme kaybı olan altı hastanın hiçbiri (%0) tedaviden yarar görmezken, tedaviye ITS eklenen grup 2'de derin işitme kaybı olan 12 hastanın altısında (%50) başarı sağlandı ($p<0.05$).

Sonuç: İntratimpanik steroidin sistemik steroid ve HBO tedavisine ilavesi, AİK olan hastalarda daha iyi sonuçlar verebilir. Ancak, ITS enjeksiyonu derin AİK olan hastalar için yararlı görünmektedir.

Anahtar Sözcükler: Hiperbarik oksijen; intratimpanik steroid; ani sensörinöral işitme kaybı.

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Sudden sensorineural hearing loss (SSHL) is defined as idiopathic loss of hearing of at least 30 dB over at least three contiguous test frequencies occurring within three days. The incidence ranges from 5 to 20 per 100,000 persons per year. As understood from the definition itself, no exact distinct etiologic factor is known. Despite a vigorous work-up, 88% of the cases remain idiopathic.[1] Although there exist numerous proposed etiologic factors such as infection, autoimmune processes, vascular disturbance, toxic substances and disruption of cochlear membranes; none of these etiologic factors have exact evidence supporting its role for each patient. It is likely that SSHL is the common condition with various etiologies. Numerous proposed factors inevitably bring innumerable treatment modalities into action. There are more than 30 different treatment modalities reported in the literature up to now. Spontaneous recovery rates without any treatment were reported to be as high as 65%.[2] Oral steroid therapy is the mainstay treatment especially for moderate to severe SSHL since the report by Wilson et al.[3] In clinical practice nearly all of the patients with SSHL are given systemic steroid treatment with or without any additional treatment modality. Intratympanic steroid (ITS) injection for SSHL was first proposed by Silverstein et al.[4] in 1996. It can be used as a primary treatment method, in conjunction with systemic steroids or as a salvage treatment in the patients with refractory SSHL. This modality is gaining popularity nowadays. Hyperbaric oxygen (HBO) has been used for SSHL treatment since 1979.[5] The other commonly proposed modalities include antiviral agents, vasodilators, diuretics, vitamins, hemodilution and carbogen gas inhalation. Shotgun therapy is the combined form of multiple modalities geared toward the hypothetical etiologies given at once. Theoretically, this approach must work better than single agents due to the multifactorial nature of SSHL. This study is a trial to see whether combination of some of the commonly preferred modalities together yield better results than the traditional approach.

PATIENTS AND METHODS

This is a prospective randomized study in a tertiary referral center with the approval of the local institutional ethics committee. All volunteers were provided with information about the procedures, and written informed consent was obtained before the study. Approval from the institutional review board of our institution was obtained. Fifty-eight patients with SSHL presenting within 72 hours who had been diagnosed as idiopathic and met the inclusion criteria were included. All patients underwent magnetic resonance imaging to exclude any neoplasm. Among these, the patients with any other ear disease; previous history of hearing loss in any type, radiation, trauma, meningitis and exposure to ototoxic medications were excluded from the study. Oral steroid treatment was oral prednisone (Prednol; Mustafa Nevzat, Istanbul, Turkey) 1 mg/kg tapered over 14 days. Hyperbaric oxygen therapy was applied as 2.5 atm pressures for 90 minutes once daily for 10 days. Intratympanic steroids were started with the beginning of oral steroid and HBO treatment. The procedure was performed in supine position with the head tilted 45 degree towards the normal side under a microscope, using a 25-gauge spinal needle. Local anesthesia was achieved by lidocaine (Xylocaine; Astra AB Södertalje, Sweden) spray. One milliliter doses of 40 mg/mL of methylprednisolone (Prednol-L; Mustafa Nevzat, Istanbul, Turkey) were injected into the middle ear through the posteroinferior quadrant of the tympanic membrane. The patient was not allowed to swallow or move for 30 minutes. The procedure was applied three times, three days apart. The patients who had received oral steroids with HBO treatment were classified as group 1 (11 males, 9 females; mean age 45.3±21 years; range 24 to 66 years). The patients who had ITS injection treatment in addition to oral steroid and HBO were classified as group 2 (19 males, 19 females; mean age 41.6±16 years; range 25 to 61 years). Success of the treatment was assigned using Siegel's criteria. Successful recovery at one month after therapy was defined as complete or partial recovery. Complete recovery was defined as final hearing better than 25 dB and partial recovery as a hearing gain exceeding 15 dB and the final hearing was between 25 and 45 dB. Profound hearing loss was defined as a pure-tone average (PTA: averaged threshold at 0.5, 1, 2, 4 kHz) of greater than 90 dB.

Statistical analysis

NCSS 2007 & PASS 2008 Statistical Software (Utah, USA) program was used for all statistical

Table 1. Hearing improvement in both groups in terms of pure tone average

	Pure tone average (dB) (before treatment)	Pure tone average (dB) (after treatment)	*p*
Group 1 (Systemic steroid + HBO)	77.55	53.65	<0.05
Group 2 (Systemic steroid + HBO + ITS	75.63	51.13	<0.05

HBO: Hyperbaric oxygen; ITS: Intratympanic steroid.

analysis. Paired sample t test was used for intragroup assessment of normally distributed parameters. Yates' chi square test was used for comparison of success rates between groups. Fisher's exact test was used for comparison of success rates in patients with profound hearing loss between groups. Significance was determined to be at the confidence level of $p<0.05$.

RESULTS

The initial and post-treatment PTA were 77.55±27.52 dB and 53.65±38.53 dB respectively in group 1, 75.63±20.94 dB and 51.13±31.07 dB in group 2. The improvement of PTA after treatment was statistically significant in all groups (Table 1). There was no statistically significant difference in the level of improvement in terms of dB between groups (Table 2). Distribution of the number of patients according to the success (Siegel's criteria) of the treatment is shown in Table 3. There was 55% success in group 1 and 63% in group 2. This was not statistically significant (Table 4). With regards profound hearing loss, no success was seen in a total of six patients (0%) in group 1. Addition of ITC to the protocol yielded success in six patients (1 complete, 5 partial success) over 12 (50%) in group 2 ($p<0.05$) (Table 5).

Table 2. Comparison of improvement in pure tone average between groups

Pure tone average	Decibel	*p*
Group 1	23.9	>0.05
Group 2	24.5	

Table 3. Success rate in both groups according to Siegel's criteria

	Improvement (n)			No improvement (n)
	Complete	Partial	*Total*	
Group 1	6	5	11	9
Group 2	11	13	24	14

DISCUSSION

Treatment of SSHL is one of the most debatable issues among otolaryngologists. This ongoing debate possibly originates from the absence of a recognized definitive, specific etiologic factor. There are more than 30 different treatment modalities proposed in the literature. Some physicians prefer not to use any medication. Although recovery rates without any medication were reported to be as high as 65%,[2] there are not many studies because of ethical concerns about not using any medication. In clinical practice, it may be stated about systemic steroids that they are the most commonly used agents at SSHL treatment with or without any additional medication. Actions of steroids are attributed to its anti inflammatory action,[6] increasing cochlear blood flow,[7] preventing cochlear ischemia[8] and regulation of inner ear de novo protein synthesis.[9] Also, inner ear glucocorticoid and mineralocorticoid receptors were identified by Rarey et al.[10] So, it is possible for steroids to effect endocochlear potential by regulating electrolyte and fluid balance. Systemic steroids were proven to effective in randomized, prospective, double-blind, placebo-controlled trials.[3,11] Hyperbaric oxygen treatment is applied with the idea to attempt to increase the supply of oxygen to the inner ear and prevent damage caused from

Table 4. Comparison of success rate between groups

Improvement	n	%	*p*
Group 1	11	55	>0.05
Group 2	24	63	

Table 5. Comparison of success rate in patients with profound hearing loss between groups

	Improvement (n)			No improvement (n)	
	Complete	Partial	*Total*		*p*
Group 1	0	0	0	6	<0.05
Group 2	1	5	6	6	

ischemia.[12,13] It was reported to be effective when used as adjunctive to oral steroid while some authors declared no additional benefit.[14,15] Since the report by Silverstein et al.[4] in 1996, ITS has been increasingly used for treatment of SSHL. It was proven that application of steroids transtympanically result in higher concentrations in perilymph when compared with systemic application.[16,17] This route of application possibly reduces systemic absorption as well, sparing patients from the various hazardous side effects of steroids. Reported complications are rare. These are pain, permanent perforation, otitis media, dysgeusia, otorrhea and vertigo. It can be used as a primary, adjunctive or as a salvage treatment.[18-20] Several studies report ITS injection as an effective and safe treatment modality when used as a salvage treatment. These studies differ in their choice of type of steroid and method of application. Haynes et al.[21] emphasized better hearing with earlier injections. Battaglia et al.[22] reported better results of combination therapy of intratympanic and oral steroids than systemic steroids alone. Lautermann et al.[23] reported that the addition of ITS to basic treatment did not provide an additional benefit. Battista[24] reported its use to be effective if applied within 11 days of onset when used alone. We preferred to use it as adjunctive to oral steroids and HBO. Although the addition of ITS application to HBO and systemic steroids had provided an increase in the success rate, there was no statistically significant difference between the hearing recovery levels of the groups. The severity of hearing loss is the most important prognostic factor among several factors for the outcome.[2,3,11] Both oral steroids alone and oral steroids plus HBO treatment were definitely unsuccessful in all of the patients with profound hearing loss. However, the addition of TTS to the protocol worked well in six of twelve patients. This was statistically significant (p=0.045). Unfortunately, the sample size of the patients with profound hearing loss was not enough to establish a significant relation or to make an evidence based conclusion. When regarding worse prognosis of profound hearing loss in the literature and the failure of oral steroid treatment in patients with profound hearing loss in this study, it seems reasonable to carry out a prospective study solely in the situation of profound hearing loss with a larger sample size in order to compare the efficacy of these combined treatment modalities with systemic steroids alone. It is well known that patients with SSHL most often present first to a general practitioner or in the emergency room. In a study about treatment of SSHL by referring physicians, it was noted that 30% of general practitioners treat this disorder on their own and these physicians tend to use lower dosages and shorter courses of steroids than otolaryngologists.[25] It is wise to advise these physicians to refer at least the patients with profound hearing loss for ITS application.

Conclusion

Although the addition of ITS injection to oral steroids and HBO treatment resulted in better but not statistically significant results, patients with profound hearing loss may benefit only when these three treatment modalities are applied together.

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