The importance of the first three days and other diagnostic indicators in sudden hearing loss

Ani işitme kaybında ilk üç günün ve diğer tanı göstergelerinin önemi

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ABSTRACT

Objectives: This study aims to compare different therapy methods used for sudden sensorineural hearing losses, to determine the prognostic factors and particularly to investigate the importance of starting the therapy within the first three days of the prognosis.

Patients and Methods: Between January 1995 and December 2008, the files of 213 patients who were treated in our clinic were reviewed. A total of 155 patients who met the inclusion criteria were included in the study. The study groups were classified according to the prognostic and audiometric factors.

Results: With regard to the effectiveness of treatment options, post-treatment audiometric improvement was significantly better in the patients treated with carbogen in addition to the medical therapy compared to the other groups (p=0.018). In terms of the patient characteristics at the time of admission, having vertigo, presence of a descending type audiogram curve and severe hearing loss affected the success of treatment negatively, while mild hearing loss and presence of an ascending type audiogram curve had a positive effect. The recovery rate was higher in patients who were admitted within the first three days (p=0.005).

Conclusion: It was found that starting the therapy within the first three days and adding the carbogen to the conventional medical treatment may improve the outcome of the treatment.

Keywords: Carbogen; first three days; prognosis; sudden hearing loss.

ÖZ

Amaç: Bu çalışmada ani sensörinöral işitme kayıpları için kullanılan farklı tedavi yöntemleri karşılaştırıldı, prognostik faktörler belirlendi ve özellikle prognozun ilk üç gününde tedaviye başlamanın önemi araştırıldı.

Hastalar ve Yöntemler: Bu çalışmada Ocak 1995 - Aralık 2008 tarihleri arasında kliniğimizde tedavi edilen 213 hastanın dosyaları incelendi. Çalışma kriterlerini karşılayan toplam 155 hasta çalışmaya dahil edildi. Çalışma grupları prognostik ve odyometrik faktörlere göre sınıflandı.

Bulgular: Tedavi seçeneklerinin etkililiği ile ilgili olarak, tıbbi terapiye ek olarak karbojen ile tedavi edilen hastalarda tedavi sonrası odyometrik iyileşme diğer gruplarla karşılaştırıldığında anlamlı olarak daha iyiydi (p=0.018). Başvuru sırasında hasta özellikleri açısından baş dönmesi, odyogramda alçalan eğri ve ciddi işitme kaybı tedavinin başarısını olumsuz etkilerken, hafif işitme kaybı ve odyogramda yükselen eğrinin varlığı tedavi için olumlu bir etkiye sahiptir. İlk üç gün içinde başvuran hastalarda iyileşme oranı daha yüksekti (p=0.005).

Sonuç: Tedaviye ilk üç gün içinde başlamanın ve konvansiyonel tıbbi tedaviye karbojenin eklenmesinin tedavinin sonucunu iyileştirebileceği gözlendi.

Anahtar Sözcükler: Karbojen; ilk üç gün; prognoz; ani işitme kaybı.

Sudden hearing loss (SHL) is defined as a sensorineural hearing loss of 30 dB or over in at least three consecutive speech frequencies within a period of three days or less.[1] The incidence of SHL has been reported as approximately 5-20/100.000 per year. However, because it is improved spontaneously in most cases and these patients will never seek medical consultation, the actual incidence is likely to be higher than estimated.[2,3] Studies have reported that the disease is least in people aged 20-30 years (4.7/100.000) and most in those aged 50-60 years (15.8/100.000).[4] The SHL is unilateral in more than 90% of the patients.[5]

There are many different diseases and factors leading to SHL, most of which can be diagnosed by the history, physical examination and/or various tests. However, no cause can be identified in the majority of cases of SHL. Histopathologic examinations have identified the major causes as viral infections, vascular events, immunological reactions, and labyrinthine membrane rupture.[6-8]

Steroid therapy is one of the most widely accepted treatment protocols in idiopathic cases due to its anti-inflammatory effects.[9,10] However, the effect of medical therapy on prognosis is controversial, because up to 65% of the cases recover spontaneously.[11,12]

The present study aimed to evaluate the effect of early initiation of treatment and the effectiveness of treatment protocols directed to eliminate the etiologic factors. We also evaluated the effect of various prognostic factors on the course of the disease in order to contribute to the literature.

PATIENTS AND METHODS

In the present study, 213 patients admitted with the SHL and hospitalized in Uludag University, Faculty of Medicine, Department of Otorhinolaryngology between January 1995 and December 2008 were evaluated. We excluded a total of 41 patients in whom perilymph fistula, acoustic neuromas, hearing loss due to Meniere disease and psychotic hearing loss were identified. Also, 17 patients additional who missed audiological follow-up visits were also excluded. The remaining 155 patients fulfilling the diagnostic criteria and who had post-treatment audiometric evaluations were enrolled

in the study. The study protocol was approved by the Uludağ University Medical Faculty Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

A detailed history including the time when the complaints has began, previous upper respiratory tract infections, exposure to barotrauma or acoustic trauma, the presence of vertigo and/or tinnitus, and comorbidities was obtained in all patients admitting with SHL. The neurological examination consisted of a complete otorhinolaryngological examination, pure tone audiometric tests, tympanometry, vestibular tests and examination of the cranial nerves.

All patients were hospitalized for treatment. In addition to investigating any systemic etiologic factors, hemogram, sedimentation, peripheral blood smear, folic acid - vitamin B12 levels, blood lipid levels and thyroid function tests were studied. Auditory canal and cranial magnetic resonance imagings (MRIs) were obtained to evaluate the auditory canal, brainstem and other cranial structures.

The pure tone audiometry analyses at 500, 1000, 2000 and 4000 Hz were performed before treatment and at 5, 10 and 30 days after treatment. In addition, audiometric evaluation was performed in 37 patients at the one-year follow-up visit. Hearing loss was classified according to the pure tone average hearing thresholds at 500, 1000, 2000 and 4000 Hz as mild (20-40 dB), moderate (41-60 dB), severe (61-80 dB), profound (81-90 dB), and total hearing loss (90 dB ↑).[5,13] Auditory data were also classified according to the configuration of the audiogram into six subgroups including ascending type (hearing loss at 250-500 Hz), descending type (hearing loss at 4000-8000 Hz), flat type (hearing loss with a 10 dB or less difference between the best and worst thresholds), total and near-total (85 dB and above), cookie bite and reverse cookie bite hearing losses.[4,5,14,15] The patients were also classified according to their age as 7-40 years, 41-53 years and 54-87 years.[16]

The patients were divided into two groups by the receiver operating characteristic (ROC) analysis method as those treated within the first three days and those treated after three days. Also, considering previous studies, patients were

divided according to the timing of the initiation of the treatment into subgroups consisting of the first three days, 4-6 days, 7-15 days and after 15 days.[16]

All patients received bed rest and conventional medical therapy (CMT) including plasma expanders (dextran-40 400 mL; 3 hour infusion for 10 days), vasodilators (pentoxifylline 300 mg; 3 hour infusion in the morning-evening for 10 days), sedative agent (10 mg mianserin for 10 days), anticoagulants (100 mg acetylsalicylic acid) and vitamin complex. The patients with severe or very severe hearing loss and/or those not benefited by CMT within five days were additionally treated with systemic (oral) steroids (40 mg prednisolone or 16 mg dexamethasone in adult patients and 1 mg/kg prednisolone in pediatric patients with tapering off the dose and discontinuing the steroids on day 10). Intratympanic steroid (dexamethasone 4 mg; once a week for 3 weeks) was administered to the patients in whom no improvement was obtained with systemic steroids and who could not be treated with systemic steroid therapy due to the associated concomitant diseases. Because it was a routine practice in our clinic since 2000, all patients also received carbogen (95% oxygen + 5% carbon dioxide) inhalation for five days in addition to CMT.

The pre- and post-treatment audiograms were compared between treatment groups according to the percentage changes estimated. In addition, pre- and post-treatment audiometric pure tone threshold averages were evaluated and those with a 10 dB or less difference were classified as "no recovery," 10-30 dB difference as "slight recovery," 30 dB or greater difference as "moderate recovery," and having a post-treatment pure tone threshold average of <20 dB as "complete recovery."[13]

Of the 155 patients, although 36 (23.2%) were treated only with CMT, the other 25 patients (16.1%) received CMT + systemic steroids (CMTS), 37 patients (23.9%) received CMT + carbogen (CMTC), 34 patients (22.0%) received CMT + systemic steroid + carbogen (CMTSC), nine patients (5.8%) received CMT + systemic-intratympanic steroids + carbogen (CMTSCI) and seven patients (4.5%) received CMT + intratympanic steroids + carbogen (CMTCI). Seven additional patients (4.5%) were treated with carbogen and/or intratympanic steroids and hyperbaric oxygen.

Statistical analysis was performed using SPSS for Windows version 13.0 (SPSS Inc., Chicago, IL, USA) statistical package program. Shapiro-Wilk test was used to analyze data normality. Mann-Whitney U test was used for two-group comparison of non-Gaussian distributed variables. The relationships between the variables were examined by using Spearman correlation coefficient. Categorical data were analyzed by Pearson's chi-square test and Fisher's exact chi-square test. The cut-off day was calculated by using ROC analysis and by comparing the post-treatment improvement in hearing loss with the first day of the treatment. The level of significance was set at $p<0.05$.

RESULTS

The average time to admission was 14.3±24.4 days. Symmetrical involvement of both ears was found in seven patients (4.5%). Of the remaining patients, hearing loss was in the right ear in 64 patients (41.3%) and in the left ear in 84 patients (54.2%). Of the patients included in the study, 47 (30.3%) were smoking and nine (5.8%) were consuming alcohol. Hearing loss was classified according to the pure tone audiogram at the time of admission as mild in 41 patients (26.4%), moderate in 37 patients (23.9%), severe in 28 patients (18.1%), profound in 12 patients (7.7%) and total in 37 patients (23.9%).

According to the post-treatment average pure tone audiometric changes, it was found that 39 patients (25.2%) had complete recovery, 12 patients (7.7%) had moderate recovery and 31 patients (20%) had slight recovery. There was no recovery in 73 (47.1%) patients. Of the patients, 131 (84.5%) had tinnitus and 52 (33.5%) had vertigo. In addition, 37 patients (23.9%) described a feeling of fullness in the ear.

Receiver operating characteristic analysis showed that initiation of treatment within the first three days results in significantly better outcomes (p=0.005). In addition, patients were divided into subgroups according to the time of the initiation of treatment, in which treatment had been initiated within the first three days in 47 patients (30.3%), on day 4-6 in 20 patients (12.9%), on day 7-15 in 53 patients (34.2%) and after day 15 in 35 patients (22.6%). The subgroup

Table 1. The effect of days of initiating treatment on audiometric outcomes in patients with sudden hearing loss

Days of initiating the treatment	Group 1 First 3 days		Group 2 Day 4.-6		Group 3 Day 7.-15		Group 4 Day 16 or later	
	n	%	n	%	n	%	n	%
Pre-treatment-post-treatment percent change	47	35	20	25	53	20	35	11
P value				0.009				
					0.032			

Days of initiating the treatment	Group 1 First 3 days	Group 2 Day 4.-6	Group 3 Day 7.-15	Group 4 Day 16 or later
	Ratio	Ratio	Ratio	Ratio
Pre-treatment-post-treatment audiometric improvement	2.61	2.35	1.92	1.57
P value		0.021		
		0.001		
			0.008	

analysis showed that the earlier treatment results in significantly better outcomes (Table 1). Compared to other patients, early initiation of treatment had a significant effect on the complete recovery in hearing in patients with complete audiometric improvement (p<0.001). Patients had no systemic disease that could cause SHL.

The recovery rate was significantly higher in patients treated with medical treatment plus carbogen (40.5%) compared to those treated with other treatment modalities (20.3%) (p=0.018) (Table 2).

In our study, the audiogram configurations were analyzed and found to be ascending type in 35 cases (22.7%), descending type in 51 cases (32.9%), and flat type in 18 cases (11.6%), in cookie bite form in seven cases (4.5%) and in

reverse cookie bite form in seven cases (4.5%). On the other hand, there was a total or near-total hearing loss in 37 cases (23.9%). Following treatment, the percent change in audiogram was 40.5% in patients with a pre-treatment audiogram of ascending type with being significantly better in patients with a pre-treatment audiogram showing descending-type, flat-type, total or near-total hearing losses (Table 3).

With regard to the pre-treatment pure tone audiogram averages, total hearing loss was present in 37 cases (23.9%). The audiometric improvement was significantly different in this group of patients compared to the other groups (p=0.028), that is, complete recovery was found in only one of 37 patients (2.7%) with total hearing loss but in 38 of 118 patients (32.2%) from other groups (Table 4).

Table 2. The effect of treatment regimens on audiometric outcomes in patients with sudden hearing loss

Treatment regimen	CMTCI[1]	CMT[2]	CMTC[3]	CMTS[4]	CMTSCI[5]	CMTSC[6]	Other[7]
Number of patients	7	36	37	25	9	34	7
Audiometric complete recovery	1	6	15	6	1	9	
Other audiometric improvements	6	30	22	19	8	25	
P value	0.680	0.272	0.018	1	0.451	0.826	

[1]Conventional medical therapy (CMT) + intratympanic steroids + carbogen; [2]CMT; [3]CMT + carbogen; [4]CMT + systemic steroids; [5]CMT + systemic-intratympanic steroids + carbogen; [6]CMT + systemic steroid + carbogen; [7]Carbogen and/or intratympanic steroids and hyperbaric oxygen.

Table 3. The effect of initial pattern in audiogram on recovery in patients with sudden hearing loss

Audiogram pattern	Ascending type		Descending type		Flat type		Cookie bite		Reverse cookie bite		*Total* near-total	
	n	%	n	%	n	%	n	%	n	%	n	%
Pre-treatment-post-treatment percent change	35	40	51	16	18	0.3	7	56	7	39	37	17
P value												

0.001 (Ascending–Descending)

0.004 (Ascending–Flat)

0.001 (Ascending–Total near-total)

Audiogram pattern	Ascending type	Descending type	Flat type	Cookie bite	Reverse cookie bite	*Total* near-total
	Ratio	Ratio	Ratio	Ratio	Ratio	Ratio
Pre-treatment-post-treatment audiometric improvement	2.91	1.76	1.66	3.71	2.57	1.67
P value						

<0.001 (Ascending–Descending)

0.002 (Ascending–Flat)

<0.0001 (Ascending–Total near-total)

The mean age of the patients was 36.5±12 years in patients with complete recovery and 43.8±16.9 years in the remaining patients. In addition, the treatment outcome, namely audiometric improvement at the end of treatment, was significantly better in patients aged 7-40 years than those in other age groups (p=0.021) (Table 5). In our study, Patients age under 18 years, the data are in (Table 6).

A history of upper respiratory tract infection, gender, the side of hearing loss, pathological findings in vestibular tests, and smoking and alcohol consumption were found to have no effect on the treatment outcome. Although there was no difference in treatment outcome between the groups in terms of the presence of tinnitus and feeling of fullness in the ear, the response to therapy was significantly worse in patients with acute hearing loss associated with vertigo. In the pre-treatment evaluation, vertigo was present in 52 patients (33.5%) in whom the percent change of improvement was 15.7% in this group of patients and 27.4% in patients without vertigo (p=0.009) (Table 7).

It was found that a sample size of 155 achieves 91% power with a significance level (alpha) of 0.05.

Table 4. The effect of pre-treatment severity of hearing loss on treatment outcomes in patients with sudden hearing loss

Severity of hearing loss	Mild (20- 40 dB)	Moderate (41- 60 dB)	Severe (61- 80 dB)	Profound (81- 90 dB)	Total (90↑ dB)
Number of patients	41	37	28	12	37
Audiometric complete recovery	24	6	8	0	1
Other audiometric improvements	17	31	20	12	36

* p=0.028
** p=0.089

* According to the pre-treatment-post-treatment audiometric improvement; ** According to pre-treatment-post-treatment percent change.

Table 5. The effect of age on treatment outcomes in patients with sudden hearing loss

Age group	7-40 years			41-53 years			54-87 years		
	n	%	Ratio	n	%	Ratio	n	%	Ratio
Number of patients	73			45			37		
Pre-treatment-post-treatment percent change		29			18			18	
Pre-treatment-post-treatment audiometric improvement			2.42			1.86			1.78
Number of patients with audiometric complete recovery	27			8			4		
Number of patients with other audiometric improvements	46			37			33		

The pre-treatment-post-treatment audiometric improvement was significantly different in 7-40 years age group compared to other two age groups * (p=0.021).

DISCUSSION

Because the etiologic factors are not clear in idiopathic SHL cases, spontaneous recovery is common in patients with certain good prognostic factors, the annual incidence of the SHL is relatively low and thus the number of prospective controlled studies is limited, it is difficult to assess the treatment outcome and qualified studies on this issue are lacking.[17,18] In cases of SHL, patients are usually advised bed rest and to avoid stress, smoking, alcohol, and ototoxic drugs.[19] Cinamon et al.,[20] in their prospective double-blind study including the patients in four groups of treatment with prednisone tablet, placebo tablet, carbogen inhalation and inhalation of room air, found no difference between these treatment regimens. Carbogen is a central nervous system vasodilator and is a gas mixture of 5% carbon dioxide (CO_2) and 95% oxygen (O_2). Fisch[21] stated that carbogen will increase the perilymphatic oxygenation. The author has reported in a randomized, prospective study that carbogen inhalation results in better outcomes compared to intravenous infusion of papaverin and low molecular weight dextran and have suggested that carbogen may serve as a safe and non-invasive alternative option for SHL.

Chen et al.[22] evaluated 318 patients in their 10-year retrospective study and demonstrated the effectiveness of systemic steroid therapy when patients with low frequency hearing loss and those with an average pure tone of <60 dB were excluded from the analysis. On the other hand Ho et al.[11] administered weekly intratympanic steroids for three consecutive weeks to the 39 patients who had not recovered despite oral steroid therapy. In that study, a total of 14 patients received the standard treatment. The authors have reported a higher recovery rate in those treated with intratympanic steroids (p<0.05). In our previous study, although we found no significant difference between treatment modalities, the recovery rate was slightly higher in patients treated with medical treatment plus carbogen

Table 6. Patients under 18 years of data

Age	Days of initiating the treatment	Pre-treatment-post-treatment audiometric improvement	Treatment regimen	Severity of hearing loss	Audiogram pattern
7	Group 3	Moderate recovery	CMTSC	Total	Total, near-total
9	Group 3	Slight recovery	CMTCİ	Total	Total, near-total
13	Group 1	No recovery	CMTS	Total	Total, near-total
14	Group 3	Slight recovery	CMTSC	Severe	Ascending type
15	Group 2	Slight recovery	CMT	Moderate	Ascending type
16	Group 4	Slight recovery	CMTSC	Total	Total, near-total
16	Group 1	Complete recovery	CMTC	Mild	Ascending type

Table 7. The effect of initial tinnitus and vertigo on treatment outcome in patients with sudden hearing loss

	Tinnitus							Vertigo						
	Yes			No				Yes			No			
	n	%	Ratio	n	%	Ratio	p	n	%	Ratio	n	%	Ratio	p
Pre-treatment-post-treatment percent change		24			20		0.458		15			27		0.009
Pre-treatment-post-treatment audiometric improvement			2.12			2.00	0.664			1			2	0.026
Number of patients with audiometric complete recovery	34			5			0.783	10			29			0.311
Number of patients with other audiometric improvements	97			19				42			74			

compared to the other treatment groups.[23] The 'favorable' recovery (Sigel's type 1 and 2) rate of the carbogen group was significantly higher than that of the lipo-PGE1 group and the control group.[24] Whereas in the present study, there was a significant difference in the medical treatment plus carbogen group compared to the other groups in terms of treatment outcome. The difference found between our two studies might be due to the increased number of patients in the latter.

In patients with SHL, response to therapy has been suggested to be affected by several factors including the initial severity of hearing loss, vertigo, audiogram configuration and the time elapsed between the onset of SHL and initiation of therapy.[4,11,18,25,26] The most widely accepted concept is that the treatment outcome will be better when treatment is initiated within the first 7-10 days.[4,18] In a study including 326 patients, Huy and Sauvaget[16] found no difference in treatment outcome between day 1 and day 6 when the treatment was initiated within the first week. In our previous study of 115 patients, we compared the patients in whom treatment was initiated within the first five days and on day 6-15 and found a positive effect of early treatment on prognosis.[23] In another study, the treatment initiation in the first three days and between 4-7 days did not show any statistically significant difference, the seven days and after seven days treatment initiation was a statistically significant negative prognostic effect according to earlier treatment.[27] In a study by Atay et al.,[28] the cut-off value for the initiation of treatment was determined to be five days. When patients with unchanged hearing were compared, starting therapy in the first five days was found to have a statistically significant positive prognostic effect (p<0.05).[28] In the present study, on the other hand, we compared the patients in whom the treatment was initiated within the first three days, on day 4-6, on day 7-15 and after the day 15 in order to evaluate the effectiveness of earlier initiation of treatment. The results of the present study suggest that treatment outcome is significantly better when treatment was initiated within the first three days compared to treatments initiated onwards (Table 1).

The prognosis has been suggested to be better in SHL patients suffering from tinnitus. Anadolu et al.[29] has reported a recovery rate of 68% in patients with tinnitus. In a study including 60 patients with acute hearing loss, Danino et al.[30] achieved partial or complete recovery in 80% of the patients, and acute hearing loss presented with tinnitus in 71% of the patients. In our study, although tinnitus was present in 131 patients (84.5%), the response to treatment was not different between the patients with and without tinnitus (Table 7).

Age is another well-known prognostic factor in acute hearing loss. The prognosis is poor in patients over 50-60 years of age and in children.[4,18,31-33] In our previous study, we found no significant difference in terms of prognosis between patients aged over and below 55 years.[23] However, in the present study, the treatment outcome was significantly better in patients aged 7-40 years compared to the other age groups (Table 5).

Şanlı[34] have reported relatively lower improvement in hearing in patients with SHL associated with vertigo. However,

Fetterman et al.[33] have found no effect of vertigo on the reversal of hearing loss in patients with SHL. In the present study, the percent change of 15.7% in patients with vertigo increased to 27.4% in patients without vertigo (Table 7), suggesting that presence of vertigo is a poor prognostic factor for the treatment of SHL.

With regard to the relationship between treatment outcome and audiometric results, hearing loss at low frequencies (ascending-type) has been suggested to be a good prognostic factor.[6,14] In a retrospective study by Celik et al.,[35] the reversal of hearing loss was most in those with ascending-type pattern and least in those with hearing loss at 100 dB or over. According to audiological configuration, the distribution of subjects did not show any statistically significant difference (p=0.245).[28] In the present study, the improvement in hearing was found to be significantly better in patients with ascending-type hearing loss compared to those with descending, flat, total or near-total hearing losses (p<0.001) (Table 3). The recovery rate was 40.5% in patients with ascending type hearing loss, whereas it was 17.7% in those with total or near-total hearing losses being the worst among all the groups.

In conclusion, our study shows that the success of treatment will be reduced when initiated late and in patients who had vertigo and an audiological finding of total hearing loss. Conversely, treatment was found to be more effective in patients with a hearing loss at low frequencies (ascending-type), aged under 40 years, with mild hearing loss, without vertigo, and in whom treatment was initiated within the first three days. All these results suggest that the treatment modality as well as other associated factors may be effective on prognosis. In addition, the carbogen added to the conventional medical therapy was found to result in better outcomes and thus it should be considered to be integrated into the treatment regimen.

Declaration of conflicting interests

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