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ORIGINAL ARTICLE

Comparison of the Outcomes of Four Different Treatment Protocols in Idiopathic Sudden Hearing Loss

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OBJECTIVE: To compare effectiveness of four different treatment protocols in idiopathic sudden hearing loss (ISHL). Patients and Methods: The patients with ISHL were divided into four groups according to the treatment protocols applied; Group 1 (n=67) was treated with rheomacrodex, pentoxyphiline, heparin, papaverine, famotidine, and methylprednisolone 1 mg/kg/day iv. Group 2 (n=39), group 3 (n=19) and group 4 (n=60) were treated with acyclovir, famotidine, and methylprednisolone (1 mg/kg/day, 2 mg/kg/day and 3 mg/kg/day, respectively). The symptoms and audiologic parameters were compared between the groups.

RESULTS: The PTAs (pure tone averages), and HG (hearing gain), RHG (relative hearing gain) and RR (recovery rate) scores of the groups were not significantly different ($p>0.05$). When the commencement of treatment was <5 days; the HG in group 1 was better than group 3; the RHG in group 4 was better than group 3; and the RR in group 1 was better than group 3 ($p<0.05$). When the commencement of treatment was between 5 and 10 days, there was no significant difference between the HG, RHG and RR scores of the groups ($p>0.05$). When the commencement of treatment was >10 days, the HG, RHG and RR scores in group 3 were better than in the other groups ($p<0.05$), respectively.

CONCLUSION: Overall comparison of the treatment protocols did not reveal significant difference between the outcomes.

Idiopathic sudden hearing loss (ISHL) can affect 5 to 20 per 100.000 people [1]. Although ISHL can result from a variety of factors like viral infection, vascular problems, rupture of membranous labyrinth or autoimmune diseases, which can cause cochlear dysfunction or degeneration [2-4], a specific etiology can be found only in 10-25% of cases.[5-7]. However, viral and vascular pathologies are mostly assumed to be responsible for ISHL. [8].

Treatment of ISHL is still controversial as its pathophysiology still remains obscure. There is a consensus on the effectiveness of the corticosteroid treatment [9,10]. Several treatment protocols using different combinations of drugs like antivirals, vasodilators, plasma volume expanders, diuretics, anticoagulants, histamine analogues, intravenous contrast agents, tissue plasminogen activators, vitamins, gingko biloba extracts, local anesthetics and prostacycline, and different therapeutic options like hypervolemic hemodilution, hyperbaric oxygen and stellate ganglion blockage have been used [9,11-13]. However, no standard treatment protocol has been established yet. In this study, we aimed to compare effectiveness of different protocols in the treatment of SHL.

MATERIALS AND METHODS

Patients:

Medical records of the patients who were treated for ISHL between 1984 and 2005 were evaluated retrospectively, and 185 patients were included in the study. The inclusion criterion was the presence of at least 20 dB sensorineural hearing loss in 3 contagious frequencies over a period of < 3 days. There were 89 women (mean age 42.7 years) and 96 men (mean age 43.4 years). None of the patients had a specific etiology for SHL such as acoustic tumor, Meniere's disease, perilymphatic fistula and acoustic trauma, or a previous history of SHL, ear surgery or hearing loss.

Otolaryngologic, audiologic (pure tone and speech audiometry, tympanometry) and radiological (magnetic resonance imaging) examinations were performed. Pure tone average (PTA) was calculated at the frequencies 500, 1000, 2000 and 4000 Hz, and speech discrimination scores (SDS) were calculated as percentages.

Treatment protocols:

All patients were hospitalized at least for 10 days for medical treatment. The choice of treatment given to each subject was determined by the otolaryngologists who prefered different tratment protocols. Thus, the patients were divided into four groups according to the treatment protocol applied.

Group 1 (n=67); 10 days of treatment was made with rheomacrodex 500 cc/day iv, pentoxyphiline 1200 mg/day iv, heparin 5000 U/day iv and papaverine 120 mg/day po, and methylprednisolone, 1 mg/kg/day iv, which was tapered after 10 days.

Group 2 (n=39); treated with acyclovir 4000 mg/day po for 2 weeks, and methylprednisolone, 1 mg/kg/day, which was tapered after 10 days.

Group 3 (n=19); treated with acyclovir 4000 mg/day po for 2 weeks, and methylprednisolone, 2 mg/kg/day, which was tapered after 10 days.

Group 4 (n=60); treated with acyclovir 4000 mg/day po for 2 weeks, and methylprednisolone, 3 mg/kg/day, which was tapered after 10 days.

Evaluation of the outcome:

The classification proposed by Saeki was used for evaluation of the pretreatment audiogram types (Table-1) [7, 14]. Since the audiograms of the patients prior to the hearing loss did not exist, the hearing level of the healthy ear was considered a reference for post-treatment comparisons. All patients had normal hearing in the contralateral ear. Audiologic evaluations were performed in the first, fifth and tenth day of admission. The treatment result was expressed as hearing gain (HG), relative hearing gain (RHG) and recovery rate (RR), which were calculated as described below [15-18].

Table-1: Description of audiograms types.

Audiogram	Definition
Up-sloping	SHL tends to increase in lower frequencies Decreases towards higher frequencies (4000 - 8000 Hz) Interfrequency difference is more than 20dB
Flat	SHL affects at least consecutive 3 frequencies between 250-8000 Hz Interfrequency difference does not exceed 15dB
Down-sloping	SHL increases towards higher frequencies (4000, 8000 Hz) Decreases toward lower frequencies (250-500 Hz) Interfrequency difference is more than 20dB
Spoon	SHL is more prominent in middle frequencies

HG was defined as the difference between the initial and after treatment pure tones in the affected ear in 5 frequencies between 250-4000 Hz. In other words, HG equals hearing after treatment minus hearing before treatment.

RHG was calculated in frequencies between 250-4000 Hz according to the following formula; % (hearing after treatment minus hearing before treatment) / hearing before treatment.

RR was calculated according to the following formula; % (hearing of the affected ear after treatment minus hearing of the affected ear before treatment) / (hearing of the affected ear before treatment minus hearing of the contralateral ear before treatment) [7, 9, 10, 19].

Statistics:

One-Way ANOVA was applied to compare the parameters of the groups. Regression analysis and Pearson correlations were performed to find our correlation between the parameters within each group. Independent samples t test was used for the remaining comparisons.

RESULTS

There was no significant difference between the groups regarding age, gender, initial admission day, history of upper respiratory infection, tinnitus and vertigo (Table 2). The types of initial audiograms are shown in Table 3. The mean ages of the patients who had down-sloping, up-sloping, flat and spoon-like audiogram were 46.8±15 (18 to 72), 40±11 (11 to 65), 42.9±16 (6 to 79) and 40.8±16 (13 to 77) years, respectively (p>0.05). There was no correlation between the type of initial audiogram and HG, RHG

Table-2: Demographic and some clinical parameters of the patients

Parameter	Group 1 (n = 67)	Group 2 (n = 39)	Group 3 (n = 19)	Group 4 (n = 60)	Statistics
Gender					
No. Female (%)	32	17	7	32	p>0.05
No. Male (%)	35	22	12	28	
Age (year)					
Mean ± sd	43.5±16	40.7±15	43.9±17	44.1±15	p>0.05
Range	6 to 79	7 to 72	22 to 69	11 to 78	
Admission after onset (day)					
Mean ± sd	7.6±9	8±8	6±4	6.2±6	p>0.05
Range	1-65	1to 30	1 to 15	1 to 30	
Vertigo present (n)	23	17	7	15	p>0.05
Tinnitus present (n)	61	30	14	49	p>0.05
URTI history (n)	6	9	4	5	p>0.05

URTI; upper respiratory tract infection

Table-3: Demographic and some clinical parameters of the patients

Audiogram	Group 1 (n = 67)	Group 2 (n = 39)	Group 3 (n = 19)	Group 4 (n = 60)
Up-sloping	8 (11.9%)	3 (7.6%)	5 (26.3%)	12 (20%)
Flat	38 (56.7%)	19 (48.7%)	8 (42.1)	32 (53.3%)
Down-sloping	13 (19.4%)	12 (30.7%)	5 (26.3%)	8 (13.3%)
Spoon	8 (11.9%)	5 (12.8%)	1 (5.2%)	8 (13.3%)

and RR scores (p>0.05) except for the difference between down-sloping and spoon type audiograms. The RHG of the patients who had down-sloping audiogram was lower than those with spoon type audiogram (p=0.016).

Vertigo was not related with upper respiratory infection, type of audiogram, the day of admission, age, gender, RHG, HG and RR (p>0.05). However, the presence of vertigo was a poor prognostic factor in terms of PTAs of the patients. The initial, 5th day and 10th day PTAs of the patients who had vertigo were 78.9.9±24 dB, 70.5±29 dB, 51.6±35 dB, respectively. The corresponding values in the patients who did not have vertigo were 65.9±24 dB, 49.3±30 dB, 36.4±28 dB, respectively. The PTAs of the patients without vertigo were better than the patients with vertigo in the initial admission (p=0.001), and in 5th (p<0.001) and 10th days (p=0.001) of treatment.

Tinnitus was not related to age, gender, day of admission, type of audiogram, HG and RR scores (p>0.05). However, it was related to RHG scores, which were higher in the patients with tinnitus compared to the patients without tinnitus (30.4±31 versus 19.7±25) (p=0.012). The PTAs on first, fifth and tenth days of treatment were not significantly different between the groups (p>0.05). Although the SDSs of the groups were not significantly different on initial admission (p>0.05), a significant improvement was observed in SDSs in group 2 and group 4 in the fifth (p=0.034) and tenth (p=0.021) days of treatment (Table 4). The HG, RHG and RR scores of the groups were not significantly different (p>0.05) (Table 5).

DISCUSSION

ISHL has been a controversial entity for past several decades especially regarding its management. Although numerous treatment protocols have been suggested, there is no consensus on its management. Spontaneous recovery ranges from 31 to 65%, and the rates for treatment success in many studies are similar to the results of spontaneous recovery [2,8,9,19,20].

The presence of vertigo was reported in 40% of ISHL patients, and considered to be a poor prognostic factor [21]. In the present study, vertigo was not related with upper respiratory infection, type of audiogram, the day of admission, age, gender, RHG, HG and RR. However, the presence of vertigo was a poor prognostic factor in terms of PTAs of the patients. The PTAs of the patients without vertigo were better than the patients with vertigo in the initial and 10th days. These suggest that vertigo does not alter the treatment response. Rather, presence of vertigo shows a severe disease in which a good recovery is unlikely. Tinnitus accompanies ISHL in 75% of cases, and its presence is considered a good prognostic factor [14, 21]. In our study, tinnitus was not related to age, gender, the day of admission, type of audiogram, HG and RR. However, it was related to RHG scores, which were higher in the patients with tinnitus compared to the patients without tinnitus. Therefore, presence of tinnitus may be considered a good prognostic factor considering the better RHG scores.

It has been suggested that the prognosis of ISHL was influenced by the slope of the initial audiogram, and down-sloping type audiograms were associated

Table-4: Pure tone averages and speech discrimination scores of the patients

Parameter	Group 1 (n = 67)	Group 2 (n = 39)	Group 3 (n = 19)	Group 4 (n = 60)	Statistics
Pure tone average (dB)					
Initial					
Mean ± sd	75±23	73±23	62±28	65±26	
Range	26 to 100	21 to 100	22 to 100	17 to 100	
Day 5					
Mean ± sd	60.2±31	63.2±29	55.9±32	48.5±31	
Range	5 to 105	20-100	6 to 100	2-100	p>0.05
Day 10					
Mean ± sd	40.9±31	45.1±31	44.8±32	38.4±30	
Range	5 to 105	5 to 100	5 to 100	5 to 100	
Contralateral					
Mean ± sd	15.8±11	16.8±17	13.8±10	13.8±13	
Range	3 to 71	3 to 100	5 to 50	2 to 85	
Speech discrimination score (%)					
Initial					
Mean ± sd	31.1±39	28.8±36	42.9±40	40.4±39	p>0.05
Day 5					
Mean ± sd	43.9±44	33.9±39*	41.2±42	57.2±40*	p = 0.034
Day 10					
Mean ± sd	49.3±44	41.5±41*	51.1±43	66.3±37*	p = 0.021

Table-5: Demographic and some clinical parameters of the patients

Parameter	Group 1 (n = 67)	Group 2 (n = 39)	Group 3 (n = 19)	Group 4 (n = 60)	Statistics
HG (%)					
Mean ± sd	35.4±32	27.1±37	17.6±30	27±24	p>0.05
Range	-48 to 100	-25 to 100	-40 to 100	-8 to 100	
RHG (%)					
Mean ± sd	0.45±0.38	0.32±0.4	0.28±0.4	0.44±0.32	p>0.05
Range	-1.12 to 1	-0.5 to 1	-0.89 to 1	-0.13 to 1	
RR (%)					
Mean ± sd	0.61±0.5	0.36±0.47	0.43±0.58	0.57±0.4	p>0.05
Range	-1.5to 1.45	-0.67 to 1.25	-1.14 to 1.13	-0.15 to 1.35	

with poor prognosis [10, 22, 23]. In this study, there was no correlation between the type of initial audiogram and HG, RHG and RR scores except for the difference between down-sloping and spoon type audiograms. The RHG of the patients who had down-sloping audiogram was lower than spoon type audiogram. The only agent in ISHL treatment that is shown to be more effective than placebo is corticosteroids [9, 10]. The recovery rates with corticosteroids range between 61% and 89% [7, 9, 10, 24]. These rates are better than those for spontaneous recovery. The purpose of steroid treatment is to resolve edema, if any, in the inner ear.

Inflammation may result from a viral infection, autoimmune mechanisms or ischemia [8]. Methylprednisolone is a steroid subtype that reaches higher concentrations and has a better pharmacokinetic profile in the endolymph and perilymph than hydrocortisone and dexamethasone [25].

Although the steroid therapy is widely used for the treatment of ISHL, its optimal dose associated with recovery is not clear. A wide range of steroid doses have been applied, fromvery low doses to intravenous high doses [26-28]. The main aim of steroid treatment is to activate glucocorticoid receptors in the cochlea. Cochlear damage seemed to be limited by the anti-inflammatory properties of glucocorticoids and it has been suggested that more potent inhibition of inflammation may facilitate the recovery [29]. Accordingly, increasing the dose of steroids might be considered to result in higher drug concentration in the inner ear fluids. In randomized and controlled studies concerning specific anti-viral treatment, it was determined that addition of anti-viral drug to treatment protocol provided no extra benefit [29,30]. Since the viral multiplication ends after 14 days, additional use of acyclovir is considered ineffective [29-32]. Although the effect of anti-viral agents on recovery rates are not assessed specifically in this study, similar RR, HG and RHG scores of the groups suggest that antiviral treatment is not effective in the treatment of ISHL.

In this study, the patients with ISHL were divided into four groups according to the treatment protocols. All groups received methylprednisolone treatment with different doses or drug combinations. Pretreatment and post treatment hearing results were compared using HG, RHG and RR scores, and no difference was found between the groups on overall comparisons. When we consider the side effects of the drugs, especially corticosteroids, it is plausible to suggest that only 1 mg per kg methylprednisolone should be used in the treatment of ISHL. However, in the light of our results, this assumption can be changed when we consider SDSs of the patients and commencement of the treatment. A better recovery in SDSs was observed when group 2 and group 4 protocols were used. Therefore, considering the side effects of high dose corticosteroids in group 4, group 2 protocol can be advocated in the patients who have poor SDSs on initial admission.

In conclusion, overall comparison of the treatment protocols did not reveal significant difference between the outcomes.

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