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Original Article

Intratympanic Methylprednisolone versus Dexamethasone for the Primary Treatment of Idiopathic Sudden Sensorineural Hearing Loss

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OBJECTIVES: The aim of the present study was to compare the therapeutic effectiveness of intratympanic (IT) methylprednisolone and dexamethasone in the initial treatment of patients with idiopathic sudden sensorineural hearing loss (ISSHL).

MATERIALS and METHODS: A total of 46 patients with ISSHL who had been treated with IT methylprednisolone or dexamethasone were included in the present study. Dexamethasone (4 mg/mL) and methylprednisolone (20 mg/mL) were given transtympanically to 22 and 24 patients, respectively, one dosage per day for 5 consecutive days. Audiologic evaluations were performed pretreatment, daily in inpatient clinics, and in the first week and second month after discharge, using four-frequency pure-tone average (PTA) and speech discrimination score (SDS). Audiologic improvement was classified according to the Furuhashi criteria.

RESULTS: According to the Furuhashi criteria, the therapeutic success rate was 62.5% (complete improvement 16.7% and marked improvement 45.8%) in the methylprednisolone group, whereas it was 54.6% (complete improvement 27.3% and marked improvement 27.3%) in the dexamethasone group. Therapeutic success was higher in the methylprednisolone group; however, it was not statistically significant. When the audiologic improvement was accepted as >10 dB in PTA, the therapeutic success rates were 83.3% in the methylprednisolone group and 72.8% in the dexamethasone group. The mean (±SD) improvement of PTA before and after treatment was 30.8±21.4 in the methylprednisolone group and 24.7±2.5 in the dexamethasone group. The mean improvement in SDS was 32.6±25 in the methylprednisolone group and 23.7±26.9 in the dexamethasone group.

CONCLUSION: IT steroids are safe, effective, and well-tolerated agents in the initial treatment of patients with ISSHL. Despite having different pharmacokinetic characteristics, IT methylprednisolone and dexamethasone have no superiorities over each other in the primary treatment in patients with ISSHL.

KEYWORDS: Idiopathic sudden hearing loss, intratympanic treatment, methylprednisolone, dexamethasone

INTRODUCTION

Idiopathic sudden sensorineural hearing loss (ISSHL) is a condition in which there is loss of >30 dB in three consecutive frequencies over a period of <3 days. The etiology of ISSHL may be idiopathic, but other causes include viral infection, vascular compromise, and immunologic diseases. The difficulty in identifying the exact etiology of hearing loss led to a lack of consensus in the management of ISSHL. Spontaneous recovery rates without treatment range from 32% to 65% [1].

The treatment of ISSHL remains controversial. There are several treatment modalities including the use of vasodilators, diuretics, anticoagulants, plasma expanders, corticosteroids, apheresis, and hyperbaric oxygen, individually or in combination. Corticosteroids have been accepted as the standard treatment ever since Wilson et al. [2] described their efficacy. The perilymphatic concentration of steroids must be adequate in order to be effective. This is achieved with high systemic doses. Intratympanic (IT) steroid injection has the advantage of direct steroid uptake through the round window membrane and higher perilymph steroid levels. Steroid concentrations were higher when administered intratympanically than orally and intravenously as has been proven through animal studies [3, 4]. Owing

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to different steroids and dosages, the efficacy of IT steroid treatment in ISSHL has not yet been determined [5]. The most common steroid used in IT steroid treatment is dexamethasone, followed by methylprednisolone [6]. On the other hand, Parnes et al. [3] demonstrated that the concentration of methylprednisolone is the highest and remains for the longest duration in both perilymph and endolymph when compared with dexamethasone and hydrocortisone. The concentration of methylprednisolone declines slowly below the detection level in 24 h in the perilymph, whereas dexamethasone and hydrocortisone can be detected only up to 6 h after middle ear injection [3, 4].

The aim of the present study was to compare the therapeutic efficacy of different IT steroids including methylprednisolone and dexamethasone in the treatment of ISSHL.

MATERIALS and METHODS

This observational clinical study was conducted retrospectively from January 2013 to December 2015. A total of 46 patients who were diagnosed with unilateral ISSHL were included in the present study. The Institutional Review Board of the Çukurova University approved the study. Written informed consent was obtained from each patient who participated in the study.

Patients with sudden sensorineural hearing loss of at least 30 dB over three consecutive frequencies, initiating within 72 h; aged between 18 and 85 years; no history of medical treatment; and unilateral hearing loss were included in the study.

Patients with trauma (acoustic, head, and barometric); autoimmune hearing loss; acute and chronic otitis media; Meniere's disease or history of fluctuating hearing loss; retrocochlear disease; and ototoxic drugs, radiation-induced hearing loss were excluded from the study.

Audiometric Assessment

Standardized methods for pure-tone average (PTA), speech discrimination score (SDS), stapedius reflex testing, and tympanometry were used to evaluate the patients. PTA was calculated by measuring the mean values of 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz frequencies.

The serologic tests, brain and cerebellopontine angle magnetic resonance imaging with contrast, and temporal bone high-resolution computed tomography were performed routinely in addition to audiometric measurements.

IT Steroid Protocol

Before injection, each patient was evaluated under a microscope for intact tympanic membranes and normal features of the middle and external ear. Patients were in the supine position with their heads tilted at a 45° angle to the opposite ear. Local anesthesia was achieved using a cotton sponge impregnated with 10% lidocaine solution (Xylocaine 10 mg/dose; AstraZeneca Korea, Seoul, Republic of Korea) on the tympanic membrane. After 10 min, the sponge was removed, and any remaining fluid was cleared from the external canal using a 25-gauge spinal needle. The injections were introduced into the posteroinferior portion of the tympanic membrane. Methylprednisolone 0.5-0.7 mL (Prednol-L 20 mg/mL; Mustafa Nevzat, Turkey) or dexamethasone 0.5-0.7 mL (Dekort 4 mg/mL; Deva, Turkey) was instilled through this site in each group, respectively. The patients were instructed not to move, speak, or swallow during the procedure, but due to inevitable swallowing, a second injection was applied after 10 min. The patients remained in the same position for an additional 10 min. IT procedures were applied for 5 consecutive days for each group.

Table 1. Characteristics of patients

	IT methylprednisolone	IT dexamethasone
Age (years) (mean±SD, range)	50.0±12.4 (26-75)	47.3±14.6 (18-71)
Male/female	14/10	9/13
Side (right/left)	17/7	12/10

IT: intratympanic; SD: standard deviation

Evaluation of Hearing Improvement

The Furuhashi criteria were used to evaluate the audiologic improvement, and results were classified as complete recovery (PTA <25 dB), marked improvement (PTA improvement >30 dB), slight improvement (PTA improvement between 10 and 30 dB), or no recovery (PTA improvement <10 dB) [7]. The complete recovery and marked improvement were identified as therapeutic success, whereas the slight improvement and no recovery were categorized as unsuccessful treatment.

Statistical Analysis

The Kolmogorov–Smirnov and Shapiro–Wilk tests and histograms were used to analyze normality for each continuous variable. Comparisons between the groups were applied using the Student's t test for normally distributed data and Mann–Whitney U test for non-normally distributed data. Categorical variables between the groups were analyzed by using the chi-square test. A p-value <0.05 was considered to be significant. Results were expressed as mean±SD, median (min–max), and n (%). All reported p-values are two-tailed. The Statistical Package for the Social Sciences (SPSS) version 20 (IBM Corp.; Armonk, NY, USA) was used for statistical analysis.

RESULTS

The two study groups were classified as the IT methylprednisolone group (n=24, mean age: 50.0±12.4 years; range: 26-75 years) and the IT dexamethasone group (n=22, mean age: 47.3±14.6 years; range: 18-71 years). Table 1 shows the audiometric and demographic features of each group at the time of diagnosis. The time interval between onset of symptoms and administration of the IT treatment was measured as the average of 2 days in both groups.

The PTA and SDS of all patients were evaluated in the first week and in the second month after treatment. Table 2 shows the treatment values of PTA and SDS before and after. Although the improvement in PTA was higher in the methylprednisolone group than in the dexamethasone group, the difference was not statistically significant (p<0.361). Similarly, the improvement in SDS was higher in the methylprednisolone group, and the difference was also not statistically significant (p<0.213).

According to the Furuhashi criteria, the therapeutic success rate was 62.5% (complete improvement 16.7% and marked improvement 45.8%) in the methylprednisolone group, whereas it was 54.6% (complete improvement 27.3% and marked improvement 27.3%) in the dexamethasone group. Therapeutic success was higher in the methylprednisolone group but not statistically significant (Table 3). When

the audiologic improvement was accepted as >10 dB in PTA, the therapeutic success rates were 83.3% in the methylprednisolone group and 72.8% in the dexamethasone group.

The distributions of PTA and SDS that were performed before treatment, in the first week, and in the second month after treatment are demonstrated again in boxplots (Figures 1 and 2). The black line indicates the median value.

Table 2. PTA and SDS values of the IT methylprednisolone and dexamethasone groups before and after treatment

		Groups Mean±SD Median (min–max)		
		IT methylprednisolone	IT dexamethasone	p
PTA (dB)	Pretreatment	71.6±24.3	66.5±26.4	0.435
		76 (33-110)	60 (30-117)	
	Week 1	54.2±25.6	50.4±34.4	0.560
		48 (13-95)	41 (7-105)	
	Month 2	40.8±25.3	41.8±35.2	0.717
		36 (8-93)	23 (5-101)	
	Improvement	30.8±21.4	24.7±22.5	0.361
		30 (-7-67)	23 (-25-80)	
SDS (%)	Pretreatment	33.9±29.6	41.7±32.9	0.407
		22 (0-84)	37 (0-88)	
	Week 1	53.7±34.7	59.3±40.9	0.529
		54 (0-96)	82 (0-100)	
	Month 2	66.5±28.9	65.4±41.6	0.309
		72 (12-100)	94 (0-100)	
	Improvement	32.6±25	23.7±26.9	0.213
		26 (-2-76)	16 (-12-84)	

T: intratympanic; PTA: pure-tone average frequencies at 0.5, 1, 2, and 4 kHz; dB: decibels; SDS: speech discrimination score; SD: standard deviation

Table 3. Audiologic improvement based on the Furuhashi criteria in the IT methylprednisolone and dexamethasone groups

	Groups			
	IT methylprednisolone		IT dexamethasone	
	n	(%)	n	(%)
Complete recovery (PTA <25 dB) *	4	(16.7)	6	(27.3)
Marked improvement (PTA improvement >30 dB) *	11	(45.8)	6	(27.3)
Slight improvement (PTA improvement=10–30 dB)	5	(20.8)	4	(18.2)
Non-recovery (PTA improvement <10 dB)	4	(16.7)	6	(27.3)

IT: intratympanic; PTA: pure-tone average frequencies at 0.5, 1, 2, and 4 kHz; dB: decibels
Complete recovery+marked improvement=therapeutic success

No serious complications were observed in the patients after IT treatment. Self-limiting otalgia was the most common symptom reported. Three patients continued with systemic treatment because they could not tolerate the injections and were excluded from the study. Of the three patients, two have had methylprednisolone injections, and one had dexamethasone injections. Eight patients reported symptoms of vertigo for approximately 1 min, in which three had methylprednisolone injections, and five had dexamethasone. Complications, such as perforation of the tympanic membrane and acute otitis media, were not observed.

DISCUSSION

Clinical ISSHL is an otologic emergency and must be evaluated carefully in addition to appropriate and specific treatment. The treatment regimens for ISSHL are not standardized because its etiology is not yet well known. The recovery rate of patients with ISSHL varies between 30% and 60% in follow-up without treatment or in their medical history [4]. Several factors, such as the type and intensity of hearing loss, the time between onset of symptoms and beginning of treatment, the duration of treatment, and through which route the steroid was administered, affect the results. Despite all these variable parameters, corticosteroids are the most accepted agents in the treatment of ISSHL. Methylprednisolone and dexamethasone are the most commonly used molecules, and each can be administered at

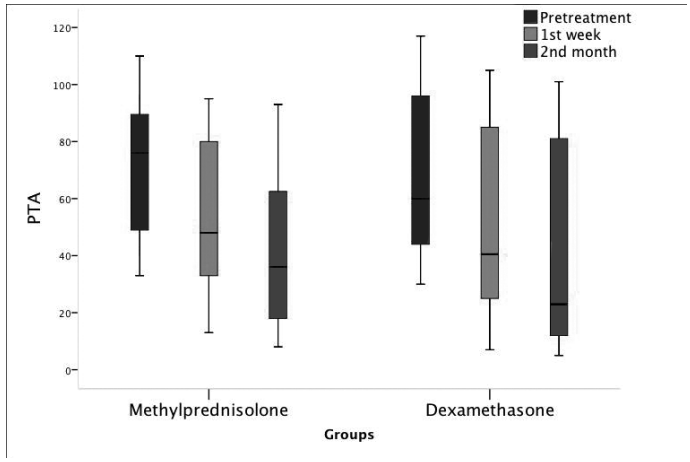

Figure 1. The distribution of PTA before treatment, in the first week, and in the second month after treatment.

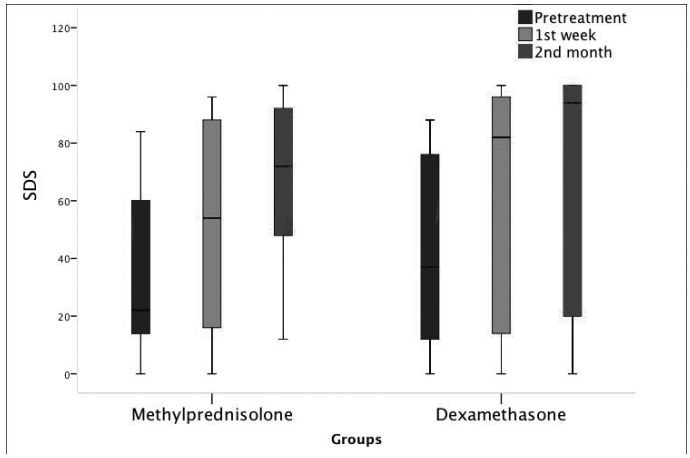

Figure 2. The distribution of SDS before treatment, in the first week, and in the second month after treatment.

different frequencies and amounts. The effects of corticosteroids in the inner ear are not clear to date. However, the known mechanisms of action of corticosteroids are defined as reducing inflammation in the inner ear, protecting against ischemia, increasing cochlear blood flow, and regulating endocochlear potentials and protein synthesis [8, 9]. Corticosteroids do not affect the outer hair cell function and also reduce the size of the degenerated portion of the stria vascularis [10, 11].

Systemic steroids have serious adverse effects, such as uncontrolled diabetes, hypertension, gastrointestinal bleeding, and avascular necrosis of the hip. In addition, adverse effects, such as insomnia, gastritis, flushing, and irritability, are more frequent but less severe [12]. IT steroids allow the inner ear to achieve high concentrations and prevent adverse effects caused by systemic steroid administration.

Systemic steroids have limited access to the inner ear due to the blood–labyrinthine barrier. However, the IT administration of steroids provides a direct route for steroid absorption to the inner ear through the round window membrane. Chandrasekhar et al. [4] compared the efficacy and concentrations of dexamethasone in the blood and perilymph by administering it via the IT and intravenous routes. The effect of the IT steroid and perilymph concentrations was higher than that of the systemic route.

Several meta-analyses have suggested favorable results in salvage treatment with IT steroid for ISSHL after failure of primary treatment with systemic steroids [13-15]. On other hand, a number of studies have shown that IT steroid is the initial treatment of ISSHL [12, 16-18]. It was stated in our previous study that IT dexamethasone has better audiologic results than oral methylprednisolone in patients with ISSHL [18].

Parnes et al. [3] demonstrated in their animal study that the IT administration of steroids provides higher concentrations in the inner ear. Guinea pigs were used in the assessment of the concentrations of corticosteroids, such as hydrocortisone, methylprednisolone, and dexamethasone in the blood, cerebrospinal fluid, and perilymph with intravenous, oral, and IT administration. Thus, it was demonstrated that the maximum concentration in the inner ear is achieved by IT administration, and methylprednisolone is the corticosteroid that attained the highest inner ear concentration. After IT administration, the concentrations of methylprednisolone in the inner ear reached the peak concentration in 2 h and remained increased for the first 6 h; then, it started to decline slowly until it reached 0 after 24 h [3]. Similar results have been demonstrated in subsequent human studies [12].

Naci Ozluoglu et al. [19] demonstrated the perilymph concentration of IT dexamethasone versus systemic dexamethasone and IT buffered papaverine+dexamethasone in their animal study. This also showed that IT is superior to systemic administration, but buffered papaverine+dexamethasone reaches a higher concentration than dexamethasone alone.

In patients with ISSHL, the IT injections are made with different corticosteroid molecules and doses. Although the comparison of systemic and IT administration has been discussed often in previous studies, there are limited studies comparing the IT administration of different corticosteroids. There are two studies in the literature that compared IT methylprednisolone and dexamethasone in the treatment of ISSHL [20, 21]. Yang et al. [20] applied IT dexamethasone (5 g/L/day) to 24 patients and IT methylprednisolone (40 mg/L/day) to 23 patients for at least 7 days in their study of 47 patients with ISSHL. Despite there being improvements in PTA in both IT applications, there was no significant difference between the effect of dexamethasone and methylprednisolone. In contrast, Berjis et al. [21] found that the overall hearing improvement rate is 64% in the dexamethasone group, which was significantly higher than 84% in the methylprednisolone group with 50 patients with refractory ISSHL. At the same time, complete recovery rates were 24% in the methylprednisolone group and 12% in the dexamethasone group.

The different results obtained from these studies can be explained by many reasons, such as the dosage of drugs, duration, interval, route of administration, and patients having primary and/or refractory ISSHL. The excess of variables makes it difficult to establish standard treatment protocols.

CONCLUSION

Intratympanic steroids are safe, effective, and well-tolerated agents in the initial treatment of patients with ISSHL. Despite having different pharmacokinetic characteristics, IT methylprednisolone and dexamethasone have no superiority over each other in the primary treatment of patients with ISSHL.

Ethics Committee Approval: Ethics committee approval was received for this study from The Institutional Review Board of the Çukurova University.

Informed Consent: Written informed consent was obtained from each patient who participated in the study.

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