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ORIGINAL ARTICLE

Intratympanic Steroid Treatment as a Primary Therapy in Idiopathic Sudden Sensorineural Hearing Loss

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Objectives: Therapy for idiopathic sudden sensorineural hearing loss (ISSHL) is still controversial. Intratympanic (IT) administration of steroids appears to be an attractive method of management of ISSHL. The purpose of this study was to evaluate the efficacy and safety of IT administered methylprednisolone (IT-MP) on ISSHL patients as a primary therapy, by comparing the results with intravenously administered dexamethasone (IV-DEX) treatment.

Materials and Methods A prospective, nonrandomized, comparative study was conducted for 44 patients presenting with ISSHL. Twenty patients were treated with intratympanic methylprednisolone as a primary therapy, and 24 with intravenous dexamethasone. The hearing level was described using the pure tone average (PTA in dB) hearing level at 4 frequencies (0.5, 1, 2 and 4 kHz). The PTA in unaffected ear was used as the presumed premorbid hearing (baseline) in the affected ear. Hearing gain was expressed as absolute hearing gain and relative hearing gain. Complete hearing recovery was defined as the final PTA within 10dB of baseline. Partial recovery was defined as a final PTA with a ≥ 50% relative recovery.

Results: Mean hearing improvement was significantly higher in IT MP group than in IV DEX group (50.7±22.11, versus 29.5±28.0, p<0.01). There was significant difference between hearing level of the unaffected ear (hearing threshold was worse in the IV DEX group) and it had an influence on high rate of relative recovery of hearing in IV DEX group. There was no difference in mean relative recovery between the two groups. Similar percent of patients in both group had complete recovery, but in the IV DEX group 42% patients had no recovery (versus 10% in IT MP group).

Conclusion: Intratympanic treatment of ISSHL may be a preferable choice as primary treatment option, since it can be performed in outpatient settings, with no serious side effects and complication rate.

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Idiopathic sudden sensorineural hearing loss (ISSHL) was defined as a 30dB loss over 3 continuous frequencies occurring in less than 3 days, with no marked vestibular symptoms and no identifiable cause. The most common theories of the etiology of ISSHL include viral infection, vascular occlusion, intralabyrinthine membrane breaks[1]. Due to the uncertainties regarding etiology and pathogenesis, the treatment of ISSHL has been highly empirical.

Different treatment protocols and agents have been proposed to treat ISSHL but the most accepted is systemic steroids. Although proven to be effective in randomized, double-blind, placebo- controlled trials1; other studies have questioned the efficacy of systemic steroids in the treatment of ISSHL[2-4]. Recently, intratympanic (IT) administration of steroids appears to be an attractive method of management of ISSHL. The use of IT steroids has evolved into three protocols for treatment of ISSHL: as initial or primary treatment, as adjunctive treatment given concomitantly with systemic steroids and after failure of systemic steroids for ISSHL. The majority of the literature concerning the use of IT steroids in the treatment of ISSHL has

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reported the experience in treatment after failure of systemic therapy[5-8]. Two studies, however, have studied the effects of IT steroids as a primary treatment for patients with ISSHL used adjunctively with systemic steroids[9,10]. Only two studies evaluated the efficacy of IT administered steroids on ISSHL patients as an initial and only therapy[11,12].

The purpose of this study has been to evaluate the efficacy and safety of IT administered methylprednisolone (IT-MP) on ISSHL patients as a primary therapy, by comparing the results with intravenously administered dexamethasone (IV-DEX) treatment.

Materials and Methods

From January 2006 to November 2007, a prospective, nonrandomized, comparative study was conducted for 44 patients presenting with ISSHL.

Forty four patients presenting with unilateral sudden sensorineural hearing loss. All patients underwent a standard evaluation protocol (ENT examination, basic audiometry, laboratory investigations, including full blood count ,biochemistry and serology for borreliosis and lues in selected cases, antigen nonspecific serologic tests and thyroid function tests; auditory brain stem response and magnetic resonance imaging with contrast only in patients with no recovery of hearing). The hearing level was described using the pure tone average (PTA in dB) hearing level at 4 frequencies (0.5, 1, 2 and 4 kHz). Pure tone audiometry was performed just before the treatment and each injection, three weeks and two months after the treatment.

Randomization was not possible because some of the patients refused any invasive procedure to treat their hearing loss and they were treated with IV DEX. The patients were informed about the new treatment and the possible benefits and risks. Informed consent was obtained from all patients, who agreed with IT MP treatment. The present study was approved by the institutional Ethical boards of the University Hospital "Zemun", Medical School, University of Belgrade.

The IT MP group consisted of 20 patients. The IT MP treatment consisted of 0.3-0.8 mL sterile aqueous suspension of methylprednisolone (Lemod Solu, Hemofarm, Vrsac, Serbia) warmed to body temperature, in a concentration of 80mg/mL instilled slowly with a fine needle (21 gauge) and 1mL-syringe through the posterior-inferior quadrant of the tympanic membrane of the affected ear. Local anesthesia was achieved with topical lignocaine chloride 2% (Lidokain hlorid, Galenika, Belgrade, Serbia). MP was allowed to perfuse the middle ear for 30 minutes with the patient`s head tilted at 45 degree . Patients were instructed to swallow as little as possible and stay still. The procedure was performed four times within a 13-day period. The IV DEX group consisted of 24 patients. They were treated intravenously with 40mg of dexamethasone for 3 consecutive days followed by 3 days of 10mg. Furthermore, they received protection against peptic ulcer disease with oral ranitidine during steroid treatment.

The PTA in unaffected ear was used as the presumed premorbid hearing (baseline) in the affected ear. Hearing gain was expressed either as absolute hearing gain (dB values from initial PTA minus dB values from final PTA) or as relative hearing gain (absolute hearing gain divided by initial PTA minus baseline PTA). A threshold value of 100 dB HL was assumed if the average hearing loss exceeded the limits of the audiometric equipment. Complete hearing recovery was defined as the final PTA within 10dB of baseline. Partial recovery was defined as a final PTA with a ≥ 50% relative recovery.

Quantitative variables have been described by mean ± standard error of mean (SEM), whereas frequency distribution tables have been used for categorical variables. Data analysis was performed using independent sample Student t-test. All tests have been 2-sided and level of statistical significance was set at 5%.

Results

Forty nine patients presented to our hospital with sudden sensorineural hearing loss during study period. Nevertheless, five patients were excluded because intratympanic steroid treatment was a secondary

treatment after a failure of primary treatment (2 patients), two patients used ototoxic drugs and one had acoustic trauma. Therefore, 44 patients were enrolled in the study.

Twenty patients were treated with intratympanic methylprednisolone as a primary therapy, and 24 with intravenous dexamethasone.

Table 1 summarizes the profiles of the patients in IT MP and IV DEX groups. There were no significant differences in age, duration between onset and treatment and initial hearing loss between the two groups, but there was a difference in hearing threshold in unaffected ears (Student's t test).

In the IT MP group, 12 (60%) of the 20 patients showed complete recovery, six had partial, whereas two patients showed no hearing recovery. Both of them had more than 30 days between onset and treatment. Four patients had initial hearing loss more than 100dB, and all of them had relative recovery about 80%.

In the IV DEX group, 12 (50%) of the 24 patients showed complete recovery, whereas ten patients had no hearing recovery. Table 2 summarizes the clinical outcomes in the IT MP and IV DEX groups.

The recovery status for all patients is summarized in Figure 1.

In IT MP group, the average amount of medication injected ranged between 0.3-0.8ml (mean 0.5 ml) for each injection. Most of patients received 4 injections (4 had three, and one had two injections). The reason for discontinuation of treatment was complete recovery of hearing. The average amount of time elapsed between injections was 4 days and average total time from the first injection to the last injection was 13 days, ranging from 8 days to 15 days.

No unexpected adverse events occurred during the injections or follow-up period. Five patients had a mild ear pain occurring during the first post- injection hour. No perforation or infection was noticed in any of the patients at their last follow -up visit.

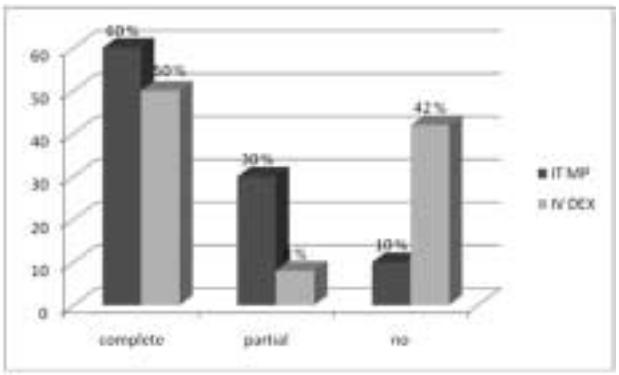

Figure 1. Recovery was defined as complete- ears with final measurement of PTA within 10dB of contra lateral ear; partial- ears with relative recovery ≥50%; no recovery- ears with relative recovery <50%. Graph depicts recovery status of two groups of patients.

Table 1. General data regarding IT MP and IV DEX groups

	IT-MP	IV-DEX	p (Student's t- test)
Number of patients	20	24	
Age (yr)			
Mean± SEM	47.3 ± 10.8	53.6 ± 15.5	t=0.06, p>0.05, NS
Range	30 - 61	19 - 72	
Duration before treatment (d)			
Mean± SEM	11.5 ± 11.9	11.4 ± 9.6	t=0.03, p>0.05, NS
Range	2 - 43	2 - 30	
Initial hearing level (dB)			
Mean± SEM	81.3 ± 12.4	72.9 ± 20.2	t=1.6, p>0.05, NS
Range	60 - 100	45 - 100	
Hearing level of unaffected ear (dB)			
Mean ±SEM	14.5 ± 11.57	25.0 ± 11.8	t=2.92, p<0.01, SIG

IT-MP, intratympanically administered methylprednisolone treatment; IV-DEX, intravenously administered dexamethasone treatment; SEM, standard error of the mean; NS, not significant; SIG, significant

Table 2. Recovery after IT MP and IV DEX treatment

	IT-MP	IV-DEX	p (Student's t- test)
Number of patients	20	24	
Absolute recovery (dB)			
Mean± SEM	50.7 ± 22.11	29.5 ± 28.0	t=2.71, p<0.01, SIG
Range	0 - 80	0 - 80	
Relative recovery (%)			
Mean± SEM	78.38 ± 29.52	58.39 ± 45.19	t=1.73, p>0.05, NS

IT MP, intratympanically administered methylprednisolone treatment; IV DEX, intravenously administered dexamethasone treatment; SEM, standard error of the mean; NS, not significant; SIG, significant

Discussion

To evaluate the influence of IT steroids on hearing levels in patients with ISSHL we included patients with no previous treatment and compared with patients who received systemic steroids.

Here, we used methylprednisolone (80mg/mL) injected through the tympanic membrane toward the round window, in the dose of 0.3-0.8 mL four times within 13-day period. Described techniques for steroid perfusion of the middle ear for ISSHL differ in many aspects, including the type of steroid used. Dexamethasone is the most common steroid used for intratympanic use[6-,8,10,12] followed by methylprednisolone[5,9,13]. Reports in literature also differ in the strength of the solution (2-4mg/ml[6] to 25mg/ml[7] dexamethasone; 32mg/ml9 to 62.5mg/ml[5] methylprednisolone. The amount injected into the middle ear in most studies is between 0.3 and 0.5 mL, the approximate volume of the middle ear space. Techniques also differ in method of delivery: transtympanic needle injection[6,8,9,12], delivery through a myringotomy[7], delivery through a myringotomy with a tube[9]. The length of time and number of injections in which patients are treated with intratympanic steroids also differs ranging from a single day to weekly transtympanic injections[5,6,9] to transtympanic injections given several times per week[7,9,14]. Further randomized, prospective, clinical studies are needed to elucidate the optimal dosages, technique and frequency of administration of steroids.

Animal experiments show that local application of corticosteroids into the middle ear results in higher inner ear concentration as compared to systemic application[13]. Parnes[13] compared pharmacokinetic of methylprednisolone, dexamethasone and hydrocortisone in inner ear, and concluded that methylprednisolone had the highest concentration and longest half-life in perilymph.

In the current study, there were no significant differences in age, duration between onset and treatment and initial hearing loss between the two groups.

Mean hearing improvement was significantly higher in IT MP group than in IV DEX group (50.7±22.11, versus 29.5±28.0, p<0.01). There was significant difference between hearing level of the unaffected ear (hearing threshold was worse in the IV DEX group) and it had influence on high rate of relative recovery of hearing in IV DEX group. There was no difference in mean relative recovery between the two groups. Similar percent of patients in both group had complete recovery, but in the IV DEX group 42% patients had no recovery (versus 10% in IT MP group).

Only two papers have studied the effects on intratympanic corticosteroids as a primary therapy[11,12]. Banarjee and Parnes[11] reported successful hearing improvement in 50% (mean PTA improvement was 27dB) when intratympanic methylprednisolone was used as a primary treatment. Kakehata et al[12] published a case-control study, showing that intratympanic treatment was also effective as initial therapy in ISSHL, with less toxicity than systemic steroids. They compared a group of 10 diabetic patients who were treated with intratympanic

dexamethasone and showed successful hearing improvement in 70% (mean PTA improvement was 41dB), and historical group of 21 patients who were treated with intravenous dexamethasone and had successful hearing improvement in 62% (mean PTA improvement was 25 dB).

However, our results are based on small sample sizes like in the other studies, and variance in intratympanic treatment response is wide, between 27dB[11] (trial with 26 patients) and 41dB[12] (trial with 10 patients). We need larger sample sizes to establish valid conclusion of intratympanic steroid treatment as primary therapy of ISSHL. Also, reporting the hearing improvement should be a more objective and standardized.

Furthermore, it is not totally clear whether this effect was actually from intratympanic steroid or the natural course of disease. A main limitation of the study was no control group with any treatment. Weinaug[15] reported a spontaneous hearing recovery rate without treatment for sudden hearing loss of 25.6 dB and a relative hearing gain of 47%. The spontaneous recovery rate, defined as a hearing gain of at least 30 dB, was 73% as reported by Mattox and Simmons[3]. Wilson et al.[1] reported that 29 of 52 non-treated patients regained normal hearing ability (i.e., 56%). The average absolute hearing gain between the initial audiogram and the final audiogram in IT MP group was 50.7dB; the mean relative recovery was 78%. The recovery rate of our IT MP group seems high compared to other reports of spontaneous recovery rates.

In our study, no unexpected adverse events occurred during the injections or follow-up period. Five patients had a mild ear pain treated with analgesics. Reported complications have been rare and included pain, vertigo, otitis media, tympanic membrane perforation, dysgeusia, chronic otitis media and further hearing loss[5,6,10,12,13].

Conclusion

Following these encouring results, it seems that intratympanic treatment of ISSHL may be a preferable choice as primary therapy, since it can be delivered in outpatient settings, with no serious side effects and low complication rate. Furthermore, future controlled studies with larger sample sizes should contribute even more to confirmation of these findings.

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