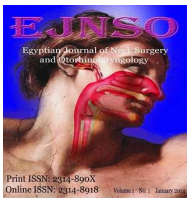
EJNSO



Transtympanic Injection of Methylprednisolone for Sudden Sensorineural Hearing Loss: Is It of Value after Failure of Systemic Therapy?

Mohamed Abd Al-Ghaffar[a], Badawy Shahat[b], Yossri Osman[c], Al Hussein Awad Ali[b]

[a] Audiology Unit, ENT Department, Faculty of Medicine, Sohag University .
[b] ENT Department, Faculty of Medicine, Sohag University.
[c] ENT Department, Faculty of Medicine, Al-Azhar University, Assiut Branch.

Received: February 18th, 2014.
Revised: March 19th, 2014
Accepted: August 28th, 2014

Keywords: sudden sensorineural hearing loss, intratympanic injection, methylprednisolone.

ABSTRACT

OBJECTIVE: Transtympanic steroids are increasingly used in the treatment of inner ear disorders; especially in patients with sudden sensorineural hearing loss (SSNHL).The aim of the present study was to verify the efficacy and the prognostic factors of transtympanic Methylprednisolone to treat sudden sensorineural hearing loss after failure of systemic steroid therapy.

MATERIALS AND METHODS: A prospective study was conducted on patients affected by idiopathic sudden sensorineural hearing loss who were treated before with systemic therapy, but without recovery of hearing. A solution of Methylprednisolone acetate (MP) 40 mg/ml was then injected through the posterior-inferior quadrant filling completely the middle ear. The follow-up in the following 6 weeks included an audiogram at one, three and six weeks after the injection.

RESULTS: 38 patients treated with Methylprednisolone acetate. It was done with a mean delay of 31.4 days from the onset of symptoms. Mean of Pure-tone audiometry (PTA), performed before transtympanic treatment, was 81.3 ± 24.5 SD dB. After six week of local steroid administration, mean PTA was 42.5 ± 21.6 SD dB.

CONCLUSIONS: Transtympanic Methylprednisolone should be suggested to all patients who failed the first systemic treatment.

INTRODUCTION:

Sudden sensorineural hearing loss (SSNHL) is one of the causes of otologic emergencies. It is defined as 30 dB or more of hearing loss over at least 3 contiguous frequencies occurring within 3 days [1, 2]. The incidence of SSNHL is estimated in 5 to 20 per 100000 every year [3]. Aetiologically, many causes, such as viral cochleitis, vascular injury, autoimmune inflammation and inner ear membrane rupture have been proposed[4]. Spontaneous recovery occurs in approximately 30% of cases [5] and

recovery occurs mainly within the first 2 weeks after onset.

Steroids have been demonstrated to be effective [1]. Early administrations of systemic steroids have been shown to increase the rate of hearing recovery [5]. On the other hand, high doses of steroids can be associated with systemic effects and cannot be used in all patients.

The transtympanic route presents two main advantages: i) it is possible to obtain a higher concentration of the drug in the inner ear and, ii) it reduces the side-effects due to systemic absorption.

Effectiveness of local application of steroids in SSNHL has been reported by many Authors[6]. Steroids have been used also in Ménière's disease [7] and in other inner ear conditions [8]. Optimal dosage, drug and route of administration still remain a matter of debate.

Corticosteroids have multiple mechanisms of action including immune suppression, anti-inflammatory action, membrane stabilization, ion balance regulation and increased perfusion [9].

Based on these considerations, we designed our work aiming to treat SSNHL patients, not responding to traditional therapy, with transtympanic steroids in order to better understand the real effectiveness of this treatment and to evaluate the prognostic factors for that line of treatment.

PATIENTS AND METHOD:

38 SSNHL patients, 21 females and 17 males, recruited to the study from November 2011 to December 2013. They were not responding to traditional treatment. All patients were informed about their condition and the treatment options. All patients gave their consent to the treatment. All patients completed a follow-up of at least 6weeks after transtympanic injection of steroids.

Exclusion criteria:

Any identifiable etiology for sudden SNHL as, patients with Meniere disease, retro-cochlear disease, autoimmune HL, trauma, fluctuating HL, radiation-induced HL, noise-induced HL was excluded from the study.

All patients under the study were submitted to the following:

1- history taking
2- Otoscopic examination
3- Blood pressure measurement
4- Blood tests including complete blood picture, cholesterol level, LDL, and Blood sugar, fasting and 2 hours postprandial.
5- Pure- tone audiometry
6- Tympanometry
7- Acoustic reflex
8- MRI on Cerebellopontine angle and Internal auditory canals.

Patient variables as they related to recovery were studied and included patient age, time to onset of therapy, status of the contra-lateral ear, presence of diabetes, severity of HL, special habits as smoking, and configuration of hearing loss

A change ≥ 15 dB in mean pure tone (PTA, 4 frequencies 0.5, 1, 2, 3 kHz) was considered significant improvement.

All patients were treated with a steroid therapy (1 mg/kg), If the patient showed no improvement with the systemic therapy after 2 weeks of treatment, transtympanic steroids were given. One ml of Methyl-Prednisolone, (MP), Depo- Medrol ®, 40 mg/ml was buffered with 1 ml of sodium bicarbonate in order to obtain a less acid solution. After local anesthesia, a transtympanic injection, usually in the round window (RW) area, was performed and approximately 0.5-1 ml of the solution was placed in the middle ear. The patient was then invited not to swallow and to remain with his/her head turned to the opposite side for 20-30 minutes. Antibiotic therapy was given to all patients for 3 days.

Statistical methods

-A t test for paired data was used to compare the PTA data before transtympanic injection of Methylprednisolone and after injection by one, three and six weeks.

-Correlation Coefficient (r) test was done to evaluate the effect of the variables on the outcome of the administrated drug.

RESULTS:

Thirty eight patients with SSNHL included in the study, 21 females and 17 males.

Pure-tone audiometry (PTA), performed before transtympanic treatment, showed a severe to profound hearing loss in 29 patients and a moderate hearing loss in the remaining nine. Overall, mean PTA was 81.3 ± 24.5 SD dB.

Mean age of the patients was 49 ± 20 SD years (range 18-67). The mean interval between the onset of SSNHL and transtympanic therapy was 31.4 ± 19.2 SD days (range 16-93). 36 patients received a single injection, two received two. Middle ear disease was ruled out in all patients.

Mean PTA before transtympanic treatment was 81.3 ± 24.5 SD dB; at the end of first week it was 49.7 ± 25.1; it was 45.3 ± 22.3 the end of third weeks and lastly at the end of 6th weeks, after local steroid administration, mean PTA was 42.5 ± 21.6 SD dB.

PTA improvement was documented in 31 patients after local administration of MP; in 26 of these, improvement was significant.

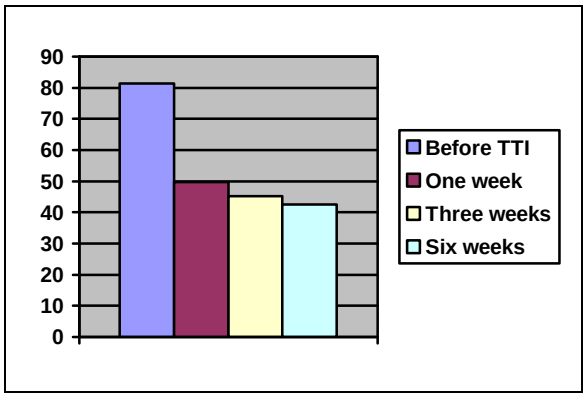


Fig. 1: Mean of PTA values before treatment and 1, 3 and 6 weeks after transtympanic injection

The results obtained with t test for paired data and correlation coefficient test indicate:

1. Comparing PTA before injection in one hand with PTA-1 week, PTA 3 weeks, and PTA 6 weeks a statistically significant difference was found ($p < 0.001$).
2. There were strong negative correlation between age of patients, smoking, diabetes mellitus and PTA improvement.
3. There were moderate negative correlation between the time elapsed till the onset of transtympanic injection, elevated cholesterol level and PTA improvement.
4. No correlation was found between PTA improvement and shape of audiogram, nor between the degree of hearing loss and PTA improvement.

No patient suffered any complications from the transtympanic application of MP.

DISCUSSION:

SSNHL is not a disease per se; it has to be considered as a manifestation of an underlying pathology.

Many drugs have been used in SSNHL treatment and steroids have been demonstrated effective in clinical trials [5]. Despite recognized clinical efficacy, the real mechanism of action of steroids on cochlear function is still unknown. Traditionally, their effect has been attributed to the anti-inflammatory and immunosuppressive activity of these drugs; neuroprotective, antioxidant and antiapoptotic effects have also been reported [10]. Steroids seem to be able to control the immunologically mediated vasculitis by inhibiting cytochine secretion [11]; in fact, they have also been shown to act not only on hair cells but also on cochlear vessels [11].

Aquaporins (AQP) have been demonstrated in the inner ear [12]. These molecules are involved in a homeostatic mechanism in the inner ear regarding water and ion balance [13]. Transtympanic steroids have been demonstrated to up-regulate AQP1 mRNA in a dose-dependent manner [14]. It is possible that local administration of steroids can modulate the inner ear environment, via the AQP1 pathway, thus balancing inner ear fluids. Moreover, they have proven to increase Na^+-K^+ exchange in the stria vascularis, thus restoring normal endolymph ion balance [15] and consequently endocochlear potential[15].

Systemic administration of these drugs is often complicated with troublesome side-effects and not all patients can be treated with steroids. The transtympanic route has 2 advantages; firstly, it allows a greater concentration of drugs in the perilymph and, secondly, it minimizes systemic effects and absorption [16].

Steroids are taken into the inner ear via RW [8]; many factors seem to affect the passage of the substances through the RW into the inner ear

In this study, we administered MP, via a transtympanic route, in patients with

SSNHL in whom a conventional therapy had failed. A significant response (defined as PTA improvement ≥ 15 dB) was obtained in 26of the 38 patients.

Our results suggest that the PTA improvement neither depend on the degree of hearing loss nor to the shape of audiogram. Moreover, we observed 19 patients that almost recovered their previous hearing level (estimated on the opposite side) and they were having severe to profound hearing loss. For those who did not achieve complete recovery, earlier transtympanic therapy might have obtained a better outcome. Overall, the average PTA improvement was 38.8 ± 21.4 SD dB.

We found also the variables that strongly affect the outcome of transtympanic injection of MP were age of the patients, smoking and diabetes mellitus. All of these variables adversely affect the response of the administrated drug.

In contrast with our previous evaluation, statistical evaluation seems to confirm that the main hearing improvement occurs during the first week after transtympanic therapy, from 81.3 dB to 49.7 dB. However, we have noted that hearing improvement may be seen even 6 weeks after steroid administration as it reached to 42.3 dB. This is probably due to various causes including inner ear environment improvement and different absorption profiles.

Interestingly, we did not observe any patient with worsening of the PTA even the two patients who had repeated injections. Based on our data, we think that transtympanic steroids represent an effective option in the management of SSNHL not responding to traditional therapy.

Furthermore, it should be stressed that control of diabetes mellitus, stop smoking and early intervention with transtympanic injection with MP that will give good outcome in patient with SSNHL. Also, we think, in accordance with many Authors that transtympanic therapy can also be used as a first line therapy, especially in patients with severe to profound SSHL or for whom systemic therapy is contraindicated.

CONCLUSIONS:

Transtympanic steroid treatment represents an effective and safe solution in patients with SSNHL in whom conventional treatment has failed.

REFERENCES:

1. Haberkamp TJ, Tanyeri HM. Management of idiopathic sudden sensorineural hearing loss. Am J Otol 1999;20:587-95.
2. Gianoli GJ, Li JC. Transtympanic steroid for treatment of sudden hearing loss. Otolaryngol Head Neck Surg 2001;125: 142-6.
3. Byl FM Jr. Sudden hearing loss: eight years experience and suggested prognostic table. Laryngoscope 1984;94: 647-61.
4. Rauch SD. Intratympanic steroids for sensorineural hearing loss. Otolaryngol Clin N Am 2004;37:1061-74.
5. Wilson WR, Byl FM, Laird N. The efficacy of steroids in the treatment of

idiopathic sudden hearing loss. A double-blind clinical study. Arch Otolaryngol 1980;106:772-6.

6. Guan-Min H, Hung-Ching L, Min-Tsan S, Cheng-Chien Y, Hsun-Tien T. Effectiveness of intratympanic dexamethasone injection in sudden-deafness patients as salvage treatment. Laryngoscope 2004;114:1184-9.

7. Barrs DM, Keyser JS, Stallworth C, McElveen JT Jr. Intratympanic steroid injections for intractable Ménière's disease. Laryngoscope 2001;111:2100-4.

8. Parnes LS, Sun AH, Freeman DJ. Corticosteroid pharmacokinetics in the inner ear fluids: an animal study followed by clinical application. Laryngoscope 1999;109(Suppl 91):1-17.

9. Shimmer BP, Parker KL. Adrenocorticotrophic hormone; adrenocortical steroids and their synthetic analogs; inhibitors of the synthesis and actions of adrenocortical hormones. In: Hardman JG, Limbird LE, Molinoff PB, Gilman AG, editors. Goodman and Gilman's the pharmacological basis of the therapeutics. 9th Edition. New York, NY: McGraw-Hill; 1996. p. 1459.

10. Liles WC, Dale DC, Klebanoff SJ. Glucocorticoids inhibit apoptosis of human neutrophils. Blood 1995;86:3181-8.

11. Gloddek B, Lamm K, Arnold W. Pharmacological influence on inner ear endothelial cells in relation to the pathogenesis of sensorineural hearing loss. Adv Otorhinolaryngol 2002;59:75-83.

12. Takumi Y, Nagelhus EA, Eidet J, Matsubara A, Usami S, Shinkawa H, et al. Select types of supporting cell in the inner ear express aquaporin-4 water channel protein. Eur J Neurosci 1998;10:3584-95.

13. Mhatre AN, Steinbach S, Hribar K, Hoque AT, Lalwani AK. Identification of aquaporin 5 (AQP5) within the cochlea: cDNA cloning and in situ localization. Biochem Biophys Res Commun 1999;264:157-62.

14. Fukushima M, Kitahara T, Fuse Y, Doi K, Kubo T. Effects of intratympanic injection of steroid on changes in rat inner ear aquaporin expression. Acta Otolaryngol 2002;122:600-6.

15. Gross ND, Kempton JB, Trune DR. Spironolactone blocks glucocorticoid-mediated hearing preservation in autoimmune mice. Laryngoscope 2002;112:298-303.

16. Chandrasekhar SS. Intratympanic dexamethasone for sudden sensorineural hearing loss: clinical and laboratory evaluation. Otol Neurotol 2001;22:18-23.