Intratympanic Versus Oral Steroids in the Management of Idiopathic Sudden Sensorineural Hearing Loss

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Abstract

Objective: To study and compare the efficacy of intratympanic steroid and oral steroid in the improvement of hearing in patients with idiopathic sudden sensorineural hearing loss (ISSHL).

Patients and Methods: This study is a prospective non-randomized comparative study done on 24 patients with sudden sensorineural hearing. These patients have normal otoscopic examination and do not have apparent causes of SSHL as detected by radiologic and laboratory investigation. There were two groups with 12 patients each: group A, which was treated with oral prednisolone, and group B, which was treated with intratympanic methyl prednisolone. Baseline pure tone audiometry (b-PTA) was done prior to treatment and was compared to the PTA taken on the 7th day (PTA-7), 14th day (PTA-14), and 30th day (PTA-30) after treatment.

Results: Group A has a mean b-PTA of 80.5 ± 14.24 SD and PTA-30 of 47.5 ± 9.88 SD respectively. Group B has a mean b-PTA of 81.91 ± 17.31 SD and PTA-30 of 50.83 ± 20.06 SD. A statistically significant difference found between b-PTA and PTA-14 and PTA-30 in both groups. A statistically significant difference was also found between b-PTA and PTA-7 in group B.

Conclusion: Intratympanic steroid leads to significant improvement of hearing that is little bit lower than oral steroids after 1month of starting treatment in patients with ISSHL. Intratympanic steroid treatment is well tolerated and relatively easy to perform with no reported complication.

Key Words: Intratympanic – Steroids -- Idiopathic sudden sensorineural -- Hearing loss.

Introduction

SUDDEN sensorineural hearing loss (SSHL) is considered an ear, nose, and throat (ENT) emergency. The definition of the hearing loss includes abrupt hearing deterioration of 30 dB or more in at least 3 consecutive frequencies that occur during no more than 3 days [1]. The etiologies of sudden hearing loss are many, but only about 10-15% of cases have an identifiable cause [2]. Etiologically, many causes, such as viral cochleitis, vascular injury, autoimmure inflammation and inner ear membrane rupture have been proposed [3]. Many factors appear to affect recovery; the degree of hearing loss, the shape of the audiogram, the presence of vertigo and the time between the onset of SSHL and therapy [4].

Several treatment protocols have been proposed for treating SSHL, but no one treatment is accepted by all [8]. The diversity of treatment protocols is due to the lack of a fully understood ethiopathogenesis of the disease. The confusion is enhanced because there is also a spontaneous recovery rate without any treatment [6]. Conversely, SSHL should be approached as an emergency, given that early intervention is associated with the best prognosis [7,8]. Corticosteroids, antiviral agents, anticoagulants, vasodilators, anti-inflammatory drugs, and other approaches have been suggested for treating SSHL; there are reports of some benefit from most of these therapies. At present, the most commonly accepted treatment is systemic corticosteroid therapy [9].

Corticosteroids have multiple mechanisms of action including immune suppression, anti-inflammatory action, membrane stabilization, ion balance regulation and increased perfusion [10]. However, the efficacy of systemic steroids for the treatment of SSHL has been called into question by several investigators and that high doses of steroids can be associated with systemic effects and cannot be used in all patients [11]. The first report of intratympanic steroid therapy in the treatment of ISSHL was by Silverstein in 1996 followed by Parnes in 1999 [12,13].

Reported complications of intratympanic steroid are rare, and include pain, vertigo, otitis media,
perforated tympanic membrane, acne, dysgeusia, chronic otitis media, and subsequent hearing loss [13]. Based on these considerations, we started treating SSHL patients, by comparing traditional oral steroid therapy, with intratympanic steroids in order to better understand the real effectiveness of this treatment.

**Patients and Methods**

The study included 24 patients who were diagnosed as cases of SSHL between March 2009 and March 2011. All patients were submitted to a standard protocol for etiological investigation in the form of: (A) Full clinical otolaryngology examination with especial interest to otological and tuning fork assessment; (B) Auditory assessment comprised pure tone audiometry (PTA) tympanometry with acoustic reflex and speech recognition test; (C) Labrotaory studies: lab studies were directed according to history and clinical examination in the form of (1) CBC count and differential for infection; (2) Fasting blood glucose for diabetes mellitus; (3) Cholesterol and triglycerides for hyperlipidemia; (4) International normalized radio (INR), activated partial thromboplastin time (aPTT), and clotting time for coagulopathy; (5) Thyroid-stimulating hormone (TSH) for thyroid disease; (6) Antinuclear antibodies (ANA), rheumatoid factor, and erythrocyte sedimentation rate (ESR) for autoimmune diseases (D) Radiological assessment: Magnetic resonance imaging (MRI) with gadolinium of the brain and internal auditory canals.

The criteria for inclusion in this study were as follow (1) 30 dB loss in 3 consecutive frequencies in <72 hours; (2) Normal or near normal hearing in the contralateral ear; (3) hearing loss not more than 2 weeks; (4) normal otoscopic exam; (5) Normal MRI with contrast of the brain and internal auditory canals; (6) Negative serologic studies for infectious and inflammatory disease.

Exclusion criteria in this study were as follow (1) children to rule out congenital malformation; (2) history of chronic otitis media; (2) history of trauma (head, acoustic, or barometric); (3) history of Meniere's disease, hydrops, or fluctuating hearing loss; (4) history of meningitis; (5) history of prior ear surgery; (6) history of radiation; (7) exposure to ototoxic medications.

Patients were divided into 2 groups: Group A treated with oral prednisolone and Group B treated with intratympanic methyl prednisolone (MP). Informed consents were taken from all patients in both groups after getting approval from the local ethical committee.

All patients started treatment as early as possible after the presentation. In group A, patients were treated with prednisolone 1mg/kg/day, with tampering after 5 days and complete withdrawal at the end of three weeks. In group B patients, intratympanic methylprednisolone (MP) was given. Methylprednisolone was selected for the present study based on preliminary literature on the pharmacokinetics of its distribution in the inner ear [14].

**Technique of intratympanic methyl prednisolone (MP):** Prior to any procedure, patients were oriented as to the risks and expectations about the procedure and signed a free informed consent form. EMLA cream was applied for topical anesthesia. EMLA cream was placed in the outer ear canal and the tympanic membrane and left for 30 to 45 minutes, after which it was removed. Next, the patient's head was placed at 45º towards the unaffected ear. A 40mg/mL methylprednisolone solution was warmed to body temperature in a water bath. About 0.3 to 0.5mL of the solution was injected into the middle ear; two orifices were made with a 21 gauge needle, one immediately below the umbus (where the drug will be administered) and another on the postero-superior region (vent hole). No ventilation tubes were needed.

After intratympanic application of the steroid, the patient was invited not to swallow and to remain with his/her head turned to the opposite side for 20-30 minutes to maximize exposure of the round window membrane to the solution. Patients were asked to avoid water in the treated ear for at least two weeks. Injections were repeated at approximately one-week intervals for a total of 3 injections (3 injections over approximately 14 days). No patient suffered any complications from the intratympanic application of MP.

Audiological assessment was repeated one day, one week, two weeks, one month, two months and three months consecutively after starting treatment for all patients in both groups. A change of greater than or equal to 15 dB in mean pure tone (PTA, 4 frequencies-0.5, 1, 2, 4kHz) was considered significant.

The statistical analyses were performed in which paired sample $t$-test used to compare values of PTA before treatment and during follow-up.

**Results**

This study is a prospective non-randomized comparative study done on 24 patients with SSHL:
17 of them were males (70.8%) and 7 were females (29.2%). The age of patients ranged from 22 to 64 years with the mean age of 44. The right ear was affected in 14 patients (58.33%) and the left ear was affected in 10 patients (41.66%). The presence of tinnitus was observed in 100% of the cases. As to configuration of audiometric curve, flat losses reaching all frequencies were the most frequent ones, observed in 12 patients (50%); ascending curves were observed in 6 cases (25%), descending in 3 patients (12.5%), and in 3 patients (12.5%) hearing loss affected preferably medium frequencies.

In group A patients, as to severity of hearing loss at the diagnosis: 4 patients (33.3%) had moderate loss, 3 patients (25%) had severe, and 5 patients (41.6%) had profound loss. The interval between the onset of SSHL and oral therapy ranged from 2 to 12 days with a mean of 5.41 ± 3.21 SD days.

In group B patients, as to severity of hearing loss at the diagnosis: 4 patients (33.3%) had moderate loss, 3 patients (25%) had severe, and 5 patients (41.6%) had profound loss. The interval between the onset of SSHL and intratympanic steroid ranged from 2 to 13 days with a mean of 5.25 ± 3.30 SD days.

In all patients, PTA after one day (PTA-1) is similar to that before treatment (b-PTA). So, PTA-1 not used for comparison in the statistic because no improvement was detected at that time for all patients. Also, PTA after one month (PTA-30) of starting treatment was similar to that after 2 and 3 months consecutively, so PTA-30 was used in the statistics because it is the least duration to get best recovery post therapy. The numerical values of PTA used in the study means the degree of hearing loss by decibels.

In group A, the mean PTA before oral steroid (b-PTA) and at one month after starting treatment (PTA-30) were 80.5 ± 14.24 SD and 47.5 ± 9.88 SD respectively. No patient showed improvement of PTA ≥ 15 db after 7 days (PTA-7) and 3 patients (25%) improved after 2 weeks (PTA-14) and 11 patients (91.6%) improved after 1 month treatment and 1 patient failed to improve.

In group B, the mean PTA before intratympanic steroid and at one month after starting treatment were 81.91 ± 17.31 SD dB and 50.83 ± 20.06 SD respectively. Two patient (16.6%) showed improvement of PTA ≥ 15 db after 7 days, 10 patients (83%) improved after 2 weeks and 12 patients after 1 month.

The statistical results, obtained with t-test for paired data, showed:
- Comparing b-PTA with PTA-7, PTA-14 and PTA-30 in group A: A statistically significant difference was found between b-PTA and PTA-14 and PTA-30 (p<0.05). No statistically significant difference was observed between b-PTA and PTA-7. These data (mean values and p-values) are summarized in Table (3).
- Comparing b-PTA with PTA-7, PTA-14, and PTA-30 in group B: A statistically significant difference was found between b-PTA and PTA-7, PTA-14 and PTA-30 (p<0.05). These data (mean values and p-values) are summarized in Table (4).
- No correlation was found between PTA improvement (ΔPTA) and age, nor between the time of starting treatment and PTA improvement (ΔPTA) in group A or group B patients.

Table (1): Mean PTA and Standard deviation in group A.

<table>
<thead>
<tr>
<th>PTA</th>
<th>Mean</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before oral</td>
<td>80.5</td>
<td>14.24</td>
</tr>
<tr>
<td>7 days</td>
<td>79.66</td>
<td>13.24</td>
</tr>
<tr>
<td>14 days</td>
<td>70.58</td>
<td>14.43</td>
</tr>
<tr>
<td>1 month</td>
<td>47.5</td>
<td>9.88</td>
</tr>
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</table>

Table (2): Mean PTA and Standard deviation in group B.

<table>
<thead>
<tr>
<th>PTA</th>
<th>Mean</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before intratympanic (TT)</td>
<td>81.91</td>
<td>17.31</td>
</tr>
<tr>
<td>7 days</td>
<td>77.76</td>
<td>18.22</td>
</tr>
<tr>
<td>14 days</td>
<td>56.66</td>
<td>20.45</td>
</tr>
<tr>
<td>1 month</td>
<td>50.83</td>
<td>20.06</td>
</tr>
</tbody>
</table>

Table (3): The relationships between PTA values before and during follow-up (before treatment and 7, 14 and 30 days after treatment) for patients in group A.

<table>
<thead>
<tr>
<th>PTA</th>
<th>Paired difference Mean</th>
<th>SD</th>
<th>95% confidence interval of the difference</th>
<th>t</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before oral and 7 days</td>
<td>0.83</td>
<td>1.466</td>
<td>−9.86 - 1.76</td>
<td>1.968</td>
<td>0.075</td>
</tr>
<tr>
<td>Before oral and after 14 days</td>
<td>9.91</td>
<td>11.21</td>
<td>2.79 - 17.04</td>
<td>3.064</td>
<td>0.011*</td>
</tr>
<tr>
<td>Before oral and after 1 month</td>
<td>23.08</td>
<td>10.91</td>
<td>16.14 - 30.01</td>
<td>7.325</td>
<td>0.000*</td>
</tr>
</tbody>
</table>

* Means statistically significant.
The intervals between the onset of SSHL and steroid therapy were almost similar in both groups. Group A have a mean of 5.41 ± 3.21 SD days and...
group B have a mean of 5.25±3.30 SD. As such allowed the comparison of the two way of steroid therapy with less bias.

In this study, two patients in group A have different ages (age 24 and 62 consecutively) both have the same b-PTA and treatment was started all at the same time resulting to the same PTA-30. Group B has the same in its three patients. From this previous finding, there were no correlation found between the age and the degree of improvement of PTA after treating each group. As such can be because of the small number of patients per group and thus allowed us to compare with less bias. This finding is similar to the study done by Raymundo et al. [9] who reported that there are no statistically significant relationships between age and improvement after intratympanic steroids.

It was found in this study that, three patients in group A have the same age, b-PTA and 30-PTA but started the treatment at different times-day 2, day 7 and day 12 consecutively after SSHL. Group B has the same in four patients. So, no correlation was found between the time of starting therapy after SSHL and the degree of improvement in both groups. This finding is different from the study of Bittar et al. [30], which observed a significant inverse linear correlation between time from SHL onset to time of starting treatment and the audiometric progression (baseline PTA minus final PTA: ΔPTA). This may be due to that in our study, all patients started treatment less than two weeks from the onset of SSHL but in the study done by Bittar et al., they included patients up to 30 days from onset of SSHL.

This study suggests that the PTA improvement does not depend on the basal PTA levels, this is different from the research done by Ferri et al. [31] who reported that Patients with severe losses greater than 90dB had a poorer recovery (7.2%) compared with losses less than 90dB (35.6%). As far as concerns this observation, it must be borne in mind that our study refer to a small group of patients, on the other hand the study done by Ferri et al., was on 159 patients.

In this study, the degree of PTA improvement after 7 days of starting treatment (PTA-7) in group A patients was not significant as p-value was 0.075. On the other hand, it was significant in group B patients as p-value was 0.03 (Tables 3,4). This finding was very encouraging to patients treated by intratympanic steroids because they improved very early.

In our study, the degree of PTA improvement after 14 days of starting treatment (PTA-14) was significant in both groups, but it was significant in group B (p-value was 0.00) more than group A patients (p-value was 0.011). On the other hand, the degree of PTA improvement on the day 30 after starting treatment (PTA-30) was significant in group A (p-value was 0.000) more than group B patients (p-value was 0.002 in group B) (Tables 3,4).

The results of this study agreed with the research conducted on 250 patients by Rauch et al. [32]. The latter concluded that the improvement in PTA at 2 months in the intratympanic methylprednisolone group was not inferior to PTA improvement in the oral prednisone group.

The mean b-PTA, PTA-7, PTA-14 and PTA-30 in group A patients were 80.5, 79.6, 70.5 and 47.5 respectively (Table 1). This implied that most of patients treated with oral steroids for SSHL would improve after one month of starting treatment, whereas after two weeks would show lesser improvement. Relatively, if patients treated with oral steroids for SSHL showed no response after one week, treatment must be continued for a higher chance of improvement after a month. On the other hand, in group B patients the mean b-PTA, PTA-7, PTA-14 and PTA-30 were 81.91, 77.1, 56.66 and 50.83 respectively (Table 2). It means that most of patients treated with intratympanic steroids showed improvement after 2 weeks, this is an early indicator for the patients who will improve by this modality of treatment. The present study is little similar to the research of Ito et al. [33], who assessed 90 SHL patients and found that patients recovered within 2 weeks had more chances of recovering more completely.

From the previous finding, we can assume that oral or intratympanic steroids leads to significant improvement after one month of treatment, provided that we started treatment less than two weeks from the onset of SSHL. Moreover, intratympanic steroids leads to significant improvement of hearing that is not so much lower than oral steroids, but the potential benefit of intratympanic treatment over oral is reduced systemic steroid exposure and associated systemic adverse effects. Adverse effects from oral steroids are well known and usually manageable. They include change in appetite, mood, or sleep pattern; weight gain; gastritis; and increased thirst. More serious medical effects can include hypertension, hyperglycemia, cataract formation, and avascular necrosis of the hip. Another advantage of the intratympanic steroids is
the possibility of using this method if there is any contraindication or hazardous effects of using oral steroids in patients with hypertension, diabetes mellitus, osteoporosis or hyperacidity. Even, patients who are afraid or cannot be convinced of using oral steroids, they can accept using intratympanic steroids as good effective alternative way.

There were no side effects observed from injecting intratympanic steroid. The present study was conducted only on a small number of patients and further studies are needed on a large number of patients with long duration of hearing loss.

**Conclusion:**

Intratympanic steroids leads to significant improvement of hearing after 1 month of starting treatment in patients with SSHL that is not so much lower than oral steroids considering that intratympanic steroid treatment started within 2 weeks from the onset of SSHL. Moreover, Intratympanic steroid leads to significant improvement of hearing more than oral steroids after 7 days and 14 days of starting treatment. Intratympanic steroid treatment is well tolerated, relatively easy to perform and represents an effective and safe solution in patients with SSHL in whom oral steroids is contraindicated or hazardous.

**References**


