Introduction

Idiopathic sudden sensorineural hearing loss (ISSNHL) is considered an otologic emergency requiring immediate and careful clinical intervention, followed by appropriate and specific treatment (Ahn et al., 2007). ISSNHL is defined as the rapid decline in hearing in less than 3 days >20 dB in >3 contiguous audiometric frequencies without any identifiable cause (Byle, 1984). ISSNHL occurs over a short period of time and its degree may vary from a mild to profound hearing impairment in otherwise normal hearing individuals. The disorder has an estimated incidence of 5-20 cases per100,000 populations (Mattox et al., 2005). The hearing drops over a few minutes or few hours, or patients awaken in the morning with hearing loss. This condition however constitutes a medical emergency because the window of opportunity for treatment is narrow and early administration of steroids is more efficacious than watchful waiting (Rauch, 2004). No single treatment exists leading to complete recovery to pre-hearing loss levels. Proposed treatments have included vasodilators, steroids (Intratympanic or systemic), antiviral agents, hyperbaric oxygen and plasmapheresis (Slattery et al., 2005). The use of steroids is due to the work of Wilson, (1983) who demonstrated recovery rate of 60% after systemic steroid therapy. IT

The primary reason for the use of IT steroid without systemic steroids is in patients who can’t tolerate systemic steroids or those who at greater risk for complications from systemic steroids e.g. Diabetes mellitus (Lefebre and Staeker, 2002).

The uses of Intratympanic steroids have evolved into 3 main protocols for treatment of ISSNHL:

- As an initial or primary treatment for ISSNHL without systemic steroids.
- As adjunctive treatment given concomitantly with systemic steroids for ISSNHL.
- As salvage therapy after failure of systemic steroids for ISSNHL (Haynes et al., 2007).

Meta-analysis is a quantitative statistical procedure that synthesizes findings across many studies, overcoming the problems of small samples and diverse outcomes and programs. According to Tobler (1986), the computation of the effect size is dependent on statistically significant results. Instead of discounting the studies whose results do not reach statistical significance, as would be the case in a literature review, the quantitative results of each study are converted into a common metric (effect size) allowing comparison of results across studies.

Methods:

Searching at the pub-med (Medline database) for articles including the following keywords:

- Intratympanic steroids in ISSNHL.
- Efficacy of Intratympanic steroids in ISSNHL. The search was limited to articles published in English language and human studies till 1/5/2013 the search resulted in 248 abstract out of them 52 articles was relevant to the target.

Table (1): Summary of screening of articles.

<table>
<thead>
<tr>
<th>Keywords</th>
<th>Number of articles and their abstracts</th>
<th>Relevant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intratympanic steroids, ISSNHL, efficacy of IT steroids in SHL</td>
<td>248</td>
<td>52</td>
</tr>
</tbody>
</table>

The screening form of articles was used by the investigators to screen the articles which were yielded by the Medline search after blinding the author name and journal name. Screen form of the articles:

1) Irrelevant articles: articles that miss one or more of the above keywords.
2) Relevant articles: articles which contain the above keywords.
3) Included articles: These are 8 articles which fulfilled the following inclusion criteria:

- Randomized control trial studies.
- Number of patients were mentioned in study and control group.
- Acute onset of hearing loss within 24-72 hours.
- Unilateral or bilateral hearing loss.
- Hearing loss of 20 dB or more in at least 3 contiguous audiometric frequencies.
- No otologic history in the affected ear.
- Description of the approach.
- Using IT steroids as primary treatment, salvage treatment or in combination with systemic steroids.
- Functional outcome is mentioned.

Results:

The data were collected from the chosen 8 articles fulfilling the previously mentioned criteria. Data analysis was performed utilizing Meta-analytic Review Manager (RevMan 5) software. The results of the data collected from the chosen articles were fed into the above mentioned (RevMan 5) software.
Table 2: Meta-analysis for Intratympanic steroids use in ISSNHL.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Intratympanic steroid</th>
<th>Control/systemic steroid</th>
<th>Odds Ratio</th>
<th>M.A. Fixed 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahm et al 2008</td>
<td>16</td>
<td>50</td>
<td>50</td>
<td>13.7%</td>
</tr>
<tr>
<td>Ho et al 2004</td>
<td>7</td>
<td>15</td>
<td>13</td>
<td>7.5%</td>
</tr>
<tr>
<td>Kars et al 2007</td>
<td>4</td>
<td>26</td>
<td>21</td>
<td>11.9%</td>
</tr>
<tr>
<td>Klif et al 2007</td>
<td>5</td>
<td>13</td>
<td>18</td>
<td>14.3%</td>
</tr>
<tr>
<td>Lee et al 2008</td>
<td>18</td>
<td>35</td>
<td>18</td>
<td>6.1%</td>
</tr>
<tr>
<td>Lee et al 2011</td>
<td>21</td>
<td>21</td>
<td>25</td>
<td>9.5%</td>
</tr>
<tr>
<td>Muon et al 2011</td>
<td>34</td>
<td>90</td>
<td>59</td>
<td>28.1%</td>
</tr>
<tr>
<td>Xie &amp; al 2006</td>
<td>10</td>
<td>15</td>
<td>18</td>
<td>3.4%</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>263</td>
<td>243</td>
<td>102</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi^2 = 20.98, df = 7 (P = 0.004), I^2 = 67%
Test for overall effect: Z = 4.24 (P < 0.0001)

Table 3: A comparison between many articles done on intratympanic steroid perfusion in ISSNHL (Haynes et al, 2007).

<table>
<thead>
<tr>
<th>Author</th>
<th>Criteria for Improvement</th>
<th>Current Study With Applied Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silvershtam et al, 1996</td>
<td>Complete recovery (OR)</td>
<td>OR within 10 dB of unaffected ear</td>
</tr>
<tr>
<td>33.3%</td>
<td>Partial: 33%</td>
<td>NR less than 10 dB Improvement</td>
</tr>
<tr>
<td>Jackson, 1996</td>
<td>Complete recovery (OR)</td>
<td>OR within 10 dB of unaffected ear</td>
</tr>
<tr>
<td>33.3%</td>
<td>Partial: 33%</td>
<td>NR less than 10 dB Improvement</td>
</tr>
<tr>
<td>Ho et al, 2004</td>
<td>Complete recovery (OR)</td>
<td>OR within 10 dB of unaffected ear</td>
</tr>
<tr>
<td>33.3%</td>
<td>Partial: 33%</td>
<td>NR less than 10 dB Improvement</td>
</tr>
<tr>
<td>Heer and Marozzi, 2005</td>
<td>Complete recovery (OR)</td>
<td>OR within 10 dB of unaffected ear</td>
</tr>
<tr>
<td>33.3%</td>
<td>Partial: 33%</td>
<td>NR less than 10 dB Improvement</td>
</tr>
<tr>
<td>Bartlett, 2006</td>
<td>Complete recovery (OR)</td>
<td>OR within 10 dB of unaffected ear</td>
</tr>
<tr>
<td>33.3%</td>
<td>Partial: 33%</td>
<td>NR less than 10 dB Improvement</td>
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There was a significant difference between systemic steroids and Intra-tympanic steroids administration.
Discussion:

Sudden sensorineural hearing loss is an otologic emergency; which represents a symptom or clinical sign rather than a disease. It occurs in 5-20 per 100,000 populations. Although various methods of management have been used in the literature, systemic steroids were the most widely used medication.

In this study we aimed to compare the effect of IT steroids in the treatment of ISSNHL; while treating another group of patients with systemic steroids as a control. The search was done through the Pubmed, where 52 articles relevant to the target were found, in which 44 articles were excluded because they didn’t fulfill the inclusion criteria and only 8 articles fulfilled the inclusion criteria. Data analysis was performed utilizing Meta-analytic Review Manger. Meta-analysis is a systematic approach to identify, appraise, synthesize and combine the results of relevant studies to reach to conclusions. All the studies analyzed during this meta-analysis were randomized controlled trials. The results of this Meta-analytic study as regard response of hearing to IT steroids showed that there is a significant improvement in hearing results in patients receiving local steroids against to the control group that received systemic steroids alone.

The total number of patients included in the meta-analysis were 506 suffers from ISSNHL, 263 received Intratympanic steroid therapy and 243 received systemic steroids, among them 158 patients improved after receiving Intratympanic steroids, and only 81 patients improved after receiving systemic steroids. The included studies were HO, 2004; Kara, 2010; Kilic, 2007; Lee, 2011; Moon, 2011; and Xenellis, 2006 and their colleagues. All these studies showed significant improvement of hearing with intratympanic steroids therapy versus systemic steroids. On the contrary Ahn et al., 2007 and Lee et al., 2008 state that there is no significant improvement of hearing after addition of intratympanic steroids to systemic steroids. The results of this Meta-analytic study support the former theory; that is, intratympanic steroid therapy is significantly effective in treatment of ISSNHL. These findings also agree with Xenellis et al., 2006; Moon et al., 2011; Lee et al., 2011; Kilic et al., 2007; Kara et al., 2010 and Ho et al., 2004.

IT steroids administration as an alternative modality for ISSNHL appears attractive because it avoids the systemic side effects of steroids and also obtains a higher inner ear concentration than systemic steroids. Steroids seem to be efficacious regardless of the etiology involved because of their anti-inflammatory effect which is based on the inhibition of pro-inflammatory cytokine secretion, immunosuppressive activity, neuroprotective, antioxidant and antiapoptotic effect. These drugs are the only form of treatment that has been shown to be effective in clinical trial, as there are glucocorticoid and mineralocorticoid receptors in the inner ear.

IT steroid therapy is used either as an initial therapy or adjuvant therapy with systemic steroids or as salvage therapy after systemic steroids failure. Parnes et al., 1999 and Chandrasekhar, 2001 reported relatively successful results with IT steroids therapy as an initial therapy in ISSNHL instead of systemic steroids, but in our study no one of included studies used IT steroids as initial therapy. It was found that IT steroids have better concentration in the inner ear fluids than systemic steroids (Chandrasekhar, 2001). Comparing the perilymph steroid concentration between the intravenous and IT administration of
the drug, the local usage was significantly more effective than systemic administration.

Conclusion:

Intratympanic steroid therapy is effective in treatment of ISSNHL either as a salvage therapy after failure of systemic steroids or in combination with systemic steroids.

References:

6-Dallan Lacopo, Luca Bruschini, Andrea Nacci, Paolo Bruschini, Claudio Traino, Ferdinando
7-Rognini and Bruno Fattori.: Transtympanic steroids as a salvage therapy in SHL preliminary results. ORL 2006; 68:247-252.


