

# Intratympanic Steroid Therapy for Treatment of Idiopathic Sudden Sensorineural Hearing Loss

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**In the primary treatment of ISSHL, achieving the correct diagnosis rapidly is paramount, as early initial treatment greatly increases the chance of hearing recovery.**



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## Abstract

**Idiopathic sudden sensorineural hearing loss (ISSHL) is the sudden loss of unilateral hearing of unknown etiology. The standard treatment consist of a high dose oral steroid taper. This article serves to review the current literature on intratympanic steroid injections for ISSHL. Current literature suggested intratympanic steroids are equivalent to oral steroid therapy, primary combined therapy is superior to either alone and intratympanic steroids should be offered for salvage therapy in ISSHL.**

## Introduction

A sudden decrease in sensorineural hearing from an unknown etiology broadly defines idiopathic sudden sensorineural hearing loss (ISSHL). There is no consensus regarding the exact degree and time frame of ISSHL, but the most common definition used is a 30 decibel (dB) loss over three continuous frequencies occurring within three days. A more general definition of any noticeable and measurable loss of hearing function over the course of minutes to days is often used.<sup>1</sup> A recent article estimates the incidence in the U.S. to be 27 out of 100,000 people with a slight male predominance.<sup>2</sup> Hearing loss is usually unilateral and associated symptoms include feeling of ear fullness, tinnitus and dizziness/vertigo.<sup>1</sup>

A number of different etiologies

have been proposed to explain ISSHL including viral infection, intracochlear membrane rupture, vascular insults, and autoimmune processes; however none of these have been proven definitively in humans.<sup>3</sup> A recent review article found that hypertension, diabetes, smoking history, heavy alcohol use and short sleep durations were more common in patients with ISSHL than controls.<sup>4</sup> The same article also found that genetic mutations associated with thromboembolic events were more common in patients with ISSHL. Most likely, each of these underlying etiologies contributes to some proportion of the total incidence of ISSHL.

Treatment strategies used for ISSHL are nearly as diverse as the proposed etiologies. Cochrane reviews exist for the use of oral steroids, antivirals, vasodilators/ vasoactive substances and hyperbaric oxygen.<sup>5,6,7,8</sup> These reviews concluded that the benefit of oral steroids remains unclear and the effectiveness of vasodilators remains unproven. Hyperbaric oxygen therapy significantly improved hearing, but secondary to the few number of patients and poor reporting, clinical significance remains unclear. There are ongoing reviews for intratympanic steroids, antioxidants and acupuncture. A multitude of other interventions have been attempted with minimal clinical response. Currently, the most widely used treatment for ISSHL is systemic glucocorticoids. The first published article looking at oral

steroid therapy was in 1980.<sup>9</sup> This placebo controlled, double blind study with 67 patients found that oral steroids resulted in 61% of patients recovering hearing as compared to 32% of the placebo group. A recent Cochrane review concluded that the evidence supporting the use is unclear<sup>8</sup> and a recent multicenter placebo-controlled, triple-blind study concluded that oral steroids did not seem to influence the recovery of hearing in ISSHL in 93 patients.<sup>10</sup>

The American Academy of Otolaryngology published a recent clinical practice guideline detailing recommendations regarding ISSHL.<sup>11</sup> By definition, ISSHL results in a sensorineural hearing loss so it is imperative to rule out a conductive hearing loss (such as cerumen impaction) by physical exam and audiometry. The history and physical should also assess patients for bilateral sudden hearing loss, recurrent or fluctuating hearing loss and focal neurological deficits, as these can point to underlying etiologies. The guideline recommended against routine CT scan or laboratory testing, but recommended MRI or auditory brainstem response to rule out retrocochlear pathology such as vestibular schwannoma. The guideline stated that oral corticosteroids could be offered, but then acknowledged the paucity of studies to support their use. It was stated that clinicians should not “routinely prescribe antivirals, thrombolytics, vasodilators, vasoactive substances, or antioxidants”. The guideline suggested that intratympanic steroids were an alternative for primary treatment and recommended them after failure of initial management. Just as the Cochrane review suggested some benefit from hyperbaric oxygen<sup>7</sup> the guideline recommended offering patients with ISSHL hyperbaric oxygen treatment within three months of diagnosis. The difficulties of obtaining hyperbaric oxygen treatment were mentioned, including the relatively few number of treatment centers and lack of insurance coverage/cost to patient. Finally, the guideline reiterated the importance of follow up audiometry and offering hearing amplification for those who do not fully regain hearing.

The use of intratympanic steroid injections for inner ear disorders was described in the mid 1990s for use in patients with Meniere’s disease, autoimmune inner ear disease and sudden sensorineural deafness.<sup>12</sup> Since that time it has grown in popularity for several reasons. As described above, the most common treatment for ISSHL is oral corticosteroids. Although no clear side effects of steroids used in ISSHL was reported in the Cochrane review<sup>8</sup>, the side effects of long term use can include fluid and electrolyte abnormalities, hypertension, hyperglycemia, increased susceptibility to infection, osteoporosis, myopathy, behavioral disturbances, cataracts, growth arrest, fat redistribution, striae and ecchymosis.<sup>13</sup> Minimal systemic absorption of intratympanic steroids has been reported and the risk of systemic side effects is minimized.<sup>14</sup> Studies have shown that cochlear perilymph concentrations are on the order of 100



Figure 1  
Injection of Intratympanic steroids using binocular otoscope. Patient in supine position. Topical phenol applied to anteriosuperior quadrant followed by injection of steroids.

fold higher with intratympanic administration of steroids vs IV or oral.<sup>14</sup> Injection of steroids through the tympanic membrane comes with some associated risk such as residual perforation or increased susceptibility to infection, however few actual complications were reported in the studies reviewed in this article.

Intratympanic steroid injections are relatively simple to perform, and an increasing percentage of generalist ENTs perform them. The general procedure at this institution is similar to ones described in studies reviewed by this article. The patient is placed supine in a chair. (See Figure 1.) Topical anesthetic (often phenol) is placed on the anterosuperior quadrant of the tympanic membrane. An aqueous solution of steroid (dexamethasone, methylprednisolone) is then injected through the anesthetized region until the middle ear is full. (See Figure 2.) The patient remains supine with the injected ear pointed up for 20-30 minutes, to facilitate passage of steroid across the round window membrane. Overall the procedure is no more difficult than an in office myringotomy, which most general otolaryngologists are comfortable performing.

It has been shown that intratympanic steroids are safe and minimize the side effects associated with systemic steroids while resulting in much higher cochlear concentrations than IV or oral preparations. The questions that remain, like many of the treatments for ISSHL, is does it work and when should it be used? There are a number of articles in the literature that describe the use of intratympanic steroids for use in ISSHL. Some of the articles describe using intratympanic steroids as primary treatment, with or without other treatments (usually oral steroids). Others describe the use as secondary or salvage treatment after initial treatment has failed or there is residual hearing loss. This article will review



**Figure 2**

Materials for intratympanic injection: steroid (methylprednisolone and dexamethasone pictured), phenol, ear speculum, syringe with luer lock needle.

the current literature on intratympanic steroids and their use in ISSHL. The review will concentrate on randomized studies with preference for placebo controlled trials.

### Literature Review

#### *Intratympanic Therapy*

#### *as Primary Treatment for ISSHL*

First studies looking at the effects of intratympanic steroid therapy as a primary treatment were considered. A single randomised, placebo controlled, triple blind study comparing intratympanic steroids to a placebo therapy was found.<sup>15</sup> The study consisted of 50 patients with moderate unilateral ISSHL. 25 were placed in the experimental group and received intratympanic prednisolone once a day for 3 consecutive days. The control group consisted of the other 25 patients and received saline injections for 3 consecutive days. The primary outcome measured was improvement in pure tone averages. Anyone who did not show a complete recovery on day 7 in either group was treated with an oral steroid taper. Notable findings included a complete recovery in 76% of the intratympanic group on day 7 and only 20% of the control group on day 7. Also noted was no recovery on day 7 in 4% of the experimental group and 80% of the saline group. By the end of the study (after patients who did not recover by day 7 had the oral steroid taper), there was no statistical difference in the hearing thresholds of the two groups. Also of note, if a patient failed to completely respond to intratympanic steroids, they did not further benefit from additional steroids. Overall, the authors suggested that the study supported the use of steroids, whether intratympanic or oral, for first line treatment for ISSHL.<sup>13</sup> The article also concluded that when intratympanic steroids were used

as monotherapy for primary treatment of ISSHL systemic steroids do not seem to offer any benefit when used as salvage treatment.

Another group of papers looked at primary intratympanic steroid treatment with or without systemic steroids versus systemic steroid treatment alone. A study out of Turkey in 2013 with 79 patients compared treatment of unilateral ISSHL with oral steroid therapy vs 4 intratympanic injections of methylprednisolone plus oral steroid therapy.<sup>16</sup> They showed an improvement of 44 dB in the intratympanic plus oral group pure tone average vs a 26 dB improvement in the oral steroid only group. The results were statistically the same for patients with an initial pure tone average of less than 70, but showed improved results with the intratympanic and oral group in those with a pure tone average of at least 70. The study concluded that the combination therapy, oral plus intratympanic steroids, was superior for primary treatment of ISSHL especially with severe hearing loss. A similar study with 158 patients out of Turkey compared systemic steroids alone vs systemic steroids in combination with intratympanic methylprednisolone.<sup>17</sup> They showed an improvement of 13 dB in the systemic steroid only group compared to 20 dB in the combination group. This was statistically significant and this group similarly recommended combination therapy as a primary treatment for ISSHL. Another similar article with 120 patients published in 2008 out of Korea reached a different conclusion.<sup>18</sup> The study compared oral steroid therapy to combination therapy with intratympanic dexamethasone. This study found a statistically significant improvement at only one frequency (250 Hz). They concluded that intratympanic steroids offered no benefit in ISSHL in comparison to oral steroid therapy alone.

The literature search also revealed multiple papers that compared systemic steroids alone vs intratympanic steroids alone; some of which had a third combined treatment group. A study out of Italy with 46 patients compared intratympanic dexamethasone alone and oral prednisone alone.<sup>19</sup> They found an improvement in hearing of at least 10 dB in 80% of the intratympanic group and 81% of the oral group. they concluded that either intratympanic or oral steroids alone would be equally effective in treatment of ISSHL. A Korean study from 2009 compared oral prednisone alone and intratympanic dexamethasone alone as primary therapy for ISSHL.<sup>20</sup> They found statistically better results in the high frequencies for oral therapy, but concluded that either modality alone could be used for primary treatment of ISSHL. A study out of the US with 51 patients compared three different groups; placebo and intratympanic dexamethasone, oral prednisone and intratympanic saline and oral prednisone and intratympanic dexamethasone.<sup>21</sup> They found an improvement of at least 15 dB in pure tone average in 71% of the intratympanic dexamethasone group, 44% of the oral prednisone group and 88% of the combined therapy group. There was a statistically significant improvement in the combined group vs either of the other groups. Of note this

study used a placebo for systemic therapy and intratympanic saline in the control groups. The study concluded that combined therapy was superior to intratympanic or oral steroids alone.

A study of 250 patients in the United States with ISSHL compared oral prednisone alone to four intratympanic injections of methylprednisolone alone for initial treatment.<sup>22</sup> The pretreatment pure tone average was 86.7 for the oral steroid group and 86.4 for the intratympanic steroid group. Following treatment the pure tone average improved 30.7 dB in the oral group and 28.7 in the intratympanic group. This was found to be statistically equivalent. This study concluded that intratympanic steroid treatment is not inferior to oral steroid treatment. In subgroup analysis, the authors noted a trend for better recovery with oral steroids in those with a pretreatment pure tone average of at least 90 dB and those who presented with dizziness.

### *Intratympanic Therapy as Salvage Treatment for ISSHL*

In addition to initial therapy in ISSHL, intratympanic steroid injections are also being used in salvage or secondary therapy after failure of initial therapy with systemic steroids. A study from China studied 65 patients who had been admitted for treatment of ISSHL and treated with IV prednisolone who showed no improvement in hearing.<sup>23</sup> The patients were split into three groups: intratympanic methylprednisolone alone, methylprednisolone drops onto the tympanic membrane alone and a group that received no further treatment. 38% of the intratympanic group showed an improvement in pure tone average of at least 10 dB with zero patients in the ear drop or control group showing this degree of improvement. The authors recommended intratympanic steroid therapy for those who failed systemic steroid treatment for ISSHL. Another placebo controlled, blinded study compared intratympanic dexamethasone to intratympanic saline injections in patients who failed systemic steroid therapy.<sup>24</sup> The study showed an improvement of at least 10 dB in 44.4% of the intratympanic steroid group compared to only 11.1% of the intratympanic steroid group. The authors again recommended the use of intratympanic steroids after failure of systemic steroid therapy. A Korean study compared the use of intratympanic dexamethasone to no further treatment in patients with ISSHL who failed systemic steroid treatment.<sup>25</sup> Similar to the other studies mentioned, 47.6% of the intratympanic steroid group showed improvement compared to only 16.0% of the controls. The authors recommended use of intratympanic steroids following failure of systemic steroids.

A single study was found that compared the use of additional systemic steroids to the systemic steroids with intratympanic methylprednisolone in patients that failed initial systemic therapy.<sup>26</sup> Patients in the study failed

conventional systemic steroids and were determined to have a 'poor prognosis'. Poor prognosis was defined as hearing loss greater than 70 dB, age older than 60, a flat or high high frequency hearing loss on audiogram, presence of severe vertigo or time exceeding 2 weeks from onset of initial treatment. 20.5% of the additional systemic steroids alone group showed an improvement of at least 15 dB in comparison to 45.9% treated with additional systemic steroids in combination with intratympanic steroids. The authors concluded that patients with 'poor prognosis' ISSHL may benefit from transtympanic therapy in combination with oral steroids for salvage treatment.

### **Discussion**

Given the obvious morbidity associated with ISSHL, it is clear that effective treatments are needed. The "gold standard" in the United States has been high dose oral steroid therapy, but recent review articles have concluded that the efficacy of this treatment is questionable.<sup>8,10</sup> Reviewing the literature reveals that intratympanic steroid therapy is proving to be beneficial for patients with ISSNL.

The studies described here seem to suggest that intratympanic steroid injections alone or systemic steroid therapy alone are equally effective in the treatment of ISSHL.<sup>15,19,20,22</sup> Patients with uncontrolled diabetes or other medical problems may not be able to tolerate high dose systemic steroid therapy, making initial treatment with intratympanic steroids a good choice. However, in certain communities, patients may not have access to an ENT who performs intratympanic injections and patients need to be able to see this specialist as soon as possible and 3-5 times over a two week period for injections.

Although monotherapy with either systemic or intratympanic steroids appears to be equally effective, the literature described above suggests that primary combined therapy is superior to monotherapy.<sup>16,17,21</sup> There were, however, studies that did not conclude combined therapy was superior.<sup>18</sup> The study that did not recommend combined therapy did show statistically significant improvement at 250 Hz.<sup>18</sup> When seeing a patient with ISSHL, offering both intratympanic and oral steroid therapy initially seems reasonable.

Studies suggest that the use of intratympanic steroids for secondary/salvage treatment is more effective than no additional treatment.<sup>23,24,25</sup> Many patients present to the ER or primary care physicians with ISSNL and are treated with oral steroid therapy. It is important for these physicians to know that patients who fail to respond to initial oral steroids may still benefit from intratympanic steroids. Most protocols in the literature initiated intratympanic injections immediately after failure of oral steroids. Physicians should promptly refer patients to an ENT comfortable performing transtympanic steroid injections.

Optimal delivery of transtympanic steroids and absorption into the cochlea is an active area of research. A study from Taiwan advocated the use of a MicroWick placed through the tympanic membrane and had patients place a dexamethasone solution in the external auditory canal twice a day<sup>27</sup> in an attempt to provide continual cochlear absorption of the steroid. Other companies are investigating ways to inject steroid into the middle ear that resorb much slower than the aqueous solutions currently being used, so that only one injection is needed.

There are multiple questions regarding intratympanic steroid treatment for ISSHL that remain unanswered. First, there is no universally accepted protocol for the use of intratympanic steroids. In the articles reviewed, the number of injections varied from 3 to 8 performed over a 1 to 4 week period; dexamethasone was most commonly used followed by methylprednisolone. Future studies determining the ideal steroid and the number and frequency of injections are needed. The treatment window for ISSHL remains uncertain. It is also unclear why some patients benefit from intratympanic steroids while others do not. As described above, multiple etiologies have been proposed to explain ISSHL. Likely, only certain underlying pathologies are amenable to steroid therapy. Subgrouping patients with ISSHL may result in better treatment strategies.

Perhaps the biggest hurdle in treatment of ISSHL with intratympanic steroids is recognizing the diagnosis and achieving timely access to care. A sudden drop in hearing in one ear is often incorrectly ascribed to fluid behind the ear drum or otitis media, and treated with decongestants or oral steroids. In the absence of a formal audiogram, a Weber tuning fork test can be used to ascertain if a hearing loss is conductive or sensorineural. The test is performed by holding a tuning fork (ideally 512 Hz) firmly against the forehead. Patients with a conductive hearing loss from otitis media or similar will hear the tuning fork louder in the affected ear, while patients with ISSHL will hear it better in the non affected (normal) ear. If a tuning fork is not available, a mobile phone or pager turned to its vibrate function and pressed against the forehead will work quite well. It is distinctly clear that rapid initiation of therapy for ISSHL profoundly increases the chance for a good outcome.

## Conclusion

In the primary treatment of ISSHL, achieving the correct diagnosis rapidly is paramount, as early initial treatment greatly increases the chance of hearing recovery. All patients with ISSHL should be evaluated for retrocochlear pathology by MRI with contrast, even if the hearing loss recovers. Both intratympanic steroids or systemic steroids alone appear equally effective, however the use of both intratympanic and systemic steroids together is likely superior to either used alone. Intratympanic steroids likely offer additional benefit as

a secondary/salvage therapy in patients who fail initial systemic steroid therapy. Hyperbaric oxygen treatment may play a role in ISSHL treatment, although robust data is lacking and patient access to hyperbaric oxygen therapy is limited.

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## Disclosure

None reported.

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