Transtympanic steroids for treatment of sudden hearing loss

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OBJECTIVES: **To determine whether transtympanic steroid administration may be an effective treatment for sudden onset sensorineural hearing loss (SSNHL) in patients for whom systemic steroid treatment has failed or who were not candidates for systemic steroids.**

METHODS: **The standard medical regimen for SSNHL usually involves systemic steroid therapy. Unfortunately, some patients do not respond successfully to or are poorly tolerant of systemic steroids. Transtympanic administration of steroids has been suggested as an alternative to systemic therapy. A prospective study was designed to evaluate the hearing outcomes in SSNHL patients treated with transtympanic steroids. Patients received transtympanic steroids if oral steroids had failed to work or if they were not able to tolerate oral steroids. Transtympanic steroids were administered through a ventilation tube placed with the patient under local anesthesia. Steroid administration was performed on 4 separate occasions over the course of 10 to 14 days. Hearing was assessed immediately before therapy and within 1 to 2 weeks after therapy.**

RESULTS: **Hearing improvement was documented in 10 of 23 patients (44%) who underwent transtympanic steroid administration. This represents a 44% hearing salvage in patients for whom steroid treatment would otherwise have been considered a failure.**

CONCLUSION: **Transtympanic steroid therapy may be an alternative treatment for patients with SSNHL for whom systemic steroid therapy had failed or who could not tolerate systemic steroid therapy.**
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Sudden sensorineural hearing loss (SSNHL) is defined as the rapid decline (≤3 days) in hearing (≥20 dB in ≥3 audiometric frequencies) without any identifiable cause. Approximately 4000 cases of SSNHL occur annually in the United States.[1] It has a variable recovery rate to a functional level that is usually quoted as 65%, but may range from 5% to 90%.[2]

One of the most popular theories of the etiology for SSNHL is viral-induced inflammation. Systemic steroid therapy has been a mainstay of treatment among those who suspect a viral inflammatory etiology and has been supported with controlled studies. Unfortunately, some patients do not respond successfully to or are poorly tolerant of systemic steroids. Transtympanic administration of steroids has been suggested as an alternative to systemic therapy. The purpose of this study is to determine whether transtympanic steroid administration may be an effective treatment for sudden hearing loss in patients for whom systemic steroid treatment has failed or who were not candidates for systemic steroids.

METHODS AND MATERIAL

Study Design

A prospective study was designed to evaluate the efficacy of transtympanic steroid administration for SSNHL. The diagnosis of SSNHL was defined as >20 dB of hearing loss in 3 or more contiguous audiometric frequencies occurring within 3 days. Patients were selected for inclusion in this study if they met the criteria for diagnosis of SSNHL and either failed to improve after a course of high-dose systemic steroid (1 mg/kg/day of prednisone for a minimum of 1 week, or equivalent) or could not tolerate systemic steroid therapy.

Technique

With the patient under local anesthesia (either topical EMLA cream or phenol application) a posterior-inferior tympanotomy was performed. The round window was then inspected with endoscopic visualization. Any adhesions of the round window niche were removed with micro-picks. A ventilation tube was placed through the tympanotomy. Steroids (either dexamethasone 25 mg/mL or methylprednisolone 125 mg/2 mL) were administered through a ventilation tube placed with the patient under local anesthesia. The steroid was instilled in the middle ear with the patient's head tilted 45

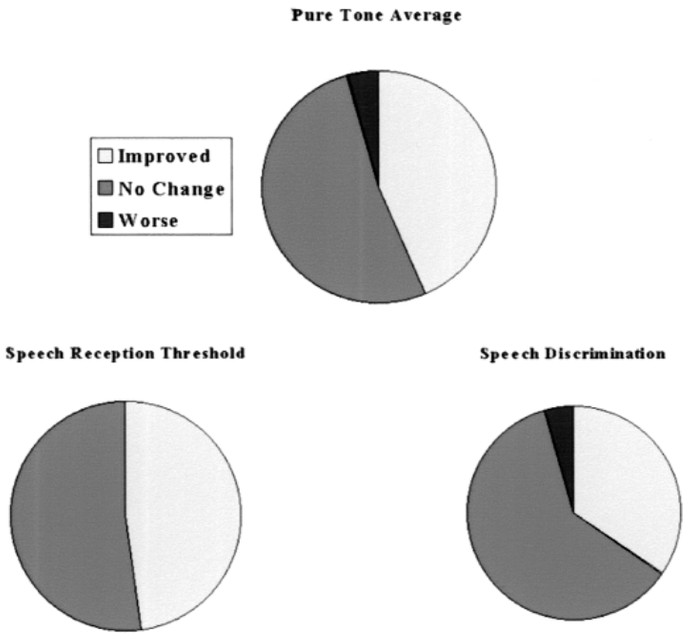

Fig 1. Overall results for all study participants for pure tone average, speech reception threshold, and speech discrimination.

degrees away. The instillation was performed such that the tip of the needle extended through the ventilation tube and into the middle ear. This was done to allow air escape and prevent bubble formation. Approximately 0.4 to 0.6 mL of medication were used in each perfusion. The steroids were allowed to perfuse the middle ear for 30 minutes. Steroid administration was performed on 4 separate occasions over the course of 10 to 14 days. Hearing was assessed by pure tone and speech audiometry immediately before and within 1 to 2 weeks after therapy was discontinued.

Data Collected

Data collected included audiometry, age, sex, time to treatment, and type of steroid perfused. Audiometric data collected included pretreatment and posttreatment pure tone averages, speech reception thresholds, and speech discrimination.

Criteria for Outcome

A change of greater than or equal to 10 dB in the pure tone average or speech reception threshold was considered significant. A change of greater than or equal to 10% in speech discrimination was considered significant. Any changes of lesser magnitudes were interpreted to be no change in hearing status.

Statistical Analysis

Group comparisons were analyzed with χ^2 or Fisher exact tests where indicated.

RESULTS

Twenty-three patients were enrolled in the study. Of these, prior steroid therapy had failed in 22, and 1 had not been able to tolerate steroid therapy. The average age of the patients was 63 years with a range of 34 to 83, and there were 12 men and 11 women. Time of onset to therapy averaged 72 weeks and ranged from 0 to 520 weeks. Methylpredisolone was perfused in 12 patients and dexamethasone in 11 patients. There was one complication. One patient had otitis media develop, which resolved after administration of oral and topical antibiotics.

Overall, pure tone average improvement was documented in 10 patients (44%) after transtympanic steroid administration (Fig 1). The average change in pure tone average for those with significant improvement was 15.2 dB. Twelve patients (52%) had no significant improvement in pure tone average. The 1 patient (4%) who had postperfusion otitis media develop had a drop in the pure tone average of 10 dB; the pure tone average returned to baseline after the infection cleared.

Overall, the speech reception threshold improved in 11 patients (48%) (Fig 1). The average improvement among these patients was 15 dB. Twelve patients (52%) noted no change, and there were no patients with a significant decline in the speech reception threshold.

Speech discrimination was improved in 8 patients (35%) with an average improvement of 21% (Fig 1).

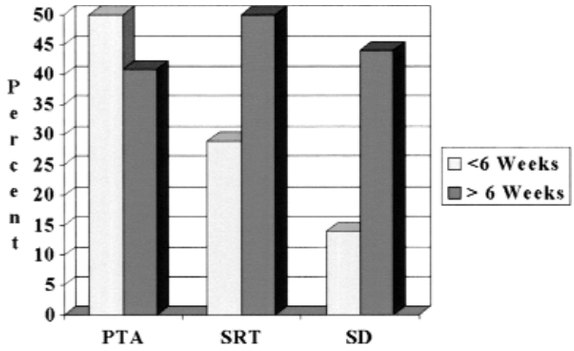

Fig 2. Hearing results comparing time to transtympanic steroid therapy, before or after 6 weeks from onset of hearing loss.

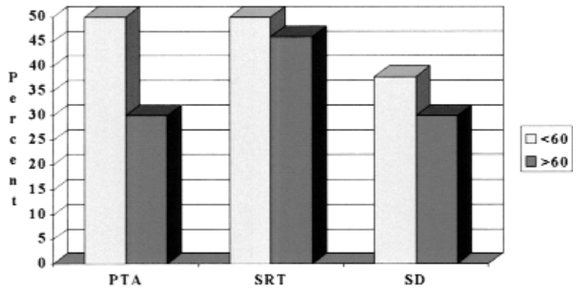

Fig 3. Hearing results compared by age greater than 60 or less than 60 years.

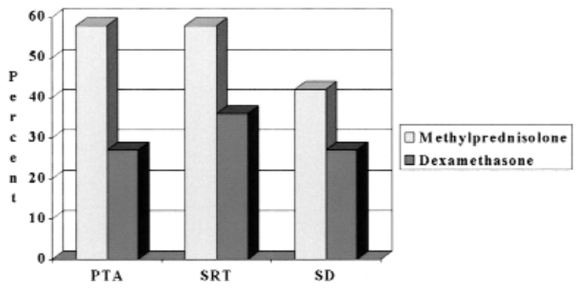

Fig 4. Hearing results comparing outcome for methylprednisolone- and dexamethasone-treated patients.

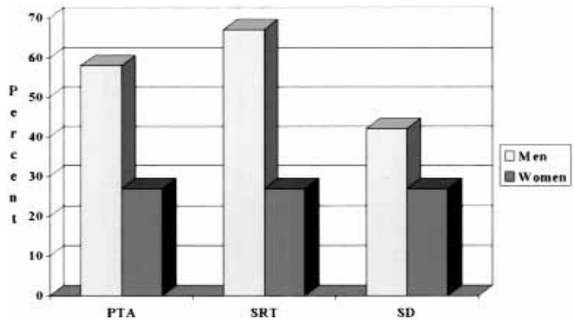

Fig 5. Hearing results comparing men and women.

Fourteen patients (61%) had no change in speech discrimination, and 1 patient (4%) had a decline in speech discrimination of 16%.

Patients were stratified by time to therapy before or after 6 weeks from the onset of hearing loss (Fig 2). Seven patients received therapy before 6 weeks and 16 received therapy after 6 weeks from onset. No statistically significant differences were noted for pure tone average, speech reception threshold, or speech discrimination for therapy instituted before or after 6 weeks.

Patients were also stratified by age (Fig 3). There were 10 patients less than 60 years of age and 13 older than 60. Comparing the patients over 60 with those younger than 60, there was no statistically significant difference for pure tone average, speech reception threshold, or speech discrimination. However, there was a trend for more favorable results for the younger patients.

There were 12 patients treated with methylprednisolone and 11 treated with dexamethasone (Fig 4). Although there was no statistically significant difference in these groups, more than twice as many of the patients treated with methylprednisolone (58%) had improved pure tone averages compared with the patients treated with dexamethasone (27%). Similar trends were noted for speech reception threshold (58% vs 36%) and speech discrimination scores (42% vs 27%).

No statistically significant differences were noted for outcomes comparing men and women (Fig 5). However, men had more favorable outcomes twice as often as the women for pure tone average (58% vs 27%), speech reception threshold (67% vs 27%), and speech discrimination (42% vs 27%).

DISCUSSION

SSNHL is the clinical entity defined by the rapid loss of hearing with no identifiable cause. Rapid has been defined as 3 days or less, although most patients note the onset as a sudden event. Hearing loss has been defined as a drop of ≥20 dB in 3 or more contiguous audiometric frequencies. Because there is usually no premorbid audiogram available for comparison, the loss is usually considered in comparison with the nonaffected ear. Because there is no identifiable cause, this disease entity most likely represents several etiologies. The leading theories are viral inflammation and vascular occlusion.

Haberkamp and Tanyeri[3] recently authored a review on the management of SSNHL. Currently, systemic corticosteroids are the only treatment for SSNHL that has been shown efficacious in rigid clinical trials. In a prospective randomized, double-blinded study, Wilson et al[4] demonstrated a significantly improved recovery rate for systemic corticosteroids compared with placebo. In a prospective randomized study, Moskowitz et al[5] reported a statistically significant improved rate of recovery from SSNHL for steroid-treated patients compared with placebo. Administration of systemic corticosteroids has become widely used for treatment of SSNHL and is arguably the treatment of choice.

If corticosteroids are responsible for hearing improvement, it would seem logical that the site of action is in the cochlea. An alternative method of delivering medication to the cochlea is by means of the round window membrane, or transtympanic. The advantages of this route of administration would be that higher concentration of medication would reach the inner ear while limiting systemic distribution. This technique could eliminate or reduce side effects and complications associated with systemic steroid therapy. Parnes et al[6] demonstrated much higher inner ear concentrations of hydrocortisone, methylprednisolone, and dexamethasone with transtympanic administration compared with oral or intravenous administration in the guinea pig model. Of these drugs, the authors determined that methylprednisolone had the best absorption profile.

Similarly, Chandrasekhar[7] measured much higher perilymphatic concentrations of dexamethasone in a guinea pig model when it was administered through a transtympanic route compared with intravenous administration. She also compared different facilitating agents that may enhance transtympanic delivery of dexamethasone. Her experimental groups included intravenous dexamethasone, intratympanic dexamethasone (IT-DEX), IT DEX with histamine, IT-DEX with hyaluronic acid, and IT-DEX with dimethylsulfoxide. The addition of histamine significantly improved perilymphatic concentrations of dexamethasone compared with hyaluronic acid, dimethylsulfoxide, or no facilitating agent. Additionally, the studies by both Parnes et al[6] and Chandrasekhar[7] report successful treatment of SSNHL with transtympanic steroid therapy in a small number of human patients. Silverstein et al[8] also reported treatment results for intratympanic perfusion.

In the present study, we administered steroids through a transtympanic route to patients with SSNHL for whom prior treatment with systemic steroids had failed. We reasoned that because the transtympanic route results in much higher inner ear steroid concentrations, some of the patients for whom systemic therapy had failed might respond to transtympanic therapy. The resultant 44% response justifies our rationale. Although 44% seems like a poor response compared with most studies addressing the treatment of SSNHL, it must be emphasized that this is a salvage number from a group of patients for whom treatment with conventional therapy was already considered to be a failure.

Although not statistically significant, we noted better outcomes in younger patients, men, and those patients treated with methylprednisolone. Prior studies have commented on better outcomes with younger patients. The higher success seen in the methylprednisolone group could possibly be attributable to the better absorption profile compared with dexamethasone noted by Parnes et al.[6] Conversely, we noted no significant difference in successful outcomes when comparing time to therapy. This is in contradistinction with most studies published on the treatment of SSNHL; most studies suggest a time window after which success diminishes. This discrepancy could simply be caused by the statistical problems of small numbers. However, this could also represent a new finding of a residual inflammatory process in these ears that is responsive to very high concentrations of steroids.

Although the findings in this study are encouraging, this must be tempered with the knowledge that the average hearing improvement in the successful patients was quite small: 15.2 dB. There were a few patients with nearly full return of hearing, but many more had only small improvements. From a clinical standpoint, some of our patients who experienced success noted no subjective improvement in hearing. For example, one patient with a pretreatment pure tone average of 90 dB improved to 70 dB after treatment (20 dB improvement). Although this would qualify as a successful outcome in this study, because the patient had a pure tone average of 5 dB in his unaffected ear, he noted no subjective improvement in his hearing.

Transtympanic steroid therapy for SSNHL deserves further evaluation in clinical trials and could be considered as a possible first-line treatment in place of systemic steroids. Hearing improvement was demonstrated in this study among patients who would normally be considered beyond therapeutic reach. Future trials should focus on better and more consistent drug delivery systems and facilitating agents. Additional data need to be collected as to optimal timing of therapy.

CONCLUSIONS

In conclusion, in this study we have demonstrated a 44% response rate in patients with sudden hearing

loss for whom treatment from systemic steroid therapy would be considered a failure. No statistical differences were noted for our comparison groups, but there was a trend for better results in younger patients, men, and those who were treated with methylprednisolone. It is also important to point out that, because this was a pilot study, statistical significance may not have been reached because of the small numbers. Transtympanic steroid therapy may be an alternative treatment for patients with sudden hearing loss for whom systemic steroid therapy has failed or who cannot tolerate systemic steroid therapy. Although we are encouraged by these results, we have noted that the results are somewhat limited with only an average improvement of 15 dB in pure tone averages, 15 dB in speech reception threshold, and 21% in speech discrimination in those patients who responded to therapy.

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