Intratympanic Steroid Therapy as a Salvage Treatment for Sudden Sensorineural Hearing Loss After Failure of Conventional Therapy: A Meta-analysis of Randomized, Controlled Trials

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ABSTRACT

Purpose: Systemic steroid therapy (SST) for sudden sensorineural hearing loss (SSNHL) is considered the only effective treatment, but the results are not satisfactory in clinical practice. Intratympanic steroid (ITS) treatment has been adopted as a salvage treatment for patients in whom previous SST failed. However, the uncertain results of ITS treatment as a salvage treatment present patients with the dilemma of accepting or refusing ITS treatment. The goal of this study was to review relevant studies and analyze the pooled data to determine whether ITS treatment is effective for SSNHL after the failure of SST.

Methods: A literature search of the PubMed, Embase, and Cochrane databases to May 2014 was performed without restrictions regarding the language of publication. The studies were screened after reading the abstract and full text. Only prospective, randomized, controlled trials that evaluated the effect of ITS therapy on SSNHL adult patients after SST failed were included in the meta-analysis. Improvements in pure tone averages and the number of patients with no improvement were extracted and entered into RevMan software to meta-analyze the overall effect of ITS on SSNHL after SST failed.

Findings: A total of 543 studies were identified, and 41 of these studies were found to be eligible and related to ITS therapy after SST failed. Ultimately, 5 randomized, controlled trials containing data from 102 patients in the ITS group and 101 control subject were included. The pooled results revealed that ITS therapy was able to improve the hearing levels of SSNHL patients who had responded poorly to SST.

Implications: ITS therapy might be an effective approach to the treatment of SSNHL after SST fails. (*Clin Ther*. 2015;37:178–187)

Key words: failure, meta-analysis, steroid, sudden sensorineural hearing loss.

INTRODUCTION

Sudden sensorineural hearing loss (SSNHL) is typically defined as the sudden hearing loss of >30 dB across 3 contiguous frequencies within 72 hours and is commonly encountered in clinical practice. SSNHL is thought to affect 5 to 20 people per 100,000.[1,2] Although spontaneous recovery occurs in 32% to 65%[3] of patients with SSNHL, starting treatment as soon as possible is recommended.[4] The treatments include steroids, antiviral drugs, anticoagulants, antioxidants, vasoactive agents, and hyperbaric oxygen. The effectiveness each of these treatments is ~65% at present.[5] Of these treatments, systematic steroid therapy (SST) seems to be generally acknowledged as the most effective treatment in use.[6,7] Steroids can be administered intravenously, orally, or via local application to the middle ear as a single agent or in combination with other drugs. The efficacy rate of steroid treatment ranges from 49% to 89%.[1,8] However, ~30% to 50% of patients still respond poorly to SST.[9,10] For these

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poorly responding patients, long-term application of steroids might not be feasible because long-term administration of systemic steroids is associated with side effects (although these effects are rare) and is contraindicated in certain pathologic situations.[11]

In such cases, alternative treatments have become popular for patients who are refractory to SST. The guidelines of the American Academy of Otolaryngology–Head and Neck Surgery recommend that clinicians offer intratympanic steroid (ITS) administration when patients exhibit incomplete recovery from SSNHL after initial management fails. The advantage of using ITS is that a higher concentration of steroid reaches the cochlea compared with systemic therapy,[12,13] which results in a reduction in systemic absorption and avoids the side effect of long-term SST, such as vascular necrosis of the femoral head, hypertension, osteoporosis, gastric ulcer and so on. Most studies have shown encouraging outcomes with ITS use in the treatment of SSNHL in patients in whom previous systemic therapy failed.[14–16] However, other studies have reported no improvements in hearing levels after ITS treatment in patients who failed to respond to SST.[17,18] Overall, the success rates of ITS as a salvage treatment range from 12% to 100%[15,16,19–21] depending on, for example, the steroid, the application method, the dose, previous therapies, the time of therapy initiation, and patient inclusion criteria. The results of different studies need to be summarized to clarify the effects of ITS treatment for SSNHL after SST fails.

To the best of our knowledge, this study is the first meta-analysis of the effect of ITS treatment for SSNHL after SST failed. This study differs from previous meta-analyses in the following aspects: (1) this study focuses on the effects of ITS on SSNHL, whereas SST has been the main topic of previous meta-analyses[22–24]; (2) this study focuses on the effects of ITS as a salvage treatment after SST failed and not on ITS therapy as a first-line treatment for SSNHL; and (3) this study included only randomized, controlled trials (RCTs), which are thought to be most suitable studies for meta-analysis.

METHODS

Materials and Methods

Our meta-analysis was conducted in strict accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement, which is the reporting guideline for meta-analyses.[25]

The search was performed in the PubMed, Embase, and Cochrane databases to May 2014. To avoid missing any articles related to ITS therapy as a salvage treatment, we did not include any term related to salvage treatment. The search terms were *sudden deafness* OR *sudden sensorineural hearing loss* OR *sudden sensorineural deafness* OR *idiopathic sudden sensorineural hearing loss*, AND *steroid*. No restrictions regarding the language of publication were applied. Additionally, we manually searched for relevant published studies and review articles.

The inclusion criteria for the current meta-analysis were the following: (1) only RCTs; (2) studies that included only adults (older than 18 years of age); (3) only studies that obtained consent from the patients; (4) only studies that included SSNHL patients who had undergone SST; (5) only studies that included patients who had responded poorly to SST; (6) only studies with control patients who were given normal saline solution or no treatment after failure to respond to SST; (7) only studies including ITS treatment; and (8) only studies including pure tone average (PTA) measurements before and after ITS treatment.

Two investigators (H.L. and G.F.) independently screened all identified studies using the aforementioned criteria. When any disagreement emerged, a third reviewer (Y.F.) participated in the resolution of the issue by discussion.

Meta-Analyses

Meta-analyses were then conducted regarding the PTA improvements in decibels (ie, the difference between the PTA before and after ITS therapy) and the numbers of patients exhibiting no improvement (defined as PTA improvement <10 decibels (dB)). The mean differences (MDs) and 95% CIs were estimated for the PTA improvement, and the risk ratio (RRs) and 95% CI were estimated for the numbers of patients with no improvement. Cochrane's I^2 index was calculated to assess heterogeneity, and if the data were not significant ($I^2 < 40\%$), the MDs and RRs were pooled according to the fixed-effects model. Otherwise, the random-effects model was used. The statistical significance of the pooled MD and RR was evaluated using the Z test. Possible publication bias was assessed with funnel plots and fail-safe numbers at $P = 0.05$ ($N_{fs0.05}$). The meta-analyses were performed using RevMan software, version 5.2 from the Cochrane Collaboration.[26]