Meta-Analysis Comparing Steroids and Diuretics in the Treatment of Acute Low-Tone Sensorineural Hearing Loss

Yueying Zhu, BS1,2, Guangqi Li, MD1,2, Huiwen Zhuang, MD1,2, Zijun Yang, BS1,2, JinCangjian Sun, BS1,2, Guangxia Xiong, MD1,2, and Xianren Wang, MD1,2

Abstract
Objective: Our objective was to perform a meta-analysis to compare the effectiveness of steroids and diuretics in the treatment of acute low-tone sensorineural hearing loss (ALHL).

Methods: PubMed, Google Scholar, and Sci databases were searched for randomized controlled trials (RCTs) examining the treatment of ALHL with steroids and diuretics. The Cochrane Reviewer’s Handbook 5.0 evaluation criteria were used to evaluate the quality of the included RCTs. Meta-analysis was performed using Revman 5.3 software to compare the recovery rate of low-tone hearing levels between patients treated with steroids and diuretics.

Results: A total of 3 RCTs were included. There was no heterogeneity between the 3 studies ($\chi^2 = 2.61, P = .27, I^2 = 23\%$); thus, a fixed-effects model of analysis was used. Meta-analysis showed there was no significant difference in the recovery rate of patients treated with steroids and those treated with diuretics (odds ratio $= 1.48$, 95% confidence interval: 0.64-3.40, $P = .36$).

Conclusion: Steroids and diuretics are equally effective for the treatment of ALHL.

Keywords
acute low-tone sensorineural hearing loss, steroids, diuretics, meta-analysis

Introduction
Acute low-tone sensorineural hearing loss (ALHL) is a clinically common disease. Acute low-tone sensorineural hearing loss patients have tinnitus, ear fullness, a slight sense of dizziness, and low-tone hearing loss. The diagnostic criteria for ALHL are not yet clear. Most scholars currently refer to the diagnostic criteria from the Japan Foundation’s Acute Profound Deafness Research Committee of the Ministry of Health, Labor and Welfare: (1) patient attendance at department within 7 days of symptom onset; (2) hearing loss is purely sensorineural and has normal tympanic membrane performance, and a radiological examination of temporal bone and brain ruling out possible organic causes; (3) pure tone audiometry: The sum of hearing loss is 70 dB or higher at 3 low frequencies (125, 250, and 500 Hz), and the sum of hearing loss is 60 dB or less at 3 high frequencies (2, 4, and 8 kHz). In the past, ALHL was considered to be an idiopathic sudden sensorineural hearing loss (SNHL). However, in 1982, Abe1 for the first time described ALHL as an independent disease. Endolymphatic hydrops2-5 and an autoimmune response6 are considered to be possible causes of ALHL. In addition, more than half of ALHL patients’ hearing is automatically recovered without treatment. However, for all that, there are still some patients who develop symptoms of deafness or progress to the possibility of progression to Ménière disease. Therefore, patients with ALHL should be actively treated rather than managed conservatively, not just waiting for natural recovery. In view of the lack of systematic reviews related to the treatment of ALHL, the purpose of this study was to conduct a meta-analysis of the current literature to compare the effectiveness of steroids and diuretics for the treatment of ALHL.

1 Department of Otorhinolaryngology, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China
2 Institute of Otorhinolaryngology, Sun Yat-sen University, Guangzhou, China

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Corresponding Author:
Xianren Wang, MD, Department of Otorhinolaryngology, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou 510080, China.
Email: wangxren@mail.sysu.edu.cn
**Methods**

**Search Strategy**
Pubmed, Google Scholar, Embase, and Sci databases were searched for randomized controlled trials (RCTs) examining the treatment of ALHL with steroids and diuretics. The search terms were “acute low-tone hearing loss,” “acute low frequency hearing loss,” “low frequency sensorineural hearing loss,” “low-tone hearing loss,” “therapy,” “treatment,” and “RCT.” And the year of the search was from 1990 to 2017.

**Inclusion and Exclusion Criteria**
The inclusion criteria were RCTs comparing steroids versus diuretics for the treatment of ALHL. The diagnosis of ALHL was required to conform to ALHL diagnostic criteria. Patient age, sex, ethnicity, and time of illness were not restricted and were required to be the same between the steroid treatment group and the diuretic treatment group. The primary outcome measure was the recovery rate of low-frequency hearing after treatment. Studies were excluded if the data of interest were incomplete and if the relevant outcome indicator was not provided.

**Quality Assessment**
Quality assessment of studies was performed by 2 trained persons. Disputes were resolved by discussion with a third person. The Cochrane Reviewer’s Handbook 5.0 evaluation criteria were used to evaluate the quality of the included RCTs. Evaluation measures were (1) random sequence generation (selection bias), (2) allocation concealment (selection bias), (3) blinding of participants and personnel (performance bias), (4) blinding of outcome assessment (detection bias), (5) incomplete outcome data (attrition bias), (6) other bias. Each measure was classified as “yes,” “unclear,” and “no.” “Yes” represents low risk of bias, “unclear” means that the risk of bias is uncertain, and “no” represents high risk of bias.

**Data Extraction**
Data extraction was performed using predesigned forms independently by the 2 persons who did the quality assessment. Data extracted included the name of the first author, year of publication, article title, patient characteristics, interventions, disease course, and final outcome.

**Data Analysis**
Data were analyzed with RevMan 5.3 software. Evaluation of heterogeneity between included studies was done using the $I^2$ test. When the value of $P$ was $\geq .1$ and $I^2$ was $\leq 50\%$, there was no statistically significant heterogeneity between studies, and a fixed-effects model of analysis was used. A value of $P < .1$ and $I^2 > 50\%$ was considered to indicate statistically significant heterogeneity between studies, and a random-effects model of analysis was used, or sources of heterogeneity were analyzed, and subgroup analysis based on heterogeneity sources was performed. As recovery rate is a noncontinuous variable, treatment efficacy was expressed as odds ratio (OR). Interval estimates were expressed using a 95% confidence interval (CI). A value of $P < .05$ was considered to indicate statistical significance.

**Result**

**Literature Search**
Twenty-five articles were identified in the database searches and were screened based on the inclusion and exclusion criteria. Finally, 3 RCTs meeting the criteria were included in the analysis. None of the included studies were performed in China. The 3 studies included a total of 123 patients; 74 patients were treated with steroids and 49 were treated with diuretics. A flow diagram of the literature screening is shown in Figure 1, and general information of the included studies is shown in Table 1.
Quality Assessment

All studies mentioned "randomized research." However, none of the studies described the randomization method, the allocation concealment method, or the blinding method. All of the studies provided outcome data of interest. Quality assessment results are summarized in Figure 2.

Meta-Analysis

There was no heterogeneity between the 3 studies ($\chi^2 = 2.61$, $P = .27$, $I^2 = 23\%$); thus, a fixed-effects model of analysis was used. Results of the meta-analysis showed there was no significant difference in the recovery rate of patients treated with steroids and those treated with diuretics (OR = 1.48, 95% CI: 0.64, 3.40, $P = .36$; Figure 3).

Abbreviations: ALHL, acute low-tone sensorineural hearing loss; RCT, randomized controlled trial.

Discussion

In 1994, Yamasoba et al reported that 63% of patients with ALHL had an increase in summing potential/compound action potential ratio of electrocochleogram (ECochG), and 74% had a positive glycerol test (74%). Studies have found that in the endolymphatic hydrops and Ménière disease, glycerol test and ECochG results are similar to ALHL results. At the same time, Im et al found that the greater the low-tone hearing loss, the higher the ECochG value (the severity of endolymphatic hydrops). The authors concluded that ALHL is caused by endolymphatic hydrops. With ALHL, the more severe the low-frequency hearing loss, the better the hearing recovery, which is different than recovery after SNHL. In addition, the autoimmune response is also considered to be one of the causes of ALHL. McCabe recognizes that patients with sensorineural hearing loss have an autoimmune response based on diagnostic studies and patient response to immunosuppressant agents such as cortisone. A study has shown that although ALHL patients do not have vertigo, it is not uncommon to have abnormal vestibular function. The water caloric test suggests that some patients with early-stage ALHL have different degrees of vestibular dysfunction. Acute low-tone sensorineural hearing loss not only involves the top of the cochlear but can be complicated with vestibular dysfunction, which may be a cause of progression to Ménière disease. As such, treatment of ALHL is important.

Various treatments have been used to treat ALHL. One study reported that low salt and low solute diets have a positive effect on ALHL patients. Drug therapy is considered to be the most effective way to treat ALHL, and the most widely used drugs are steroids and diuretics. The degree of low-frequency hearing level changes in patients with ALHL after treatment is classified into 5 grades: (1) complete recovery, defined as a hearing threshold reduced to $\leq 20$ dB, which is within normal range, at all frequencies below 500 Hz; (2) partial recovery, defined as an improvement in hearing threshold at low frequencies by 10 dB or more compared to the initial hearing threshold; (3) progression, defined as an increase in the low-frequency hearing threshold of more than 10 dB compared to the initial hearing threshold; (4) fluctuation, defined as an average loss of 30 dB or more at low frequencies seen after "complete recovery" or "partial recovery"; (5) unchanged, defined as a $<10$ dB difference in hearing thresholds from before to after treatment. These outcome criteria are based on the model of the Study Group for Acute Profound Deafness Research Committee of

Table 1. Basic Characteristics of the Included Studies.

| Studies     | Type of Study | Sample                  | Data Collection Time       | Intervention | Control Group | Outcome |
|-------------|---------------|-------------------------|---------------------------|--------------|---------------|---------|
| Morita et al | RCT           | 89 patients with ALHL   | April 2000 to March 2009   | Steroids     | Diuretics     | Recovery rate |
| Park et al  | RCT           | 15 patients with ALHL   | June 2005 to June 2015     | Steroids     | Diuretics     | Recovery rate |
| Fuse et al  | RCT           | 19 patients with ALHL   | May 1996 to July 1998      | Steroids     | Diuretics     | Recovery rate |

Abbreviations: ALHL, acute low-tone sensorineural hearing loss; RCT, randomized controlled trial.
The contralateral ear is a healthy ear, the low-frequency hearing loss is greater than high-frequency hearing loss. Even if it is determined that patients' unaffected ears low-frequency hearing loss is greater, there are much higher than males, and unilateral ALHL female cases are unilateral ALHL, and very few cases are bilateral, the remainder was unilateral ALHL. Most of the current clinical studies mentioned that the subject was a bilateral ALHL and the contralateral ear is still needed in the future. In the study we included, only one study reported that patients with vertigo had a higher possibility of developing Ménière disease (40%) than those without vertigo (12%). At present, the relationship between ALHL and Ménière disease is not fully understood, and relevant research is still needed in the future. In the study we included, only one study mentioned that the subject was a bilateral ALHL and the contralateral ear is a healthy ear, the low-frequency hearing is slightly damaged compared to the high frequency. The issue of bilateral ALHL, unilateral ALHL, and repetitive ALHL deserves further discussion.

Meta-analysis holds an important place in the field of evidence-based medicine. Although its advantages are obvious, there are still some limitations. An excellent meta-analysis incorporates homogeneous, high-quality studies. Generally, statistically significant results are more easily accepted for publication, and positive results are easier to publish than negative results. Because the drawing of a funnel plot requires a minimum of 5 studies, we were unable to perform a funnel plot analysis. With respect to homogeneity, the 3 trials included in this study exhibited good homogeneity and were suitable for combined analysis. The number of studies and the number of patients in this meta-analysis were small, so there are shortcomings in the strength of argumentation. In the future, large sample size, well-designed, multicenter RCTs are needed to arrive at more reliable conclusions to guide clinical practice and provide evidence supporting treatment options for ALHL patients.

Declaration of Conflicting Interests
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ORCID iD
Xianren Wang https://orcid.org/0000-0002-6760-3258

References
1. Abe T. Acute sensorineural hearing loss in low frequencies. Otolaryngol (Tokyo). 1982;54:385-392.
2. Aso S, Kimura H, Takeda S, Mizukoshi K, Watanabe Y. The intravenously administered glycerol test. Acta Otolaryngol Suppl. 1993;504:51-54.
3. Merchant SN, Adams JC, Nadol JB Jr. Pathophysiology of Ménière’s syndrome: are symptoms caused by endolymphatic hydrops? Otol Neurotol. 2005;26(1):74-81.

4. Yamasoba T, Kikuchi S, Sugasawa M, Yagi M, Harada T. Acute low-tone sensorineural hearing loss without vertigo. Arch Otolaryngol Head Neck Surg. 1994;120(5):532-535.

5. Fuse T, Hayashi T, Oota N. Immunological responses in acute low-tone sensorineural hearing loss and Ménière’s disease. Acta Otolaryngol. 2003;123(1):26-31.

6. Fuse T, Aoyagi M, Funakubo T, Sakakibara A, Yoshida S. Short-term outcome and prognosis of acute low-tone sensorineural hearing loss by administration of steroid. ORL J Otorhinolaryngol Relat Spec. 2002;64(1):6-10.

7. Morita S, Suzuki M, Iizuka K. A comparison of the short-term outcome in patients with acute low-tone sensorineural hearing loss. ORL J Otorhinolaryngol Relat Spec. 2010;72(6):295-299.

8. Park MJ, Kim SH, Kim SS, Yeo SG. Clinical characteristics and short-term outcomes of acute low frequency sensorineural hearing loss with vertigo. Clin Exp Otorhinolaryngol. 2018;11(2):96-101.

9. Yamasoba T, Sugasawa M, Kikuchi S, Yagi M, Harada T. An electrocochleographic study of acute low-tone sensorineural hearing loss. Eur Arch Otorhinolaryngol. 1993;250(7):418-422.

10. Im GJ, Kim SK, Choi J, Song JJ, Chae SW, Jung HH. Analysis of audio-vestibular assessment in acute low-tone hearing loss. Acta Otolaryngol. 2016;136(7):649-654.

11. McCabe BF. Autoimmune sensorineural hearing loss. Ann Otol Rhinol Laryngol. 1979;88(5):585-589.

12. Kimura M, Hamamura R, Umehara T. Caloric test in low-tone sensorineural hearing loss. Nihon Jibiinkoka Gakkai Kaiho. 2009;112(8):615-622.

13. Suzuki M, Otake R, Kashio A. Effect of corticosteroids or diuretics in low-tone sensorineural hearing loss. ORL. 2006;68(3):170-176.

14. Chang J, Yum G, Im HY, Jung JY, Rah YC, Choi J. Short-term outcomes of acute low-tone sensorineural hearing loss according to treatment modality. J Audiol Otol. 2016;20(1):47-52.

15. Hong SK, Nam SW, Lee HJ, et al. Clinical observation on acute low-frequency hearing loss without vertigo: the role of cochlear hydrops analysis masking procedure as initial prognostic parameter. Ear Hear. 2013;34(2):229-235.