Therapeutic Effect on Idiopathic Sudden Sensorineural Hearing Loss with Duration of Onset More Than 3 Months

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Abstract The purpose of this study was to evaluate the therapeutic efficacy and stability upon idiopathic sudden sensorineural hearing loss (ISSNHL) patients with duration of onset more than 3 months. Twenty-eight patients diagnosed as ISSNHL were treated by intravenous injection and another 26 by oral medication. Pure tone tests were undertaken at pre-therapy, the 3rd, 7th, 10th, 14th day of post-treatment, and 1 and 2 months of follow-up respectively. A total of 54 ISSNHL patients with duration of onset ranged from 3 months to 19 years were concerned. In the group administrated by intravenous injection, the total effective rate was 64.29 % including 2 cases total recovery, 3 excellent and 13 partial recovery. In the oral administration group, there was no recovery or excellence case, and 8 (30.77 %) showed partial recovery. There was significant difference between the two groups in total effective rates ($P < 0.05$). The treatment efficacy were stable in both two groups, and the difference in stability was no statistical significance ($P = 0.397$). There was therapeutic value for ISSNHL duration of onset more than 3 months, especially for patients with mild and moderate hearing loss. The administration by intravenous injection should be the optimization.

Keywords Sensorineural hearing loss · Sudden deafness · Patient history · Pharmacotherapy

Introduction

Idiopathic sudden sensorineural hearing loss (ISSNHL), the acute onset of hearing loss of at least 30 dB in 3 connected frequencies occurring instantaneously or over a period of up to 3 days [1], has an estimated incidence between 10 and 20 per 100,000 persons per year [2]. ISSNHL occurs mainly in patients between the ages of 30 and 60 years, with equal sex distribution, and can be devastating for the patient. Therefore, sudden hearing loss should be treated as a medical emergency. As the term idiopathic implies, the etiology and pathophysiology of hearing loss are unknown. Treatment options include steroids, antivirals, vasodilators, diuretics, hyperbaric oxygen therapy, and vitamins [3, 4]. The current treatment period for idiopathic hearing loss is 1 ~ 3 months from onset of hearing loss. Over 3 months history, it is considered the lost hearing is hard to recovery [5]. However, in clinical practice, we found there was a subgroup of ISSNHL patients whose impaired hearing could be improved by medication administered after 3 months of hearing loss. Even more, the pure tone average (PTA) of the hearing thresholds at 500, 1,000, 2,000 Hz in the affected ear is recovery to normal (<25 dB PTA) individually.

The present study evaluated the therapeutic efficacy and stability upon ISSNHL patients with long history (more than 3 months) accepted treatment of injection by intravenous or oral medication respectively, and the pure tone tests were undertaken at pre-therapy, the 3rd, 7th, 10th, 14th, 30th, and 60th day of post-treatment respectively.

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Materials and Methods

Patients

Eligibility criteria included an age of at least 18 years and a unilateral sensorineural hearing loss that developed at least 30 dB in three contiguous frequencies within 72 h, and with duration of onset 3 months or more without receiving prior treatment. PTA, calculated as the arithmetic mean of the hearing thresholds at 500, 1,000, 2,000, and 4,000 Hz in the affected ear, in the affected ear must have been at least 30 dB worse than that in the contralateral ear in at least 1 of the 4 PTA frequencies. The hearing loss must have been deemed idiopathic following a suitable otolaryngologic evaluation, including detailed medical and otologic history and extensive systems review, head and neck and otologic and neurotologic physical examination, audiometry, blood tests, and imaging to rule-out structural or retrocochlear pathology, such as vestibular schwannoma, stroke, or demyelinating disease.

Patients with ear disease that could be confused with idiopathic sudden hearing loss and patients with systemic disease who might be at increased risk of adverse effects from steroid treatment. Otologic exclusion criteria included a previous history of hearing loss in either ear, hearing asymmetry prior to onset, congenital hearing loss, fluctuating hearing or Meniere disease, history of genetic hearing loss with family history, history of chronic inflammatory or suppurative ear disease, cholesteatoma or otosclerosis, history of prior ear surgery of any kind (except ventilating tubes), physical trauma or barotrauma to the ear immediately preceding hearing loss, history of luetic deafness [6]. Systemic exclusion criteria included history of tuberculosis or prophylactic therapy for positive purified protein derivative skin test, insulin-dependent diabetes mellitus, rheumatic disease, active atherosclerotic vascular disease, serious psychiatric disease, prior treatment with chemotherapy agents or other immunosuppressive drugs, pancreatitis, known human immunodeficiency virus, chronic renal insufficiency, alcohol abuse, active herpes zoster infection, severe osteoporosis, history of head and neck cancer, or history of radiation therapy.

This study was approved by the Clinical Otorhinolaryngology Division of the Provincial Hospital Affiliated to Shandong University. And written informed consent was obtained from each individual.

Interventions

After screening for eligibility, patients consenting to enroll were randomized to receive either oral administration or medication by intravenous injection. The randomization codes were computer generated using SAS software (SAS

Institute Inc, Cary, North Carolina). The participants and treating physicians were not blinded to treatment. The oral group took oral medication with Ginaton (extract of Ginkgo biloba leaves) tablets 80 mg/time and 3 times per day for 14 days, prednisone 1 mg/kg (60 mg/day maximum) daily for 5 days followed by a 5-day taper (50, 40, 30, 20, and to 10 mg) for a total of 10 days of treatment, and mecobalamin tablets 500 µg/time and 3 times/day for 14 days. The intravenous group administered by intravenous injection received Ginaton injection with a dose of 105 mg every day by intravenous injection for 14 days, dexamethasone 10 mg/day for 5 days followed by a dose of 5 mg/day for 5 day, and mecobalamin injection 500 µg/day by intravenous injection for 14 days.

In addition to checking vital signs and otological physical examination, safety monitoring laboratory studies including complete blood cell count, serum glucose measurement and urinalysis, were performed before or on the first day of treatment. Other safety testing was performed at the discretion of the treating physician as indicated by the patient's medical history. Patients who required specific therapy for diabetes, hypertension and dyslipidemia were treated in association with the proposed standard therapy. No surgical intervention was performed during the 2-month period of follow-up.

Audiology Examination

All participants underwent a standard audiometric evaluation consisting of pure tone audiometry, speech audiometry, tympanometry curve with determination of acoustic reflexes, distortion product otoacoustic emission and auditory brain-stem response examination. The hearing involvement was monitored by successive audiometric tests of air- and bone-conducted pure tone audiometry and speech audiometry at screening: on the day of presentation, at 3, 7, 10, and 14 days after treatment, and at 1 and 2 months of follow-up. Audiologists were blinded to treatment. Pure tone audiometry yields hearing threshold values (dB PTA) and speech audiometry yields a word recognition score, the highest percentage of monosyllabic words identified correctly from digitally recorded standardized 50-word lists presented to each ear of each participant.

A PTA of 500, 1,000, 2,000, and 4,000 Hz was used to categorize the losses as mild (26–40 dB), moderate (41–60 dB), severe (61–80 dB), profound or total (>80 dB). The therapeutic effect was evaluated basing on the change in hearing threshold from the first audiogram (tested before treatment) to the 1-month follow-up audiogram. The stability of hearing restoration was measured by the differences in hearing threshold values and word recognition scores at 1 and 2 months posttreatment. It was considered as total

recovery that the PTA, calculated based on thresholds of 500, 1,000, 2,000, and 4,000 Hz, recovered to normal hearing threshold (<25 dB), or to hearing level of contralateral unaffected ear or prior level. It was considered as excellent recovery that the PTA improved 30 dB or more, partial recovery the PTA value improved between 15 and 30 dB, and lack of recovery below 15 dB.

Statistical Analysis

Improved measurements in the PTA from baseline to 1 month between the two study groups were analyzed using one-way analysis of variance (ANOVA). To assess the effect of treatment we compared the total effective rates between oral and intravenous groups using χ^2 test, and the total effective rate of hearing recovery included subjects with total recovery, excellent recovery, and partial recovery. The Fisher's exact test of probabilities was employed to analyze the stability of hearing restoration between oral and intravenous groups, and to assess differences in total effective rate among the four categories of the hearing loss degree. The correlation between curative effect and the history from hearing loss onset was also analyzed by statistical method of Spearman's rank correlation. All results were considered significant at the level of 0.05.

Results

Fifty-four patients (54 affected ears) with ISSNHL presence more than 3 months were enrolled in this study between August 2010 and February 2012, and were divided into two groups. (1) The intravenous group ($n = 28$) given medication by intravenous injection had a median age 57.0 years (range 30–79) and there were 16 males (57.14 %). There were 13 (46.43 %) in left ears. The mean time period elapsed since onset of hearing loss was 7.6 years (range 0.25–17). The initial audiograms of the 28 ears showed mild hearing loss in 7.14 % (2/28), moderate in 35.71 % (10/28), severe and profound in 28.57 % (8/28) respectively. (2) The oral group ($n = 26$) was administered by mouth with a median age of 59.5 years (range 37–74). There were 16 male patients (61.54 %), and the affected ears in left were 10 (38.46 %). The mean time period elapsed since onset of hearing loss was 8.2 years (range 0.5–19). The initial audiograms of the 26 ears showed mild hearing loss in 7.69 % (2/26), moderate in 23.08 % (6/26), severe in 46.15 % (12/26), and profound in 23.08 % (6/26). The mean baseline PTA in the oral and intravenous groups were 72.0 dB (range 36.0–107.1 dB) and 71.2 dB (range 35.8–110.0 dB), respectively. Mean word recognition scores in the oral and intravenous groups were 35.0 % (range 0–77.6 %) and 37.9 % (range 0–78.4 %), respectively. Between the two

groups, there were no significant baseline differences in demographics, otologic history, physical characteristics, ear examination, tuning fork test results, neurological examination, cerebellar and vestibular testing, and audiometric measures of pure tone threshold and word recognition scores (Table 1).

In the intravenous group, the initial mean auditory threshold in this group was 71.2 dB and the final mean threshold at 1 month was 52.1 dB. 7.14 % of these ears (2 of 28) achieved total recovery of hearing in PTA threshold of 500, 1,000, 2,000, and 4,000 Hz, 10.71 % (3 of 28) had excellent recovery, and 46.43 % (13 of 28) partial improvement. There was no recovery in 35.71 % (10 of 28). The total effective rate was 64.29 % (18 of 28). In the oral treatment, the initial mean PTA value was 72.0 dB and the final mean threshold at 1 month was 64.2 dB. There was no subject with total or excellent recovery in the oral treatment group. The total effective rate, that was partial recovery, was 30.77 % (8 of 26), and there was no recovery in 69.23 % (18 of 26) (Table 2). None of the total 54 participants showed significant worsening of hearing from baseline. In the intravenous group, PTA from baseline to 1 month after randomization improved 19.1 dB compared with 7.8 dB in the oral group. The estimate of the difference between the oral and intravenous groups in the mean change in PTA is significance ($P < 0.05$). Comparing the total effective rate between the two groups, a significant difference was observed ($\chi^2 = 6.07$, $P < 0.05$). Thus, improvement in PTA at 1 month in the intravenous group was inferior to PTA improvement in the oral group.

Table 3 showed a distribution of hearing recovery correlated with the degree of hearing loss in intravenous group. In the oral administration group, 8 patients observed partial recovery in PTA included 4 of 6 patients (66.7 %) with moderate hearing loss and 4 of 12 (33.3 %) with severe hearing loss. Although it showed a trend for better outcome with mild or moderate than severe or profound hearing loss, there was no statistical significance among subgroups categorized by degree of hearing loss because of limited cases ($P > 0.05$).

Considering the stability of hearing restoration, there were 2 participants in the oral and intravenous groups respectively, showed 2-month worse than 1-month hearing, which was 10–15 dB worse. There was not statistically significant between oral and intravenous groups in the stability of hearing restoration ($P = 0.397$).

Spearman's rank correlation test indicated there was no correlativity between therapeutic effect and duration of onset of hearing loss prior to entry into the study ($P < 0.05$). In the intravenous group, the histories whose hearing recovered to normal (<25 dB) in PTA at 500, 1,000, 2,000, and 4,000 Hz, were 2 and 5 years respectively, and 0.25, 11, 13 years whose hearing excellent recovery. The correlation of treatment effective and history could be observed in Fig. 1.

Table 1 Baseline Characteristics

Characteristics	Oral administration (<i>n</i> = 26)	Intravenous administration (<i>n</i> = 28)	All (<i>N</i> = 54)
Age (year), median (range)	59.5 (37–74)	57.0 (30–79)	57.5 (30–79)
Male–female	1.6:1	1.3:1	1.5:1
Duration from onset of deafness (year), mean (range)	8.2 (0.5–19)	7.6 (0.25–17)	7.8 (0.25–19)
Affected ear in right–left	1.6:1	1.2:1	1.3:1
Degree of hearing loss (<i>n</i>)			
Mild	2	2	4
Moderate	6	10	16
Severe	12	8	20
Profound	6	8	14
PTA (dB) of affected ear, mean (range)	72.0 (36.0–107.1)	71.2 (35.8–110.0)	71.6 (35.8–110.0)
Word recognition scores (%) of affected ear, mean (range)	35.0 (0–77.6)	37.9 (0–78.4)	36.5 (0–78.4)

There was no significant difference in baseline characteristics between the oral and intravenous administration group

Table 2 Comparison in hearing recovery between intravenous and oral administration groups

Groups	Total recovery	Excellent recovery	Partial recovery	Ineffective rate	Total effective rate
Intravenous (<i>n</i> = 28)	7.14 % (2)	10.71 % (3)	46.43 % (13)	35.71 % (10)	64.29 % (18)
Oral treatment (<i>n</i> = 13)	0 (0)	0 (0)	30.77 % (8)	69.23 % (18)	30.77 % (8)

Comparing the total effective rate between the two groups, a significant difference was concluded ($\chi^2 = 6.07$, $P < 0.05$)

Table 3 Distribution of hearing recovery correlated with the degree of hearing loss in patients with intravenous administration

Hearing recovery	Degree of hearing loss			
	Mild (<i>n</i> = 2)	Moderate (<i>n</i> = 10)	Severe (<i>n</i> = 8)	Profound (<i>n</i> = 8)
Ineffective (10)	0	2	5	3
Partial recovery (13)	1	5	3	4
Excellent recovery (3)	0	2	0	1
Total recovery (2)	1	1	0	0
Total effective (18)	2 (100 %)	8 (80 %)	3 (37.5 %)	5 (62.5 %)

There was no statistical significance among subgroups categorized by degree of hearing loss ($P > 0.05$)

Discussion

ISSNHL, or sudden deafness, is an intriguing clinical condition. The natural course is characterized by spontaneous recovery among approximately 50 % of patients. As the term idiopathic implies, the etiology and pathophysiology of hearing loss are unknown. Possible causes include infections (especially viruses), autoimmune disease, circulatory problems, and neurological disease, including multiple sclerosis. As a result of the high rate of spontaneous resolution [7, 8], multiple potential causes, absence of validated tests for etiological identification, differences in patient demographics, and the existence of multiple factors involved in its genesis, [9] the evaluation of treatment effectiveness is difficult.

Fig. 1 Correlativity between treatment effect and duration of onset from hearing loss in intravenous groups

In routine practice, the medicine for idiopathic hearing loss is emergent within 1 month [8, 10, 11], and the lost hearing is hard to recovery after 3 months from onset of ISSNHL. In the current study, we observed the therapeutic effect on ISSNHL patients with duration of onset more than 3 months and comparison of efficacy of oral and intravenous medicine. We found there still was restoration of hearing loss delayed in treatment more than 3 months. Statistical analyses showed inferiority of intravenous to oral administration for restoration of hearing loss. The prognosis for hearing recovery was poorer in oral group of patients with no significant hearing improvement, although some cases did improve partially. The degree of initial hearing loss was also evaluated as a prognostic item. The optimal efficacy was observed in patients with mild or moderate hearing loss whose competence of speech communication was obviously improved. The importance of degree of hearing loss in patients of the present study deserved some comments, although there was no significant difference among the four categories of the hearing loss degree on account of small quantity of subjects. We also analyzed the correlation of efficacy and duration of ISSNHL, and there was no statistical correlativity. In the intravenous group, the histories whose hearing recovered to normal in speech frequencies were 2 and 5 years respectively, and 0.25, 11, and 13 years whose hearing excellent recovery. Considering the stability of hearing restoration, only 4 patients among those who received hearing improvement were observed hearing worsen 10–15 dB during a 2-month follow-up, suggesting that the treatment results for the long history of idiopathic hearing loss were stability.

Similarly to the case report that a complete recovery of hearing delaying approximately 9 month postonset of the ISSNHL [12], this current outcomes of delayed recovery in hearing may indicate the pathological cause for the ISSNHL involved a process that was capable of repair or regeneration, thus ruling out pathologies related to cochlear hair cell destruction or nerve fiber loss. There are a number of obvious hearing loss treatment questions that remain unanswered. And further studies are needed to confirm the true effects of duration of onset hearing loss.

Conclusion

Although more than 3 months had elapsed since onset of hearing loss and the probability of total recovery of lost hearing grew downwards, there might have important

treatment outcomes on hearing improvement. For ISSNHL patients with mild or moderate hearing loss, there would be probable to obviously improve the competence of speech communication. For severe and profound hearing loss, the hearing threshold in PTA improved by 15–30 dB, that would offer an opportunity to fit with hearing aid or consumedly improves the hearing aid quality. Owing to the limited cases, it is impossible to conclude from our study if the medication played an important role in the hearing recovery. In future analyses, we hope to explore data for possible predictors of treatment outcome.

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References

1. National Institute on Deafness and Other Communication Disorders (2000) Sudden deafness. National Institutes of Health, Bethesda
2. Finger RP, Gostian AO (2006) Idiopathic sudden hearing loss: contradictory clinical evidence, placebo effects and high spontaneous recovery rate—where do we stand in assessing treatment outcomes? *Acta otolaryngol* 126(11):1124–1127
3. O'Malley MR, Haynes DS (2008) Sudden hearing loss. *Otolaryngol Clin North Am* 41(3):633–649
4. Kuhn M, Heman-Ackah SE, Shaikh JA et al (2011) Sudden sensorineural hearing loss: a review of diagnosis, treatment, and prognosis. *Trends Amplif* 15(3):91–105
5. Bittar RS, Oiticica J, Zerati FE et al (2009) Sudden hearing loss: a ten-year outpatient experience. *Int Tinnitus J* 15(2):196–202
6. Darmstadt GL, Harris JP (1989) Luetic hearing loss: clinical presentation, diagnosis, and treatment. *Am J Otolaryngol* 10(6):410–421
7. Nosrati-Zarenoue R, Arlinger S, Hultcrantz E (2007) Idiopathic sudden sensorineural hearing loss: results drawn from the Swedish national database. *Acta Otolaryngol* 127(11):1168–1175
8. Labus J, Breil J, Stützer H et al (2010) Meta-analysis for the effect of medical therapy vs. placebo on recovery of idiopathic sudden hearing loss. *Laryngoscope* 120(9):1863–1871
9. Ziegler EA, Hohlweg-Majert B, Maurer J et al (2003) Epidemiological data of patients with sudden hearing loss—a retrospective study over a period of three years. *Laryngorhinootologie* 82:4–8
10. Lee SS, Cho HH, Jang CH et al (2010) Fate of sudden deafness occurring in the only hearing ear: outcomes and timing to consider cochlear implantation. *J Korean Med Sci* 25(2):283–286
11. Roebuck J, Chang CY (2006) Efficacy of steroid injection on idiopathic sudden sensorineural hearing loss. *Otolaryngol Head Neck Surg* 135(2):276–279
12. Ortmann AJ, Neely JG (2012) Sudden sensorineural hearing loss and delayed complete sudden spontaneous recovery. *J Am Acad Audiol* 23(4):249–255