The Journal of International Advanced Otology

J Int Adv Otol 2020; 16(2): 201-6 • DOI: 10.5152/iao.2020.8341

Original Article

The Outcome of Prompt Concomitant Single-Dose High-Concentration Intratympanic and Tapered Low-Dose Oral Systemic Corticosteroid Treatment for Sudden Deafness

Špela Kordiš, Domen Vozel, Manja Hribar, Nina Božanić Urbančič, Saba Battelino

Department of Otorhinolaryngology and Cervicofacial Surgery, University Medical Centre Ljubljana, Ljubljana, Slovenia (SK, DV, MH, NBU, SB)
University of Ljubljana School of Medicine, Ljubljana, Slovenia (SK, DV, MH, NBU, SB)

ORCID iD of the authors: Š.K. 0000-0001-7397-4795; D.V. 0000-0002-9992-5892; M.H. 0000-0002-7488-2777; N.B.U. 0000-0003-3407-2064; S.B. 0000-0003-1478-0573.

Cite this article as: Kordiš Š, Vozel D, Hribar M, Božanić Urbančič N, Battelino S. The Outcome of Prompt Concomitant Single-Dose High-Concentration Intratympanic and Tapered Low-Dose Oral Systemic Corticosteroid Treatment for Sudden Deafness. J Int Adv Otol 2020; 16(2): 201-6.

OBJECTIVES: To investigate the efficacy of prompt concomitant corticosteroid treatment with single application of high-concentration intratympanic (IT) dexamethasone and tapered low-dose systemic methylprednisolone of an idiopathic sudden sensorineural hearing loss (ISSNHL).

MATERIALS and METHODS: Between September 2017 and September 2019, 86 adult patients met the criteria for the diagnosis of ISSNHL at baseline evaluation. The patients received immediate concomitant treatment with single high-concentration (24 mg/mL) IT dexamethasone and low-dose (48 mg) oral methylprednisolone for 1 week followed by tapered doses. Improvement in pure-tone average (PTA) and word recognition score (WRS) was determined after 1 and 6 months.

RESULTS: A total of 63 patients met the requirements for the analysis. PTA improved in 71% and WRS improved in 59% of patients with ISSNHL. PTA and WRS were statistically significantly different at different time points during the intervention ($p<0.0005$). Hearing improved in all measured frequencies from 125 to 8000 Hz until the second follow-up. In 65.4% of patients with tinnitus, the WRS has improved compared with 27.3% without tinnitus ($p<0.05$). In 69.2% of patients without vertigo, the WRS has improved compared with 41.7% with vertigo ($p<0.05$).

CONCLUSION: Prompt concomitant single high-concentration IT and low-dose systemic corticosteroid treatment is efficient in recovering hearing loss and speech discrimination in ISSNHL. Tinnitus positively predicts hearing outcome. Vertigo negatively predicts speech discrimination recovery.

KEYWORDS: Audiometry, speech, dexamethasone, tinnitus, vertigo, sudden deafness

INTRODUCTION

Corticosteroids (CSs) are the main treatment option for an idiopathic sudden sensorineural hearing loss (ISSNHL). Although their use has been widely investigated for the treatment of ISSNHL, there is no definite conclusion on their efficacy. Compared with systemic CSs, intratympanic (IT) CSs offer several advantages, such as delivering a higher concentration of CSs to the inner ear fluids and causing less adverse effects. According to the American Academy of Otorhinolaryngology-Head and Neck Surgery (AAO-HNS) guidelines, an IT CS should be offered to a patient whose hearing fails to recover after initial systemic CS treatment [1]. The AAO-HNS guidelines [1] and other studies [2] recommend low-dose systemic CS treatment (i.e., methylprednisolone 48 mg/d), whereas the German guidelines recommend high-dose treatment (i.e., methylprednisolone 200 mg/d) [3]. Low-dose systemic CS treatment can be considered as superior due to the less frequent side effects [4].

Because the treatment delay negatively affects the hearing outcome [5-7], we aimed to determine the efficacy of prompt concomitant single high-concentration IT and low-dose systemic CS treatment for ISSNHL in a prospective clinical study.

Corresponding Address: Saba Battelino E-mail: saba.battelino@kclj.si

Submitted: 03.20.2020 • **Revision Received:** 05.01.2020 • **Accepted:** 05.05.2020
Available online at www.advancedotology.org

MATERIALS AND METHODS

Patients

The study approved by the Republic of Slovenia National Medical Ethics Committee (No. 0120-475/2017-4) was performed at our tertiary referral center from September 2017 to September 2019. The procedures followed in the study were in accordance with the ethical standards of the Republic of Slovenia National Medical Ethics Committee on human experimentation and with the Helsinki declaration. Written informed consent was obtained from the patients following a detailed explanation of the procedures.

We prospectively recruited adult patients with ISSNHL for the treatment according to our protocol. ISSNHL was defined as ≥30 dB hearing loss (HL) over ≥3 contiguous frequencies that developed in ≤3 days without other identifiable causes of sudden HL (e.g., Meniere's disease and fluctuating HL). Patients with diabetes, history of peptic ulcer, immune dysfunction, and thyroid gland abnormalities were excluded from the study. The presence of these conditions was screened at each subsequent follow-up because some causes of sudden HL become identifiable later, during the diagnostic work-up, e.g., magnetic resonance imaging (MRI) for vestibular schwannoma.

Audiometry and vestibular function tests

Standardized tympanometry, pure-tone audiometry, and word recognition score (WRS) test were performed to assess hearing at admission, 1 month (i.e., first follow-up), and 6 months (i.e., second follow-up) after the start of the treatment.

Because HL can occur at different frequencies, assessing only the speech frequencies from 500 to 4000 Hz could cause bias. Therefore, a wide range of frequencies (125, 250, 500, 1000, 2000, 4000, 6000, and 8000 Hz) was used to calculate the pure-tone average (PTA) up to 120 dB. The patients were classified in five grades according to the severity of HL: normal (≤25 dB), mild (26-40 dB), moderate (41-60 dB), severe (61-80 dB), and profound (>80 dB) HLs. WRS test was carried out in silence with the nonaffected and nonafflicted ear masked. We used the Freiburg monosyllabic word test, adapted for Slovenian language [8]. Improvement of PTA >10 dB or improvement of WRS >15% was considered as clinically significant improvement. The intensity, frequency, and laterality of tinnitus were evaluated. The patients were asked if they had vertigo. The vestibular function was assessed with a bithermal caloric test (Variotherm plus, Atmos Medizintechnik, Lenzkirch, Germany) or video head-impulse test (EyeSeeCam vHIT 1.2.0 and Otoaccess 1.4.0, Interacoustics, Middelfart, Denmark).

Treatment Protocol

All patients received a single high-dose IT dexamethasone (DEX) and low-dose systemic methylprednisolone immediately after admission. Approximately 0.5-1 mL of filtered IT DEX (dexamethasone sodium phosphate; 24 mg/mL; Krka d.d., Novo mesto, Slovenia), previously warmed in a bottle to body temperature, was given as a single injection through a myringotomy under topical anesthesia. A 5-cm-long sterile cotton wick prepared from 1 cm x 10 m tamponade gauze (ref: 9190, Tosama d.o.o., Domžale, Slovenia) was inserted in the outer ear canal for 1-2 days. The patients were instructed to protect the ear against water and to avoid significant pressure changes (e.g., forceful nose blowing). They had to stay recumbent for 30 min after the IT CS application with the affected ear turned upward.

Methylprednisolone (Medrol; Pfizer SARL, Luxembourg; Grand Duchy of Luxembourg) was administered orally at a dose of 48 mg daily for 1 week, followed by a taper of 32, 16, and 8 mg each for 2 days. To prevent gastric upset, a proton pump inhibitor was administered orally at a dose of 40 mg daily while administering methylprednisolone.

Adverse Effects

At the beginning of the treatment and at each follow-up, adverse events were looked for. Adverse events attributed to IT CS treatment could be persistent tympanic membrane perforation following myringotomy, vertigo, dizziness or nausea after IT CS application, signs or symptoms of middle ear infection, more severe HL, tinnitus reported within 24 hours of IT CS treatment, and disturbed sense of taste. Momentary vertigo and dizziness or nausea during the injection were not considered as adverse effects. Because patients were covered sterile over the head, we could not observe nystagmus.

Adverse events attributed to our systemic CS treatment protocol could be sleeplessness, mood swings, psychotic reactions, anxiety, a sense of well-being, a sense of fullness, weight gain, gastric upset, blood pressure elevation, ocular hypertension, glaucoma, and blood glucose elevation [4].

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 23, (IBM Corp., Armonk, NY, USA) and Microsoft Excel for Mac (version 16 and later, Microsoft corporation, Redmond, Washington). Specific statistical tests were used depending on the group characteristics as shown in Table 1. $p<0.05$ was considered as statistically significant.

RESULTS

At baseline evaluation, 86 adult patients met the criteria for the diagnosis of ISSNHL. During follow-up, 23 patients were excluded from the study because of lack of data for the analysis (13 patients did not perform all the tests and 6 missed the follow-up), vestibular schwannoma diagnosed with MRI (2 patients), and additional hyperbaric oxygen treatment administration (2 patients). Patients who had other identifiable causes of HL (e.g., enlarged vestibular aqueduct) were excluded. Thus, the final analysis included 63 patients.

MAIN POINTS

- Prompt concomitant single high-concentration IT and low-dose systemic corticosteroid treatment is safe and efficient in the treatment of ISSNHL, since the hearing recovered to serviceable level in 77 % of patients.
- The median PTA improved from 60 dB to 43 dB in 6 months and 37 % of patients improved hearing to normal.
- The hearing threshold at low frequencies improves better than at high frequencies.
- Tinnitus is considered a good prognostic sign in ISSNHL.
- Vertigo is considered a poor prognostic sign in ISSNHL.

Table 1. Descriptive statistics and relationships of demographical and clinical characteristics.

		PTA outcome		WRS outcome	
Outcome	**Descriptive statistics**	**Improvement**	**No improvement**	**Improvement**	**No improvement**
Age[a] (years)	54.79 (15.633)	53.31 (16.923)	58.50 (11.388)	55.08 (2.539)	54.38 (3.176)
Statistics		p=0.369[1], τ_b = -0.095	p=0.863[2], r_{pb} = 0.022		
Gender[b]					
Male	35 (55.6)	27 (77.1)	8 (22.9)	20 (57.1)	15 (42.9)
Female	28 (44.4)	18(64.3)	10 (35.7)	17 (60.7)	11 (39.3)
Statistics		p=0.262[3], Δ% = 0.128	p=0.775[3], Δ% = 0		
Tinnitus[b]					
Yes	49 (77.8)	35 (71.4)	14 (28.6)	34 (65.4)	18 (34.6)
No	14 (22.2)	10 (71.4)	4 (28.6)	3 (27.3)	8 (72.7)
Statistics		p=1.000 [4], Δ% = 0	p=0.040 [4], Δ% = 0.381		
Vertigo[b]					
Yes	24 (38.1)	14 (58.3)	10 (41.7)	10 (41.7)	14 (58.3)
No	39 (61.9)	31 (79.5)	8 (20.5)	27 (69.2)	12 (30.8)
Statistics		p=0.071[3], Δ% = 0.212	p=0.031[3], Δ% = 0.460		
Caloric test and/or vHIT[b]					
Normal	54 (85.7)	41 (75.9)	13 (24.1)	31 (57.4)	23 (42.6)
Pathological	9 (14.3)	4 (44.4)	5 (55.6)	6 (66.7)	3 (33.3)
		p=0.104[4], Δ% = 0.315	p=0.725[4], Δ% = 0.089		
Time to th[c] (days)	4 (2-7)	p=0.510[5], r_s = -0.085	p=0. 976[5], r_s = -0.04		

PTA: pure-tone average; WRS: word recognition score; + : improvement; - : no improvement; vHIT: video head-impulse test; th: therapy; p: p-value; τ_b : Kendall's tau-b; r_{pb} : point-biserial correlation coefficient; r_s : Spearman rank-order correlation coefficient; Δ% : difference in proportions, [a] : data are given as mean (SD) for continuous variables with normal distribution; [b] : data are given as number (percentage) for categorical variables; [c] : data are given as median (Q1-Q3) for continuous variables without normal distribution; [1] : Kendall's tau-b; [2] : Point-biserial correlation; [3] : Chi-square test of homogeneity; [4] : Fisher's exact test; [5] : Spearman's rank-order correlation. Shapiro-Wilk test was initially used to determine group distributions. p<0.05 was considered as statistically significant.

Relationships of baseline demographic and clinical characteristics with an improvement in PTA and WRS are shown in Table 1.

HL grade according to PTA at admission and at the first (Avg=33, SD=7 days) and second follow-ups (Avg=183, SD=30 days) is depicted in Figure 1. PTA improved in 71% of patients after 6 months. By that time, in 37% of patients, hearing regained to the normal level, in 11% of patients, hearing improved to mild HL, in 29% of patients, hearing improved to moderate HL, and in 14% patients, HL was severe. Furthermore, 9% of patients remained deaf. After the treatment, hearing improved in all patients with mild HL, in 63% of patients with moderate HL, in 79% of patients with severe HL, and in 58% of patients with profound HL at admission. However, a Cochran-Armitage test of trend did not show a linear trend between the HL grade at admission and PTA improvement (p=0.235).

A Friedman test was performed to determine the differences in PTA and WRS at admission, first follow-up, and second follow-up because of nonnormal distributions of data. To perform pairwise comparisons, a Bonferroni correction for multiple comparisons was applied.

PTA was statistically significantly different between admission, first follow-up, and second follow-up, $\chi^2(2)=53.696$, p<0.0005 (Figure

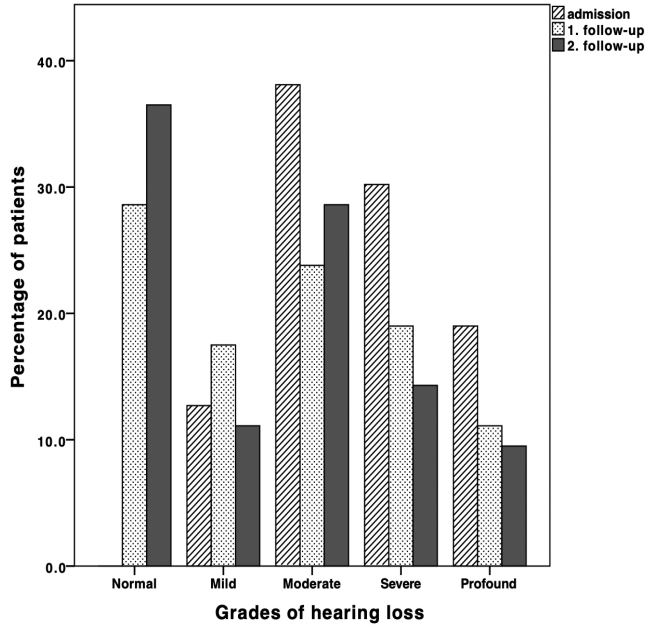

Figure 1. Hearing loss (HL) severity according to pure-tone average at admission and at first and second follow-ups.

2). A post hoc analysis revealed statistically significant differences between PTA at admission (Mdn=60 dB) and PTA at first follow-up (Mdn=44 dB) (p<0.0005) and between PTA at admission and PTA at the second follow-up (Mdn=43 dB) (p<0.0005). There was no statistically significant difference between PTA at the first and PTA at the second follow-up (p=1.000).

WRS improved in 59% of patients after 6 months. In 50% of patients with mild HL, in 58% with moderate HL, in 74% with severe HL, and in 42% with profound HL at admission, hearing improved after 6 months. WRS was statistically significantly different between admission, first follow-up, and second follow-up, $\chi^2(2)=80.983$, p<0.0005 (Figure 3). A post hoc analysis revealed statistically significant differences between WRS at admission (Mdn=38%) and WRS at the first follow-up (Mdn=80%) (p<0.0005) and between WRS at admission and WRS at the second follow-up (Mdn=80%) (p<0.0005) but not between the follow-ups (p=1.000).

Figures 4 and 5 represent WRS and PTA at admission and follow-ups in accordance with the AAO-HNS guidelines [9]. Figure 5 shows data plotted up to 100 dB, therefore, seven patients are not presented because of a higher PTA.

Hearing improved in all frequencies according to differences in median pure-tone hearing thresholds. The hearing threshold at admission

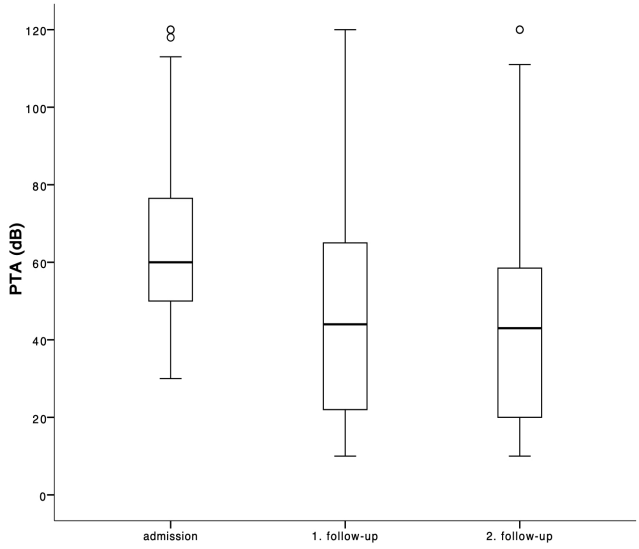

Figure 2. Boxplots of pure-tone averages (PTAs) at admission and at first and second follow-ups.

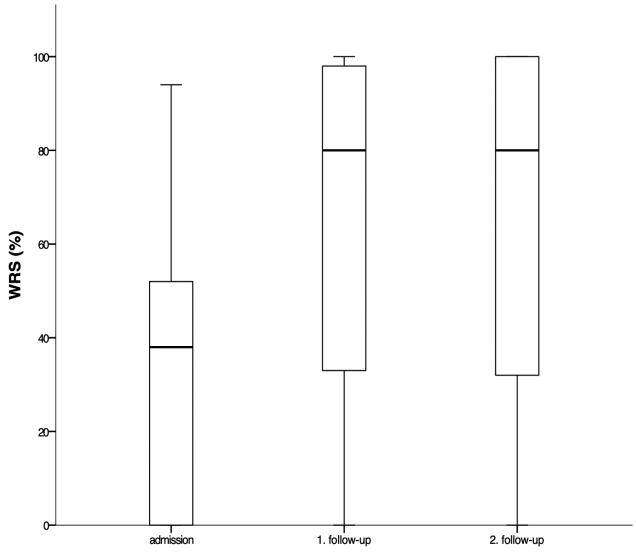

Figure 3. Boxplots of word recognition score test (WRS) at admission and at first and second follow-ups.

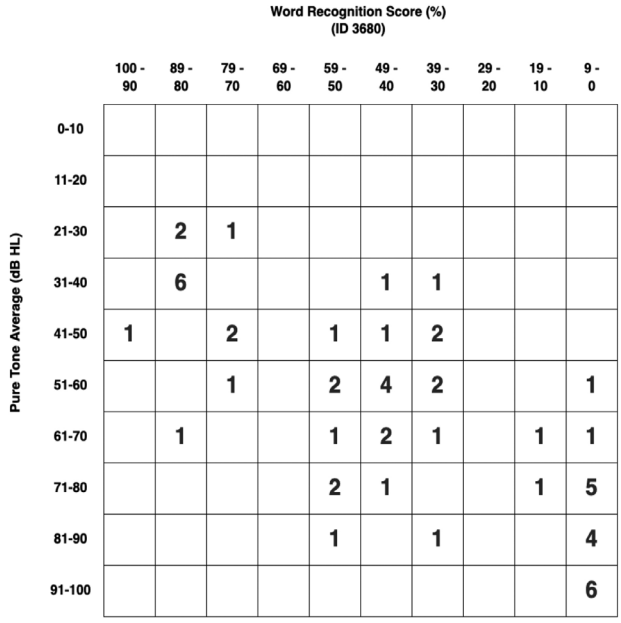

Figure 4. Scattergram of pretreatment hearing levels. Each box depicts the number of patients.

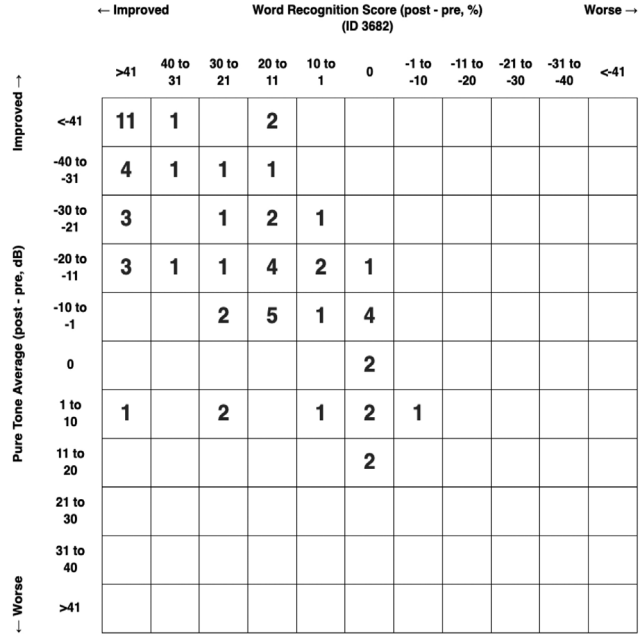

Figure 5. Scattergram of hearing levels for admission versus second follow-up. The patients whose pure-tone average and WRS improved are depicted in the boxes of upper left quadrant.

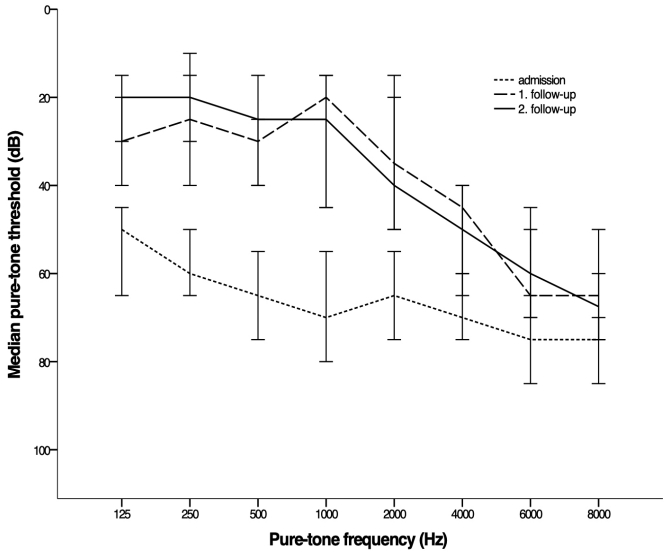

Figure 6. Median pure-tone hearing thresholds with 95% confidence intervals (i.e., error bars) due to nonnormal distributions at admission and at first and second follow-ups.

was higher in high frequencies compared with the hearing threshold in low frequencies. Furthermore, hearing thresholds in high frequencies improved less than hearing threshold in low frequencies. Therefore, high frequencies were more affected than low frequencies. Although the medians were different for all frequencies, there was an overlap of confidence intervals at frequencies 4000, 6000, and 8000 Hz. For that reason, there was no significant improvement in these frequencies (Figure 6).

No adverse effects were detected.

DISCUSSION

CSs are recommended for the treatment of ISSNHL. Several studies showed the benefit of CS use for the treatment of sudden HL [10–12], although some meta-analyses do not support that [13]. Only a few clinical studies compared the efficacy of glucocorticoids and placebo, but the question of spontaneous recovery remains open because of small sample sizes and limited methodological validity [7, 10, 14-16]. Data on the dose of systemic and IT CSs are inconclusive. The AAO-HNS guidelines [1] and other studies [2] recommend low-dose CS treatment (prednisone 1 mg/kg/d, usually a maximal dose of 60 mg/d or methylprednisolone 48 mg/d or dexamethasone 10 mg/d), whereas the German guidelines recommend high-dose CS treatment (250 mg prednisolone or an equivalent steroid dose) [3]. To avoid possible adverse effects, low-dose systemic CS treatment with a proven efficacy was used in our study [17, 18]. IT CSs were shown to be beneficial for treating ISSNHL either as salvage [5, 18, 19] or primary treatment [20-23]. Although studies by Nakache [24] and Ashtiani [25] did not show any difference between systemic, IT, or combined CS treatments for sudden deafness, IT combined with systemic CSs was found to be more effective than systemic CSs combined with hyperbaric oxygen therapy [26]. According to the CS dose–dependent effect described by Alexander [6], we treated ISSNHL concomitantly with high-concentration (24 mg/mL) IT dexamethasone and low-dose methylprednisolone orally (48 mg daily for 1 week, followed by a taper every 2 days).

Assessment of hearing improvement differs in the literature. Some researchers consider hearing is improved when PTA improves for ≥10, ≥15, or ≥30 dB [12]. Others evaluate hearing using the Wilson's [14] or the Siegel's criteria [27]. As PTA presents an average hearing threshold for the tested frequencies, HL in only a few frequencies does not significantly affect the PTA, yet it can affect WRS. For that reason, evaluating only PTA can be deceiving, and WRS improvement serves as an additional indicator of hearing recovery; therefore, PTA and WRS were analyzed in our study [28, 29].

As PTA improved in 65% of patients, and 29% of the patients recovered completely until the first follow-up, we can support an early efficacy of treatment protocol. Additionally, PTA and WRS were statistically significantly different between admission and the first follow-up. Despite some authors reporting a delayed improvement in PTA and WRS [24, 29], our results refute this. Although PTA improvement rate increased to 71% and WRS to 59% of patients after 6 months, the difference between the follow-ups was not statistically significant. In 37% of patients, the hearing level regained to normal, and in 11% of patients, hearing improved to the mild HL grade. Furthermore, 9% of patients remained deaf. Patients with serviceable hearing levels (43%), i.e., moderate (29%) and severe HLs (14%) were offered a hearing aid. However, there was no linear trend between the HL grade and PTA improvement. Patients with mild HL recovered better and those with profound HL recovered worse, which is consistent with the results of other studies [23, 30].

Our study confirms that the hearing thresholds at low frequencies improved better than at high frequencies [10, 18, 24, 31, 32]. Age did not have a statistically significant influence on the hearing outcome, which is consistent with the results of other studies [6, 33].

Patients with associated tinnitus had a better prognosis for improvement of WRS but not PTA. This is because word recognition is impaired by tinnitus in addition to HL. When tinnitus subsides, WRS improves although PTA does not improve. Therefore, tinnitus, especially of short duration, is considered a good prognostic sign, as already described [28, 34].

Vertigo was associated with statistically significantly worse hearing improvement compared with patients without vertigo, which is consistent with the results of other studies [35]. Therefore, vertigo is considered a poor prognostic sign.

According to published studies, statistically significant better hearing improvement is achieved if IT CS treatment is prompt [6, 21]. Our results show that patients in our study received treatment earlier than the time to therapy reported by Alexander et al. [6] (Avg=9.2 days, SE=1.3) and Battaglia et al. [21] (Avg=7.2 days, SD=7.6 days). The majority (75%) of our patients received treatment within 7 days. For that reason, we did not detect a statistically significant high correlation between the time to therapy and PTA or WRS improvement.

Although our study lacked a control group, a randomized placebo-controlled clinical study by Filipo et al. [36] confirmed the efficacy of IT CS treatment for sudden HL. Because of possible ethical concerns, our study was not placebo controlled similar to few other studies [11, 18, 33].

CONCLUSION

Prompt concomitant single high-concentration IT and low-dose systemic CSs are efficient for the treatment of ISSNHL, especially in

patients with associated tinnitus or absent vertigo. More than one-third of the patients recovered their normal hearing. Our treatment regimen yielded hearing improvement without adverse side effects.

Ethics Committee Approval: The study was approved by the Republic of Slovenia National Medical Ethics Committee (No. 0120-475/2017-4). The procedures followed in this study were in accordance with the ethical standards of the Republic of Slovenia National Medical Ethics Committee on human experimentation and with the Helsinki Declaration.

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – S.B., Š.K., D.V., N.B.U.; Design - S.B., Š.K., D.V., N.B.U.; Supervision – S.B.; Resource - S.B., Š.K., D.V., N.B.U ; Materials S.B., Š.K., D.V., N.B.U, M.H.; Data Collection and/or Processing - S.B., Š.K., D.V., N.B.U, M.H..; Analysis and/or Interpretation - S.B, Š.K., D.V., Literature Search - S.B., Š.K., D.V., N.B.U., Writing - S.B., Š.K., D.V..; Critical Reviews - S.B., Š.K., D.V., N.B.U., M.H.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Chandrasekhar SS, Tsai Do BS, Schwartz SR, Bontempo LJ, Faucett EA, Finestone SA, et al. Clinical practice guideline: sudden hearing loss (update) executive summary. Otolaryngol Neck Surg 2019; 161: 195-210. [Crossref]
2. Hultcrantz E, Nosrati-Zarenoe R. Corticosteroid treatment of idiopathic sudden sensorineural hearing loss: analysis of an RCT and material drawn from the Swedish national database. Eur Arch Otorhinolaryngol 2015; 272: 3169-75. [Crossref]
3. Plontke SK. Diagnostics and therapy of sudden hearing loss. GMS Curr Top Otorhinolaryngol Head Neck Surg 2018; 16: Doc05.
4. Richards RN. Side effects of short-term oral corticosteroids. J Cutan Med Surg 2008; 12: 77-81. [Crossref]
5. Kordiš Š, Battelino S. The role of high dose intratympanic dexamethasone as salvage therapy for idiopathic sudden sensorineural hearing loss. J Int Adv Otol 2017; 13: 318-21. [Crossref]
6. Alexander TH, Harris JP, Nguyen QT, Vorasubin N. Dose effect of intratympanic dexamethasone for idiopathic sudden sensorineural hearing loss: 24 mg/mL is superior to 10 mg/mL. Otol Neurotol 2015; 36: 1321-7. [Crossref]
7. Mattox D, Simmons F. Natural history of sudden sensorineural hearing loss. Ann Otol Rhinol Laryngol 1977; 86: 463-80. [Crossref]
8. Marvin T, Derganc J, Battelino S. Adapting the Freiburg monosyllabic word test for Slovenian. Linguistica 2017; 57: 197-210. [Crossref]
9. Gurgel RK, Jackler RK, Dobie RA, Popelka GR. A new standardized format for reporting hearing outcome in clinical trials. Otolaryngol Neck Surg 2012; 147: 803-7. [Crossref]
10. Alexiou C, Arnold W, Fauser C, Schratzenstaller B, Gloddek B, Fuhrmann S, et al. Sudden sensorineural hearing loss: does application of glucocorticoids make sense? Arch Otolaryngol Neck Surg 2001; 127: 253-8. [Crossref]
11. Gallo DE, Khojasteh E, Gloor M, Hegemann SCA. Effectiveness of systemic high-dose dexamethasone therapy for idiopathic sudden sensorineural hearing loss. Audiol Neurotol 2013; 18: 161-70. [Crossref]
12. Han X, Yin X, Du X, Sun C. Combined intratympanic and systemic use of steroids as a first-line treatment for sudden sensorineural hearing loss: a meta-analysis of randomized, controlled trials. Otol Neurotol 2017; 38: 487-95. [Crossref]
13. Crane RA, Camilon M, Nguyen S, Meyer TA. Steroids for treatment of sudden sensorineural hearing loss: a meta-analysis of randomized controlled trials. The Laryngoscope 2015; 125: 209-17. [Crossref]
14. Wilson WR, Byl FM, Laird N. The efficacy of steroids in the treatment of idiopathic sudden hearing loss: a double-blind clinical study. Arch Otolaryngol 1980; 106: 772-6. [Crossref]
15. Moskowitz D, Lee KJ, Smith HW. Steroid use in idiopathic sudden sensorineural hearing loss. The Laryngoscope 1984; 94: 664-6. [Crossref]
16. Veldman JE, Hanada T, Meeuwsen F. Diagnostic and therapeutic dilemmas in rapidly progressive sensorineural hearing loss and sudden deafness a reappraisal of immune reactivity in inner ear disorders. Acta Otolaryngol (Stockh) 1993; 113: 303-6. [Crossref]
17. Slattery WH, Fisher LM, Iqbal Z, Liu N. Oral steroid regimens for idiopathic sudden sensorineural hearing loss. Otolaryngol Neck Surg 2005; 132: 5-10. [Crossref]
18. Taha A, Shlamkovitch N, Abu-Eta R, Yeheskeli E, Muallem-Kalmovich L, Gavriel H, et al. High dose of intratympanic steroids for sudden sensorineural hearing loss salvage. Otol Neurotol 2019; 40: 1134-8. [Crossref]
19. Amarillo E, Navarro A, Hernández-García E, Plaza G. Intratympanic steroids for combined treatment of idiopathic sudden hearing loss: when is it too late? Acta Otolaryngol (Stockh) 2019; 139: 632-5. [Crossref]
20. Battaglia A, Burchette R, Cueva R. Combination therapy (intratympanic dexamethasone + high-dose prednisone taper) for the treatment of idiopathic sudden sensorineural hearing loss. Otol Neurotol 2008; 29: 453-60. [Crossref]
21. Battaglia A, Lualhati A, Lin H, Burchette R, Cueva R. A prospective, multi-centered study of the treatment of idiopathic sudden sensorineural hearing loss with combination therapy versus high-dose prednisone alone: a 139 patient follow-up. Otol Neurotol 2014; 35: 1091-8. [Crossref]
22. Gundogan O, Pinar E, Imre A, Ozturkcan S, Cokmez O, Yigiter AC. Therapeutic efficacy of the combination of intratympanic methylprednisolone and oral steroid for idiopathic sudden deafness. Otolaryngol Neck Surg 2013; 149: 753-8. [Crossref]
23. Kim SH, Jung SY, Kim MG, Byun JY, Park MS, Yeo SG. Comparison of steroid administration methods in patients with idiopathic sudden sensorineural hearing loss: a retrospective observational study. Clin Otolaryngol 2015; 40: 183-90. [Crossref]
24. Nakache G, Migirov L, Trommer S, Drendel M, Wolf M, Henkin Y. Steroid-based treatments for patients with total sudden sensorineural hearing loss. Acta Otolaryngol (Stockh) 2015; 135: 907-13. [Crossref]
25. Ashtiani MK, Firouzi F, Bastaninejad S, Dabiri S, Nasirmohtaram S, Saeedi N, et al. Efficacy of systemic and intratympanic corticosteroid combination therapy versus intratympanic or systemic therapy in patients with idiopathic sudden sensorineural hearing loss: a randomized controlled trial. Eur Arch Otorhinolaryngol 2018; 275: 89-97. [Crossref]
26. Suzuki H, Hashida K, Nguyen KH, Hohchi N, Katoh A, Koizumi H, et al. Efficacy of intratympanic steroid administration on idiopathic sudden sensorineural hearing loss in comparison with hyperbaric oxygen therapy. The Laryngoscope 2012; 122: 1154-7.[Crossref]
27. Siegel LG. The treatment of idiopathic sudden sensorineural hearing loss. Otolaryngol Clin North Am 1975; 8: 467-73.
28. Kim JY, Han JJ, Sunwoo WS, Koo JW, Oh SH, Park MH, et al. Sudden sensorineural hearing loss in children and adolescents: clinical characteristics and age-related prognosis. Auris Nasus Larynx 2018; 45: 447-55. [Crossref]
29. Noguchi Y, Takahashi M, Ito T, Fujikawa T, Kawashima Y, Kitamura K. Delayed restoration of maximum speech discrimination scores in patients with idiopathic sudden sensorineural hearing loss. Auris Nasus Larynx 2016; 43: 495-500. [Crossref]
30. Byl FM. Sudden hearing loss: eight years' experience and suggested prognostic table. The Laryngoscope 1984; 94: 647-61. [Crossref]
31. Lee JB, Choi SJ, Park K, Park HY, Choo OS, Choung Y-H. The efficiency of intratympanic dexamethasone injection as a sequential treatment after initial systemic steroid therapy for sudden sensorineural hearing loss. Eur Arch Otorhinolaryngol 2011; 268: 833-9. [Crossref]
32. Jun HJ, Chang J, Im GJ, Kwon S-Y, Jung H, Choi J. Analysis of frequency loss as a prognostic factor in idiopathic sensorineural hearing loss. Acta Otolaryngol (Stockh) 2012; 132: 590-6. [Crossref]
33. Bhandari A, Jain S. Early intratympanic methylprednisolone in sudden SNHL: a frequency-wise analysis. Indian J Otolaryngol Head Neck Surg 2019; 71: 390-5.[Crossref]
34. Hikita-Watanabe N, Kitahara T, Horii A, Kawashima T, Doi K, Okumura SI. Tinnitus as a prognostic factor of sudden deafness. Acta Otolaryngol (Stockh) 2010; 130: 79-83. [Crossref]
35. Shih CP, Chou YC, Chen HC, Lee JC, Chu YH, Wang CH. Analysis of caloric test responses in sudden hearing loss. Ear Nose Throat J 2017; 96: 59-64. [Crossref]
36. Filipo R, Attanasio G, Russo FY, Viccaro M, Mancini P, Covelli E. Intratympanic steroid therapy in moderate sudden hearing loss: a randomized, triple-blind, placebo-controlled trial. The Laryngoscope 2013; 123: 774-8. [Crossref]