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Original Article

Is it Beneficial to Treat Patients Presenting Three Weeks or Longer after the Onset of Sudden Sensorineural Hearing Loss?

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OBJECTIVES: The accepted treatment for idiopathic sudden sensorineural hearing loss (ISSNHL) consists of oral or intratympanic steroids. The time from onset to treatment is considered as an important prognostic factor, although there is no clear cutoff point when treatment is no longer beneficial. This study aimed to assess the efficacy of treatment with oral or intratympanic steroids and carbogen, in patients presenting 21 days or later after the onset of hearing loss.

MATERIALS and METHODS: A total of 895 patients with ISSNHL was seen in our center between 2010 and 2018. The study cohort included 103 patients treated with oral or intratympanic steroids or both with carbogen 21 days or longer after experiencing hearing loss. Retrospective analysis of files and audiometry was conducted, and pre- and post-treatment audiograms were compared. Improvement was defined by SRT (≥15 dB improvement), discrimination (≥15% improvement), or 15 dB improvement at specific frequencies (250-500, 4000-6000 Hz).

RESULTS: Hearing improvement, according to the study definition, was seen in 22.3% (23/103) of patients within the time period of the treatment. All the 23 patients had functional hearing after treatment and 16 of them returned to their baseline or normal hearing. While the time from onset of ISSNHL to treatment varied, most patients demonstrating improvement were treated 21-30 days after onset.

CONCLUSION: In this patient cohort treated late for sudden sensorineural hearing loss (SSNHL), a small but significant number of patients improved during the time of treatment. Although the lack of a control group makes it difficult to prove that the improvement resulted from the treatment, we recommend not to rule out treatment systematically in patients presenting late after ISSNHL. Additional prospective studies are warranted.

KEYWORDS: Sudden sensorineural hearing loss, intra-tymanic steroids, late treatment

INTRODUCTION

Sudden sensorineural hearing loss (SSNHL) is a debilitating condition, which is traditionally considered an otologic emergency. It is defined as sensorineural hearing loss of 30 decibels (dB) or more over at least 3 contiguous frequencies (on audiometry) with an onset of 3 days or less [1]. The entity is divided into cases with an underlying etiology and those that are idiopathic. The incidence of idiopathic sudden sensory neural hearing loss (ISSNHL) is approximately 5 to 20 per 100,000 people [2] with a spontaneous recovery rate ranging between 32%–65% [1, 4-6]. There are numerous treatment regimens proposed in the literature of which the main groups are steroids (oral or intratympanic [IT]), hyperbaric oxygen, vasodilators, and anti-viral medication. It is widely accepted that steroids are the main treatment modality for ISSNHL [3]. Several publications compared the efficiency of steroid therapy to spontaneous recovery; Wilson et al. [7] in their report presented a recovery rate of 61% in the steroid treated group compared with 32% in the placebo group. Recent studies questioned the efficacy of steroids in the treatment of ISSNHL, an example is a meta-analysis by Crane el al.[9] which reviewed 3 clinical trials comparing oral steroid treatment to placebo and concluded that there is no statistical benefit.

It is believed that starting treatment within 7 days from symptom onset leads to a higher rate of recovery, and the early treatment serves as an important positive prognostic factor for these patients [6, 10, 11]. Hosokawa et al. [10] showed an improvement rate of

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82.2% in patients who received their initial treatment within 7 days of symptom onset. The authors reported that after 7 days, there was an inverse correlation between improvement rate and later treatment time [10]. This study aimed to assess the efficacy of treatment with steroids, oral or IT or both along with carbogen inhalations, in patients presenting 21 days or later after the onset of hearing loss.

MATERIALS AND METHODS

A total of 895 patients diagnosed with ISSNHL (ICD-9) were seen in Shaare Zedek Medical Center between 2010 and 2018. Of the 895 patients identified from the electronic records search, 116 were admitted 21 days or more after the initial occurrence of hearing loss. Exclusion criteria included acoustic trauma, inner ear, or retro-cochlear pathology, external or middle ear disease, prior diagnosis of Meniere's disease, and a history of congenital otologic pathology. Thirteen patients were excluded based on these criteria. After exclusion, a final cohort of 103 patients was analyzed. There were 49 females and 54 males, and the age distribution is shown in Table I. The information collected included demographic details, associated symptoms, prior treatments by primary care physicians, time elapsed between the hearing loss and presentation to our center, treatment modality, and initial and follow-up audiograms.

Our center's treatment protocol for ISSNHL in most patients begins with a 1-week course of 60 mg/day of oral prednisone (PO) along with inhalations of carbogen (95% oxygen and 5% CO_2) 4 times daily. Most patients are hospitalized making it easier to receive the 4 times daily treatments of carbogen and undergo an audiogram every other day to closely monitor hearing improvement. In addition, we find it useful being able to monitor patients with hypertension and/or diabetes under steroid therapy. For patients who do not return to their baseline hearing or reach normal hearing levels under oral steroid treatment, a myringotomy using a CO_2 laser is performed and a week of salvage daily treatment of dexamethasone 10 mg/mL by IT injections is initiated. Carbogen therapy is continued even with IT treatment and is stopped only if side-effects, such as headache or dizziness occur. Our protocol for carbogen treatment is 20 minutes 4 times daily, 8–10 L directly from the container. Vital signs, dizziness, and facial flush are monitored.

In general, initial oral steroid treatment is offered to patients admitted with symptoms lasting 2 weeks or less and IT injections to those who present within 2–4 weeks from symptom onset and/or in patients suffering from unstable hypertension and/or diabetes mellitus to spare the systemic side effect of oral steroids. Moreover, for patients admitted 4 weeks or later from symptom onset, we do not usually propose treatment due to lack of valid data supporting improvement in that group of patients. Nonetheless, our protocol is flexible regarding this issue and in some cases in which the patient insists, we treat after realistic expectations are discussed. This ensured that we could gather a cohort for this study, which included patients presenting later than 21 days who were treated locally, systemically, or both.

Audiometry was performed by certified audiologists in our medical center, the test was performed in soundproof booths using Grason-Stadler (GSI-61/AudioStar Pro) audiometer (Minnesota, USA) with standard audiometric parameters. The audiometers were calibrated annually. Pure tone average (PTA) was calculated using 500, 1,000, and 2,000 Hz. Speech discrimination (SD) and speech reception threshold (SRT) were included for analysis. Recorded media was used for speech audiometry. Each patient in our cohort had at least 2 audiograms: one prior to treatment initiation and another at the end of treatment under hospitalization. "Improvement" was defined by one of the following: (i) ≥15 dB improvement in SRT, (ii) ≥15% improvement in discrimination, and (iii) 15 dB improvement on specific frequencies (250–500, 4000–6000 Hz), in case of high/low frequency ISSNHL.

The study was approved by the Shaare Zedek Medical Center Institutional Review Board.

RESULTS

The final cohort included 103 patients who were admitted and treated 21 days or longer after the onset of hearing loss. The time from onset of ISSNHL to treatment varied, with a mean of 32 days. The majority of the patients presented between 21–30 days after symptom onset with one patient presenting 90 days after hearing loss occurred (Figure 1). The treatment modality among the final cohort varied. Fifty-three percent (55/103) of the patients received IT injections with dexamethasone, 32% (33/103) received systemic steroids followed by local steroids, and 14% (15/103) received only oral treatment (Figure 2a). All patients, regardless of treatment modality, received carbogen inhalations according to our protocol.

MAIN POINTS

- In this study, 23 out of 103 patients (22.3%) treated with oral or IT steroids and carbogen 21 days or later after onset of ISSNHL demonstrated improvement in hearing during the time of treatment.
- All 23 patients who showed improvement had functional hearing after treatment, and 16 of them returned to baseline or normal hearing.
- Although, due to the lack of a control group it is difficult to prove that the improvement resulted from the treatment, we recommend not systematically ruling-out treatment in patients presenting late after ISSNHL.

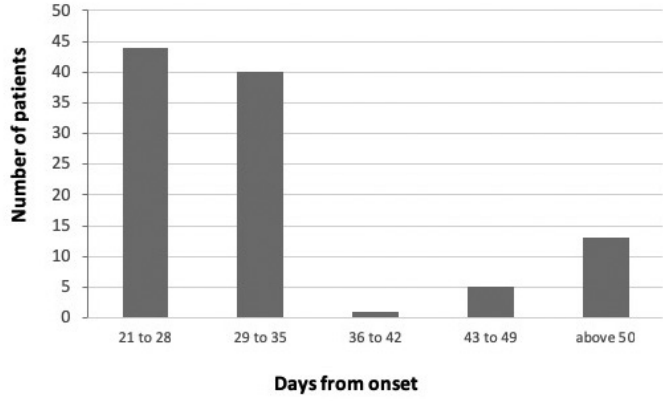

Figure 1. Number of patients according to presentation time after hearing loss.

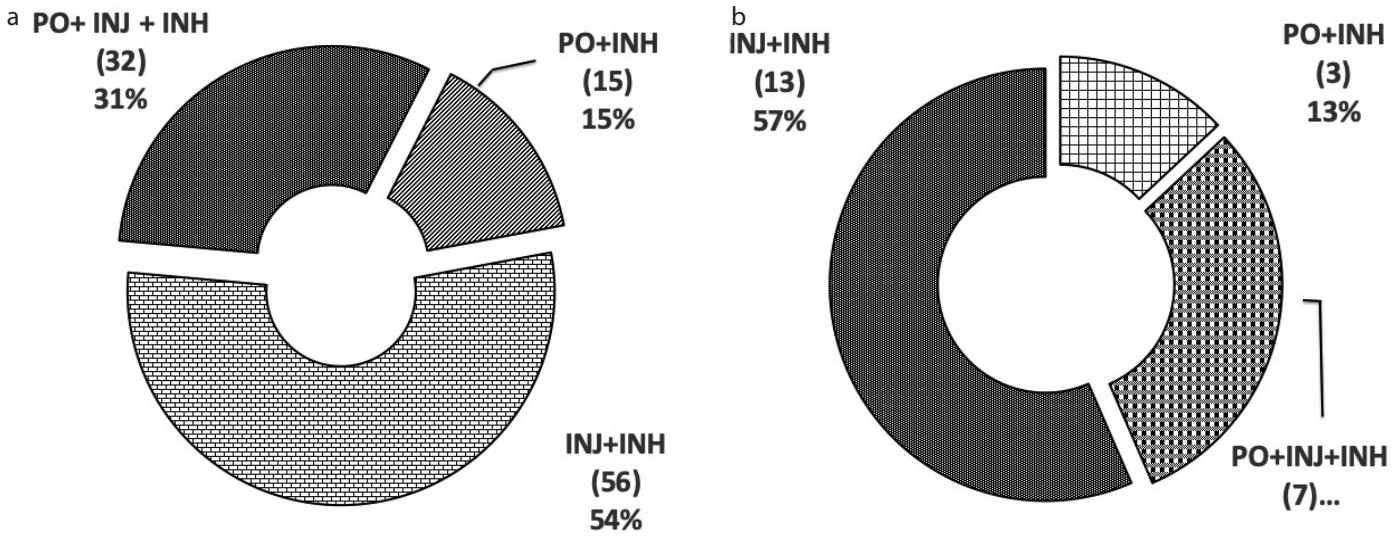

Figure 2. a, b. (a) Patient groups according to treatment modality (PO – Oral steroid, INJ – Intratympanic steroids, INH – Carbogen inhalations). (b) Patients who improved according to the treatment modality (PO – Oral steroid, INJ – Intratympanic steroids, INH – Carbogen inhalations)

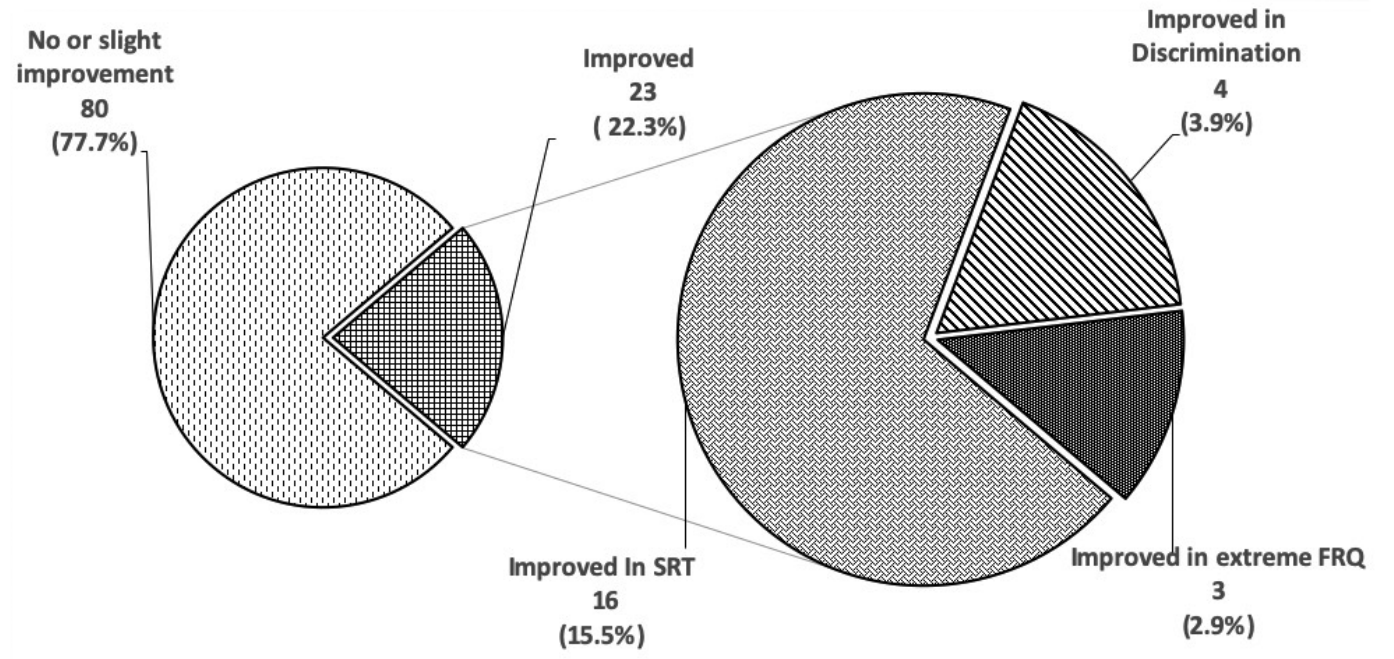

Figure 3. Final cohort improvement rates, along with the division to the improvement criteria.

Hearing improvement, according to the study definition, was seen in 22.3% (23/103) of the patients within the time period of the treatment. In the majority of these patients (16/23), improvement was demonstrated by a decrease of at least 15 dB in SRT thresholds; 4/23 showed an improvement of at least 15% in discrimination scores, and 3/23 improved in extreme frequencies (250–500, 4000–6000 Hz). The improvement rates are presented in Figure 3.

Sixteen of the 23 patients that showed improvement according to the study criteria returned to their baseline hearing level or to normal hearing, the remaining 7 improved substantially but were left with hearing loss. All 23 patients had functional hearing after treatment.

When looking at hearing improvement as a function of the treatment modality, it was seen that the highest rates of improvement (57%) were in those patients treated with IT injections along with carbogen inhalations. Thirty percent of the patients that improved were treated with systemic steroids followed by IT injections along with carbogen inhalations, and 13% of the patients who improved were treated with systemic steroids only along with carbogen inhalations (Figure 2b).

The percentage of patients that improved in every age group is shown in Table 1. Generally, it does not seem that age affected the chance of improvement; however, unfortunately, the small sample size of our cohort study does not enable us to statistically confirm this.

Table 1. Distribution of the study cohort and improvement rate according to age

Age group (years)	Number of patients Final study cohort	Number of patients improved	Improvement rate by age (%)
1-9	2	0	0
10-19	7	0	0
20-29	9	2	22
30-39	10	3	30
40-49	17	5	29
50-59	26	3	11
60-69	21	7	33
70-79	9	2	22
80-89	2	1	50

DISCUSSION

The focus of this study was to evaluate hearing improvement in patients diagnosed with ISSNHL who presented late for treatment regardless of the type of hearing loss and the severity. We questioned the efficacy of steroid treatment among those patients. We saw an improvement of 22.3% with steroidal treatment (either systemic or local) along with carbogen inhalations in these patients who presented 21 days or later from symptom onset. As mentioned, we defined improvement in 3 separate ways, either a 15 dB decrease in the SRT threshold, a 15% increase in discrimination, or in case of hearing loss at extreme frequencies (250–500, 4000–6000 Hz), improvement with increase of 15 dB at those specific frequencies.

It was noted that in most of the patients, the improvement was demonstrated in SRT thresholds (70%), which can be explained by the fact that most of the audiograms were with either mid-frequency hearing loss or involvement of more than 3 frequencies. Importantly, all 23 patients who demonstrated improvement had functional hearing after treatment; 16 of them returned to their baseline hearing level or normal hearing and the remaining 7 had the potential to benefit from hearing aids.

While there is an agreed definition for ISSNHL[1], other aspects of ISSNHL are controversial[12]. For example, there is no definite data on the benefit of steroidal treatment in general, the specific benefit of treatment among those who present late, and the rate of spontaneous recovery. This results in an ongoing debate in the literature about the modalities of treatment in general and steroidal treatment in particular for ISSNHL. Some studies do not demonstrate a significant difference between placebo and steroid treatment [9]. As mentioned earlier, the rate of spontaneous recovery is 32%–65% [4-6], but there is no clear information regarding the timeframe of spontaneous recovery and common definition of what is considered recovery. The time between symptom onset and treatment is currently considered as a prognostic factor [6, 10, 11]. Although in all of the above-mentioned articles, data are given to support the importance of treatment timing in relation to outcome, there is no sufficient emphasis on the benefit of steroidal treatment on late presenters compared with spontaneous recovery. In order to examine this direct relationship between treatment and recovery in late presenters, we assessed hearing improvement during the treatment itself. We assumed that those who presented late and improved during the timeframe of treatment, had probably benefited from the treatment itself, rather than from improving spontaneously.

In our cohort, the mean time from symptoms onset to treatment was 32 days, with one patient presenting 90 days from symptoms onset. Interestingly, this specific patient improved under treatment with oral prednisone + carbogen inhalations. The majority of the patients that improved presented between 21-30 days from symptom onset.

A significant limitation of this study is the lack of a control group. It is difficult to differentiate between improvement as a result of treatment and spontaneous recovery. Another weakness of this study is the definition of improvement. As there is no standard definition agreed upon, in this study we adopted a comprehensive definition.

CONCLUSION

In this cohort of 103 patients treated over 21 days after onset of SSNHL, a small but significant number of patients (23/103) improved during the time of treatment. All the 23 patients had functional hearing after treatment, and 16 of them returned to baseline or normal hearing. Although the lack of a control group makes it difficult to prove that the improvement resulted from the treatment, we recommend not to rule out treatment systematically in patients presenting late after ISSNHL. Additional prospective studies are warranted.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Shaare Zedek Medical Center.

Informed Consent: Informed consent is not necessary due to the retrospective nature of this study.

Peer-review: Externally peer-reviewed.

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

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