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Original Research Article

Intratympanic Dexamethasone for the Treatment of Sudden Sensorineural Hearing Loss among Adult Patients: An Institutional Study

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Abstract:

Background: Sudden sensorienural hearing loss (SSNHL) is an otological emergency. Steroids, in various forms still the treatment of choice. Intratympanic steroids avoid systemic side effects. Higher concentration of drug is achieved in the end organ. Topical application of steroids in low dose is therefore, preferred.

Methods: Prospective study of 36 months. Total 59 patients were included in the study. Intratympanic dexamethasone were given twice a week for 4 weeks, weekly for 3 months and once in 2 weeks up to 6 months. Pure tone audiograms (PTA) were taken on the day of first presentation (pre-treatment) and 1 month, 3 month and 6 month post treatment. They were compared to know the effect of local treatment.

Results: Complete recovery noticed in 36 (61%) patients, partial recovery in 15(25.4%) patients and no improvement shown by 8 (13.6%) patients. Early initiation of treatment is the key to success. No serious side effects were noticed in our study.

Conclusion: Intratympanic dexamethasone is cost effective, widely available. Intratympanic dexamethasone therapy can lower the total amount of steroid administration. It reduces the systemic toxicity, duration of treatment. This is one among the best option for treatment of SSNHL patients. The dosage and duration of this medication is individual to each patient. Nanocarrier - based therapy can diffuse into inner ear allowing direct drug delivery. Targeted delivery of certain type of nanoparticles is the latest therapy of SSNHL. Direction towards less toxic nanoparticles might be the future research with respect to therapy of SSNHL.

Keywords: Sudden sensorineural hearing loss (SSNHL), Intratympanic steroid, Dexamethasone, Audiogram, Round window membrane (RWM), Nanoparticles (NP), Recovery.

Introduction

Sudden sensori-neural hearing loss (SSNHL) is still an otological emergency. In this modern era of technology, many a times the early and correct diagnosis of SSNHL is being missed. Ischemia, viral infection, systemic illness, immune reaction, retrocochlear pathology, temporary rupturing inner ear membrane are the different aetiologies associated with its pathogenesis.

The golden window period for initiation of treatment is very narrow. Earlier the treatment initiated, better the outcome. Nearly 50% of SSNHL patients has got tinnitus and giddiness associated with it at the time of diagnosis. The exact incidence of SSNHL is not clear. Spontaneous recovery occurs and missing the treating otologist occurs many a time. Incidence range from 11 to 77/100,000 people per year. The most common age group is 47-62 years [1].

Dosage of steroid treatment and the duration of steroid treatment is not correctly defined in medical

literature pertaining to SSNHL. Mostly, steroids are picked up empirically rather than accurate therapy.

Low dose of systemic steroid may not create an ideal therapeutic effect due to its limited capacity to penetrate the hematoperilymphatic barrier. Recent pharmacokinetics and its research show that the intratympanic (IT) steroid therapy allows direct penetration of this drug via the round window membrane and thereby produces high perilymphatic concentration of the drug. Thereby reducing strong toxic side effects and negligible absorption of steroids to the systemic circulation [2,3].

Dexamethasone is quite inexpensive and easily available in most areas of the world. It has got high affinity to glucocorticoid receptors (GRs) of inner ear than other steroids. So we have chosen dexamethasone as intratympanic agent in SSNHL patients [4].

Aim of Study

1) To arrive at an earlier and correct diagnosis of SSNHL.
2) To study the efficacy of intratympanic dexamethasone in its treatment among adult patients presenting with SSNHL.
3) To study the factors affecting the success of treatment.
4) To evaluate the complications associated with its treatment.

Materials and Methods

Ours is a prospective study of 36 months. The study period was between August 2020 to July 2023. Patients presented to the ENT department at Heritage Institute of Medical Sciences, Varanasi, Uttar Pradesh, India with complaints of sudden hearing loss and tinnitus were evaluated in our study. Total number of patients were 59. Patients presented to ENT OPD with SNHL of 30dB or more on 3 consecutive frequencies over less than 72 hrs. of duration were selected. The patients who took treatment previously were not considered.

Inclusion Criteria

1. Age≥18 years
2. Patients with SNHL and tinnitus

Exclusion Criteria

1. Age<18 years
2. Mixed and conductive hearing loss
3. Ototoxicity
4. Middle ear tumours
5. Pregnant women with hearing loss

Each patient was evaluated in terms of general, systemic and ENT examinations. Audiometric evaluation done with pure tone audiometry (PTA machine-Labat company-audilite model-2016 make) and Impedance Audiometry (Impedance machine- Interacoustic company AT235 model-2018 make). If required HRCT temporal bone and MRI brain was taken.

Intratympanic Dexamethasone (4mg/1ml) was given to each patient twice a week for four weeks, after initial dose. Vasodilators like Pentoxifylline (400mg thrice a day) and Xantinol Nicotinate (500mg twice a day) were given for 3 weeks as adjuvant therapy. PTA was repeated on day four of first treatment. There after every week for first one month. Then it was repeated monthly for six months.

The efficacy of local treatment was assessed by pure tone audiograms (PTA) before and after therapy. The averages of 500, 1000 and 2000 Hz were calculated to determine the hearing level.

Treatment outcome was divided into 3 groups, namely complete recovery, partial recovery and no improvement. Complete recovery audiogram was measured, when the hearing level became stable.

- 40-50dB improvement from first PTA (before treatment) was considered partial recovery.
- 60-80dB improvement from first PTA (before treatment) was considered complete recovery.

Results

The mean age of patients in our study is 60.4. Majority of patients fall under the age group 56-65 (28.8% patients). The sex distribution among patients was same. Complete recovery was seen in 36 patients (61%). Partial recovery was seen in 15 patients (25.4%). No improvement was seen in 8 patients (13.6%).

The number of patients presented to ENT OPD in less than 4 days was 39. Late presentation was noticed among 20 patients. Complete recovery and early presentation were interlinked. Among our patients of 36 months, only 3 were having bilateral SSNHL. The efficacy of treatment with intratympanic dexamethasone was influenced by factors like age, severity of hearing loss, shape of the audiogram, time of initiation of therapy, associated vertigo and tinnitus. The therapy efficiency was not influenced by associated vertigo and tinnitus.

Younger age and initiation of treatment less than 4 days were the major factors which influenced the success rate in our study. Patients with age more than 40 years and beginning of treatment after 7 days showed poor results. Precipitously falling hearing loss (shape of audiogram) has shown a poor progress with the treatment.

Results are shown in table 1-5 and Figures 1-6.

Table 1: Presentation of patient

<4Days	>4Days
39	20
66.1%	33.9%

Table 2: Distribution (Unilateral/Bilateral)

Unilateral	56	94.2%
Bilateral	3	5.8%

Table 3: Distribution (Age-wise)

Age distribution	Number of patients	% of patients
18-25	3	5.1%
26-35	5	8.5%
36-45	8	13.6%
46-55	14	23.7%
56-65	17	28.8%
>65	12	20.3%

Table 4: Treatment Outcome

Complete recovery	36	61.0%
Partial recovery	15	25.4%
No improvement	8	13.6%

Table 5: Complications

Transient pain	7	11.9%
TM perforation	1	1.7%
Transient tinnitus	6	10.2%
Vertigo	9	15.3%
Further decline of hearing	0	NA

Discussion

Different types of hearing loss are a prevailing health issue worldwide. The magnitude of this clinical condition is high. 1.5 billion People worldwide affected by hearing loss in a year. The sensory inner ear cell, once damaged, do not regenerate in mammals. This leads to permanent sensorineural hearing loss. Still, spontaneous recovery is seen usually in 30-65% cases of SSNHL patients. Mostly recovery occurs in the first two weeks after the initiation of therapy. In a study by Zhao et al., it is noted that the therapy initiated within two weeks is better for treatment outcome [5]. Several methods are recommended for the evaluation of recovery in SSNHL patients. Various factors associated with recovery in SSNHL are early visit to ENT doctor, initiation of therapy, age, unilateral or bilateral type of SSNHL. Disruption of the blood –labyrinthine barrier is evaluated by 3-Tesla MRI scan. The contrast enhancement of the inner ear is studied by administration of gadolinium contrast [6].

In a study, Salt and Plontke postulated agents delivered to round window membrane were not regularly distributed. Rather it demonstrated a base-to-apex gradient of concentration. Basal parts of the cochlea receive far high concentration of the drug compare to apical parts. This fact likely to explain the greater efficacy of intra tympanic steroids over the high –frequency range than lower frequencies [7].

Dexamethasone is a glucocorticoid medication with chemical formula$C_{22H_{29}FO_5}$. Its melting point is 262℃ (504℉). The effects of dexamethasone usually seen within a day and last for about 3 days. Bioavailability is 80-90%. Its biological half-life is 36 to 54 hours. Plasma half life is 4 to 5 hours. Dexamethasone first synthesized in 1957 by Philip Showalter Hench. It was approved for medical use in 1958 [8-11]. Dexamethasone is a pregnancy category C medication. It should only be used when the benefits are greater than the risks, during pregnancy. It should not be taken during breast feeding time [12, 13].

It is a agonist of glucocortico receptor (GR) and is highly selective for the GR over the mineralocorticoid receptor (MR) [14]. Dexamethasone is 25 times more potent than hydrocortisone. Its affinity (K_i) for the GR was found to be about 1.2nM in a study. It has got poor blood brain barrier penetration. But in high dosage dexamethasone override the export capacity of P-glycoprotein and enter the brain to activate the central GRs. In the inner ear, it has got high affinity to GRs compared to methylprednisolone. So intratympanic dexamethasone is more beneficial to the patients with regard to SSNHL. Potential possibility of hearing improvement in SSNHL

patients noticed when intratympanic dexamethasone is given for longer duration.

Hearing improvement is mostly seen when this drug is administered in early period of the disease as in our study. In a study by Kakehata et al. they described a higher efficacy of local steroid treatment over 8 days compared to systemic steroid therapy in patients with diabetes [15].

In our study, the efficacy of intratympanic dexamethasone is illustrated by number of complete recoveries (36 patients), partial recoveries (15 patients). The rate of complete recoveries was also seen with local treatment. It shows the capacity of hearing restoration with long course of treatment. Many a times, positive response in hearing may not be seen with systemic steroids in the initial period of treatment. This fact favours, once again the good outcome with local therapy on the period of treatment [16].

From our study we couldn't set an optimal duration of local treatment. The duration of treatment is individual for each patient. So it might be advised to continue the local treatment as long as early improvement is noticed. 2 same audiograms showing improvement in hearing is taken one month apart, and regular follow up of SSNHL patient is advised for a minimum of six months.

No serious systemic side effects were noticed in our study, related to intratympanic application of dexamethasone. Commonest side effect noticed was vertigo (9 patients), which lasted 2-3 days and settled by simple remedies. Transient pain was noticed in 7 patients, transient tinnitus in 6 patients. TM perforation seen in 1 patient. Deterioration of hearing was not seen in any patient in this study.

Recent research has contributed a lot in delivering drugs locally to the inner ear safely and in controlled manner. Newer drug delivery systems have been used to mitigate the resistance exerted by different anatomical barriers found in the end organ. Nanocarrier-based systems can easily diffuse to the inner ear, through round and oval window membranes [Fig-6]. It allows direct delivery of the drug in the end organ components. Nanoparticles is the key component of newer drug delivery system, locally. Nanoparticles are solid particles with diameters smaller than 100nm. Both organic and inorganic components are included in its structure. Various drugs can be added to nanoparticles for functionalization. It delivers the drug to specifically to target cells and regulates the structural and signaling mechanism [17,18]. Noninvasive targeted drug delivery to the inner ear is possible by the use of nanoparticles.

Encapsulation of different types of agents (small drugs, siRNA proteins, or peptides) within nanocarriers allows higher concentration and their residence time in the perilymph. Nanocarriers dispersed within hydrogels give superior efficacy. Nanocarriers migrate to the inner ear after specific targeting without losing the integrity [19].

The ability of the drug to cross the hematoperilymph barrier is enhanced by NP-based DDS. It gives a new hope for hearing loss [20]. Controlled drug delivery has got control of time, amount of drug, and location of release of the drug. It enhances the efficacy of the drug at end organ. The small size, narrow accessibility and high vulnerability of the inner ear limit the choice of therapy. So new drug delivery systems are expected to have high drug loading capacity and predictable delivery kinetics at the decide location namely inner ear. Their desired time period of drug delivery has to be good. New drug delivery system has to be non toxic. They are expected to be eliminated shortly from the body system just after release of the active substance at the end organ [21].

The toxicity of nanoparticles at end organs like inner ear, brain, testes, liver and spleen are studied by some authors [22, 23]. Nanoparticles appears to be safe for the inner ear. Its long time toxicity needs to be studied, with regard to side effects produced by nanocarrier degradation at its end organ [24]. The highlight is early visit to ENT doctor and early initiation of treatment. Conventional therapy coupled with recent research namely nanoparticle based drug therapy will give good outcome in SSNHL patients.

Conclusion

Sensorineural hearing loss remains to be an important and difficult to treat health entity. Various treatment options are available for the treatment of SSNHL. Administration of drugs via intratympanic or intracochlear routes has proven to be more effective than systemic route. Though improvement of SSNHL is not certain, intratympanic dexamethasone therapy gives good outcome in its treatment. It is cost effective and widely available. It significantly decreases the duration of treatment and adverse side effects of systemic steroid therapy. Most common age group affected is 56-65. Duration with intratympanic dexamethasone is individual to each patient. Complete recovery was shown by 61% of patients. No major side effects were noted by this form of therapy. Nanoparticles impregnated with various medicaments are the newest treatment for SSNHL. Further studies in future, might reveal the importance of nanotechnology in the treatment of various inner ear diseases.

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Compliance and Ethical Standards

Ethical Approval: The permission was taken from Institutional Ethics Committee prior to starting the project. All procedures performed in studies involving human participant were in accordance with the ethical standards of the institution and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The ethical committee number is: U/2020/08/25.

Informed Consent: Informed consent was obtained from all individual participants included in the study.

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