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***Retrospective Study***

**Intratympanic dexamethasone injection for sudden sensorineural hearing loss in pregnancy**

LyuYL *et al.* Intratympanic dexamethasone for SSNHL in pregnancy

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**Abstract**

BACKGROUND

As sudden sensorineural hearing loss (SSNHL) rarely occurs in pregnant women, there is a lack of knowledge and relevant research on its management.

AIM

To investigate the effect of intratympanic dexamethasone injection in the treatment of pregnant patients with SSNHL.

METHODS

A retrospective chart review was made for the period between June 2017 and August 2019 at our Department of Otorhinolaryngology-Head and Neck Surgery. Pregnant women who met the criteria for SSNHL were included and grouped based on the therapeutic modalities. The treatment group received intratympanic dexamethasone (2.5 mg) q.o.d. for a total of four times, while the control group received no medication other than bed rest and medical observations. All the patients were under close care of obstetricians. Pure-tone audiograms were performed before and after treatment.

RESULTS

Eleven patients who met the inclusion criteria were assigned to the treatment group (*n* = 7) and the control group (*n* = 4). The mean age of patients was 31.2 ± 3.8 years; the right ear was affected in seven (63.64%) cases. Two patients (18.2%) suffered from vertigo, 10 (90.9%) suffered from tinnitus and 6 (54.5%) suffered from aural fullness. The time from onset to clinic visit was relatively short, with a mean time of 1.3 ± 0.9 d. All the women were within the second or third trimester; the average gestation period was 26.0 ± 6.2 wk. The pure-tone averages at onset between the two groups were similar. After one wk of therapy, the treatment group had a curative rate of 57.1% and a significantly better hearing threshold and greater improvement compared to the control group (all *P* < 0.05). Some patients experienced transient discomfort from intratympanic injections that disappeared after getting rest, while none had permanent complications. All patients delivered healthy full-term neonates with an average Apgar score of 9.7 ± 0.5.

CONCLUSION

Intratympanic dexamethasone injections can be used as a first-line therapy in pregnant women with SSNHL.

**Key words:** Sudden sensorineural hearing loss; Pregnancy, Intratympanic injection; Audiometry; Dexamethasone; Obstetrics

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**Core tip:** Sudden sensorineural hearing loss (SSNHL)rarely happens in pregnant women. The lack of understanding and guidelines in this condition has caused treatment dilemma. We retrospectively analyzed our experience with intratympanic dexamethasone injections for patients with sudden deafness during pregnancy and found out that the treatment group demonstrated a significantly better hearing threshold and greater improvement than control group after a total dose of 10 mg dexamethasone. Thus, we suggest that intratympanic dexamethasone injections should be applied as a safe and effective therapy for SSNHL during pregnancy. **INTRODUCTION**

Sudden sensorineural hearing loss (SSNHL) is a common otologic disease with an estimated incidence of 5-20/100 000[1]. It is defined as an acute elevation of hearing thresholds by at least 30 dB in three consecutive frequencies within three days[2]. SSNHLrarely occurs in pregnant women. A population-based study conducted in Taiwan covering data from 2000-2009 revealed an incidence of SSNHL of 2.71 per 100 000 pregnancies, which is lower than that of the general female population[3]. Controversial results were reported by the South Korean study that compared the risks of SSNHL between pregnant females and non-pregnant populations[4]. Although vasospasm, hair cell lesions, and viral infections can explain the cause of the disease, the etiology for SSNHL in pregnant women seems to have different pathogenesis. Pregnancy induces considerable changes in women’s bodies, which can bring significant challenges to cardiovascular, hormonal, and hematological systems. These variations are likely involved in the development of SSNHL; however, these theories lack solid proof. Moreover, the insufficiency of studies in this field causes a dilemma in the management of sudden deafness in pregnancy. Previous studies have established systemic steroids as first-line therapy with a recovery rate of up to 70%[5,6] for non-pregnant SSNHL. Nevertheless, this approach does not apply to pregnant patients because of the complexity of the maternal body and the latent side effects on the fetus. The aim of this study was to present our experience in treating pregnant patients with SSNHL, and evaluate the safety and the efficiency of intratympanic dexamethasone injections.

**MATERIALS AND METHODS**

***Subjects and study design***

A retrospective chart review was performed at our hospital between June 2017 and August 2019. A total of 11 pregnant patients who were diagnosed with SSNHL which was defined as an acute decline in the hearing thresholds over 30 dB in at least 3 adjacent frequencies within 72 h by pure-tone audiogram were included in this research. All patients persisted in our treatment and followed up without any other therapies. The exclusion criteria were as follows: (1) patients had diseases that could cause sensorineural hearing loss such as chronic otitis media, otosclerosis, Ménière's disease, large vestibular aqueduct syndrome, cerebrovascular conditions or autoimmune diseases; (2) patients who recently underwent otologic surgeries; and (3) patients who had a recurrent SSNHL. Patients’ medical history in detail was acquired by an otologist and an obstetrician. The obstetricians recorded the gestation period, the basic maternal conditions, the occurrence of pregnancy-related complications, and the state of the fetus in the uterus. Otologists documented the demographic data such as age, side, time from onset to clinical visit, concomitant symptoms (vertigo, tinnitus, and aural fullness) and regular ear-nose-throat or otorhinolaryngology (ENT) manifestations.

Eleven patients were categorized into two groups based on their choice of treatment. Seven patients in the treatment group received intratympanic dexamethasone injection while four patients in the control group received no medication other than bed rest and medical observations.

All the patients were fully informed of the treatment modalities and the associated risks of medication or medical observations. The study was reviewed and approved by the Shenzhen People’s Hospital Institutional Review Board. All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

***Intratympanic dexamethasone injection***

The intratympanic dexamethasone was administered to patients in the treatment group every other day for a total of four times. The procedure was performed in the endoscopy room, with patients lying down in the supine position with the affected ear turned upwards. Before the procedure, topical anesthesia was induced with lidocaine (2%) for 10 min, which was then drained, and the ear canal was cleaned. Next, an experienced otologist punctured the tympanic membrane in the anterior inferior or inferior posterior quadrants with a 27-gauge spinal needle and slowly injected 2.5 mg/0.5 mL dexamethasone under endoscopy. The patients were required to maintain the body position without swallowing for at least 30 min afterward. The affected ear was kept from contact with water until the integrity of the eardrum had been confirmed by doctors.

***Pure-tone audiometry***

Two experienced audiologists conducted pure-tone audiometry. The values from the air conduction acuity measurements of all frequencies (250, 500, 1000, 2000, 4000, and 8000 Hz) performed at the onset and one week later were determined. All the patients underwent another pure-tone audiometry after delivery to evaluate their final hearing thresholds.

***Statistical analysis***

Descriptive variables such as age, gestational weeks, and days from onset to clinical visit are expressed as means ± standard deviations. Categorical variables, such as side and concomitant symptoms, are expressed as *n* (%). The pure-tone averages (PTAs) and the mean hearing gains are expressed as mean ± SD and were compared using a non-paired *t* test. The efficiency was evaluated according to Siegel's criteria (Table 1)[7].

All statistical analyses were two-tailed; *P* value < 0.05 was considered statistically significant. All statistical analyses were completed using SPSS software (version 22.0; SPSS Inc., Chicago, IL, United States).

**RESULTS**

A total of 11 patients who met the inclusion criteria were assigned to the treatment group (*n* = 7) and the control group (*n* = 4). The mean age of patients was 31.2 ± 3.8 years, and the right ear was affected in 7 (63.64%) cases. The time from onset to clinical visit was relatively short with a mean time of 1.3 ± 0.9 d. As to concomitant symptoms, two patients (18.2%) suffered from vertigo, ten (90.9%) suffered from tinnitus and six (54.5%) suffered from aural fullness. In obstetric fields, eight patients were at primipara and three patients were at multipara. All the women were within the second or third trimester, the average gestation period was 26.0 ± 6.2 wk. All the neonates were in good condition with an average Apgar score of 9.7 ± 0.5. Pregnancy-induced hypertension and diabetes mellitus were observed in one patient with the blood pressure and blood sugar within the normal range. The mean PTAs at onset were 83.1 ± 15.0 dB, and the PTAs were significantly elevated to 55.2 ± 25.7 dB (*P* = 0.006) after one week of medical attendance. The overall recovery rate according to Siegel’s criteria (CR + PR) was 45.4% (Table 2).

The PTAs at onset between the two groups were similar (82.5 ± 12.9 dB, 84.2 ± 20.2 dB; *P* = 0.87). Seven patients in the treatment group received a total dose of 10 mg (2.5 mg × 4 times) dexamethasone via intratympanic injection, where the curative rate was 57.1%. Three out of four patients (75%) in the control group did not benefit from medical observations or had spontaneous relief postpartum (PTAs > 75 dB with mean hearing gains < 15 dB). Other than that, the treatment group had a significantly better hearing threshold (43.8 ± 15.9 dB *vs* 75.2 ± 29.4 dB; *P* = 0.04) one week later and greater improvement (38.7 ± 7.3 dB *vs* 13.3 ± 17.0 dB; *P* = 0.006) than a control group. After giving birth to healthy babies, the patients’ final PTAs were similar with the short-term improvement (T: 42.7 ± 16.0 dB *vs* 43.8 ± 15.9 dB, *P* = 0.90; C: 74.2 ± 29.3 dB *vs* 75.2 ± 29.4 dB, *P* = 0.96, respectively) (Table 3).

Two patients from the treatment group suffered from vertigo, which was the first sign of SSHNL; the symptoms disappeared as the session ended. The aural fullness improved and gradually disappeared in six patients; ten patients experienced tinnitus, and only three patients in the treatment group who had achieved complete recovery (CR) or partial recovery (PR) reported complete disappearance of the symptom after treatment; the remaining six patients had different degrees of remittance of tinnitus after delivery. In long-term follow-up, C1 and C4 were still bothered by obvious noise.

All 11 patients had standard manifestations in obstetric fields and fetal conditions in the uterus. All the deliveries were full-term, and all neonates were healthy without any obvious malformations or complications.

Regarding the side effects of intratympanic injections, three patients (42.8%) experienced obvious but tolerable temporary otalgia, while one patient (9.1%) had transient dizziness, which spontaneously resolved after repose. No one in the treatment group had perforations or otorrhea after the procedure.

**DISCUSSION**

There are several hypotheses for the etiology of SSNHL in pregnancy, all of which are based on the tremendous physiological changes occuring in the maternal body. Since the pregnancy, the production of estrogen and progesterone considerably increases in order to prepare the mother for a new life. The hormonal changes can lead to an increase in the blood volume due to water and sodium retention as well as a hypercoagulable state with activated blood coagulation and fibrinolysis system, especially in the second and third trimester. The increased interstitial fluids may cause the endolymphatic hydrops within the cochlea, which may manifest the low-frequency hearing loss mimicking Ménière's Disease[8]. The elevated risk of hypercoagulation may lead to disturbance of microcirculation in cochlear and thromboembolism in the labyrinth artery, which can evoke SSNHL[9]. On the other hand, estrogen exerts its protective and excitatory effect on the auditory system through combination with receptors located on the spiral ganglion, outer hair cells, inner hair cells, stria vascularis, and cochlea vessels. The fluctuation of estrogen level and the antagonism of progesterone during pregnancy may trigger SSNHL as well[10,11]. SSNHL is also observed in hypertensive pregnant women, which leads to debate over hypertension to be a risk factor for hearing impairment during pregnancy[12,13]. Although previous studies have demonstrated cyclic hearing alterations during menstrual cycle[14-16], the etiology of SSNHL in pregnancy still needs to be elucidated by more concrete evidence.

Eleven patients enrolled in this study suffered from moderately severe to profound unilaterally idiopathic SSNHL (mean PTAs at onset was 83.1 ± 15.0 dB). Vertigo was observed in two patients (18.2%) and tinnitus in ten patients (90.9%). In the present study, the mean time from onset to clinical visit (1.3 ± 0.9 d) was relatively short compared with SSNHL in the general population. Accordingly, we suggest prompt hospitalization, which allows the patients to receive medication as soon as possible. The early intervention has been identified as a beneficial prognostic factor for SSNHL.

It is challenging for otologists to determine the therapeutic strategy for pregnant patients with SSNHL. Although spontaneous resolution is observed among 32%-65% of non-pregnant patients with SSNHL, mostly in the first two weeks[17], the natural history of sudden deafness in pregnant women has not yet been established. The three out of four patients in our control group did not experience any improvement in hearing throughout the whole bearing period. Moreover, despite the fact that some studies have reported that hearing thresholds return to normal after delivery without any medication[18], the postpartum PTAs in all 11 patients enrolled in the current study were comparable with that after treatment (54.2 ± 25.7 dB, 55.2 ± 25.7 dB; *P* = 0.92). Consequently, medical care is necessary to save the patients’ hearing. Yet, in clinical practice, there are many cases when pregnant women and family refuse to receive treatment because of the fear of potential maternal deterioration and perinatal side effects. Our otologists and the patients’ family jointly decided to adopt medical observations without medication after the family members were fully informed of the possibility of spontaneous recovery as well as hearing disabilities in the future. Patient 2 in the control group was a 29-year-old woman at 26 wk of gestation in her second pregnancy suffering from SSNHL in the right ear who consulted our clinic three days after the onset of sudden deafness, tinnitus, and ear fullness. She was rather healthy without pregnancy-induced complications, and she had not experienced any inner ear symptoms during her last pregnancy. The audiological examinations showed a positive Rinne test, a type-A tympanogram, and a moderately severe hearing impairment with PTAs of 65.8 dB. During history taking, the patient mentioned an episode of emotional outbursts before the onset of symptoms. She was sent home for bed rest after physical examinations, and she reported a ”gradual improvement” one week later when she came back for a pure-tone audiogram with a mean hearing gain of 38.3 dB when her final PTA was 40.8 dB. Such obvious remission was not observed in other cases; thus, it remains unclear whether it was an example of successful self-healing of SSNHL.

Systemic and localized steroid treatment has been used as mainstream for SSNHL in the non-pregnant population for decades[5,17,19,20]. Yet, the oral or intravenous steroids are not recommended for pregnant patients because the prenatal exposure can cause detrimental effects in the fetus. Intratympanic dexamethasone injection is otherwise safe and efficient due to high-precision delivery to the cochlear fluids without systematic absorption, high local concentration, and long duration of medication action that regulates sodium transport and reabsorption in the inner ear [21]. Fu *et al*[22]conducted a prospective study on intratympanic dexamethasone for SSNHL in pregnancy with a curative rate (CR + PR) of 33%, and their single dosage was 4 mg at various times of injections according to the pure-tone audiogram improvements[22]. In our study, we assessed the efficiency and safety of intratympanic dexamethasone injections for the treatment of SSNHL during pregnancy, which revealed a satisfying curative rate (57.1%). The initial PTA of the treatment group was 82.5 ± 12.9 dB, and all seven patients received intratympanic injections of a total of 10 mg dexamethasone for one week. The mean hearing gain was 38.7 ± 7.3 dB, with significant intergroup differences in the control group (13.3 ± 17.0 dB, *P* = 0.006). The postpartum hearing outcomes did not differ compared to those after treatment, which suggests that the ending of hormone fluctuation would not further restore the compromised hearing. The complications related to intratympanic steroid therapy included perforation, otorrhea, otitis media, vertigo, dizziness, ear fullness, and otalgia. In our study, four of the treatment subjects (57.1%) suffered from transient minor discomfort, and none had persistent perforations. Other studies reported similar probabilities of adverse events[16,23]. Moreover, all patients gave birth to healthy neonates with normal Apgar scores, which suggested that intratympanic therapy is safe and tolerable for pregnant women. Other recommended therapies include dextran-40 and hyperbaric oxygen therapy[24]. Wang and Yang[18] administered 3.5 L of 10% dextran-40 intravenously to six pregnant patients, achieving a success rate (PTAs < 25 dB or mean hearing gains ≥ 30 dB) of 83.3%[18]. In another retrospective study by Xu *et al*[23], 30 pregnant patients with SSNHL received 10% dextran-40 intravenously at a dose of 500 mL/d for 10 days, and 16 of them received additional intratympanic dexamethasone for 3 times. The overall recovery rate (CR + PR) was 60%, and patients with combined therapy showed greater improvement and better final hearing thresholds[23]. Although none of the underlying adverse effects of dextran-40[25] (*i.e.*, acute kidney injury, pulmonary edema or coagulopathy) were documented in these researches, considering the ratio between profit and risk, it is not safe to use a plasma expander in patients who already have elevated blood volume due to pregnancy. Hyperbaric oxygen therapy usually serves as subsidiary treatment for SSNHL. Some doctors use it as the only therapy for SSNHL in pregnant patients because the safety of short-term exposure to hyperoxic atmosphere has been confirmed by literature[26]. Nevertheless, there is no strong evidence to support the efficiency of hyperbaric oxygen therapy on SSNHL in pregnancy.

Due to the low incidence of this disease, the major limitation of this research is the small sample size. The retrospective nature of the study also weakens the validity of the results. More studies are needed to fully elucidate the SSNHL in pregnancy, and more clinical trials are needed to establish evidence-based management.

SSNHL occurs in pregnant women at a very low rate; nevertheless, the special status of maternal body and susceptibility of the fetus can lead to a clinical problem in case of positive medication therapy or passive medical observations. The interview with more than 100 otologists showed that most of them hesitated to prescribe steroids of any kind but refer to dextran-40 or hyperbaric oxygen therapy to treat SSNHL in pregnant patients. Our research suggested that timely intratympanic dexamethasone injections could be served as a safe and effective therapeutic strategy, which would help preserve the auditory function of pregnant patients.

**ARTICLE HIGHLIGHTS**

***Research background***

Sudden sensorineural hearing loss (SSNHL) is a common otologic disease in clinic while it rarely happens in pregnant women. The special status of maternal body as well as the insufficiency of research in this field causes a dilemma for both otologists and obstetricians. The doctors need a concrete treatment modality to follow when facing the problem.

***Research motivation***

hearing loss during pregnancy is a rare but severe clinical problem. Our attempt to improve their hearing thresholds motivated us to carry out this study. We aimed to help mothers deliver healthy babies safely with normal hearings.

***Research objectives***

The aim of this study was to demonstrate and promote our successful experience in treating SSNHL in pregnant patients. We hope more pregnant patients with SSNHL could be treated with timely intratympanic dexamethasone injections for their audiological impairments.

***Research methods***

We performed a retrospective chart review for pregnant women who met the criteria for SSNHL. The treatment group received intratympanic dexamethasone (2.5 mg) q.o.d. four times and control group received no medication other than bed rest and medical observations. We documented their obstetric signs and pure-tone audiometry results before and after treatment and postpartum as indicators of safety and efficiency of the therapy.

***Research results***

Eleven patients who met the inclusion criteria were assigned to the treatment group (*n* = 7) and the control group (*n* = 4). The mean age of patients was 31.2 ± 3.8 years; the right ear was affected in seven (63.64%) cases. Two patients (18.2%) suffered from vertigo, 10 (90.9%) suffered from tinnitus and 6 (54.5%) suffered from aural fullness. The time from onset to clinical visit was relatively short, with a mean time of 1.3 ± 0.9 d. All the women were within the second or third trimester; the average gestation period was 26.0 ± 6.2 wk. The PTAs at onset between the two groups were similar. After one week of therapy, the treatment group had a curative rate of 57.1% and a significantly better hearing threshold and greater improvement compared to the control group (all *P* < 0.05). All patients delivered healthy full-term neonates with an average Apgar score of 9.7 ± 0.5.

***Research conclusions***

When SSNHL occurred in pregnant women, the doctors, the patients and the families were apt to sacrifice the hearings for the safety of neonates because of the lack of information and confidence for a safe and effective therapy. Unwilling to risk the babies’ well-being for uncertain hearing improvement, both doctors and patients chose to believe the spontaneous relief of symptoms or some treatments with potential detrimental effects. Based on sufficient literature review and field work, we were confident to propose that the intratympanic dexamethasone injection is a safe therapy for neonates as well as an efficient treatment in improving hearing impairments profoundly.

***Research perspectives***

Our research needs more evidence with larger samples. We are making great efforts to conduct a multicenter RCTs on SSNHL in pregnant patients in order to verify our results. We hope, by publishing this paper, our experience will help more patients to restore their hearings.

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**Footnotes**

**Institutional review board statement:** This study was approved by the Committee of our Hospital.

**Informed consent statement:** All the patients were fully informed of the treatment modalities and the associated risks of medication or medical observations. All patients signed informed consent forms before they were enrolled in research.

**Conflict-of-interest statement:** The authors declare that there is no conflict of interest.

**Data sharing statement**: No additional data are available.

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**Table 1 Siegel’s criteria[7]**

|  |  |  |
| --- | --- | --- |
| **Treatment efficiency** | **Final PTAs/dB** | **Mean hearing gains/dB** |
| CR | < 25 | / |
| PR | 25-45 | > 15 |
| SR | > 45 | ≥ 15 |
| NR | > 75 | ≤ 15 |

CR: Complete recovery; PR: Partial recovery; SR: Slight recovery; NR: No recovery.

**Table 2 Baseline clinical information of patients and the results after treatment**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Case** | **Age/yr** | **Affected side** | **Onset/d** | **Concomitant symptoms** | **Gestation wk** | **Number of pregnancy** | **Apgar scores**  | **Onset PTA/dB** | **PTA after treatment/dB** | **Postpartum PTA/dB** | **Outcome** |
| T1 | 31 | L | 1 | N | 15 | 1 | 9 | 80.8  | 35.8 | 35.8  | PR |
| T2 | 24 | L | 1 | TF | 22 | 1 | 10 | 81.7  | 32.5  | 30.8  | PR |
| T3 | 33 | L | 0 | VTF | 28 | 1 | 10 | 103.3  | 70.8  | 69.2  | SR |
| T4 | 30 | R | 0 | VT | 27 | 1 | 10 | 95.0  | 55.8  | 55.0  | SR |
| T5 | 32 | R | 2 | T | 30 | 1 | 10 | 73.3  | 43.3  | 41.7  | PR |
| T6 | 36 | R | 2 | T | 26 | 1 | 10 | 65.0  | 22.5  | 20.8  | CR |
| T7 | 35 | R | 2 | TF | 16 | 2 | 9 | 78.3  | 45.8  | 45.8  | SR |
| C1 | 35 | R | 1 | TF | 27 | 1 | 10 | 102.5 | 99.2 | 97.5  | NR |
| C2 | 29 | R | 3 | TF | 27 | 2 | 10 | 65.8  | 42.5 | 40.8  | PR |
| C3 | 32 | R | 1 | T | 33 | 3 | 9 | 67.5  | 58.3 | 58.3  | NR |
| C4 | 26 | L | 1 | TF | 35 | 1 | 10 | 100.8  | 100.8 | 100.0  | NR |

T: Treatment group; C: Control group; T: Tinnitus; V: Vertigo; F: Aural fullness.

**Table 3 Audiology data before and after therapy in treatment and control groups**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Group** | **Pre-treatment PTAs/ dB** | **Post-treatment PTAs/dB** | **Postpartum PTAs/dB** | **Mean hearing gains/dB** | **Curative rates** |
| Treatment | 82.5 ± 12.9 | 43.8 ± 15.9 | 42.7 ± 16.0 | 38.7 ± 7.3 | 57.1% |
| Control | 84.2 ± 20.2 | 75.2 ± 29.4 | 74.2 ± 29.3 | 13.3 ± 17.0 | 25.0% |
| *P* value | 0.87 | 0.04 | 0.04 | 0.006 | / |

PTAs: The pure-tone averages.