Assessment of complications due to intratympanic injections

Yu-Chuan Liu a, Fan-Hsiang Chi b, Ting-Hua Yang a, Tien-Chen Liu a,*

a Department of Otolaryngology, National Taiwan University Hospital, Taipei, Taiwan, China
b Department of Otolaryngology, National Taiwan University Hospital, Yun-Lin Branch, Yun-Lin, Taiwan, China

Received 19 August 2015; received in revised form 12 October 2015; accepted 11 November 2015
Available online 3 February 2016

Abstract  Objective: The purpose of the study is to report and to analyze the complications following intratympanic injections (ITI) of steroids. The occurrence rate of complications at different ITI sites, four quadrants of eardrum, was also compared.

Methods: A retrospective clinical review in a medical center. Each patient received ITI twice in a week for 2–3 consecutive weeks as a salvage therapy for sudden sensorineural hearing loss. Post-injection complications, especially transient dizziness and vertigo, were recorded. Patients with acute or chronic vertigo episodes in 1 month were excluded.

Results: A total of 59 patients with sudden sensorineural hearing loss and a total of 278 times of ITI were performed in 1 year. The post-injection complications included pain, tongue numbness, transient dizziness, vertigo, tinnitus, and a small persistent perforation. There was no significant difference in the occurrence of these complications between the injections sites on the 4 quadrants of the tympanic membrane. However, there was statistical significance in the post-injection vertiginous episode after IT injections to posterior-inferior quadrant (Q3) and posterior-superior quadrant (Q4) compared to anterior-superior quadrant (Q1) and anterior-inferior quadrant (Q2) ($P = 0.0113$).

* Corresponding author. Department of Otolaryngology, National Taiwan University Hospital, No. 7, Chung-Shan South Road, Taipei, Taiwan, China. Tel.: +886 2 23123456; fax: +886 2 23946674.
E-mail address: liuent@ntu.edu.tw (T.-C. Liu).

Peer review under responsibility of Chinese Medical Association.

http://dx.doi.org/10.1016/j.wjorl.2015.11.001
2095-8811/© 2015 Chinese Medical Association. Production and hosting by Elsevier B.V. on behalf of KeAi Communications Co., Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
Corticosteroids are widely used for the treatment of Ménière’s disease, sudden sensorineural hearing loss (SSNHL), autoimmune inner ear disease, and tinnitus. Oral treatment with steroid was reported to have 88% adverse effects, such as increasing requirements for insulin or oral hypoglycemic agent (OHA) in patients with diabetes mellitus (DM), increased thirst, and sleep or appetite changes. Hypoglycemic agent (OHA) in patients with diabetes mellitus (DM), increased thirst, and sleep or appetite changes.

Recently, many studies have shown the efficacy of corticosteroid use on the cochlear function in both human and animal models. Despite wide-ranging investigations, only minimal information focused on the adverse effects induced by ITI of steroid. The complications of ITI include transient dizziness, injection pain, a burning sensation, increasing tinnitus, post-injection vertigo, tongue numbness, and a small perforation of the eardrum. The most common side effect is transient dizziness, injection site pain, and a burning sensation. The character of post-injection vertigo has not been described in detail. This article will focus on the adverse effects of ITI and a characteristic description of post-injection vertigo. In order to prevent possible annoying side effects, previous articles suggested injection of the solution into the posterior-inferior quadrant, via narrow-gauge spinal needle, to fill the middle ear space. However, there is still no consensus to it.

Materials and methods

Patient selection

This retrospective clinical study was performed from January 1st, 2013 to December 25th, 2013 in a medical center. It included 59 patients with idiopathic sudden sensorineural hearing loss (ISSHL). Six out of 59 patients had severe vertigo attack along with sudden hearing loss for the initial 2 days, then vertigo subsided and followed by mild to moderate disequilibrium. All intratympanic steroid injected were used as a salvage treatment when primary treatment with oral steroid failed to improve hearing loss and tinnitus completely. The exclusion criteria are patients under active treatment for recurrent vertigo before ITI.

Conclusion: ITI injection is recommended to be applied to the Q2 since the Q1 and Q4 injections are more likely to induce the adverse effect of tongue numbness, while the Q3 and Q4 areas are more likely to induce post-injection vertigo.
Complications due to intratympanic injections

record any discomfort they suffered after leaving the clinic. We also checked the pure-tone audiometry before the course of IT injection, weekly during the course and 1 week after completion of the treatment course. Outcome improvement is defined as the difference of 5 frequencies (256 Hz, 512 Hz, 1024 Hz, 2048 Hz, and 4096 Hz). Average hearing level improved more than 10 dB after ITI.

Injection agent

The medication we chose was Rinderon Injection (Betamethasone Disodium Phosphate 5.3 mg/mL, as Betamethasone 4 mg/mL). The dosage was about 0.4–0.8 mL into the middle ear space for each injection, according to Clinical Practice Guideline.  

Measures and statistical analysis

The crew asked patients to report (immediately and 30 min after ITI) if there were any discomforts after ITI, such as vertigo, intolerable pain, tinnitus, ear fullness, burning sensation, or tongue numbness. This was repeated in the next office hour. We were also wary of eardrum perforations. We calculated the percentage of complications and also analyzed the relationship between injection sites at the tympanic membrane and complications, using Chi-squared test by SPSS 2.0.

Results

Complications after ITI

There were 59 patients (26 male, 33 female, average age 57.2 years old, left ear 29 cases, right ear 30 cases) who received ITI (278 times in total). The most common injection site was the anterior-inferior quadrant (Q2), 120 times (43.2%), followed by the posterior-inferior quadrant (Q3), the anterior-superior quadrant (Q1), and the posterior-superior quadrant (Q4). The injection times and percentages are 92 (33.1%), 35 (12.6%), and 31 (11.2%) respectively. The injection site depends on the different technique of the senior authors and the prior injection conditions such as clot or perforation. ITI was used as initial therapy for 17 (25.9%) patients, steroid ITI was used as salvage therapy for 42 (71.2%) patients. Twenty-five (42.3%) cases had hearing improvement after ITI.

Increasing tinnitus was noted 15 out of 278 times (about 5.4%) after ITI. The transient dizziness and post-injection vertigo were noted 47 times (16.9%) and 5 times (1.8%), respectively, after injection. Most patients who received ITI underwent only mildly painful sensations, about 211 times (75.9%). There was one female who suffered from severe pain after ITI and refused further ITI therapy. The patients with underlying diseases, such as diabetes mellitus (DM), peripheral neuropathy, or a history of nasopharyngeal cancer status post-irradiation therapy or chronic otitis media with eardrum thickening, reported less pain during injection. The symptom of tongue numbness was reported by 2 patients, about 0.7%. The injection sites were the Q1 and Q4, respectively. One case had a small eardrum perforation after 6 times of ITI. A previous article reported that persistent tympanic membrane perforations are rare and most of them lasting up to 6 months.  

Post-ITI vertigo cases

The acute onset transient dizziness episodes are quite frequent. They ranged from disequilibrium for several seconds to lightheadedness for a few minutes. The duration rarely lasted longer than 10 min. It does not affect the patient’s ability to walk or his behavior. It was relieved spontaneously after a few minutes of rest.

Five patients had post-injection vertigo. They did not suffer from vertigo attack until 20–30 min after ITI, especially when getting up. We realized that the duration of post-injection vertigo ranged from 40 min to 5 h, and it was accompanied by persistent horizontal nystagmus to the unafected ear. The visual suppression was positive in all five patients. Two patients had rotatory nystagmus to the left, and one patient had rotatory nystagmus to the right. The detailed data of these 5 patients are listed in Table 1. Two out of five patients recovered after ITI. Case 1 without previous medical history has a hearing improvement from an average hearing level of 85 dB–50 dB. Case 2 has a history of breast cancer, status post operation 2 years ago, now under hormone therapy. She also has hearing improvement from an average hearing level of 79 dB–7 dB. The other 3 cases did not have obvious hearing improvements.

Injection site and post ITI dizziness and vertigo

As shown in Table 2, the Q1 statistical accumulation showed 8 patients out of 35 patients, 22.9%, who experienced transient dizziness after ITI. The Q2 statistical accumulation showed 20 patients out of 120 patients, 16.7%, who experienced transient dizziness after ITI. The Q3 statistical accumulation showed 13 patients out of 92 patients, 14.1%, who experienced transient dizziness after ITI. The Q4 statistical accumulation showed 6 patients out of 31 patients, 19.4%, who experienced transient dizziness after ITI.

Although a difference in the percentage of transient dizziness rate is noted in each quadrant, it is not statistically significant and all P values >0.05.

Comparing the incidence of post-injection vertigo between the two protocols (4 times in 2 weeks vs. 6 times in 3 weeks), the 4 times group is 1.58% and the 6 times group is 1.97%. This is based on injection numbers but not patient numbers. There is no statistical difference between these two protocols.

Discussion

The possible pathophysiology of post ITI vertigo is still unknown. The etiology may be due to the caloric test response, the lidocaine agent diffused into the inner ear,
the semicircular canal dehiscence on the middle ear cavity side or the injection agent irritating the round window. The caloric response was first described by Robert Barany in 1906. It is a test of the lateral semicircular canals. Vertigo and nystagmus may be induced immediately by warm and cold media. The duration is usually within 10 min. The clinical course is different from what we observed in post-ITI vertigo, which has much longer vertiginous time with persistent nystagmus. Besides, we always ask patients to warm up the steroid agent in the palm for 5–10 min before injection. Therefore, the Caloric test response is less likely to be the major explanation of post-injection vertigo.

The lidocaine agent diffused into the inner ear is a possible explanation of post-injection vertigo, although we always try to clean the anesthetic agent completely before injection, we think that there is still possibility that the residual anesthetic agent may leak and diffuse into the inner ear. The semicircular canal dehiscence on the middle ear cavity side is rare and possible, but if such an anomaly pre-existed, the post-injection vertigo should happen every time after ITI. It seems it is also not likely to be the etiology of post-injection vertigo.

The lidocaine agent diffused into the inner ear is a possible explanation of post-injection vertigo, although we always try to clean the anesthetic agent completely before injection, we think that there is still possibility that the residual anesthetic agent may leak and diffuse into the inner ear. The semicircular canal dehiscence on the middle ear cavity side is rare and possible, but if such an anomaly pre-existed, the post-injection vertigo should happen every time after ITI. It seems it is also not likely to be the etiology of post-injection vertigo. Another possible etiology of the post-injection vertigo is the irritation of the round window by the injection agent, which makes a micro-perilymph fistula on it. But based on the anatomy and previous experience of cochlear implantation, round window is membrane is not so fragile and easily subjected to injury. Therefore, the micro-fistula is again less likely.

One limitation of the present study is its retrospective design, which may cause biased result. Also, the injection done a less favorable condition may be a confounding factor in analyzing the post injection complications. Finally, there is no plausible explanation for the post-injection prolonged vertigo in 5 patients. However, our results do suggest that injection on the posterior quadrant or under less favorable conditions may have higher incidence of vertigo. Therefore these sites should be avoided whenever possible.

**Conclusion**

The steroid IT injection performed is suggested to be applied to the anterior-inferior quadrant (Q2) since the Q1 and Q4 injections are more likely to induce the adverse effect of tongue numbness, though there was no statistical significance in our study. The injections to the Q3 and Q4 areas display statistical significance, compared to those of the Q1 and Q2 areas, with a greater possibility of causing post-injection vertigo.

**Financial disclosure**

No.

**Conflicts of interest**

Nil.

**References**

1. Itoh A, Sakata E. Treatment of vestibular disorders. *Acta Otolaryngologica*. 1991;481(Suppl.):617–623.
2. Parnes LS, Sun AH, Freeman DJ. Corticosteroid pharmacokinetics in the inner ear fluids: an animal study followed by clinical application. *Laryngoscope*. 1999;109:1–17.
3. Belhassen S, Saliba I. Pain assessment of the intratympanic injections: a prospective comparative study. *Eur Arch Otorhinolaryngol*. 2012;269:2467–2473.
4. Stachler RJ, Chandrasekhar SS, Archer SM, et al. Clinical practice guideline: sudden hearing loss. *Otolaryngol Head Neck Surg*. 2012;146:S1–S35.
5. Haynes DS, O’Malley M, Cohen S, Watford K, Labadie RF. Intratympanic dexamethasone for sudden sensorineural hearing loss after failure of systemic therapy. *Laryngoscope*. 2007;117:3–15.

---

**Table 1** Five post-injection cases.

| Number | Age | Sex | Oral steroid therapy | Lesion side ear | Quadrant | Rotation | Nystagmus direction | Duration | Vomiting | Hearing improvement |
|--------|-----|-----|----------------------|-----------------|----------|---------|-------------------|----------|---------|-------------------|
| 1      | 71  | M   | Yes                  | Right           | Q3       | No      | Left              | 2 h 37 min | No      | Yes               |
| 2      | 56  | F   | No                   | Right           | Q3       | Clockwise | Left              | 3 h      | Yes     | No                |
| 3      | 81  | M   | Yes                  | Left            | Q4       | Counterclock | Right           | 2 h 20 min | Yes     | No                |
| 4      | 54  | M   | Yes                  | Right           | Q3       | Clockwise | Left              | 5 h      | Yes     | No                |
| 5      | 31  | F   | Yes                  | Left            | Q4       | No       | Right             | 40 min    | No      | Yes               |

Q3, posterior-inferior quadrant, and Q4, posterior-superior quadrant; M, male; F, female.

**Table 2** Injection sites and incidence of post-injection dizziness or vertigo.

| Injection site (quadrant) | Transient dizzy rate | Post-injection vertigo rate |
|---------------------------|----------------------|----------------------------|
| Q1                        | 8/35 (22.9%)         | 0/35 (0%)                  |
| Q2                        | 20/120 (16.7%)       | 0/120 (0%)                 |
| Q3                        | 13/92 (14.1%)        | 3/92 (3.3%)                |
| Q4                        | 6/31 (19.4%)         | 2/31 (6.5%)                |

Q1, anterior-superior quadrant; Q2, anterior-inferior quadrant; Q3, posterior-inferior quadrant, and Q4, posterior-superior quadrant.