Intratympanic methylprednisolone acetate versus intratympanic lidocaine in the treatment of idiopathic subjective unilateral tinnitus of less than 1-year duration: a randomized, double-blind, clinical trial

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Background
Tinnitus, which can persist for many years, usually affects the quality of life. Tinnitus is challenging to manage with a variety of options including psychotherapy and pharmacological treatment. Intratympanic (IT) injections of steroids or lidocaine (LD) are two of the pharmacological treatment options used in the treatment of idiopathic tinnitus.
Objective
The aim of the study was to evaluate the efficacy and safety of IT-methylprednisolone acetate (MPA) versus IT-LD in the treatment of idiopathic subjective unilateral tinnitus of less than 1-year duration.
Participants and methods
In this randomized, double-blind, clinical study, 46 people who had been diagnosed with idiopathic subjective unilateral tinnitus were randomly divided into two groups and treated with IT-MPA acetate or IT-LD, accordingly. Improvement was evaluated in both groups 3 months after the injections and then again after 1 year. Safety was evaluated by recording the side effects of the injections.
Results
At 3 months after the injections, the mean improvement rates (using visual analog scale) were 56.5% in the MPA group and 47.8% in the LD group. After 1 year, this declined to 30.4 and 26.1%, respectively. The difference in improvement was not statistically significant. The side effects were all minor, and were primarily reported after LD injection.
Conclusion
IT injections of MPA and LD result in moderate improvement in tinnitus, but no statistically significant differences between these treatments were found.

Keywords:
intratympanic injection, lidocaine, methylprednisolone acetate, tinnitus

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Introduction

Tinnitus is defined as a perception of involuntary sounds in the ears. Its mechanism is poorly understood, and its pathophysiological features remain unclear [1]. Sounds heard can be in the form of buzzing, hissing, or ringing, or as a combined sound that can occur continuously, intermittently, or in a pulsatile fashion with distressing annoying symptoms that affect quality of life [2]. Tinnitus can persist for many years, leading to insomnia, an inability to concentrate, and depression [3]. It can be classified as either objective tinnitus, which is generated by an internal biological source, or subjective tinnitus, which remains the most common form of the condition. It has been suggested that tinnitus is related to the presence of a cochlear lesion, as a result of its observed frequency among people with hearing loss. It is thought that the development of tinnitus is triggered in the initial stage of cochlear damage; therefore, it has been postulated that it is still possible to eliminate tinnitus during this time, when the cochlear lesion is reversible [4].

Tinnitus is rather challenging to manage, and a variety of options aim to improve a patient's quality of life. These methods include psychotherapy and pharmacological treatments [antidepressants, benzodiazepines, and local intratympanic (IT) injections], as well as electronic masking devices that aim to mask the tinnitus sound. However, the success rate of these methods remains relatively low [3,5].

IT injections of steroids or lidocaine (LD) are two of the pharmacological treatment options used in the treatment of idiopathic tinnitus. IT steroid injection has frequently been used; however, its usage has been limited to being a form of salvage therapy when other forms of management have been deemed unsuccessful [6–8]. The IT route of administration is favored over the systemic route, as it provides direct access to the inner ear without systemic side effects, and also delivers a far higher concentration of steroids to the cochlear fluids. It has been found that IT-methylprednisolone acetate (MPA) has the optimal profile within the perilymph and endolymph [9]. Tinnitus duration likely plays a very important role in treatment efficacy, particularly with regard to corticosteroids. Shim and colleagues hypothesized that, during the first 3 months of tinnitus, a phase that is also known as acute tinnitus, the cochlear damage is reversible. They found that IT injection, in addition to alprazolam medication, resulted in improvement of tinnitus within 3 months [4]. However, a recent study by Araujo and colleagues revealed that IT dexamethasone is no better than placebo in the treatment of severe disabling tinnitus that has a duration of over 1 year.

IT administration of LD has been also used in the management of tinnitus. However, vertigo is a common side effect of LD injection [10,11]; in addition to shutting down cochlear function, LD also shuts down vestibular function, resulting in temporary vertigo and vomiting, which limits its use [11,12].

We also considered the fact that many patients do not necessarily present during the first 3 months following tinnitus onset. The present study examined MPA versus IT-LD in the treatment of idiopathic subjective tinnitus of less than 1-year duration, thereby covering the gap in the available literature, by focusing on tinnitus with a duration of less than 1 year but more than 3 months.

The aim of our study was to compare between the IT injection of MPA and LD in the management of unilateral tinnitus of less than 1-year duration.

Participants and methods

A total of 46 people with idiopathic subjective unilateral tinnitus were randomly recruited from Suez Canal University Hospital, Ismailia, Egypt, between January 2009 and August 2012. Exclusion criteria were tinnitus for less than 3 months, bilateral tinnitus, any abnormality in contrast-enhanced MRI, the presence of systemic disorders, such as hypertension or disturbed thyroid function, and a history of ear disorders within the last 6 months. Those who were included had normal hearing thresholds up to 25 dB. They did not receive any other form of tinnitus management during or before the study, with the exception of counseling, which was given during their initial assessment and which lasted for 20 min. The participants were randomly allocated to one of the two study groups as follows: group A comprised 23 participants who received IT-MPA (40 mg/ml) four times over 30 days, and group B consisted of 23 participants who received LD (40 mg in 1 ml of saline) four times over 30 days.

Intratympanic injection procedure

The tympanic membrane was visualized under the operating microscope with local anesthesia (eutectic mixture of local anesthetics) applied to the upper-rear quadrant of the tympanic membrane, after which 1.2 ml of either MPA or LD was injected in the middle ear. This amount is usually sufficient to completely fill the middle ear. Each participant was supine, with the head turned ~45° toward the unaffected side [4,] and was kept in this position for 15 min after the injection [9]. They were advised to avoid swallowing during that time to prevent the escape of injected substance through the Eustachian tube [13]. Neither participants nor the administrator were informed as to whether the injected substance was LD or MPA.

The syringe used for injection was prepared with its content covered and given to the administrator. However, it was easy to identify which substance had been injected, due to the vertigo that is more associated with LD and the fact that the substance could be seen under the microscope while it was injected into the middle ear. IT injections were carried out in the ear, nose, and throat clinic in the early morning, anticipating reports of vertigo after LD injections that may require follow up [12]. The injections were repeated four times at 1-week intervals.

Assessment of efficacy and safety of intratympanic injections

Participant evaluation included a detailed medical history, as well as general and otorhinolaryngologic examinations. The evaluation included pure-tone audiometry, speech audiometry, and tympanometry. IT injection efficacy was assessed using a tailored visual analog scale (VAS questionnaire) that measured five parameters: loudness of tinnitus,

annoyance, effect on work, effect on social life, and awareness of tinnitus. These parameters were scored from 0 (no symptoms) to 10 (most severe symptoms) and calculated to a total of 100%, with 20% being assigned for each one of the five. VAS assessment was carried out before treatment, and then at 3 at months and at 1 year after the last injection. Improvement in VAS score was measured by subtracting the post-treatment score from the pretreatment score. Assessment of the frequency of tinnitus was conducted using tone matching, in which the pitch of a pure tone was matched to the most prominent tinnitus pitch perceived by the participant [14]. Any side effects of the IT injections were reported during the injections and for 6 h afterward.

Statistical analysis

Data analysis was carried out using the Statistical Package for the Social Sciences software, version 18 (SPSS Inc., Chicago, Illinois, USA). Student's *t*-test was used to compare the significance of difference for quantitative variables that followed normal distribution.

Ethical considerations

The study was approved by the ethical committee of Suez Canal University Hospital. A written informed consent was obtained from all study participants.

Results

A total of 46 individuals (31 women and 15 men) with a mean age of 41.3±2.17 years participated in the study. All participants had normal hearing thresholds and normal findings in the otorhinolaryngologic examination. Group A had a mean hearing threshold of 19±3.57 dB, whereas group B had a mean hearing threshold of 20±3.09 dB. Seven (30.4%) participants in group A had low-frequency (250, 500, and 1000 Hz) tinnitus and 16 (69.6%) participants had high-frequency (2, 4, 6, and 8 kHz) tinnitus. In group B, 10 (43.5%) participants had low-frequency (250, 500, and 1000 Hz) tinnitus, and 13 (56.5%) participants had high-frequency (2, 4, 6, and 8 kHz) tinnitus.

Comparison between tinnitus character in MPA and IT-LD groups is illustrated in Table 1.

At 3 months after treatment, the overall VAS improvement scores were 56.5% for participants in group A and 47.8% for participants in group B. When VAS was assessed again after 1 year, the mean scores had declined to 30.4% in group A and 26.1% in group B. The differences between the groups were not statistically significant at 3 months or at 1 year after treatment (Table 2).

Six participants who received MPA reported minor side effects, which were primarily mild dizziness and nausea, in addition to mild otalgia. However, 21 of the 23 participants who received LD reported dizziness that lasted up to 6 h after its administration. None of these individuals required hospitalization, they were fairly cooperative, and attended for the full course of injections. There were no major side effects that would have necessitated withdrawal from the trial, for example, hearing loss, severe otalgia, or headache.

The overall improvement rates between the two groups were recorded according to VAS in the tinnitus questionnaires as 13 (56.5%) patients in group A: IT-MPA compared with 11 (47.8%) patients in group B: IT-LD (Fig. 1).

Table 1 Comparison tinnitus character in intratympanic methylprednisolone acetate and intratympanic lidocaine groups

	IT-MPA	IT-LD	*P* value
Frequency (kHz)	5.31	6.10	NS
Loudness (dB)	8.21	8.43	NS

IT-LD, intratympanic lidocaine; IT-MPA, intratympanic methylprednisolone acetate.

Table 2 Difference between intratympanic methylprednisolone acetate and intratympanic lidocaine groups at 3 months and 1 year using visual analog scale improvement scores

	IT-MPA (%)	IT-LD (%)	*P* value
3 months	56.5	47.8	NS
1 year	30.4	26.1	NS

IT-LD, intratympanic lidocaine; IT-MPA, intratympanic methylprednisolone acetate.

Figure 1

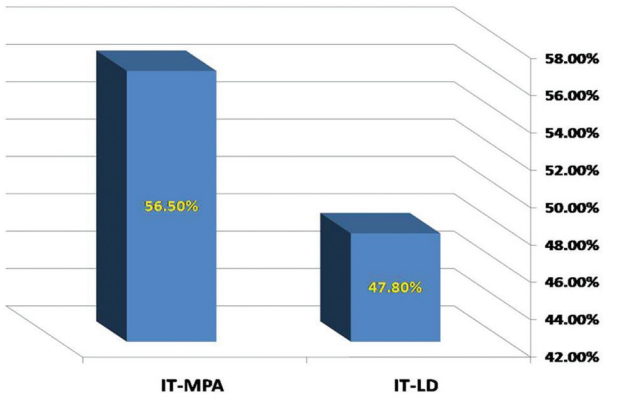

Figure (1) shows the allover improvement rates between both groups

Overall improvement rates between the two groups.

Discussion

This study assessed the efficacy and safety of IT injection of MPA versus LD in the management of subjectively reported unilateral tinnitus of less than 1-year duration. The clinical improvement observed 3 months after IT-MPA injection was 56.5%. She *et al.* [15] found that IT prednisolone or dexamethasone treatment for subjective tinnitus resulted in improvements of 48.6 and 37.5%, respectively. However, they defined improvement as a decrease in loudness of at least 5 dB after comparing tinnitus intensities obtained pretreatment and post-treatment or when persistent tinnitus became intermittent. Another study examined 54 patients who were treated with IT dexamethasone injections. Of these individuals, 34% experienced complete resolution of tinnitus, 40% experienced significant improvement, and 26% experienced no change. However, by the 6-week follow-up, complete resolution was present in only 13.5% of the study participants. At the 1-year follow-up, only two of the 54 patients studied continued to report complete resolution of symptoms [13]. Our results indicate the effectiveness of IT-MPA versus LD in people who have had tinnitus for less than 1 year. Although this result is not statistically significant, it points to the fact that improvement resulting from MPA decreases as the tinnitus moves from the acute to the chronic phase. It may also help in closing the knowledge gap between studies that focused on either acute tinnitus (<3 months in duration) and tinnitus that had already been ongoing for over 1 year [4,16].

Although the mechanism of action of IT steroids remains relatively unclear in terms of hearing-related disorders, it has been postulated that they suppress the irritability or hypersensitivity of hair cells, or abolish immune-mediated inner ear neuroepithelial dysfunction [17]. MPA remains a powerful anti-inflammatory drug, more potent than hydrocortisone and with a better inner ear fluid profile than dexamethasone. In addition, the IT approach avoids systemic side effects from steroids.

IT injection of LD showed a lower percentage of improvement compared with MPA. In group B, a 47.8% improvement was observed 3 months after the injection. LD management of tinnitus was previously attempted in the 1970s, and up to 82.8% improvement was reported [10]. The same authors reported a similar improvement rate of 81% upon treatment of cochlear tinnitus with IT-LD in 369 patients [11]. In another report, in which only nine of 52 patients completed a 5-week course of IT-LD, all nine patients showed improvement [18]. The difference between the rates of improvement after LD treatment may also be attributed to the way improvement was measured. In addition, the use of LD has been limited, due to reports of violent vertigo following its administration [12]. In our study, 21 of the 23 participants who received LD reported dizziness that lasted up to 6 h. The findings that the effects of LD injection-associated vertigo were transient warrant its possible use in treating tinnitus. However, we also observed a greater improvement rate with MPA, although there was no statistical significance versus LD. For both substances, the degree of improvement declined with time. Finally, in the present study, IT injections were not associated with any major side effects that would limit their use in the future.

Conclusion

IT injections of MPA and LD resulted in moderate improvement of unilateral tinnitus symptoms, and greater improvement was observed with MPA. The difference between the two substances was not statistically significant. LD is associated with a greater number of side effects, which limit its favorability compared with MPA. The effects of MPA decrease as tinnitus moves from the acute to the chronic phase.

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Conflicts of interest

There are no conflicts of interest.

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