https://doi.org/10.47811/bhj.87

Effectiveness of lignocaine-dexamethasone periauricular injection on treating tinnitus

Tika R. Adhikari[1], Sithar Dorjee[2], Pelden wangchuk[3], Pema Khandu[4], Sonam Jamtsho[5]

[1,3-5]*Department of Otorhinolaryngology, Jigme Dorji Wangchuk National Referral Hospital, Thimphu, Bhutan*
[2]*Khesar Gyalpo University of Medical Science of Bhutan, Thimphu, Bhutan*

ABSTRACT

Tinnitus is a highly prevalent disorder with no effective treatment. The various topical treatment used are ineffective and the benefits are mainly due to its placebo effect. A study on a series of twelve patients was carried out in a tertiary hospital in Bhutan to see the effectiveness of lignocaine-dexamethasone periauricular injection on treating tinnitus. To remove the bias in recording tinnitus by subjective response, we used a single patient as both case and control for the first time in such studies. The study found that there was no significant difference in reduction in tinnitus severity in both case and control ears even after eliminating the subjective response bias.

Keywords: Placebo; Tinnitus; Treatment.

INTRODUCTION

Tinnitus is defined as the phantom perception of sound where patient hears sound even when it is not present. It is classified as objective (somato-sounds) or subjective (true tinnitus). Objective tinnitus is produced in the body and can be heard by others whereas in subjective tinnitus there is no external sound but the patient hears it. Around 10-15% of the people have long duration of tinnitus requiring intensive medical investigations[1]. Many patients with tinnitus report symptoms such as frustration, annoyance, insomnia, anxiety, depression, irritation and concentration difficulties which are a huge burden on patients and significantly impair quality of life. Currently there is no effective approved drug in the market[2]. Although many drugs have tried in the treatment of tinnitus none of them seems to be effective[3]. The different groups of drugs that are used to treat tinnitus include antiarrhythmics (lidocaine-more commonly used as local anesthetic), anticonvulsants (carbamazepine, gabapentin), anxiolytics (diazepam), antidepressants (amitriptyline), muscle relaxants (baclofen), multivitamins, intratympanic injection of lignocaine, intratympanic injection of dexamethasone, and transdermal injections etc. Tinnitus similar to pain has a wide subjective variation to its perception in severity. So, there may be bias in responce if the case and control are different patients. This subjective response overcome if the case and control is the same subject like comparing right ear with left ear in same patient. In this study, we aimed to find the effectiveness of lignocaine-dexamethasone transdermal injection on treating tinnitus, eliminating the subjective response bias by using one ear as case and other ear as the control in the same patient. This study is first of its kind that we know of where case and control is the same patient on treatment response to tinnitus.

METHODS

The study was conducted in JDWNR hospital. This was a small pilot study conducted on twelve patients which will guide future studies to be done in a similar manner in response to treatment assessment.

Ethical clearance was obtained from Research Ethical Board of Bhutan, Ministry of Health, Bhutan vide approval letter REBH/Approval/2016/015 dated 9th May 2016.

This study was carried out to observe the effectiveness of the combination of lignocaine and dexamethasonetransdermal injection in treating tinnitus. Patients presenting with bilateral tinnitus who fit the inclusion criteria were recruited for the study. Informed written consent was obtained from the patients. The right and left ear were randomized for case and control by tossing a coin. The case ear was injected with 1 ml of 4 %lignocaine and 2 ml dexamethasone (4mg/ml) a total of 3 ml in the four quadrants of the external auditory canal and mastoid region by the ENT surgeon which is quite safe[5].The control ear was injected with 3 ml of normal saline. The patients werefollowed up on the following day and then weekly for a period of one month in the audiology unit. The patients as well as the audiologist who record the treatment response were blinded. Treatment response

Corresponding author:
Tika R. Adhikari
tikaram78@gmail.com

was assessed using validated scales like visual analogue scales (VAS), tinnitus handicap inventory (THI) and tinnitus functional index (TFI).

Inclusion criteria:

1. Patient more than 18 years and mentally sound to give consent.
2. Bilateral subjective tinnitus with no identifiable cause
3. Patient consent for transdermal route injection as a treatment method

Exclusion criteria:

1. Unilateral tinnitus
2. Objective tinnitus
3. Patient prefers other method of treatment
4. Coexistent ear diseases
5. History of allergy to lignocaine
6. Pregnant women

RESULTS

Out of 12 patients recruited, 2 patients did not follow up and another one was lost to follow up after 1st week reading. Nine patients came for follow up on day 1,8,15,22 and 29 (weekly for a month). Therefore, this data analysis was limited to 5 readings each for 9 patients (5 females and 4 males) compared with pretreatment reading. Table 1 shows the descriptive data of the nine patients that completed the study.

Table 1. Socio-demographic characteristics of patients with tinnitus at National Referral Hospital in 2016

Variable		Frequency (*n*)
Sex	Male	5
	Female	4
Occupations	Dependent	1
	Farmer	1
	Housewife	3
	Private sector	1
	Government sector	3
Age(Years)	Median	Min-Max
	50	40-78
Duration of Tinnitus (years)	Median	Min-Max
	3	1-7

Patients were from diverse occupational groups. There was no specific occupation related to tinnitus. Eight out of nine had bilateral sensorineural hearing loss ranging from mild to severe (mainly presbycusis) and only one had normal hearing. The duration of tinnitus ranged from 1-7 years with median of 3 years. Visual analogue scores (VAS) recorded pretreatment (day 1) was compared with subsequent scores on day 8,15,22,29 for case ear (0) and control ear(1) as shown in Table 2a and 2b for case and control ear respectively. It shows the minimum, 25 percentile, median, 75 percentile, maximum and mean reading of VAS score.

Table 2a. The visual analogue score reading (minimum, 25 percentile, median, 75 percentile, maximum and mean) in the treated ear (case ear), at a different point of time on a weekly basis

Time	Minimum	P25	P50 (Median)	P75	Maximum	Mean
1(Day 1)	6	6.5	8	10	10	8.12
2(Day 8)	4	6	7	8	10	6.72
3(Day15)	3	6	7	7	8	6.22
4(Day 22)	2	5	6	8	9	6
5(Day 29)	0	5	5	5	8	4.66

Table 2 b. The visual analogue score reading (minimum, 25 percentile, median, 75 percentile, maximum and mean) in the non-treated ear (control ear), at a different point of time on weekly basis

Time	Minimum	P25	P50 (Median)	P75	Maximum	Mean
1(Day 1)	4	6	8	10	10	8.12
2(Day 8)	0	4	5	6	8	6.72
3(Day15)	0	1	5.5	7	8	6.22
4(Day 22)	0	3	4	5	7	6
5(Day 29)	0	4	5	5	8	4.66

However, these raw data would not make a meaningful inference in the analysis as patients were of diverse groups and also the same ear was measured repeatedly at different point of time(weekly for a month). In such scenarios of clinical studies where different patients are repeatedly measured, an adjustment needs to be done on time and person. Thus, mixed model effect of coefficient of linear regression was used which gives the predicted value of VAS score in the treated and nontreated ear at different point of time. The trend of VAS score post treatment is the true inference which is of clinical use. For this the 2nd, 3rd, 4th and 5th reading is compared with the pretreatment reading (1st reading). As shown in Table 3 below, the mixed effect model adjusting for random effects of individual and ear as each ear has been repeatedly measured. The predicted margin of VAS scores thus obtained in case and control ear after treatment is shown in Figure 1 which gives the actual trend of decrease in tinnitus post treatment after making an adjustment for individuals and repeated measures.

Figure 1 showed that VAS score was lower in the control group compared to case group prior to the intervention which was

Table 3. The result of mixed model effect of coefficient of linear regression showing the visual analogue score for case and control ear

Variable	coefficient (95% CI)(ref(min-max)	Standard error	*p*-value	Remark
Control ear				
01	7.11(5.85-8.37)	11.07	<0.005	1st reading compared to base value
02	4.99(3.77-6.21)	8.03	<0.005	2nd reading compared to base value
03	4.55(3.28-5.82)	7.03	<0.005	3rd reading compared to base value
04	4.06(2.79-5.33)	6.28	<0.005	4th reading compared to Reference value
05	3.77(2.52-5.03)	5.89	<0.005	5th reading compared to base value
Case ear				
11	8.58(7.31-9.85)	13.23	<0.005	1st reading compared to basevalue
12	6.47(5.24-7.67)	10.39	<0.005	2nd reading compared to base value
13	6.01(4.76-7.27)	9.36	<0.005	3rd reading compared to base value
14	5.53(4.24-6.82)	8.39	<0.005	4th reading compared to base value
15	5.24(3.98-6.49)	8.19	<0.005	5th reading compared to base value

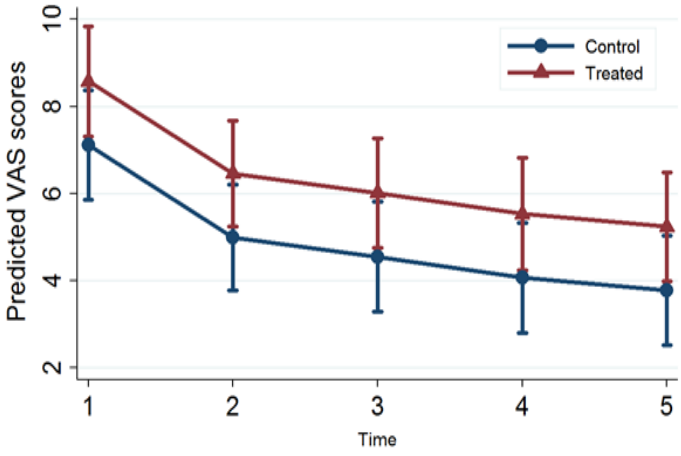

Figure 1. Predicted margins of vas scores at different time points in treated and non-treated groups

not significant statistically. After the treatment, the VAS scores for tinnitus decreased in subsequent measurements. The drop was maximum in 1st week of intervention and it plateaued after that. A similar drop in VAS score was noted for control ear.

This similar downward trend in VAS score in both case and control ear could be attributed to the following reasons. Firstly, it could be a placebo effect. Secondly, it could be a systemic effect of drugs. Although local subcutaneous injection was given in the periauricular area, systemic absorption of drug and effect on the other ear. Thirdly, it could be a feeling of psychological effect due to treatment.

Secondly, the tinnitus functional index and its subscales like intrusive, sense of control, cognitive interference, sleep disturbance, auditory, relaxation, quality of life and emotional components were also recorded. One-way analysis of variance by ranks (Kruskal-Wallis test) and chi-square tests were performed on these components. As expected there was no difference pre and post treatment as only one ear was treated. Similarly, there was also no significant difference in tinnitus handicap inventory score pre and post treatment.

This study has its own limitation. The small sample size could have a significant impact on the inference of the study. However, it is first of its kind where same patient is used as case and control and future studies may use this model to eliminate subjective bias.

DISCUSSION

The mechanism of tinnitus is poorly understood. This may be the reason why there is no standard and effective treatment for tinnitus. A wide range of systemic therapies as well as topical therapies has been in practice with conflicting results. Sakata et al (1984) showed topical treatment with intratympanic injection of lidocaine and steroid proved effective in treating tinnitus[6]. Since then many studies were done which showed different results with intratympanic treatment with steroids and lignocaine[7-17].

Savastano (2004) suggested that intradermal route of vasoactive lignocaine injection will not only improve the bioavailability and prolong the duration of action by injection in periauricular region but the distressing side effects of transtympanic injection such as sensorineural hearing loss, vertigo, vomiting, and taste disturbances can be avoided[18].

Most of the above studies did not use a control group, so it was difficult to rule out the placebo effect. To overcome this problem Aurouzo et al[19] carried out a study using 35 ears (14 control and 21 cases). However, we felt that this study has its own limitation as the case and control are different subjects and the result was analyzed based on the subjective response recorded in visual analogue scale graded 1-10.

Similar to perception of pain, the severity of perception

of tinnitus is highly variable among different individuals. This subjective response bias can be overcome by making the same patient both case and control. We used one ear of the patient as case and other ear as control so that the subjective bias on response to treatment is eliminated. This is the first study of its kind that we know of where a single patient used as both case and control (one ear case and other ear control), to assess the treatment response to tinnitus. Thus, this study eliminated the subjective response bias that was there in previous studies.

CONCLUSIONS

There was no significant difference between tinnitus VAS score in case and control group. Our study complements the above fact even after eliminating the subjective response bias by using a single patient as both case and control(right and left ear of same patient). The effect of topical treatment of tinnitus is mainly due to a placebo effect. The secondary finding of similar drop in predicted margin of VAS score post treatment suggests the systemic effect on other ear. The small sample size could have had a significant impact on the inference of the study. However, it is first of its kind where same patient used as case and control.

ACKNOWLEDGEMENTS

I would like to acknowledge the Bhutan Foundation for funding this study. I would like to thank Deki Pelzom, MoH and entire ENT department staff who contributed to conduct of this study.

REFERENCES

1. Heller AJ. Classification and epidemiology of tinnitus. Otolaryngol Clin North Am. 2003;36(2):239-48. [Full Text | DOI]
2. Langguth B, Elgoyhen AB. Current pharmacological treatments for tinnitus. Expert Opin Pharmacother. 2012;13(17):2495-509. [Full Text | DOI]
3. Espinosa-Sanchez JM, Heitzmann-Hernandez T, Lopez-Escamez JA. Pharmacotherapy for tinnitus: much ado about nothing. Rev Neurol. 2014;59(4):164-74. [PubMed]
4. Moller AR . Tinnitus and pain. Prog Brain Res. 2007;166:47-53. [PubMed | DOI]
5. Yerzingatsian KL. The dosage of dilute lignocaine for the infiltration technique of local analgesia. Ann R Coll Surg Engl. 1991;73(4):201-3. [PubMed | Full Text]
6. Sakata E, Nakazawa H, Iwashita N. Therapy of tinnitus. Tympanic cavity infusion of lidocaine and steroid solution. Auris Nasus Larynx. 1984;11(1):11-8. [PubMed | DOI]
7. Silverstein H, Choo D, Rosenberg SI, Kuhn J, Seidman M, Stein I. Intratympanic steroid treatment of inner ear disease and tinnitus (preliminary report). Ear Nose Throat J. 1996;75(8):468-71, 74, 76. [Full Text | DOI]
8. Sakata H, Kojima Y, Koyama S, Furuya N, Sakata E. Treatment of cochlear tinnitus with transtympanic infusion of 4% lidocaine into the tympanic cavity. Int Tinnitus J. 2001;7(1):46-50. [PubMed]
9. Light JP, Silverstein H. Transtympanic perfusion: indications and limitations. Curr Opin Otolaryngol Head Neck Surg. 2004;12(5):378-83. [Full Text | DOI]
10. Dodson KM, Sismanis A. Intratympanic perfusion for the treatment of tinnitus. Otolaryngol Clin North Am. 2004;37(5):991-1000. [Full Text | DOI]
11. Garduno-Anaya MA, Couthino De Toledo H, Hinojosa-Gonzalez R, Pane-Pianese C, Rios-Castaneda LC. Dexamethasone inner ear perfusion by intratympanic injection in unilateral Meniere's disease: a two-year prospective, placebo-controlled, double-blind, randomized trial. Otolaryngol Head Neck Surg. 2005;133(2):285-94. [Full Text | DOI]
12. Alles MJ, der Gaag MA, Stokroos RJ. Intratympanic steroid therapy for inner ear diseases, a review of the literature. Eur Arch Otorhinolaryngol. 2006;263(9):791-7. [Full Text | DOI]
13. Araujo MF, Oliveira CA, Bahmad FM, Jr. Intratympanic dexamethasone injections as a treatment for severe, disabling tinnitus: does it work? Arch Otolaryngol Head Neck Surg. 2005;131(2):113-7. [Full Text | DOI]
14. She W, Dai Y, Du X, Chen F, Zhang Q, Jiang P, et al. A short term study on the efficacies of intratympanic prednisolone and dexamethasone injection for subjective tinnitus. Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi. 2008;22(19):871-3, 7. [PubMed | Full Text]
15. Topak M, Sahin-Yilmaz A, Ozdoganoglu T, Yilmaz HB, Ozbay M, Kulekci M. Intratympanic methylprednisolone injections for subjective tinnitus. J Laryngol Otol. 2009;123(11):1221-5. [Full Text | DOI]
16. She W, Dai Y, Du X, Chen F, Ding X, Cui X. Treatment of subjective tinnitus: a comparative clinical study of intratympanic steroid injection vs. oral carbamazepine. Med Sci Monit. 2009;15(6):I35-9. [Full Text]
17. Meyer T. Intratympanic treatment for tinnitus: a review. Noise Health. 2013;15(63):83-90. [Full Text]
18. Savastano M. Lidocaine intradermal injection--a new approach in tinnitus therapy: preliminary report. Adv Ther. 2004;21(1):13-20. [Full Text | DOI]
19. Araújo MFS, Oliveira CA, Bahmad FM. Intratympanic Dexamethasone Injections as a Treatment for Severe, Disabling TinnitusDoes It Work? Arch Otolaryngol Head Neck Surg. 2005; 131(2):113-117. [Full Text | DOI]