

A Study of the efficacy of caroverine in the treatment of tinnitus

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Abstract

Introduction: Tinnitus is a common complaint among patients coming for auditory problems. It is a symptom which plagues the sufferer, hinders concentration, prevents sleep and haunts the mental state of the sufferer. Tinnitus prevalence rises with increasing hearing loss. Tinnitus is defined as a perception of sound in proximity to the head with the absence of an external source. It is estimated to occur in 15-20% of the world's population, with 1-3% of the cases severely affecting quality of life. **Aims and Objectives:** To Study of the Efficacy of Caroverine in the Treatment of Tinnitus. **Methodology:** The study was conducted on 60 patients of age 20-80 years and of either sex who presented with chronic tinnitus between July 2012 to July 2014, to the ENT OPD of MGM Hospital and Medical College, Aurangabad. All the patients of tinnitus were randomly divided into two groups, 1) group A caroverine and 2) group B placebo. For treatment, all patients received a single infusion of 100ml physiological saline solution. The caroverine group A (n=30), the saline solution contained 160mg caroverine (4 ampoules of 40mg caroverine each). In the placebo group B (n=30), only the physiological saline solution was given. Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean \pm SD (Min-Max) and results on categorical measurements are presented in Number (%). Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Student t test (two tailed, dependent) has been used to find the significance of study parameters on continuous scale within each group. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. McNemar test has been used to find the significance of change in each for pre and Post treatment. **Result:** THI score post treatment with caroverine showed statistically significant reduction in the immediate and 1st week post infusion period with p value = 0.002. The study showed 63.3% responded to caroverine therapy immediately after infusion. Our study looked at the effectiveness of caroverine in a selected placebo controlled group of patients. This study revealed that THI score post treatment with single infusion of caroverine had significant improvement in tinnitus severity immediately and at the first week, but no improvement in the fourth week and at 6 month follow up. **Conclusion:** Use of caroverine helps in reducing tinnitus in the immediate and first week post treatment. Caroverine is effective as a modality of treatment in suppressing tinnitus on short term basis.

Key Words: Tinnitus, Caroverine, Tinnitus Handicap Inventory (THI) score.

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INTRODUCTION

Tinnitus is a common complaint among patients coming for auditory problems. It is a symptom which plagues the sufferer, hinders concentration, prevents sleep and haunts

the mental state of the sufferer. Tinnitus prevalence rises with increasing hearing loss.¹ Tinnitus is defined as a perception of sound in proximity to the head with the absence of an external source. It is estimated to occur in 15-20% of the world's population, with 1-3% of the cases severely affecting quality of life.² It may vary in pitch and loudness and has been described by the patient as roaring, hissing, swishing, rustling or clicking type of noise. Patients may hear as a single sound or multiple sounds. It may be perceived in one ear, both ears, within the head or outside the body and the symptom may be continuous or intermittent.³ Two types of tinnitus are described. 1) Subjective, which can only be heard by the patient. 2) Objective, which can be even heard by the examiner with the use of a stethoscope. Subjective tinnitus is again sub classified into conductive, sensorineural and central. Some

of the examples are impacted wax, fluid in the middle ear, acute and chronic otitis media, abnormally patent Eustachian tube, Meniere's disease, otosclerosis, presbycusis, noise trauma, ototoxic drugs and tumors of eighth nerve. Objective tinnitus is usually caused by arteriovenous malformations, glomus tumors, palatal or tympanic myoclonus⁴. Many use the term tinnitus to designate subjective tinnitus and the term somatosound to designate objective tinnitus. Due to these different etiologies of tinnitus as well as the inability to measure the perception of tinnitus and also because of the unknown mechanism and exact physiological processes involved in tinnitus, none of the treatment modalities have demonstrated consistently good results in all patients⁵. During the second half of the 20th century, several theories for the etiology of tinnitus were proposed and treatment modalities in the form of medications and surgery were developed with varying degrees of success⁶. Even with these advances, tinnitus continues to be a debilitating condition with no definitive cure, sometimes driving the patient to suicide⁷. The problem of tinnitus in India is also an alarming and as severe as in the Western countries; but no statistics is available for Indian population⁸. There is dearth of studies in India related to tinnitus and its associated impact on the individuals. This study attempts to evaluate the efficacy of single infusion of Caroverine in the management of tinnitus. The prevalence of tinnitus has been estimated on the basis of data obtained from epidemiologic studies conducted in different countries (Brown *et al*, 1990; Office of population Census and Surveys, 1983; Sindhusake *et al.*, 2003). These studies contained at least one question about tinnitus, either written or conducted by interview, which was administered to random population samples (Davis *et al*, 2000)⁹. In spite of their limitations, these studies indicated that the prevalence of tinnitus in adults fall in the range of 10% to 15%. Hoffman *et al* (2004)¹⁰ With respect to tinnitus, its degree of severity would reflect the nature and extend of patients tinnitus related problems (Meikle *et al*, 2003)¹¹. The prevalence of tinnitus is much higher than the number of patients who seek treatment (Brown *et al*, 1990; Davis *et al*, 1995; Hinchcliffe *et al*, 1961; Leske *et al*, 1981; Office of Population Census and Surveys, 1983)^{12,13, 14, 15}, thus indicating that many individuals who experience tinnitus do not find it to be a significant or debilitating problem. The trigger for the adverse or intrusive effects of tinnitus is sometimes unrelated to the associated condition. Emotional stress, psychological factors, bereavement, unemployment, or various physical or mental illnesses can produce a repeating cycle of annoyance, mood changes, fear, anxiety, and depression- all of which are associated with tinnitus severity.

RESULT

METHODOLOGY

The study was conducted on 60 patients of age 20-80 years and of either sex who presented with chronic tinnitus between July 2012 to July 2014, to the ENT OPD of MGM Hospital and Medical College, Aurangabad. Detailed history taking and subjective assessment of the tinnitus using Tinnitus Handicap Inventory Questionnaire. Clinical examination, auditory assessment and imaging wherever appropriate. Patients were evaluated immediately, 1 week, 4 week and 6 month after infusion and were assessed with Tinnitus Handicap Inventory Questionnaire and Pure Tone Audiometry both pre and post treatment to evaluate which drug is better. Patients were randomized into study group A and control group B. All patients with tinnitus, Minimum age 20 years, Cochlear or retro cochlear pathology included into study group. Patients with psychiatric disorders, Patients with conductive hearing loss, Patients with systemic diseases such as hypertension or diabetes, Patients diagnosed with vestibular schwannoma or cerebellopontine angle tumours, Meniere's disease were excluded from the study. All the patients of tinnitus were randomly divided into two groups, 1) group acaroverine and 2) group B placebo. For treatment, all patients received a single infusion of 100ml physiological saline solution. The caroverine group A (n=30), the saline solution contained 160mg caroverine (4 ampoules of 40mg caroverine each). In the placebo group B (n=30), only the physiological saline solution was given. The rate of infusion was 2-3ml/min. The dosage of caroverine or placebo depended on the effect of tinnitus reduction and was chosen individually from patient to patient. The infusion was stopped in cases of worsening of the tinnitus. Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean \pm SD (Min-Max) and results on categorical measurements are presented in Number (%). We compare the P-Value with the level of significance. If $P < 0.05$, we reject the null hypothesis and accept the alternate hypothesis. If $P > 0.05$, we accept the null hypothesis. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Levenls test for homogeneity of variance has been performed to assess the homogeneity of variance. Student t test (two tailed, dependent) has been used to find the significance of study parameters on continuous scale within each group. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. McNemar test has been used to find the significance of change in each for pre and Post treatment.

Table 1: Comparison of Tinnitus severity using Tinnitus Handicap Inventory (THI) score pre and post treatment (immediately, 1st week, 4th week and 6 months)

		Group A(Caroverine)(n=30)	Group B (Placebo) (n=30)	Chi Square	P Value
Pre treatment	Mild	3 (10%)	3 (10%)	0.22	0.896
	Moderate	25 (83.33%)	24(80%)		
	Severe	2(6.6%)	3(10%)		
Post Treatment Immediately	Mild	12(40%)	4(13.33%)	5.12	0.042
	Moderate	16(53.33%)	21(70%)		
	Severe	2(6.67%)	3(10%)		
1st week	Mild	12(40%)	3(10%)	7.2	0.002
	Moderate	17(56.67%)	25(83.3%)		
	Severe	1(3.33%)	2(6.6%)		
4th week	Mild	8(26.67%)	4(13.33%)	2.22	0.329
	Moderate	20(66.6%)	25(83.3%)		
	Severe	2(6.6%)	1(3.3%)		
6 months	Mild	1(3.3%)	3(10%)	1.38	0.502
	Moderate	27(90%)	24(80%)		
	Severe	2(6.6%)	3(10%)		

THI score post treatment with caroverine showed statistically significant reduction in the immediate and 1st week post infusion period with p value = 0.002.

Table 2: Comparison of Mean difference of THI score pre and post treatment in the two groups at Pre-Infusion, Post infusion Immediate, 1st Week, 4th week and 6 Months

		Mean Difference	t-value	p-value
Group A (Caroverine) (n=30)	Pre Infusion Vs Post Infusion Immediate	6.80	3.34	0.002
	Pre Infusion Vs Post Infusion 1 st week	6.80	3.34	0.002
	Pre Infusion Vs Post Infusion 4 th week	5.73	3.24	0.003
	Pre Infusion Vs Post Infusion 6 month	1.73	1.89	0.068
	Pre Infusion Vs Post Infusion Immediate	1.33	1.49	0.145
Group A (Placebo) (n=30)	Pre Infusion Vs Post Infusion 1 st week	1.13	1.23	0.227
	Pre Infusion Vs Post Infusion 4 th week	0.93	1.20	0.24
	Pre Infusion Vs Post Infusion 6 month	0.20	0.47	0.639

The study showed 63.3% responded to caroverine therapy immediately after infusion. Our study looked at the effectiveness of caroverine in a selected placebo controlled group of patients. This study revealed that THI score post treatment with single infusion of caroverine had significant improvement in tinnitus severity immediately and at the first week, but no improvement in the fourth week and at 6 month follows up.

DISCUSSION

Tinnitus is a common complaint among patients coming for auditory problems. Several theories about the aetiology of tinnitus were proposed and treatment modalities in the form of medications and surgery were developed with varying degrees of success. In this study we have compared the efficacy caroverine in the management of tinnitus in a selected placebo controlled group of patients. Patients were randomized into 1 study group and 1 control group. The study group comprised of 30 patients and was administered 160 mg of caroverine single infusion. The control group

comprised of 30 patients and was given 100ml normal saline single infusion. Thus 60 patients with chronic tinnitus were evaluated and studied during this period. The two groups were matched by the distribution of age, sex and duration of tinnitus.

There was significant change in the pre and post treatment THI score (immediate and first week) with single infusion of 160mg of caroverine group with p value 0.002. The control group did not show any statistically significant change. Assessment of Management of Tinnitus: All our patients were assessed pre and post treatment with Tinnitus

Handicap Inventory Questionnaire to evaluate the efficacy of the drug. The THI Questionnaire was selected because it is a brief and easy-to-administer questionnaire that is suitable for use in busy clinical settings. The THI is a 25-item self-administered Questionnaire that aims to quantify the impact of tinnitus on daily life. It consists of three subscales: a functional subscale (THI-Functional) (12 items), an emotional subscale (THI-Emotional) (8 items) and a catastrophic subscale (THI- Catastrophic) (5 items). Respondents were asked to answer the question with Yes (4 points), Sometimes (2 points) or No (0 points). Tinnitus severity can be categorized based on the total THI score, into no handicap (0-16), mild handicap (18-36), moderate handicap (38-56) and severe handicap (58-100).¹⁶ There is paucity of literature on the use of caroverine in the management of tinnitus. However there was one study in Austria (1997) Klaus Ehrenberger *et al*¹⁷ which looked into the effectiveness of caroverine in the management of tinnitus. This was a prospective randomized clinical study on 60 patients with tinnitus. 30 were treated with caroverine and 30 patients with placebo. The response was evaluated as a reduction in tinnitus in both subjective rating and psychoacoustic measurement (tinnitus matching). The study showed 63.3% responded to caroverine therapy immediately after infusion. Our study looked at the effectiveness of caroverine in a selected placebo controlled group of patients. This study revealed that THI score post treatment with single infusion of caroverine had significant improvement in tinnitus severity immediately and at the first week, but no improvement in the fourth week and at 6 month follows up. caroverine appears to be clinically practical, promising a reduction in tinnitus on short term basis than on long term basis. However further studies involving larger group population in double blind study have to be taken for determining the definitive effect of caroverine in the management of tinnitus.

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