



## EFFECTIVENESS OF CAROVERINE VERSUS GINKGO BILOBA IN TREATMENT OF TINNITUS: PLACEBO CONTROL TRIAL

Y Prabhakara Rao<sup>1\*</sup> and Vamshi Krishna Biroj<sup>2</sup>

<sup>1</sup>Professor, Department of ENT, Malla Reddy Medical College for Women, Hyderabad- 500 055, Telangana, India.

<sup>2</sup>Assistant Professor, Department of ENT, Malla Reddy Institute of Medical Sciences, Hyderabad- 500 055, Telangana, India.

### ABSTRACT

We undertook this study to evaluate the effectiveness of Caroverine versus Ginkgo Biloba in the treatment of tinnitus. We performed a prospective randomized control study of total patients of 90 attending the outpatient department with the complaint of tinnitus. A complete detailed examination including tinnitus case history questionnaire (TCHQ) were done. Investigations were advised as required. Patients were assessed pre and post treatment by Rinne's test, Webers test and by audiometry. Observations of our study showed that the use of Ginkgo Biloba was effective for reduction of tinnitus than Caroverine. There was improvement in sensorineural hearing loss in patients with tinnitus in Caroverine group.

**Key words:** Tinnitus, Caroverine, Ginkgo Biloba, TCHQ.

### INTRODUCTION

Tinnitus defined as “ringing sensation in ear” is common condition in about 10% of population and considered a major problem in about 0.5% [1]. There are no effective pharmacological treatments for tinnitus as it is considered to have a number of underlying causes. It is unlikely that a single treatment will be effective for all the patients. All the clinical trials have produced inconsistent and ambiguous results [2].

### MATERIALS AND METHODS

A prospective randomised control study was conducted on out patients visiting at Malla Reddy hospital and NH- Malla Reddy hospital between January 2013 and September 2014. All procedures were approved by local ethical committee.

### Data Collection

Patients were randomized into two study groups and a control group. Group1 included 30 patients who were administered single dose of Caroverine injection followed

by Caroverine capsules twice a day for six months. Group 2 also had 30 patients who were administered with Ginkgo Biloba once a day for six months. B-Complex was administered for the Control group of 30 for six months.

### Exclusion criteria

- Age less than 18 years
- Recent onset of tinnitus (ex- immediate exposure to loud noise)
- Previous treatment for tinnitus
- Vascular tinnitus
- Any middle ear/inner ear disorder
- Any systemic disease that can be cause for tinnitus
- (HTN/DM)
- Patients on Anticoagulation drug therapy

### Statistical Analysis

Descriptive and inferential statistical analysis has been carried out using SPSS version 9.0 for windows.

---

Corresponding Author: - Y Prabhakara Rao Email:- mailyp@gmail.com

---

**OBSERVATIONS AND RESULTS**

All the 3 groups were matched by age, sex and duration of tinnitus. Our study had maximum age between 50-60 years. Group1 had 14 male, 16 female. Group2 had 16 male 14 female. Control group had 18 male and 12 female. Control group had 18 male and 12 female.

In this study duration of tinnitus ranged from 8 months to 2 years.

Rinne’s test , Weber’s test along with pure tone audiometric assessment were done to differentiate patients

between SNHL and CHL. Group1 had 63.3%of SHNL. Group2 had 46.7% of SNHL (Table 1). Control group had 53.3% of SNHL. Statistical improvement in hearing was present in Caroverine group. Tinnitus was scored as No Handicap (0-16) ; Mild Handicap (18-36); Moderate Handicap (38-56); Severe Handicap (58-100) according to TCHQ score. There was significant improvement in pre and post treatment TCHQ score in Group2 with a p-value <0.001. Group1 and control group did not show any significant changes (Table 2).

**Table 1. Pre-treatment and Post-treatment TCHQ score**

TCHQ score	Pre treatment	Post treatment
<b>Caroverine (n=30)</b>		
Mild	9(30%)	13(43%)
Moderate	16(53%)	14(46%)
Severe	5(17%)	3(10%)
<b>Ginkgo Biloba (n=30)</b>		
Mild	2(7%)	21(70%)
Moderate	27(73%)	9(30%)
Severe	6(20%)	0(0%)
<b>Control group (n=30)</b>		
Mild	11(37%)	12(40%)
Moderate	16(53%)	15(50%)
Severe	3 (10%)	3(10%)

Pure tone audiometry showed statistically significant improvement in hearing in those patients treated with Ginkobiloba with a p-value 0.007.

**Table 2. Pure Tone Audiometric Findings Pre-treatment and Post-treatment.**

PTA	Caroverine	Ginkgo Biloba	Control Group	p-Value
<b>Right</b>				
Pre treatment	40.69 ±15.37	32.39±15.01	34.33±14.61	0.087+
Post treatment	40.42±15.25	31.06±14.42	34.21±14.57	0.049
p-value	0.095+	0.007	0.458	
<b>Left</b>				
Pre treatment	36.82±13.10	31.69±13.30	32.73±13.99	0.301
Post treatment	36.59±12.94	30.78±13.54	32.19±14.10	0.227
p-value	0.176	0.007		

**DISSCUSSION**

Tinnitus is defined as sound perceived in the ear or head for which there is no acoustic source external to head. In attempt of a scientific definition McFadden [4] considered that “conscious expression of sound that originates in an involuntary manner in the head of its owner, or may appear to him to do so” this definition is widely accepted. Several theories of etio-pathology regarding tinnitus have been proposed.

They include

**Cochlear models**

- Spontaneous OAE by Penner [5]
- Discordant damage of Inner Hair cells and outer Hair Cells [6]
- Biochemical model [7]

- Role of serotonin in persistent tinnitus was proposed by Simpson and Davies [8]

**Non cochlear mechanisms-**

- Jastreboff neuro-physiological model
- Increased neuronal activity [9]
- Synchronization of spontaneous neural activity [10]

**Somatic modulation**

Medical treatment is presented as the best hope of various treatment methods available for the management of tinnitus. We have compared the clinical efficacy of Caroverine with Ginkgo Biloba in management of tinnitus. In our study a total of ninety patients grouped randomly

into three groups including a control group. First group were administered Caroverine injection single dose, followed by capsule twice daily for six months. Second group were administered Ginkgo Biloba twice daily for six months. The control group had B-Complex tablet once a day for six months. All the patients were followed up for six months. Caroverine a quinoxaline derivative used as a spasmolytic and *otoneuroprotective*. It acts as an N-type calcium channel blocker, competitive AMPA receptor antagonist, and non-competitive NMDA receptor antagonist [12]. It also has potent antioxidant effects. In this study Caroverine group 63.3% responded immediately to infusion typically disappearing in less than 4 hours.

The highly purified and concentrated mono extract obtained from dried leaves of Ginkgo Biloba plant extract is manufactured according to a patented standardized pharmaceutical process is made available in market. The

underlying principle behind the therapeutic action of the Ginkgo leaf extract on chronic ailments (such as neurodegenerative diseases, cardiovascular diseases and cancer) has focused on its antioxidant properties. The 2 proposed mechanisms of action are

- (1) Directly scavenging free radicals
- (2) Indirectly inhibiting formation of free radicals.

The available literature shows that there is evidence of successful treatment of tinnitus with Ginkgo Biloba extract; of note all the trials using TCHQ consistently demonstrate its superiority over placebo. In this study we found the statistical improvement in tinnitus in those treated with Ginkgo Biloba ( $p=0.007$ ).

We conclude that Ginkgo Biloba is a better drug when compared with Caroverine in long term treatment while Caroverine has a better response immediately after administration than later.

## REFERENCES

1. Tyler RS Paris A, Rafele E A. Epidemiology of tinnitus, tinnitus handbook, San Diego, CA, Singular press, 2000.
2. Ernst E and C Stevinson. Ginkgo Biloba for tinnitus a review. *Clinical Otol and allied sciences*, 24(3), 1999, 164-167.
3. Coles RR. Epidemiology of tinnitus. *J Laryngol Otol*, 1948-49, 7-15,
4. MC Fadden D. Tinnitus, facts, theories and treatment, Report of working group committee on hearing bioacoustics and biomechanics, NRC, Washington DC, National academy press, 1982.
5. Penner MJ. Spontaneous OAE and tinnitus, In, Tyler RS (ed) Tinnitus Handbook. San Diego, CA, Arch *Otolaryngol Head and Neck*, 115, 1990, 871-5.
6. Jastreboff PJ. Phantom auditory perception, mechanisms of generation and perception. *Neuro science RES*, 8, 1990, 221-54.
7. Sahey TL, Nodar Rh. A biochemical model for peripheral tinnitus. *Heart Res*, 152, 2001, 43-54.
8. Simpson J J, Davies W E. A review of evidence in support of a role for 5-HT in the perception of tinnitus. *Heart Res*, 145 (1-2), 2000, 1-7
9. Evans EF, Wilson JP. Animal models of tinnitus. In Tinnitus. Ciba Found. symp85, (D. Edward and G. Lawrenson, eds.), 108-38. London. Pitman Medical, 1981.
10. Eggermont JJ. Psychological mechanisms and neural models, tinnitus handbook, San Diego, CA, Singular press, 2000, 85-121.
11. Lavine RA. Proceedings of the 6<sup>th</sup> international tinnitus seminar, London, 1999, 193-7.
12. Udilova N, Kozlov AV, Bieberschulte W, Frei K, Ehrenberger K, Nohl H. The Antioxidant Activity of Caroverine. *Biochemical Pharmacology*, 65(1), 2003, 59-65.