

## Original Research Paper

### “CLINICAL STUDY OF EFFECTS OF INJ. CAROVERINE AND GINKGO BILOBA EXTRACT IN COCHLEAR SYNAPTIC TINNITUS”

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#### ABSTRACT

##### BACKGROUND & OBJECTIVES:

Tinnitus (ringing in the ear), is the most common problem encountered in every day of otolaryngology practices. Considerable variations exist in tinnitus prevalence with gender and age. It affects patient's life-style, general health as well as emotional status. The most common variety of tinnitus, cochlear synaptic tinnitus is diagnosed with the help of various audiological tests. There is no standardized treatment till date yet Tinnitus Retraining Therapy, medical therapy in form of psychotherapy or pharmacological therapy are commonly used one. Ginkgo biloba extract suggest greater and faster relief as compared to placebo. Recently Caroverine, a spasmolytic drug, having glutamate antagonistic activity is used for Tinnitus treatment. A randomized comparative study was designed to establish effects of Caroverine and Ginkgo biloba extract in treatment of Cochlear Synaptic Tinnitus. **METHOD:** 86 diagnosed patients of cochlear synaptic Tinnitus were treated with Inj. Caroverine (group 1, n=22) and placebo (group 2, n=21), Ginkgo biloba extract ( group 3, n=22) and placebo (group 4, n=21) and followed up at 1 month ,3 months and 6 months and improvements were evaluated in terms of Tinnitus Grading and Tinnitus Matching. Statistical analysis was done using statistical software SPSS. The baseline profile and any improvement after treatment between groups were compared using paired/ANOVA test. **RESULT:** In our study 54.4% (12 out of 22.) patients responded immediately after infusion of Caroverine and remained effective at end of 1,3 and 6 months after drug infusion while 13.6% (3 out of 21) patients responded in placebo group and reverted back to pretreatment level on subsequent follow ups. In Ginkgo biloba group 31.8% (7 out of 22) patients responded at one month follow-up, while none responded in placebo group. These responders showed further improvement in Tinnitus Matching and Tinnitus Grading at 3 months but a plateau occurred at follow-up at 6 month without further improvement. Two patients were cured in group 3 (Ginkgo biloba). **CONCLUSION:** Caroverine immediately improves tinnitus grading and matching and provides immediate relief in reducing the severity of tinnitus. Ginkgo biloba extract takes longer time to improve tinnitus but it provides greater relief on long term follow-up It is finally suggested that inj. Caroverine should be given in severe cases of tinnitus to reduce its severity immediately and then patient should be put on Ginkgo biloba extract for a period of 3 months to provide sustained and long lasting relief.

**KEYWORDS** - Cochlear Synaptic Tinnitus, Tinnitus Matching, Tinnitus Grading, Caroverine, Ginkgo biloba.

## **INTRODUCTION:**

Tinnitus is defined as sound perceived for more than five minutes at a time in absence of any external acoustical or electrical stimulation of the ear and not occurring immediately after exposure to loud noise<sup>1</sup>, phantom auditory perception<sup>2</sup> or head noise<sup>3</sup>. Prevalence of Tinnitus has been estimated as high as 30% in an adult population<sup>4</sup>. Population statistics suggested that females are more affected than males. Although considerable variations exist in Tinnitus laterality with age and gender yet studies suggested that left ear has been affected more than right ears<sup>5</sup>. Tinnitus prevalence rises with increasing hearing loss with almost 75% of patients presenting with hearing loss have Tinnitus<sup>6</sup>. It affects general status life style as well as emotional status of patients' considerably<sup>7</sup>.

Various conditions e.g. excessive noise, head trauma, hypoxia, aging or metabolic disorder lead to excess of toxic glutamate release which causes spontaneous depolarization state perceived as Tinnitus. Various classifications have been established for Tinnitus e.g. subjective Vs objective, vibratory Vs Non-vibratory, conductive/ sensorineural or central Tinnitus<sup>8,9</sup>. Cochlear Synaptic Tinnitus is synonymous with signal transfer type of sensorineural tinnitus and is the most common type of tinnitus<sup>10</sup>. Tinnitus evaluation may include proper history with its onset, course, possible cause, characteristics, loudness and severity with audiological tools as PTA, Tympanometry, SISI, ABLB or BERA for its proper categorization and various imaging modalities.

Various treatment modalities have been described as Tinnitus Retraining Therapy<sup>11</sup>, surgical therapy, instrumentation like Hearing Aids<sup>12</sup>, noise generators<sup>13</sup> or pharmacological therapy with Antidepressants<sup>14</sup>, GABA

Analouges<sup>15</sup>, Ca<sup>2+</sup> - Channel Antagonists<sup>16</sup>, Antiepileptics<sup>17</sup>, Prostaglandin Analouges<sup>18</sup>, or In. Lidocaine<sup>19</sup>. Ginkgo biloba extracts were used for Tinnitus treatment and studies have shown better and faster improvement as compared to placebo<sup>20</sup>. Selective Glutamate Receptor Antagonist like Caroverine, a smooth muscle relaxant and a neuroprotective drug which blocks post synaptic glutamate receptor, was given intravenously and reported to be effective in tinnitus<sup>21</sup>.

Reviews of the evidences for the effective treatment of tinnitus suggested that no treatment can yet be considered well established and no specific therapy is found to be satisfactory in all patients. Hence an interventional study was undertaken to establish efficacy of Caroverine and Ginkgo biloba in cochlear synaptic tinnitus.

## **AIMS AND OBJECTIVE:**

This comparative clinical study aims to evaluate the effect of inj. Caroverine and Ginkgo biloba extracts in cochlear synaptic tinnitus in term of improving tinnitus grading tinnitus matching and quality of life of patient.

## **MATERIAL AND METHODS:**

### **Study design:**

Randomized placebo controlled open labeled, hospital based interventional prospective study.

### **Subjects:**

100 patients who were having cochlear synaptic tinnitus, attending outpatient department of Otorhinolaryngology were included in study. Institutional Ethical Clearance was obtained before starting of study. Out of 100 only 86 were ready to participate in the study. Informed consent

was taken from each patient for participation in study. Patients were included irrespective of age, gender, occupation, social status and ethnicity. Patients with co-existing chronic illness, immediate post-operative, pregnancy, lactating women, Meniere's disease, masticatory movement problem influencing subjective tinnitus sensation or patients not willing to give written consent after receiving due instruction were excluded from study.

The cases were registered and given one number for each case. The age, sex, religion, socio-economic status, occupation and address of patients were recorded. The symptoms of the patient's were recorded chronologically. The history of present episode or previous such episodes were recorded. The past history of systemic disorders, oto-toxic drug use was recorded. These subjects were then given/explained a questionnaire adapted from University of Denver Tinnitus Centre. After the completion of the questionnaire the Pure Tone Audiometry (PTA) was done. Other audiological tests including Acoustic Reflex Test (ART), clinching reflex, Tympanometry, Short Increment Sensitivity Index (SISI), Alternate Binaural Loudness Balance (ABLB) and Tone Decay Test (TDT) were performed. Tinnitus frequency and loudness match using narrow band sound in the contra lateral ear was performed in the same sitting. The masking of tinnitus was done in the diseased ear using narrow band noise. Cochlear synaptic tinnitus was diagnosed based on finding from different audiological examinations, which localized pathology cochlea and excluded middle ear pathology. Tinnitus Grading was done on scale 0-10 in which "0" means no tinnitus and "10" means debilitating tinnitus.

By using computer generated block randomization method participants were randomized into four groups.

**Group 1- Caroverine-** Patients were infused with a single dose of intravenously 160 mg/8ml of caroverine in 100 ml of physiological saline at the rate of 2ml per minute.

**Group 2- Caroverine- Placebo** -patients were infused with a single dose of intravenously 8ml of caroverine placebo in 100 ml of physiological saline at the rate of 2ml per minute.

**Group 3- Ginkgo Biloba-** Patients were treated with 60 mg of Ginkgo biloba extract 12 hourly for a period of 3 months.

**Group 4- Ginkgo Biloba Placebo-** Patients were treatment with 60 mg of placebo 12 hourly for a period of 3 months. Patients were treated accordingly, followed up and evaluated over a period of six months for improvement of clinical symptoms in term of tinnitus grading and quality of life.

**Statistical analysis:** Statistical analysis was done using statistical software SPSS. The baseline profile and any improvement after treatment between groups were compared using paired/AN OVA test.

## **RESULTS:**

86 patients with Cochlear Synaptic tinnitus were the subject of our study. 22 patients were in group 1 (caroverine), 21 patients in group 2 (caroverine placebo), 22 patients in group 3 (Ginkgo biloba) and 21 patients in group 4 (Ginkgo biloba placebo).

Most of the patients in our study were in fifth decade (40.69%) followed by fourth decade (22.09%).

In the present study 67.44% (n=58) of the patients were male and 32.56% (n=28) were female. So, there was a male preponderance.

Left ear tinnitus was more common (53.4%) as compared to right ear tinnitus (36.04) and only 10.4% were having bilateral tinnitus.

77.90% (67 out of 86 patients) patients had a Tinnitus Grading of 4-6 (moderate severity). (Table I) and Tinnitus Matching between 41-

60 dB in 52.32% (45 out of 86 patients) (Table II)

**Table-I Pre-Treatment Tinnitus Grading**

Tinnitus Grading	Group 1 (N = 22)		Group 2 (N = 21)		Group 3 (N = 22)		Group 4 (N = 21)		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
<b>0 - 3</b>	1	4.55%	3	14.28%	2	9.1%	1	4.76%	7	8.13%
<b>4 - 6</b>	17	77.27%	15	71.46%	18	81.8%	17	80.95%	67	77.90%
<b>7 - 10</b>	4	18.18%	7	14.28%	2	9.1%	3	14.28%	12	13.9%
<b>Total</b>	<b>22</b>	<b>100%</b>	<b>21</b>	<b>100%</b>	<b>22</b>	<b>100%</b>	<b>21</b>	<b>100%</b>	<b>86</b>	<b>100%</b>

**Table-II Pre-Treatment Tinnitus Matching**

Tinnitus matching	Group 1 (N = 22)		Group 2 (N = 21)		Group 3 (N = 22)		Group 4 (N = 21)		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
<b>0 - 20 dB</b>	1	4.54%	2	9.52%	0	0%	0	0%	3	3.48%
<b>21 - 40dB</b>	8	36.36%	6	28.57%	12	54.54%	7	31.81%	33	38.37%
<b>41 - 60 dB</b>	11	50%	12	57.14%	10	45.46%	12	57.14%	45	52.32%
<b>61 - 80 dB</b>	2	9.0%	1	7.76%	0	0%	2	4.55%	5	5.81%
<b>Total</b>	<b>22</b>	<b>100%</b>	<b>21</b>	<b>100%</b>	<b>22</b>	<b>100%</b>	<b>21</b>	<b>100%</b>	<b>86</b>	<b>100%</b>

**Table-III Post Treatment Scoring**

	Group 1		Group 2		Group 3		Group 4	
	T.G.	T.M.	T.G.	T.M.	T.G.	T.M.	T.G.	T.M.
<b>Pre-treatment score</b>	5.26	43.84	4.91	42.82	4.79	42.08	5	45.9

<b>%immediate improvement</b>	3.57 (32.12)	29.23 (33.32)	4.69 (4.49)	41.7 (2.61)	- -	- -	- -	- -
<b>At 1 month %improvement</b>	3.57 (32.12)	29.23 (33.32)	4.91 (0)	42.82 (0)	4.08 (14.8)	35.20 (16.34)	5 (0)	45.9 (0)
<b>At 3 month improvement</b>	3.57 (32.12)	31.34 (28.51)	4.91 (0)	42.82 (0)	3.90 (18.5)	34.09 (18.98)	5 (0)	45.9 (0)
<b>At 6 month %improvement</b>	3.57 (32.12)	32.69 (25.43)	4.91 (0)	42.82 (0)	3.90 (18.5)	34.09 (18.98)	5 (0)	45.9 (0)

**T.G.-Tinnitus Grading, T.M.-Tinnitus Matching**

Figures in parenthesis shows percentage improvement from baseline.

Group 1 was better than group 2 in improving Tinnitus Grading and difference was statistically significant ( $p < 0.05$ ) immediate after infusion, at 1 month, 3 month and 6 month post infusion. (Table IV and Graph I)

**Table -IV Comparison of Tinnitus Grading (Mean±sd) between Caroverine (group 1) and Caroverine Placebo (group 2)**

Tinnitus Grading	Pre-tt	immediate	1 month	3 month	6 month
	Mean ±SD				
Group 1	5.57±1.5	3.57±1.5	3.57±1.5	3.84±1.5	3.96±1.6
Group 2	4.69±1.29	4.69±1.29	4.91±1.31	4.91±1.31	4.91±1.31
P value	$p > 0.05$				

**GRAPH I comparison of tinnitus grading (mean) between caroverine (group 1) and caroverine placebo (group 2)**

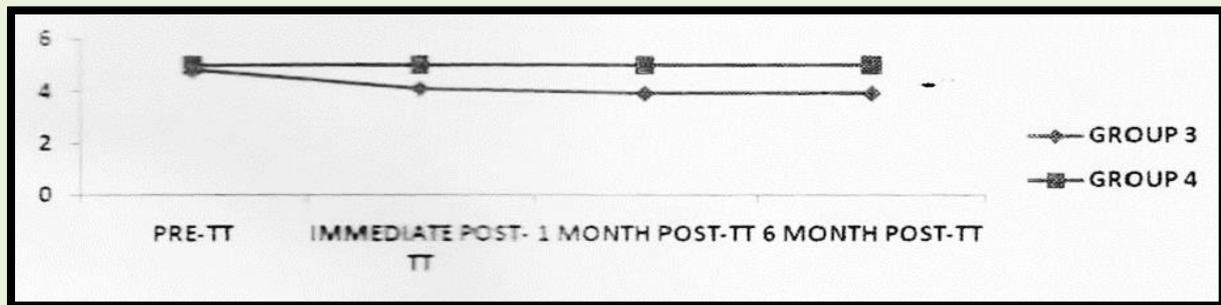


Group 3 was better than group 4 in improving tinnitus grading and it was statistically significant ( $p>0.05$ ) at 1 month, 3 month and 6 month (table V and graph II)

**Table -V Comparison of Tinnitus Grading (Mean+sd) between Ginkgo Biloba (group 3) and Ginkgo biloba Placebo (group 4)**

Tinnitus grading	Pre-TT	1 month	3 month	6 month
	Mean $\pm$ sd	Mean $\pm$ sd	Mean $\pm$ sd	Mean $\pm$ sd
Group 3	4.79 $\pm$ 2.21	4.08 $\pm$ 1.24	3.90 $\pm$ 1.44	3.90 $\pm$ 1.44
Group 4	5.0 $\pm$ 1.44	5 $\pm$ 1.44	5.0 $\pm$ 1.44	5.0 $\pm$ 1.44
P value	$p>0.05$	$p>0.05$	$p>0.05$	$p>0.05$

**GRAPH III Comparison of tinnitus Grading (Mean) between Ginkgo biloba (group3) and Ginkgo biloba Placebo (group 4)**

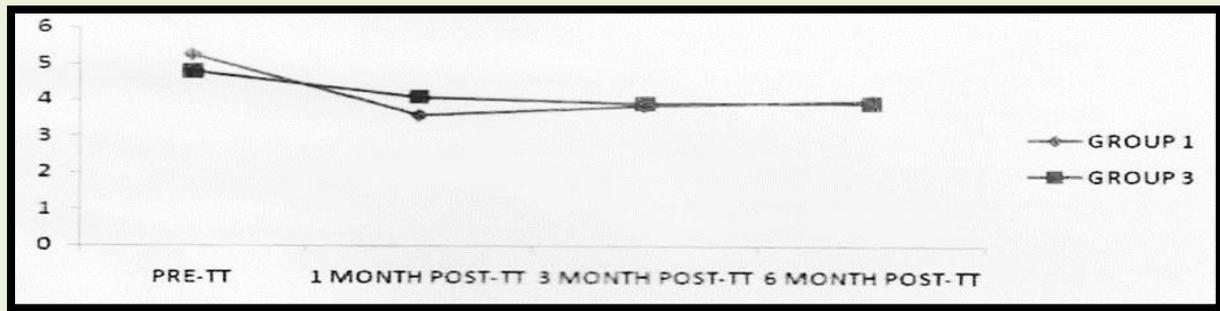


Group 1 was better than group 3 in improving Tinnitus Grading but it was statistically ( $p>0.05$ ) at 1 month and 3 month at 6 month group 3 was found to be better than group 1 but difference was statistically not significant ( $p> 0.05$ ). (Table Vi and graph III)

**Table – VI Comparison of Tinnitus Grading (Mean $\pm$ SD) between Caroverine (group 1) and Ginkgo biloba (group 3)**

Tinnitus grading	pre -TT	1 month	3 month	6 month
	mean $\pm$ SD	mean $\pm$ SD	mean $\pm$ SD	mean $\pm$ SD
GROUP 1	5.26 $\pm$ 1.21	3.57 $\pm$ 1.5	3.84 $\pm$ 1.5	3.96 $\pm$ 1.6
GROUP 2	4.79 $\pm$ 1.21	4.08 $\pm$ 1.24	3.90 $\pm$ 1.44	3.90 $\pm$ 1.44
P VALUE	$P>0.05$	$P>0.05$	$P>0.05$	$P>0.05$

**GRAPH III comparison of tinnitus grading (mean) between caroverine (group 1) and ginkgo biloba (group 3)**

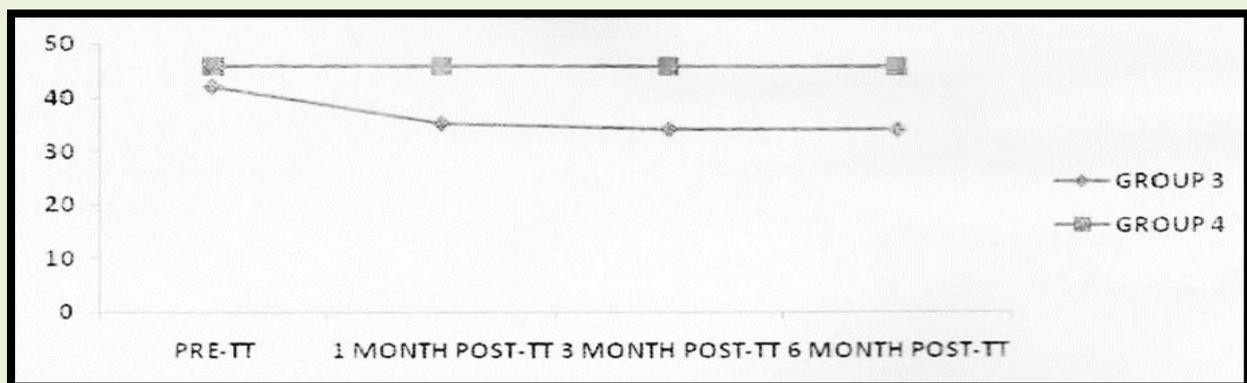


GROUP 1 was better than group 2 in improving tinnitus matching and it was statistically significant ( $p > 0.05$ ) at immediate after infusion, at 1 month, 3 month and 6 month. (Table VII and graph IV)

**Table-VII Comparison of Tinnitus Grading (Mean±SD) between Caroverine (group 1) and Caroverine Placebo (group2)**

Tinnitus grading	Pre-TT	Immediate	1 month	3 month	6 month
	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD
Group 1	43.84±14	29.23±14	29.23±14	31.34±15.39	32.69±16.32
Group 2	42.82±13	41.7±13.36	42.8±13	42.8±13	42.8±0.13
P value	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$

**GRAPH IV Comparison of Tinnitus Matching (Mean) between Caroverine (group 1) and Caroverine Placebo (group 2)**



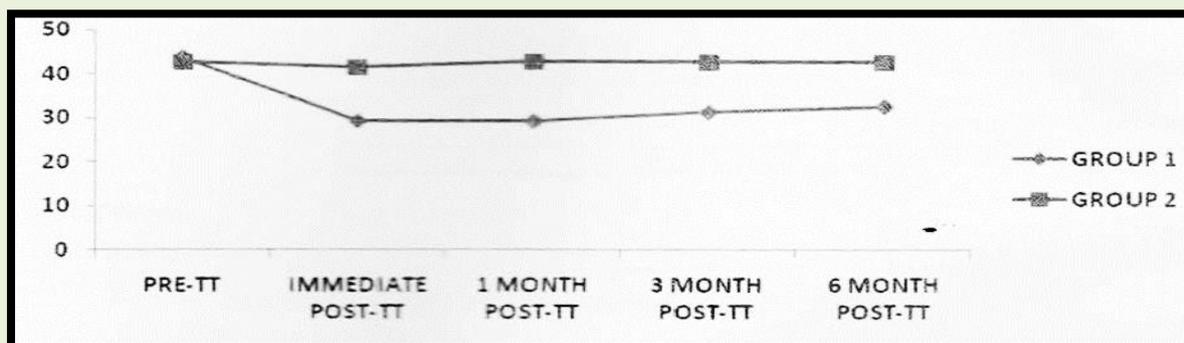
Group 3 was better than group 4 improving tinnitus matching and it was statistically significant ( $p > 0.05$ ) at 1 month, 3 month and 6 month. (Table VIII and graph)

**Table-Viii Comparison of Tinnitus Grading (Mean±SD) between Ginkgo biloba (group 3) and Ginkgo biloba Placebo (group 4)**

Tinnitus grading	Pre-TT	1 month	3 month	6 month
	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD
Group 3	42	35	35	35
Group 4	45	45	45	45

Group 1	42.08±11.69	35.2±12.7	34.09±14.27	34.09±14.27
Group 2	45.9±12.5	45.9±12.5	45.9±12.5	45.9±12.5
P value	p>0.05	p>0.05	p>0.05	p>0.05

**GRAPH V Comparison of Tinnitus Matching (Mean) between Ginkgo biloba (group3) and Ginkgo biloba Placebo (group 4)**

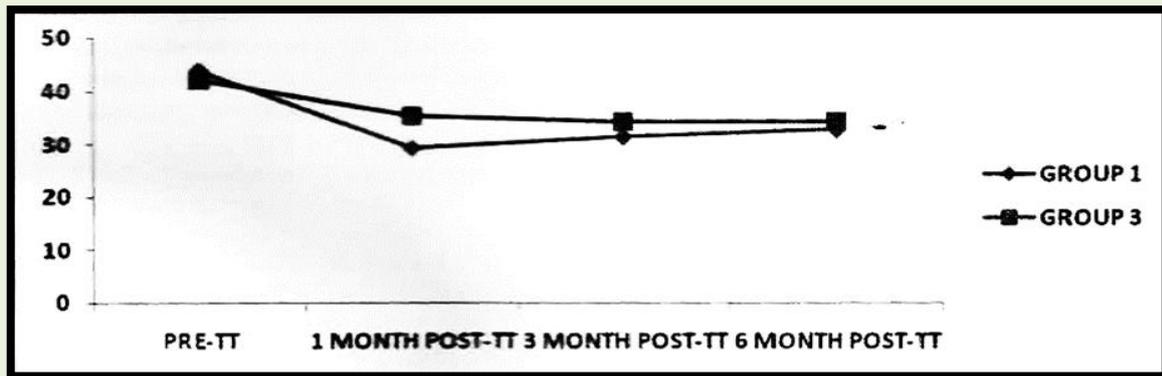


Group 1 was better than group 3 in improving Tinnitus Grading but it was statistically not significant ( $p>0.05$ ) at 1 month, 3 month and 6 month. (Table IX and Graph VI)

**Table-IX Comparison of Tinnitus Grading (Mean±SD) between Caroverine (group 1) and Ginkgo Biloba (group 3)**

Tinnitus grading	Pre tt	1 month	3 month	6 month
	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD
Group 1	43.84±14	29.23±14	31.34±15.39	32.69±16.32
Group 2	42.08±11.69	35.2±12.72	34.09±14.27	34.09±14.27
P value	p>0.05	p>0.05	p>0.05	p>0.05

**GRAPH VI Comparison of Tinnitus Matching (Mean+SD) between Caroverine (group 1) and Ginkgo biloba (group 3)**



### DISCUSSION:

Tinnitus, 'ringing in the ears,' is one of the most common problems encountered in every day otolaryngology practice. In spite of a long history of tinnitus research and a rapid increase in the understanding of the auditory system, tinnitus remains a mystery. A relatively recent shift towards recognizing that tinnitus is a phantom auditory perception and importance of various structures and systems in the brain have yielded substantial progress in the understanding and treatment of tinnitus. Many treatments have been proposed during last 30 years and the effectiveness of these treatments has increased considerably during this time.

Surgical treatment of tinnitus provided little evidence of effectiveness. Tinnitus retraining therapy has become one of the main tinnitus treatment strategies in a number of audiology departments. Noise generator & tinnitus maskers are the wearable behind-the ear or in-the-ear devices, used for presentation of sound in a controlled manner in order to reduce or eliminate the perception of tinnitus. Psychotherapy includes cognitive restructuring that is dislocation of negative emotions from the perception of tinnitus and the modification of avoidance behavior motivated by tinnitus. Antidepressant like selective serotonin reuptake inhibitor (SSRI) may also find an application for the treatment

of tinnitus in elderly in whom a down-regulation in serotonergic transmission, as a part of aging process, has been suspected.

GABA analogue like Alprazolam (benzodiazepine) has been reported to be beneficial for the treatment of tinnitus following a randomized controlled trial. Ca<sup>++</sup> channel antagonists like Flunarazine is primarily used for the treatment of migraine, but it has been demonstrated to reduce tinnitus in subset of patients with dizziness. Lidocaine is one of the most intriguing drug used in controlling tinnitus and probably the most effective one.

Many trials have been reported on the effectiveness of Ginkgo biloba<sup>20</sup>. The results suggest that the Ginkgo biloba treated group experienced greater and faster improvement in symptoms.

Caroverine, a quinoxaline derived from isoquinoline, the basic structure of papaverine, originally developed as a spasmolytic drug which may, however, exert central effects due to an unspecific calcium channel blocking action and glutamate antagonism. Experiments in guinea-pigs have shown that caroverine acted as a potent competitive alpha amino 3 hydroxyl 5 methyl -4 isoxazone proprionic acie (AMPA) receptor antagonist and, in higher dosages, a non-competitive N-Methyl d aspartate (NMDA) antagonist. Glutamate is a principal excitatory neurotransmitter in brain. In physiological

conditions glutamate releases from presynaptic vesicles of inner hair cell in response to appropriate stimulus and acts on post synaptic NMDA and AMPA receptors resulting in corresponding depolarization and impulse is conducted through the nerve. In pathological conditions when there is damage to inner hair cell membrane, excess amount of glutamate leaks through the vesicles and acts on post synaptic NMDA and AMPA receptors resulting in spontaneous depolarization state perceived as tinnitus. Due to its glutamate antagonistic activity on NMDA and AMPA receptors Caroverine reverses the spontaneous depolarization state and receptor starts responding as per the acoustic stimulus.

In our present study, 86 patients suffering from cochlear synaptic tinnitus were registered. Most of the patients were in fifth decade of life (40.69%) followed by fourth decade of life (22.09%) and age range of patients was from 18 years to 60 years The relatively lower percentage of elderly people in this study i.e. 20.93% in sixth decade of life as compared to 40.69% of fifth decade in life was not due to lower prevalence of tinnitus in elderly, but due to lower turnover of elderly patients to health-care facilities to seek help due to underlying socioeconomic conditions in this part of world. Our data correlated well with the study of Coles et al (1990)<sup>16</sup> who found that prevalence of tinnitus was a positive function of age: 38% of patients were less than 40 years of age and 62% of patients were more than 40 years of age.

In present study male to female ratio was 2.07:1 showing male preponderance. This difference might be because in Indian population males are more exposed to sound pollution in their work place or other factors which may cause tinnitus. Secondly most of the females in India are house wives and are dependent on their father, husband or

children to look after, like elderly and hence they are also often neglected. So, very few female patients reported to health-care facilities for tinnitus. However, our data does not correlate with population statistics of Cooper Jr (1994)<sup>5</sup> that suggest females (57.5%) are more affected than males (42.5%).

In the study conducted by Prof. Klaus Ehrenberg<sup>21</sup> to evaluate the efficacy of single dose infusion of caroverine in the caroverine group, 63.3% responded to therapy immediately after the infusion and the value sustained at 1, 3 and 6 month. In the placebo group, none of the patients treated showed significant response according to the defined success criteria. We conducted our study on 86 patients and also compared it with other treatment modalities i.e. Ginkgo Biloba. Patients were randomized to receive either single dose infusion of inj. Caroverine or single infusion of placebo or tab Ginkgo Biloba or Ginkgo biloba placebo.

In our study 54.4% (12 out of 22) Patients responded immediately after infusion of Caroverine and 13.6% (3 out of 21) patients responded in placebo group However, all 3 responders of placebo group reverted back to their pretreatment level at one month follow-up. All the patients who initially responded to Caroverine infusion, remained responder at 1 month follow up in the Caroverine group. At three month follow up two patients who initially responded to Caroverine reverted back to pretreatment level, so the number of responders at three month follow-up were 10 (i.e. 45.4%). At 6 month follow up, one more patient reverted back to pretreatment level and so, number of responders drop down to 9 (40.9%). One of patient in our study complained of nausea following Caroverine infusion which was amenable to intra venous ondansetron. No specific side effect was reported in

Ehrenberg's<sup>21</sup> study. However, none of the patient in Caroverine study became symptom free completely.

From our study, we found that single dose infusion of Caroverine is effective in reducing the severity of cochlear synaptic tinnitus but, it cannot abolish the tinnitus, and its effect weans off with time in 25% of responders.

Thus from our study on Caroverine it can be concluded that it may be of great use in patients who are in acute distress, to provide immediate relief. Compared to Prof Ehrenberg's<sup>21</sup> study we also found statistically significant improvement in subjective symptom (Tinnitus Grading) and psycho-acoustic measure (Tinnitus Matching) in the experimental group.

In our study 43 patients of cochlear synaptic tinnitus were randomized and treated either with 2x60mg of oral Ginkgo biloba or with placebo and patients were followed up at 1 month, 3 month and 6month time Interval tor observation of improvement in Tinnitus Matching and Tinnitus Grading In Ginkgo biloba group 31.8% (7 out of 22) patients responded at one month follow up, and none responded in placebo group. At subsequent follow up responders showed further improvement in Tinnitus Matching and Tinnitus Grading at 3 months. However, plateau occurred at subsequent follow up at 6 month with no further improvement No side effects were noted during the 6 months of follow up. Two of the patients in Ginkgo biloba group were cured after three months of treatment. Compared to study on Ginkgo biloba by Meyer, B. 1986)<sup>20</sup>, we also found statistically significant improvement ( $p < 0.05$ ) in subjective symptom (Tinnitus Grading) and psycho-acoustic measure (Tinnitus Matching) in the Experimental group. From our study on Ginkgo biloba we found that Ginkgo biloba is effective in treating cochlear synaptic tinnitus

and response increases with continuation of therapy and its effectiveness persist even after the cessation of treatment. Ginkgo biloba can also abolish the tinnitus (Table 3).

Thus Ginkgo biloba seems to be a better drug for control of cochlear synaptic tinnitus. However a further study is needed with a repeat dose of Caroverine in non-responder.

#### **CONCLUSION:**

Following conclusions were drawn from the present study:

Most of the patients suffering from cochlear synaptic tinnitus were in fifth decade (40.69%) followed by fourth decade (22.09%) while Male to female ratio was 1: 0.48.

A single dose infusion of Caroverine immediately improves tinnitus grading and matching and provides immediate relief in reducing the severity of tinnitus in 54 54% of cases.

One third of initial responders in Caroverine group reverted back to pretreatment level however rest two third of responders had sustained effect after six months of follow-up.

Ginkgo biloba is also effective in improving Tinnitus Grading and Tinnitus Matching in 31.8% of cases. There is further improvement of tinnitus grading and matching on continuation of treatment but, plateau occurred after cessation of treatment. Improvement was sustained in Ginkgo biloba group even after 3 month of cessation of treatment i.e. at 6 month follow-up Two of the patients in Ginkgo biloba group were cured after three months of treatment

Ginkgo biloba takes longer time tinnitus but it provides greater relief on long term follow-up. Due to its sustained effectiveness and without side effect, Ginkgo biloba seems to be a better drug for control of cochlear synaptic

tinnitus. It is finally suggested that inj. Caroverine 160 mg/ 8ml in 100 ml of physiological saline as intravenous infusion should be given in severe cases of tinnitus to reduce its severity immediately and then patient should be put on tab. Ginkgo biloba 60 mg twice a day for a period of 3 months to provide sustained and long lasting relief.

## REFERENCES

1. Hazell JWP. Models of Tinnitus: Generation, perception, clinical implication, In: Vernon JA, Moller AR (eds). Mechanism of Tinnitus. Needhoms Heights, MA: Allyn and Bacon, 1995; 8:221-54.
2. Jastrboff PJ Phantom auditory perception (tinnitus): Mechanism of generation and perception. Neuroscience Research. 1990; 8: 221-54
3. Fowler EP. Subjective head noises (tinnitus aurium): Genesis and differential, diagnostic significance. A few facts and several speculations. Loryngoscope.1965; 75:1610-8
4. National Centre for Health Statistics. Hearing status and ear examinations: Findings among adults. United States, 1960-1962 Vital and health statistics series, 11, no. 32,1. US Department of HEW, Washington DC. November1968.
5. Cooper Jr. Jc. Tinnitus, subjective hearing lass and well being. Health and Nutrition Examination Survey of 1971-75: port II. Journal of the American Academy of Audiology. 1994;5 37-43
6. Alberti PW Tinnitus in occupational hearing loss: Nosological aspects. Journal of Otolaryngology. 1987; 16:34-5.
7. Coles RR, Davis A, Smith O. Tinnitus. its epidemiology and management In: Jensen IN ( ed.). Proceedings of the xiv Danavox Symposium. Copenhagen: Danavox jubilee Foundation, 1990: 377-402
8. Shulman A, Goldstein B. A final common pathway for tinnitus implication for Treatment Int Tinnitus12:137-142, 1996.
9. Zenner HP, Gitter AH. Possible Roles of Hair Cell Potential and Ionic Channels Cochlear Tinnitus. In H Feldmann (ed), Proceedings of the III International Tinnitus Seminar, Karlsruhe: Harsch: 1987; 306-310.
10. Ehrenberger K, Felix D. Receptor pharmacological models for inner ear therapies with emphasis on glutamate receptors. Acta Otolaryngol 115:236-240, 1995.
11. Josttreboff PJ, Hazell JWP. A Neurophysiological approach to tinnitus clinical implications. .British Journal of Audiology.1993;27:7-17.
12. Brooks DN, Blumer D. Survey of binaural hearing aid users. Ear and Hearing. 1981;2:220-4.
13. Jasterboff PJ, Jasterboff MM. Tinnitus retaining therapy (TRT) as a method of treatment of tinnitus and hyperacsis. Journal of American Academy of Audiology.2000; 11:162-77.
14. Podoshin L, Ben-David y Fradis M, Malatesky S ,Hafner H. Idiopathec subjective tinnitus treated by aminotryptiline

hydrochloride/biofeedback,  
International

TinnitusJournal.1995;1:54-60.

15. Jhonson RM, Brummett R, Scleuning A. Use of Alprazolam for relive of tinnitus. Double -blind study .Archives of Otolaryngology, Head and Neck Surgery. 1993;119:842-5.
16. Davis E, Knox E, Donaldson I. The usefulness of nimodipine, an L-calcium channel antagonist in treatment of tinnitus. British Journal of Audiology.1994;28:125-9.
17. Murai K, Tyler RS, Harker LA, Sttoufer JL, Review of pharmacological treatment of tinnitus. American Journal of Otology.1992;13:454-64.
18. Yilmaz I, Akkuzu B, Cakmak A, Ozuloglu LN. Misoprostol in treatment of tinnitus: A double blind study.

Otolaryngology and Head and Neck Surgery.2004; 130:604-10.

19. Martin FW, Colman BH. Tinnitus :A double- blind crossover controlied trial to evaluate the use of lignocaine. Clinical Otolaryngology.1980;5:3-11.
20. Mayer B. 1986 Etude multicentrique randomissee a double insuface Gu placebo du traitementdes acouphenesparl' extraitde Ginkgo biloba. La Presse Medicare, 15,1562 1564.

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