"EFFECT OF GINGKO BILOBA VERSUS CAROVERINE IN THE TREATMENT OF TINNITUS- A ONE YEAR RANDOMIZED CONTROL STUDY''

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With reference to the above, we wish to inform you that your proposed research project titled **"EFFECT OF GINGKO BILOBA VERSUS CAROVERINE IN THE TREATMENT OF COCHLEAR TINNITUS – A ONE YEAR RANDOMIZED CONTROL STUDY",** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

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LIST OF ABBREVIATIONS

OHC	-	Outer hair cell
IHC	-	Inner hair cell
BM	-	Basilar membrane
ROS	-	Reactive oxygen species
SNHL	-	Sensory neural hearing loss
CCB	-	Calcium channel blocker
TCA	-	Tricyclic antidepressants

ABSTRACT

"EFFECT OF GINGKO BILOBA VERSUS CAROVERINE IN THE TREATMENT OF TINNITUS"- A ONE YEAR RANDOMIZED CONTROL STUDY

Introduction:

Chronic tinnitus is a prevalent condition that causes distress to at least 10-15% of the adult population which directly affects the quality of life and is commonly associated with anxiety and depression. Gingko biloba, a well-known herbal medicine exhibits anti-inflammatory, anti-oxidant, and free radical scavenging, cerebral glucose consumption, platelet aggregation inhibition, neurotransmitter modulation, and vasomotor activity. It enhances microcirculatory flow, which in turn increases blood fluidity. Caroverine is a glutamate receptor antagonist and also reduces the excitability of the nerve cell function.it is postulated that caroverine blocks both NMDA and AMPA induced firing.

Objective:

To study the effect of caroverine versus gingko biloba in the treatment of tinnitus patients.

Methodology:

A total of 80 carefully chosen tinnitus sufferers were involved in the trial, and they were randomly split into two groups, one receiving Gingko biloba 120 mg, and the other receiving caroverine 60 mg. Three months of follow-up were given to both groups. Advancement in subjective symptoms (tinnitus functional index) and an

objective assessment were used to assess treatment effects (tinnitus pitch matching and loudness).

Result:

Both groups showed improvement in tinnitus function index scores, tinnitus pitch matching and loudness at the end of 3 months.

Conclusion:

Caroverine has been proven to be a successful treatment for tinnitus and is widely accessible, affordable, and free of side effects.

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INTRODUCTION

Tinnitus is the perception of sound in the absence of any external acoustical or electrical stimulation of the ear.[1] Tinnitus lasting longer than 3 months is considered as chronic tinnitus. Tinnitus frequently presents as ringing, although the disorder can also sound like buzzing, hissing, whistling, roaring, or other combinations of these sounds.[2]

The traditional view that tinnitus is a degenerative disorder of the cochlea caused by damaged hair cells has led to a philosophy that nothing much can be done to alter it, and patients can only be helped to cope with the situation or learn to live with it. Although our knowledge of auditory processing by no means finished, enough is known to explain the basic mechanisms for the emergence and persistence of tinnitus, and to describe quite accurately the mechanism of distress caused by tinnitus.

Chronic tinnitus is a condition that causes distress to 10-15% of the adult population which affects the quality of life and is commonly associated with anxiety and depression. Approximately 25% of tinnitus sufferers claim that it disrupts their daily activities, One percent to three percent of people claim that it seriously reduces their quality of life.[2] Hearing loss is the greatest risk factor for developing tinnitus and risk increases with a history of high-level sound exposure earlier in life. Tinnitus being a common illness, does not have a standardized and effective treatment plan. Tinnitus can be mild or severely incapacitating in its severity. 93% of tinnitus patients said that the condition had an impact on their way of life. Some said their inability to sleep, the escalation of family issues, their withdrawal from or avoidance of friends, or the disruption of their employment were all caused by its presence. Finally, 70% of

patients claimed that having tinnitus had worsened their emotional struggles, including signs like despair, frustration, irritability, worry, insecurity, and a reduced capacity for relaxation or concentration.[3]

A loss of cochlear input to neurons in the central auditory system, such as occurs in cochlear hair cell damage or a lesion of the vestibulocochlear nerve, can result in abnormal neural activity in the auditory cortex perceived as tinnitus.[4] Damage to the cochlea can result in the death of OHCs or IHCs, impairment of OHC electromotility, disruption of synapses between IHCs and spiral ganglion neurons, damage to the stereocilia bundle, or rupture of BM. A lesion at any level in this circuit can manifest as tinnitus.

The two types of tinnitus are objective and subjective. Subjective tinnitus, which makes up the majority of instances, is the perception of sound by the patient alone in the absence of a discernible acoustic source. It can have otologic, metabolic, neurologic, cardiovascular, pharmacologic, or psychological origins. The term "objective tinnitus" describes the production of sound (somatosounds) close to the ear that is brought on by vascular, neurological, or eustachian tube dysfunction. In certain cases of objective tinnitus, the examiner may actually hear the sounds, typically as a result of turbulent flow of blood or uncontrolled spasms of the muscles in the middle ear or soft palate.[2] Hence, it is important to differentiate between objective and subjective tinnitus as their treatments differ vastly. This study deals with subjective tinnitus which still doesn’t have an effective mode of treatment.

One of the herbal remedies that is most frequently prescribed is ginkgo biloba. Gingko biloba, a herbal medicine, exhibits anti-inflammatory, anti-oxidant, free radical scavenging, cerebral glucose consumption, platelet aggregation inhibition,

neurotransmitter modulation, and vasomotor activity. Enhances microcirculatory flow, which in turn increases blood fluidity.[5]

The papaverine category includes caroverine, a quinoxaline derivative. Caroverine has both antioxidant and oto-neuroprotective properties. It works as a glutamate receptor antagonist to lessen nerve cells' excitability. Afferent nerve fibres of IHCs contain AMPA [2-amino-3-(5-methyl-3-oxo-1,2-oxazol-4-yl) propionic acid] and NMDA [N-methyl D- aspartate]. Caroverine inhibits the activation of both NMDA and AMPA receptors. It functions as a competitive AMPA receptor antagonist, a non-competitive NMDA receptor antagonist, and an N-type CCB.[6]

Studies have found caroverine to be immediately effective whereas gingko biloba is effective throughout the course of the treatment. Therefore, a comparative study will help us figure out the better mode of treatment among the two. This study has not been done in this part of the country and a standard guideline of treatment which is effective doesn’t exist, which is why undertaking this study is beneficial.

OBJECTIVE:

- To study the effect of oral caroverine versus oral gingko biloba in the treatment of tinnitus patients.

REVIEW OF LITERATURE

Tinnitus

Tinnitus is the perception of sound in the absence of an external acoustic stimulus or electrical stimulation of the ear.[1] A frequent and occasionally incapacitating medical problem is tinnitus. with a 10% to 15% adult prevalence estimate.

Approximately 25% of tinnitus sufferers claim that it disrupts their daily activities, One percent to three percent of people claim that it seriously reduces their quality of life.[2] The term tinnitus originates from the Latin word “tinnire,” which means “to ring.” Although ringing is the most common symptom of tinnitus, the illness can also sound like buzzing, roaring, whistling, hissing, or different combinations of these sounds. One or both ears may experience tinnitus, which can also be intermittent or continuous and pulsatile or non-pulsatile. There may be variations in the perceived intensity. The two types of tinnitus are objective and subjective. Subjective tinnitus, which makes up the majority of instances, is the patient's unique sense of sound in the absence of a discernible acoustic source. The term "objective tinnitus" describes the production of sound (somatosounds) close to the ear that is brought on by vascular, neurological, or eustachian tube dysfunction.[2] Even though the majority of tinnitus sufferers are only somewhat impacted, some go through serious life changes, sadness, and worry. Since suicide has been in tinnitus sufferers who also have a concomitant psychiatric condition, prompt identification and care are necessary in patients who also experience significant anxiety or depression in addition to their tinnitus.

History:

Tinnitus was described in the Egyptian papyri (6000 BC) and has clearly been with us a long time. It is true that the word tinnitus originates from the Latin word tinnire (to ring) and McFadden's description of tinnitus as 'the conscious expression of a sound that originates in an involuntary manner in the head of its owner or may appear to him to do so' is appropriate.[7] The increased incidence of tinnitus with age reflects the effects of ageing throughout the auditory system, but also worsening hearing. The Jastreboff model of tinnitus stresses the importance of the 'straining to hear' phenomenon as a cause of tinnitus with increased hearing loss.

In the 1950s, Heller and Bergman studied the descriptions of 180 subjects (80 with reportedly normal hearing and 100 with hearing impairment) who were interviewed regarding sounds that they perceived when introduced into a soundproof booth. Despite many subjects describing a 'ring', this was only one of 39 descriptions reported. In reality, the sound perceived by the patient does not have to be ringing, does not have to be a continuous sound, and in some cases can even represent complex sounds such as musical tunes.[8]

The United Kingdom Medical Research Council, Institute of Hearing, study on hearing (n = 48313) included the broadest analysis into the epidemiology of tinnitus to date. 9 According to this study's definition of persistent spontaneous tinnitus, which is defined as tinnitus that develops spontaneously and doesn't happen in response to sound stimuli and lasts for a period of 5 minutes or more at a time, the prevalence of this condition in the adult population is 10.1%. Five percent of those polled said their tinnitus was moderately to highly annoying, and one percent said it was badly impairing their the capacity to lead a typical life. Prevalence figures in Italy

were reported as 14.5% of the population,[10] in the US as 14.9%[11] and in Sweden as 15.8%.[12] An overall figure of 5.2% was reported from Egypt, rising to 17.7% in patients over 60 years of age.[13] In Japan, 18.6% of people aged over 65 described tinnitus[14] and in a similarly aged population sample in Nigeria the figure was 14.1%.[15]

Tinnitus has been an age old debilitating condition as far as we have known. The modality for treatment of tinnitus has evolved with time, yet complete relief is yet to be attained. Hence multiple studies are ongoing to attain complete relief from tinnitus, if not at least improve the quality of life for the bearers.

Anatomy:

Inner Ear

An essential organ for hearing and balance is the internal ear, often known as the labyrinth. It is made up of a bony labyrinth and a membranous labyrinth. Endolymph, a clear fluid, fills the membranous labyrinth, while perilymph fills the area between the membranous and bony labyrinths.

It is responsible for mechanoelectrical transduction, the conversion (transduction) of movements initiated by sound waves in the cochlea or by changes in the position of the head in space in the vestibular system into electrical signals that can then be passed to the brain along the auditory or vestibular nerves.

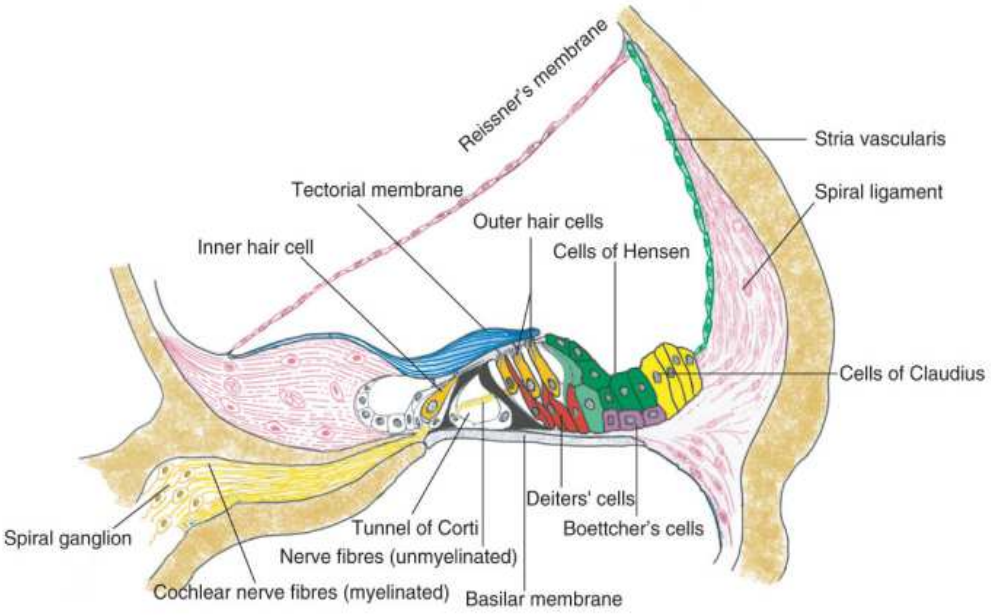


Figure 1 Cut Section Of Cochlea

A ridge of cells sitting on the BM and covered by the tectorial membrane is the mature organ of Corti. The inner and OHCs are the two different types of hair cells that make up the Corti organ (IHCs and OHCs). The IHCs are located above a slender, rigid bony protrusion from the bone that encircles the modiolus. They resemble flasks and have hair bundles that are generally straight or shallowly 'U' shaped, giving the impression that they are forming an almost continuous 'fence' along the medial or inner aspect of the organ of Corti.[16]

The cylindrical OHCs have bundles of stereocilia made of actin filaments that protrude into the scala media at their apical ends. These stereocilia move in a plane parallel to their plane of orientation as a result of BM-led tectorial membrane displacements in response to acoustic stimuli: depolarization when the movement is toward the tallest stereocilia and hyperpolarization/repolarization when the movement is towards the smallest stereocilia. The cation-selective ionic gates necessary for

transduction and the production of an action potential are opened by displacement. The stereociliary bundle is susceptible to movement by as little as 0.3 nm.[16]

The hair bundle is composed of rows of stereocilia that increase in height in one particular direction across the apical surface of the hair cell, and a single kinocilium located behind the row of longest stereocilia. Deflection of the stereocilia towards the longest ones opens MET channels, K+ enters and the hair cell becomes depolarized. Deflection in the opposite direction closes the transducer channels and the hair cell becomes hyperpolarized.[16]

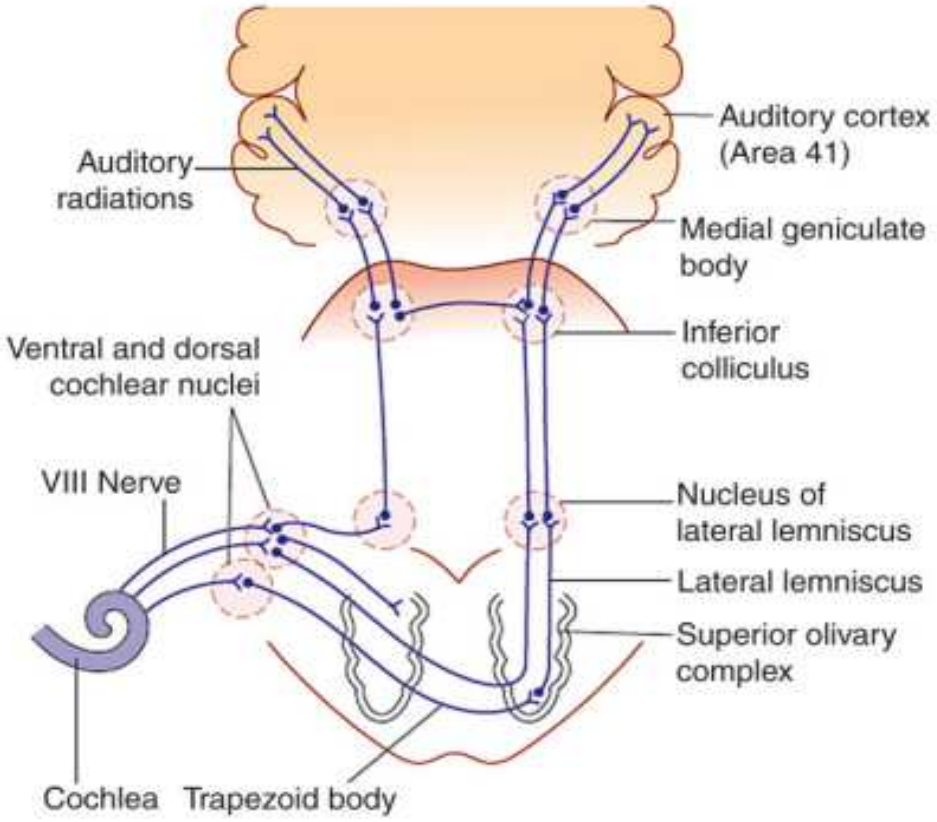


Figure 2 Auditory pathway

Two different neuronal populations give rise to the afferent ANFs that innervate the inner and OHCs. IHCs are innervated by the majority (90–95%) of myelinated type 1 neurons. OHCs are innervated by the remaining 5–10% of type 2 neurons, which are slender and unmyelinated. The spiral ganglion is a collection of both of these types of neurons' cell bodies.

Dendrites of the spiral ganglion's bipolar cells, which are located in Rosenthal's canal, innervate the hair cells (canal running along the osseous spiral lamina).

These bipolar cells' axons branch out onto the dorsal and ventral cochlear nuclei on both sides of the medulla, which are located in the cochlear division of CN VIII. Auditory circuits continue to be complex. The primary nuclei in the ascending auditory pathways from the cochlea are:

1. Superior olivary complex
2. Nucleus of lateral lemniscus.
3. The inferior colliculus
4. The medial geniculate body
5. The Auditory cortex.

The auditory fibres have many decussation locations and travel along both the ipsilateral and contralateral paths. Thus, both brain hemispheres have a representation of each ear..[16]

Any pathology that can potentially damage the auditory pathways has the potential to result in tinnitus.

Physiology:

Peripheral mechanisms

Discordant damage of cochlear hair cells

OHCs have been shown to be more susceptible than IHCs to damage by certain agents including noise and aminoglycoside antibiotics. It has been suggested that, in areas where OHCs have been damaged but IHCs remain, the tectorial membrane is no longer supported by the OHCs and can sag onto the IHCs, causing them to depolarize.[17]

Calcium channel dysfunction

Calcium is fundamental to several functions of cochlear hair cells and some drugs that are known to cause tinnitus, including salicylates and quinine, affect intracellular calcium levels. Noise also affects the concentration of intracellular calcium. It has therefore been suggested that calcium flux may be implicated in tinnitus generation.[17]

Glutamate receptors

The primary excitatory neurotransmitter within the auditory system is glutamate, and there are many glutamate receptor subgroups. The primary receptors on auditory nerve fibres beneath the IHCs are called AMPA receptors, and are in charge of the quick communication of data from cochlea to the brain. However, glutamate in large quantities is toxic to nerve fibres. This effect, which can be observed following significant noise exposure, is mediated by AMPA. Another subgroup of glutamate receptors, NMDA receptors are also present in auditory nerve

fibres though their function is still a matter of some speculation. It has been observed that pharmacological blockade of NMDA receptors can be protective against both salicylate-induced and noise-induced tinnitus in animal models. Although the evidence that glutamate receptors are directly implicated in the causation of tinnitus is at best circumstantial, they do offer a potential site for therapeutic intervention and this continues to be an active research area.[18]

Central mechanisms

Increased spontaneous firing

There is always a certain degree of electrical activity in the auditory system even when there is no sound input to the ear. Damage to the ear results in reduced activity in the auditory nerve which in turn downregulates inhibitory processes in higher auditory centres, resulting in the possibility of increased neuronal excitability in the auditory cortex, which can be heard as tinnitus.[19]

Increased central neural synchrony

Spontaneous neural activity in the auditory cortex is normally random and, when this activity becomes synchronized, this is the signal that a sound is present. If the peripheral auditory system is damaged, spontaneous cortical activity tends to become more synchronized and there is speculation that this can give rise to tinnitus.[20]

Reorganization of the cortical auditory map

The auditory system is tonotopically organized from cochlea to cortex: structures within the auditory system that deal with adjacent sound frequencies are situated beside each other. When the peripheral auditory system is damaged, one

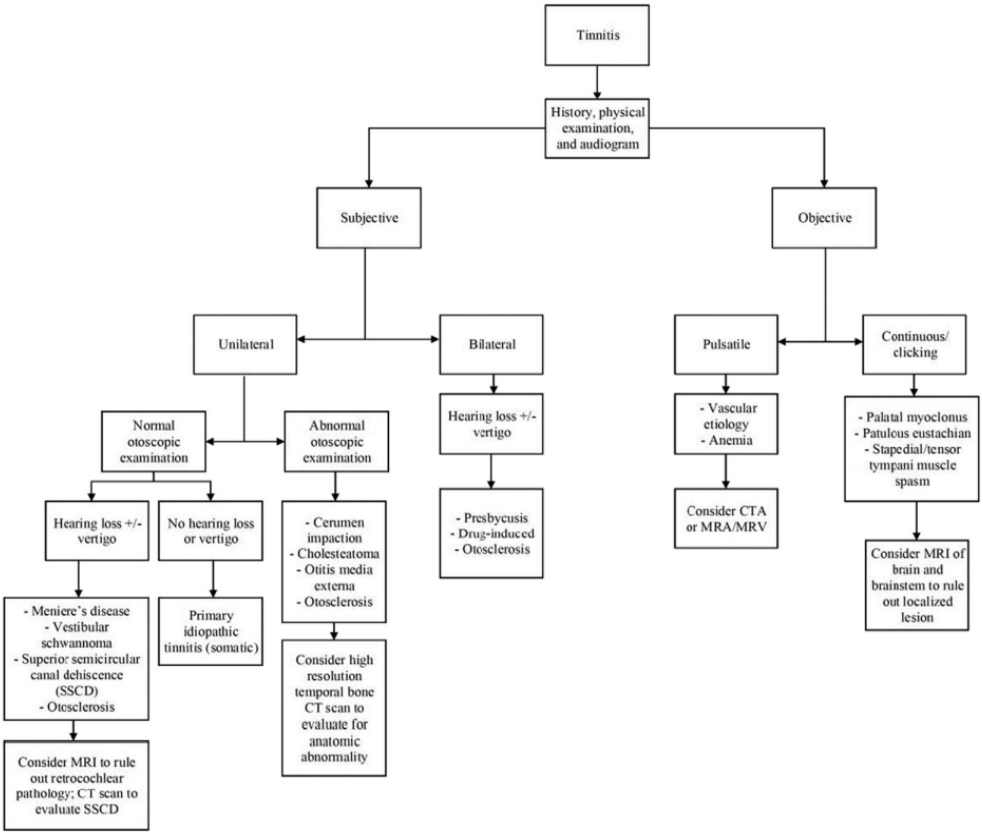
change seen in the auditory cortex is that neurons that received inputs from parts of the cochlea that have been damaged tune in to the nearest adjacent frequency input that is still active. This results in over representation of frequencies adjacent to areas of damage and increased neural activity at those frequencies.[21]

Subjective Tinnitus	**Objective Tinnitus**
Otologic ● Impacted wax Fluid in middle ear ● Acute otitis media Chronic otitis media ● Ménière's disease ● Schwannoma ● Presbycusis ● Noise-induced hearing loss ● Idiopathic sudden SNHL Metabolic ● Obesity ● Hyperlipidaemia ● Hypothyroidism ● Hyperthyroidism ● Vitamin deficiency Cardiovascular ● Anaemia ● Hypertension ● Hypotension ● Arteriosclerosis ● Cardiac arrhythmias Neurologic ● Head injury (labyrinthine concussion) ● Temporal bone fractures ● Multiple sclerosis ● Post- meningitis ● Cerebral haemorrhage ● Cerebral infarct Pharmacologic ● Certain medications ● ototoxic drugs Psychogenic ● Depression ● Anxiety	Vascular ● AV shunts ● Congenital AV malformations ● Glomus tumour of middle ear Venous hum ● Jugular bulb dehiscence. Arterial bruit ● Vascular loop pressing on internal auditory canal's fifth nerve ● High-riding carotid artery ● Carotid aneurysm ● Carotid stenosis ● Persistent stapedial artery Dental Temporomandibular joint clicks Palatal myoclonus Patulous eustachian tube Stapedial or tensor myoclonus

Diagnosis

Along with an assessment of the patient's medications and psychosocial history, a history of the date and type of the tinnitus must be gathered. The external ear should be examined, the heart and cervical arteries should be audible, and the cranial nerve functioning, including hearing, should be assessed. If there is a possibility of hearing loss, an audiogram is advised. To assess asymmetrical hearing loss or tinnitus, pulsatile tinnitus, as well as other focal neurological dysfunction, brain magnetic resonance imaging, frequently in conjunction with magnetic resonance angiography, may be necessary. A CT scan of the temporal bone may be necessary when there is a past record of cholesteatoma or mastoiditis. Testing for vascular or structural abnormalities has a rather low result in cases of bilateral tinnitus. Serum testing for conditions like anemia, polycythemia, hypercholesterolemia, hyperthyroidism, syphilis, autoimmune diseases may on occasion be necessary. Diagnostic testing should also include speech discrimination testing, and tympanometry.[2]

Frequency of the tinnitus is matched with a variety of stimuli using pitch masking, loudness matching, minimum masking level, loudness matching, loudness matching with a pure tone or noise, residual inhibition, and other audiologic measurements of tinnitus (achieving decreased or absent tinnitus after exposure to a masking tone at the pitch and intensity of the tinnitus).



DIAGNOSTIC FLOW CHART

TFI should be useful in both clinical and research settings because of its responsiveness to treatment-related change, validity for scaling the overall severity of tinnitus, and comprehensive coverage of multiple domains of tinnitus severity.

The TFI calculates the harmful effects of tinnitus. It has 25 items, and responses are graded on a Likert scale of 1 to 10. The range of sum scores is linearly converted to be 0 to 100.The items load on eight subscales:

1. Intrusive (unpleasantness, intrusiveness, persistence)

2. Sense of control (reduced sense of control)

3. Cognitive (cognitive interference)

4. Sleep (sleep disturbance)
5. Auditory (auditory difficulties attributed to tinnitus)
6. Relaxation (interference with relaxation)
7. Quality of life (quality of life reduced)
8. Emotional (emotional distress)

It has been established that a changing value of at least 13 points indicates a consistent, clinically significant improvement.[22]

Management:

Tinnitus treatment necessitates a complete knowledge of both the patient as well as the complaint being made. Patients may occasionally just want confirmation that the condition has no serious underlying cause. According to estimates, supportive counselling without specialised treatment is effective for about 80% of tinnitus patients. In other situations, the symptom is quite distressing and relief is of utmost importance.

Psychological Treatments

Psychoeducation and Counseling

Psychoeducation and counseling can help patients manage their tinnitus and any associated side effects, such as emotional anguish, sleep problems, and disruptions to their work and personal lives, although many cases of tinnitus could not be treated.

Tinnitus retraining therapy

` Tinnitus retraining therapy aims to help the patient perceive tinnitus as an unconditioned stimulus by "retraining" the brain to become accustomed to the tinnitus signal. Two main elements of tinnitus retraining therapy are audiological therapies in the form of white noise devices or masking that are kept just less than the patient's perceived tinnitus level and directive, or educational, counselling. The brain's limbic or emotional centres are thought to be activated by tinnitus, however this is being attempted to be reduced. The protocol calls for subjecting the patient to low-level, continuous audio stimulation. One attempts to blend the auditory input to the tinnitus and lessen susceptibility to it by progressively changing the tone.[23,24]

Cognitive behavioral therapy

By reorganising the patient's unhelpful ideas and actions, cognitive behavioural therapy (CBT) aims to lessen negative emotional and behavioural reactions to tinnitus. Psychoeducation, relaxation training, mindfulness-based training, imagery training, and exposure therapy make up the bulk of CBT.[25]

Auditory Stimulation

Sound therapy

White noise produced by masking equipment is meant to be calming and lessen the tinnitus. By reducing tinnitus-related hypersynchronous activity in the auditory cortex by the activation of lateral inhibition, masking aims to reduce the perceived loudness of tinnitus. Specifically, notched sound therapy is a sort of sound therapy targeted to patients in which the sound stimulus's tinnitus-causing frequency is subtracted. Complete masking and partially masking are the two main categories of

sound therapy approaches that have developed since the 1970s when sound therapy was first introduced. Devices with adjustable, frequency-specific narrowband (partial) masking have grown in popularity since extended exposure to broadband (total masking) stimulation is known to increase the risk for hearing loss. There are specialised sound generators that could be placed behind the ear, much like a hearing aid. Furthermore, some hearing aids include built-in sound generators, which would be perfect for people who additionally experience hearing loss and tinnitus.[26,27]

Hearing aids

With the high prevalence of concomitant hearing loss in tinnitus patients, hearing aids are frequently advantageous in the treatment of tinnitus. The most widely used kind of treatment, known as sound therapy (masking), involves using sound-generating equipment to cause a decrease in tinnitus loudness or an increase in quality of life associated with tinnitus. Typically, this takes the form of a hearing aid-like device which emits a soft sound to lessen the intensity of the ringing. By letting the patient set up a fan in the space, a comparable result can be obtained. Tinnitus can be made less intrusive by using a radio or television to generate an auditory stimulus. The impact of hearing aids amplifying background noise can be to disguise tinnitus. Despite the fact that many people use hearing aids, their positive effects are more noticeable in people who have tinnitus that is < 6000 Hz in frequency (ie, in the amplification range of the hearing aids). Hearing aids with integrated sound generators produce narrowband or broadband noise and offer sufficient high-frequency masking.[28]

Cochlear implants

With the exception of treating particular underlying disorders like otosclerosis or vestibular schwannomas, surgical intervention has yet not been demonstrated as an effective modality in treating tinnitus in general. However, findings indicate that tinnitus is eradicated in more than 80% of patients with bilateral significant SNHL and concomitant tinnitus after cochlear implantation.[29] Despite the type of tinnitus, patients responded the same way. Preliminary research also indicates cochlear implantation effectively reduces tinnitus in patients who have unilateral significant SNHL and normal or almost normal hearing in the other ear. According to preliminary research, this subgroup had effectiveness suppressing tinnitus. This may also be a good choice for people with severe unilateral tinnitus as unilateral cochlear implantation for one-sided hearing loss with tinnitus has become increasingly popular.

Pharmacologic Treatments

Although multiple drugs have been used to alleviate tinnitus therapeutically, the Food and Drug Administration has not yet approved any medications for treatment of primary, idiopathic tinnitus. Most of the medications examined have undesirable side effects and are ineffective.

Antidepressants

Selected serotonin reuptake inhibitors and TCA have both been investigated for treatment of tinnitus. Antidepressants have improved tinnitus measures in some trials, but because of the methodological flaws in these studies and their inability to generalise to individuals without depression, they are not routinely advised for treatment of tinnitus.[30] When compared to a placebo, amitriptyline has been

demonstrated to have considerably lessened tinnitus complaints and loudness. Another study examining the impact of nortriptyline on individuals with severe tinnitus and significant depression discovered a decrease in both the severity of the depression and the tinnitus.[31] One study found that sertraline reduced tinnitus loudness and intensity in people with concomitant depression and anxiety.[32] Although, it was discovered that in those with chronic tinnitus who did not also have comorbid depression, paroxetine had nil effect in reduction of tinnitus symptoms. When considered as a whole, these data indicate that while antidepressants may help tinnitus patients who also have depression or anxiety, they should not be utilised as a standard treatment for persistent tinnitus.

Anxiolytics

Clinical studies looking at how anxiolytics, including benzodiazepines, affect tinnitus may not always demonstrate a benefit. Alprazolam was found to lessen tinnitus loudness in a single double-blind, placebo-controlled research, although the study had limitations due to its small sample size and lack of repeatability. These drugs can also have negative consequences, such as a significant risk of drug dependence and sleepiness.

Anticonvulsants

Anticonvulsant medications like lamotrigine and carbamazepine may be able to reduce tinnitus-related central auditory hyperactivity. A Cochrane review, though, was unable to show that benefits outweighed drawbacks. Anticonvulsant side effects include nausea, vertigo, headaches.

Other compounds

Ginkgo biloba:

The most popular herbal tinnitus supplement, ginkgo biloba, includes bioactive flavonoids with vasoactive and anti-oxidant effects. Its use is typically indicated by one of three conditions: tissue damage, peripheral vascular disease, or cerebrovascular disease. The Ginkgo biloba extract EGb 761 is used in majority of randomised control trials (RCTs). A medical herb known as ginkgo biloba is utilised for its alleged capacity to improve memory and cognition. The durations range from 2 weeks to 2 years, and the dosages ranging from 80 to 720 mg/d. Increased cerebral blood flow, anti-oxidant benefits, and anti-inflammatory effects are some of the mechanisms of action. Flavone and terpene lactone components have been linked to antiplatelet actions. Although gingko is usually considered to be safe, patients should be informed that there may be an increased risk of bleeding, especially when ginkgo is combined with drugs that have synergistic effects. With the following major constituents (greater than 0.1%), composition EGb 761 is standardised to contain 24% ginkgo-flavone glycosides and 6% terpenoids: flavonol monoglycosides (such as quercetin-3-0-glucoside, quercetin-3-0-rhamnoside, and 30 -0 methylmyricetin-3-0-glucoside), flavonol diglycosides, flavonol triglycosides, coumaric esters of flavonol diglycosides, flavonoidic compound, terpenes (eg, bilobalide, ginkgolide A, ginkgolide B, ginkgolide C, ginkgolide J), organic acids, and steroids. The use of ginkgo in the treatment of neurologic, psychiatric, functional, and physiologic symptoms such as issues with memory, processing information, attention and concentration, psychomotor function, mood, tiredness, and daily activities is supported by the plant's putative neuroprotective and cognitive enhancing properties.

Common indications include Alzheimer's disease and age-related dementia, normal ageing, traumatic cerebral injury, cerebrovascular disease, multi-infarct dementia, cerebral atherosclerosis, cerebral insufficiency, cerebral edoema, inflammation, intermittent claudication, and glutamate toxicity. Other indications include the symptomatic treatment of a number of disorders, such as an improvement in pain-free walking, peripheral arterial occlusive disease (i.e., intermittent claudication), ver Action-regulatory mechanisms Ginkgo appears to work through flavones and terpene lactones, respectively, which have antioxidant and anti-platelet-activating factor (anti-PAF) activities. Ginkgo has modulatory effects on the tone of the cerebral vasculature, the activity of receptors and transmitters, the metabolism of glucose, and the electroencephalogram. Ginkgolides, which are terpene lactones, decrease PAF and improve blood flow. Ginkgo can influence venous and arterial vasoactive changes that result in improved microcirculation, peripheral and cerebral blood flow, and tissue perfusion. Ginkgo has a beneficial effect on blood perfusion, supporting its use in treating peripheral artery occlusive disease, tinnitus, and vertigo with vascular origins. The main mechanisms underlying the mitigative effects in intermittent claudication appear to be vasoregulation, platelet antagonism, and defence against postischemic oxidative damage. Properties related to metabolism, oxidation, and inflammation Putative pathways for vascular dementia include increasing blood flow, lowering ischemia-reperfusion harm, and suppressing platelets. Since the mitochondrial respiratory system is both the primary target and the generator of ROS ginkgo biloba may have direct protective properties on mitochondria that support its antioxidant properties (ROS). Scavenge ROS using flavonoids. Through intracellular signalling pathways implicated in apoptosis, where flavonoid and terpene constituents play a significant role, ginkgo may also have antiapoptotic effects. Numerous

different nutritional supplements, including melatonin and B-complex vitamins, have been researched, but no positive effects have been identified.[33]

Caroverine:

A quinoxaline derivative called caroverine, also known as 1-(diethylaminoethyl)-3-(p-methoxybenzyl)-1,2-hydroquinoxaline-2-one, was created in the 1960s. Along with its antioxidant properties, caroverine has antagonistic effects on the NMDA and -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors. The cochlear afferents' primary excitatory and neurotransmitter, glutamate, is released onto the IHC (IHC) synapse area. Excessive noise exposure can cause excitotoxic intracellular calcium overload and excessive glutamate release in some pathological conditions, which may be the cause of tinnitus. According to studies, caroverine and other glutamate receptor antagonists can specifically block glutamate receptors, such as the NMDA (N-Methyl-D aspartate) receptor, which eliminates tinnitus in a large majority of patients.[5]

Brain Stimulation

Brief magnetic pulses are sent to particular regions of the cerebrum through an unbroken scalp using the transcranial magnetic stimulation procedure. Its been demonstrated that repetitive transcranial magnetic stimulation (rTMS) lowers neuronal activity in remote brain regions that are physically related to directly stimulated brain regions. Tinnitus treatment using rTMS was suggested because aberrant central auditory system activity has been linked to the feeling of tinnitus. Few studies have indicated reductions in tinnitus severity with rTMS, Advancements in quality of life for patients have not been demonstrated in randomised studies or

comprehensive reviews or tinnitus reduction over the long term. Emerging research suggests that deep brain stimulation of the caudate nucleus may be helpful in the treatment of tinnitus. Epidural excitation of the secondary auditory cortex by implanted electrodes results in reduction of tinnitus in some patients.[34,35,36]

Some people may benefit from additional therapies such biofeedback, acupuncture, hypnosis, and stress-reduction methods. However, randomised controlled trials have been unable to show that tinnitus has improved.

In cases where objective tinnitus is brought on vascular flow turbulence, no treatment may be required. Treatment for vascular tumours, arteriovenous malformations, increased intracranial pressure, and schwannomas should focus on the root of the problem.

MATERIALS AND METHOD

Methodology

The present study was carried out at Department of Otorhinolaryngology and Head and Neck Surgery, Jawaharlal Nehru Medical College from January 2021-December 2021 to study the effect of gingko biloba versus caroverine in the treatment of tinnitus. A total of 80 patients were chosen randomly for the study.

Source of data - Patients aged between 18 and 75 years with complaints of tinnitus presenting to ENT & HNS outpatient department in KLES Dr Prabhakar Kore Charitable Hospital during the study period.

Study design: A Randomized controlled study.

Study period: January 2021 to December 2021

Study population: Patients of both sexes between the age group of 18-60 years who are attending the ENT & HNS department in KLE Dr. Prabhakar Kore charitable hospital

Sample size: 80 cases

$$n = \frac{(z_\alpha + z_\beta)^2(s_1^2 + s_2^2)}{(\bar{X}_1 - \bar{X}_2)^2}$$

where zα is linked with the level of significance and zβ is linked with the power of the test. For 5% level of the significance zα =1.96 and zβ =0.84 for 80% power of the test.

Ethical clearance: obtained from the institutional ethical committee.

Method of randomization - Computer generated Randomisation

Inclusion criteria:

Patients of both sexes between the age group of 18-75 years who are attending the ENT & HNS department in KLE Dr. Prabhakar Kore charitable hospital,

- Patients who give consent to participate in the study.
- Patients who are clinically and audiologically confirmed cases of tinnitus.

Exclusion criteria:

The following patients are excluded from the study:

- Patients not willing to participate and not given informed written consent.
- Patients with any blood disorders.
- Patients with any recent vascular injury, major surgical illness and undergone or undergoing surgery.
- Patients having excessive tobacco, nicotine or any other substance abuse.
- Pregnant females or women trying to conceive.

Statistical analysis:

The study's main objective is to compare the two groups. We will compute the mean and standard deviation for the continuous quantitative data. Utilizing appropriate statistical methods like the unpaired student's t test, the continuous

variables between groups will be compared. The student's paired t test will be utilised to compare two quantitative variables within a group. Rates, ratios, and percentages will be used to express the categorical data. Using the Chi-square test or Fisher's exact test, relationship between result, clinical, and demographic factors will be examined. Median will be used to represent discrete variables. Discrete variable comparisons will be made using non-parametric tests. Suitable graphs will be used to depict the comparison. For all the tests the value of p less than 5% (0.05) will be considered significant.

Methodology

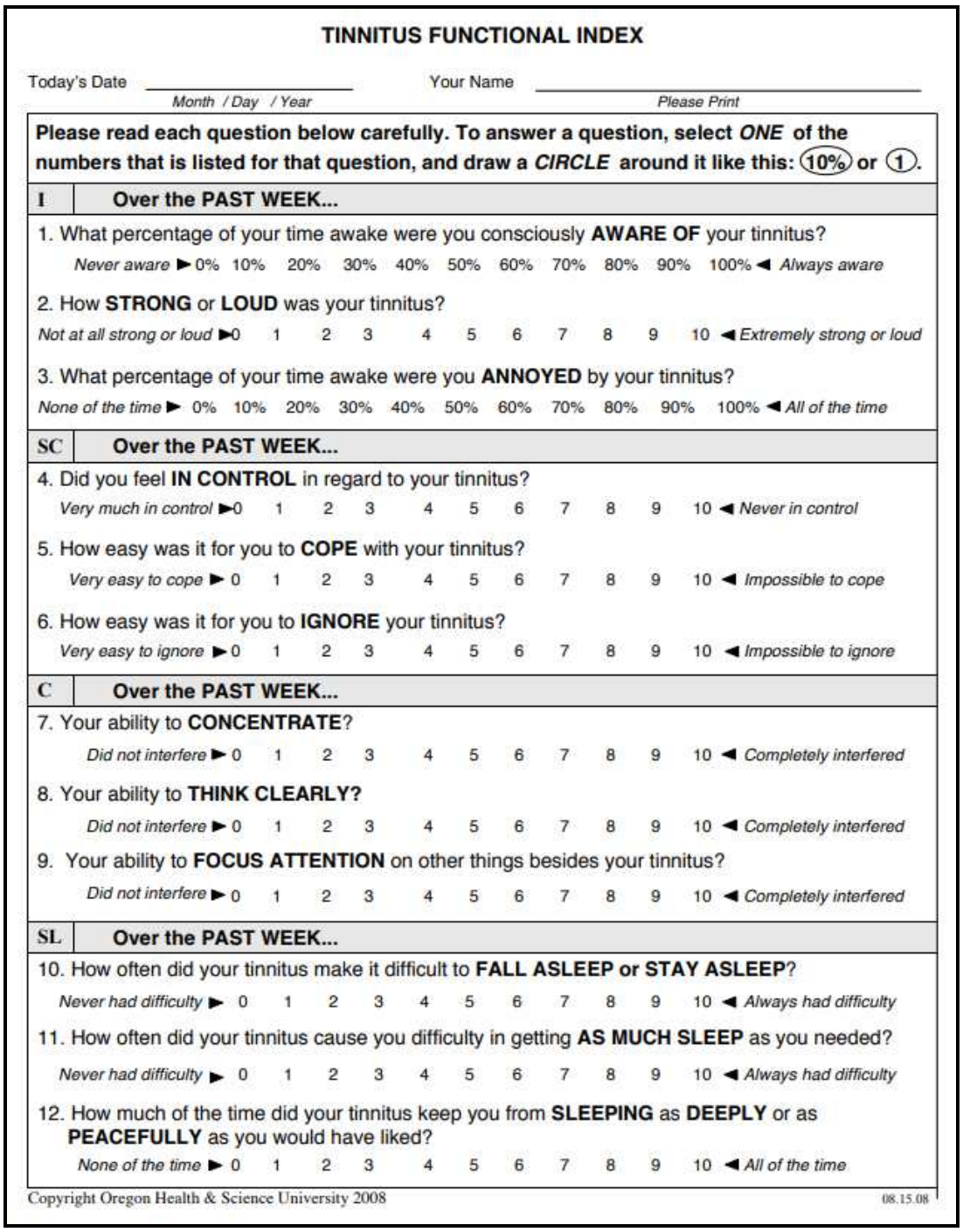
- After taking informed consent from the patient, their details and a thorough clinical history will be obtained for duration and nature of tinnitus, duration and nature of any previous treatment.
- All patients will be clinically examined including general physical examination, careful examination of the ear, nose and throat and routine blood investigations will be done.
- All patients had to undergo pure tone audiometry ranging from 0-16000Hz and tinnitus matching was done.
- All patients have to undergo blood investigations from which neutrophil lymphocyte ratio and mean platelet value will be assessed.
- All patients were asked to fill a questionnaire - Tinnitus functional index adopted from Oregon health and science university.

- All patients have to fill the questionnaire before, during and after the course of treatment being day 1, day 45 and day 90 respectively.

- A total of 80 patients of tinnitus will be considered for the trial and will be randomly divided into 2 equal groups.

- One group will be given 120mg gingko biloba divided in 3 doses for treatment of tinnitus whereas the other group will be given 60mg caroverine divided into 3 doses daily for a period of 3 months.

- Patients will be asked to follow up monthly for a period of 3 months and severity of tinnitus will be assessed.



TINNITUS FUNCTIONAL INDEX

Today's Date _____ (Month / Day / Year) Your Name _____ (Please Print)

Please read each question below carefully. To answer a question, select *ONE* of the numbers that is listed for that question, and draw a *CIRCLE* around it like this: (10%) or (1).

I — Over the PAST WEEK...

1. What percentage of your time awake were you consciously **AWARE OF** your tinnitus?
   Never aware ► 0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100% ◄ *Always aware*
2. How **STRONG** or **LOUD** was your tinnitus?
   Not at all strong or loud ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Extremely strong or loud*
3. What percentage of your time awake were you **ANNOYED** by your tinnitus?
   None of the time ► 0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100% ◄ *All of the time*

SC — Over the PAST WEEK...

4. Did you feel **IN CONTROL** in regard to your tinnitus?
   Very much in control ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Never in control*
5. How easy was it for you to **COPE** with your tinnitus?
   Very easy to cope ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Impossible to cope*
6. How easy was it for you to **IGNORE** your tinnitus?
   Very easy to ignore ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Impossible to ignore*

C — Over the PAST WEEK...

7. Your ability to **CONCENTRATE**?
   Did not interfere ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Completely interfered*
8. Your ability to **THINK CLEARLY?**
   Did not interfere ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Completely interfered*
9. Your ability to **FOCUS ATTENTION** on other things besides your tinnitus?
   Did not interfere ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Completely interfered*

SL — Over the PAST WEEK...

10. How often did your tinnitus make it difficult to **FALL ASLEEP or STAY ASLEEP**?
    Never had difficulty ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Always had difficulty*
11. How often did your tinnitus cause you difficulty in getting **AS MUCH SLEEP** as you needed?
    Never had difficulty ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Always had difficulty*
12. How much of the time did your tinnitus keep you from **SLEEPING** as **DEEPLY** or as **PEACEFULLY** as you would have liked?
    None of the time ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *All of the time*

08.15.08

Figure 3 Tinnitus Functional Index Questionnaire

TINNITUS FUNCTIONAL INDEX PAGE 2

Please read each question below carefully. To answer a question, select *ONE* of the numbers that is listed for that question, and draw a *CIRCLE* around it like this: (10%) or (1).

A	**Over the PAST WEEK, how much has your tinnitus interfered with...**	*Did not interfere*										*Completely interfered*
	13. Your ability to **HEAR CLEARLY**?	0	1	2	3	4	5	6	7	8	9	10
	14. Your ability to **UNDERSTAND PEOPLE** who are talking?	0	1	2	3	4	5	6	7	8	9	10
	15. Your ability to **FOLLOW CONVERSATIONS** in a group or at meetings?	0	1	2	3	4	5	6	7	8	9	10

R	**Over the PAST WEEK, how much has your tinnitus interfered with...**	*Did not interfere*										*Completely interfered*
	16. Your **QUIET RESTING ACTIVITIES**?	0	1	2	3	4	5	6	7	8	9	10
	17. Your ability to **RELAX**?	0	1	2	3	4	5	6	7	8	9	10
	18. Your ability to enjoy "**PEACE AND QUIET**"?	0	1	2	3	4	5	6	7	8	9	10

Q	**Over the PAST WEEK, how much has your tinnitus interfered with...**	*Did not interfere*										*Completely interfered*
	19. Your enjoyment of **SOCIAL ACTIVITIES**?	0	1	2	3	4	5	6	7	8	9	10
	20. Your **ENJOYMENT OF LIFE**?	0	1	2	3	4	5	6	7	8	9	10
	21. Your **RELATIONSHIPS** with family, friends and other people?	0	1	2	3	4	5	6	7	8	9	10

22. How often did your tinnitus cause you to have difficulty performing your **WORK OR OTHER TASKS**, such as home maintenance, school work, or caring for children or others?

Never had difficulty ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Always had difficulty*

E	**Over the PAST WEEK...**

23. How **ANXIOUS** or **WORRIED** has your tinnitus made you feel?

Not at all anxious or worried ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Extremely anxious or worried*

24. How **BOTHERED** or **UPSET** have you been because of your tinnitus?

Not at all bothered or upset ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Extremely bothered or upset*

25. How **DEPRESSED** were you because of your tinnitus?

Not at all depressed ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Extremely depressed*

 08.15.08

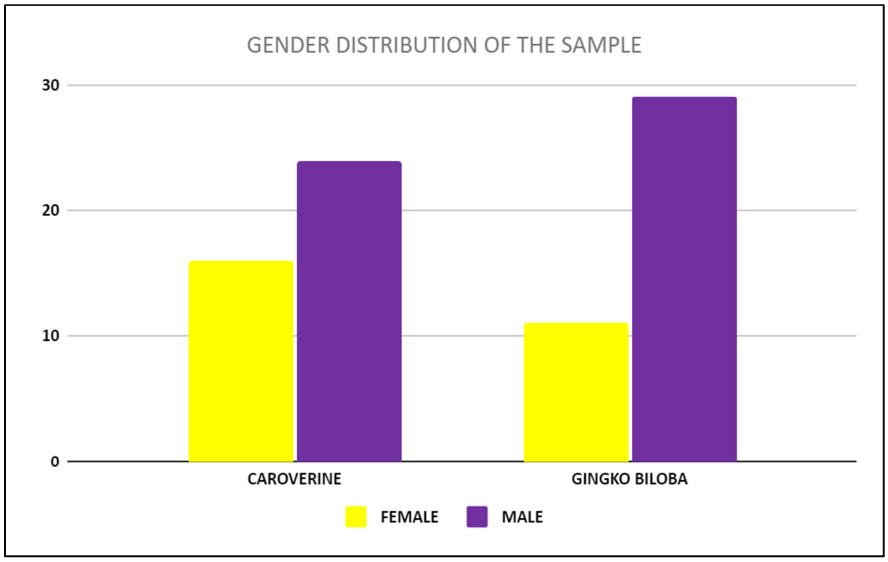
RESULTS:

Group A – received 60 mg caroverine per day, for a period of 3 months.

Group B – received 120 mg gingko biloba per day, for a period of 3 months.

Table -1: Gender wise distribution of patients in both groups.

	CAROVERINE		GINGKO BILOBA	
GENDER	**NUMBER**	**%**	**NUMBER**	**%**
FEMALE	16	40.00	11	27.50
MALE	24	60.00	29	72.50
TOTAL	40	100.00	40	100.00

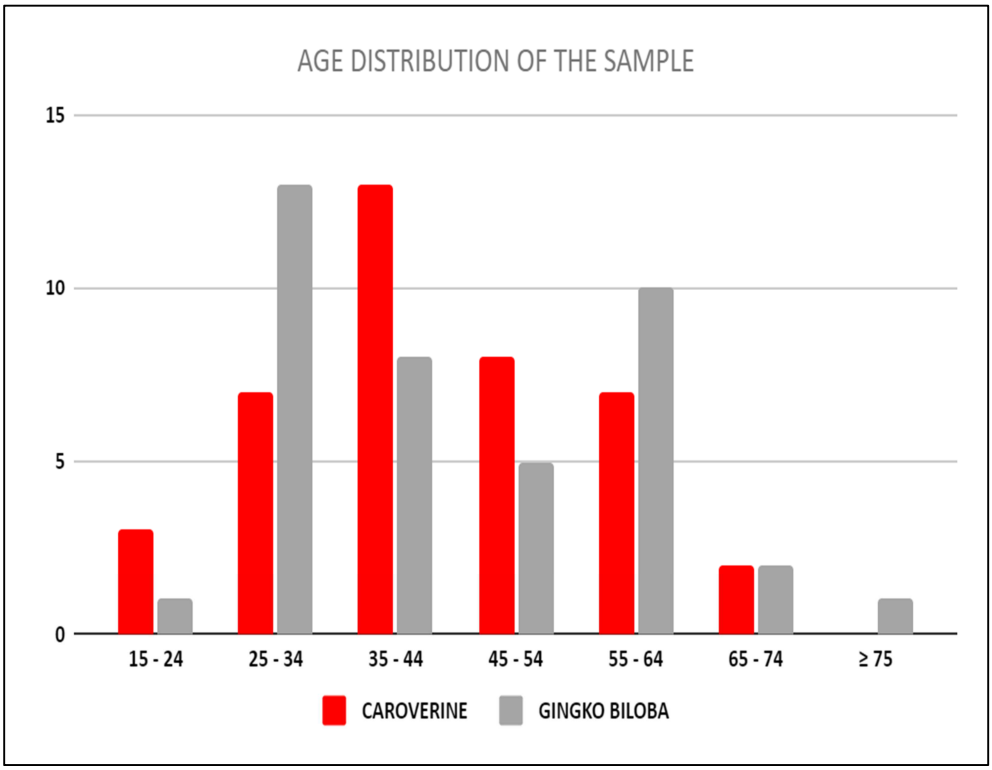


Graph -1: Gender wise distribution of patients in both groups.

Group A consisted of 16 females and 24 males (range: 18 – 75 years) and their mean age was 43.3 ± 13.7 years. There were 11 females and 29 males in group-B, and their mean age ranged from min to max at 43.9 ± 13.74 years (Table -1, Graph-1).

Table - 2: Age wise distribution of patients in both groups

	CAROVERINE		GINGKO BILOBA	
AGE	**NUMBER**	**%**	**NUMBER**	**%**
18 - 24	3	7.50	1	2.50
25 - 34	7	17.50	13	32.50
35 - 44	13	32.50	8	20.00
45 - 54	8	20.00	5	12.50
55 - 64	7	17.50	10	25.00
65 - 74	2	5.00	2	5.00
≥ 75	0	0.00	1	2.50
TOTAL	40	100.00	40	100.00



Graph - 2: Age wise distribution of patients in both groups

Table -2 and Graph -2 show the age wise distribution of tinnitus patients in this study between the age group 18-75. In group A ,13 patients (32.5%) belonged to the age group 35-44 years and in group B,13 patients (32.5%) belonged to the age group 25–44 years, comprising the majority respectively.

Table -3: Distribution of patients in both groups based on the ear involved

	CAROVERINE		GINGKO BILOBA	
EAR	**NUMBER**	**%**	**NUMBER**	**%**
LEFT	20	50.00	10	25.00
RIGHT	12	30.00	16	40.00
BOTH	8	20.00	14	35.00
TOTAL	40	100.00	40	100.00

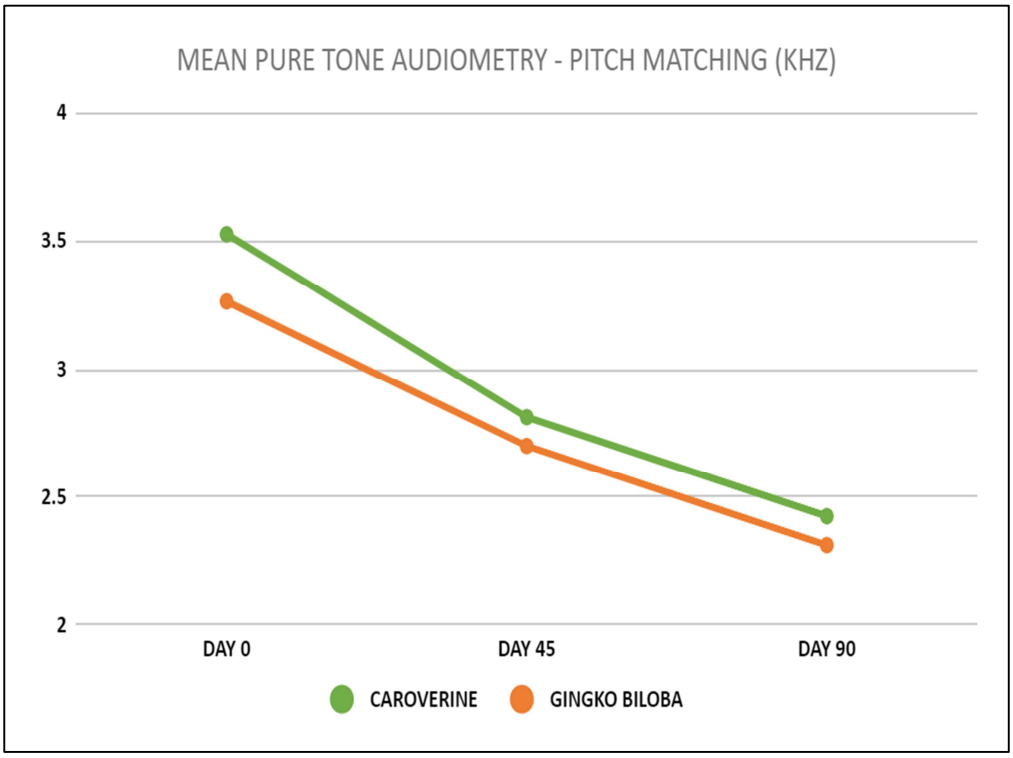
In Table-3, group A had 20 patients (50%) with only left ear being affected, group B had 16 patients (40%) with right ear affected. Tinnitus of the left ear was most common in this study.

Table – 4: Pure tone audiometry - Pitch matching (KHZ) on day 0,45,90 on caroverine

	CAROVERINE					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	3.53	1.25	1.5	6	--	--
DAY 45	2.81	1.03	1	5	0.0034	VS
DAY 90	2.43	1.02	1	4.5	< 0.0001	HS

Table – 5: Pure tone audiometry - Pitch matching (KHZ) on day 0,45,90 on gingko biloba

	GINGKO BILOBA					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	3.26	1.15	1.5	6	--	--
DAY 45	2.70	1.09	1	5	0.0140	S
DAY 90	2.31	0.95	1	5	0.0001	HS



Graph-3: Pure tone audiometry - Pitch matching(kHz) on day 0,45,90 between both groups

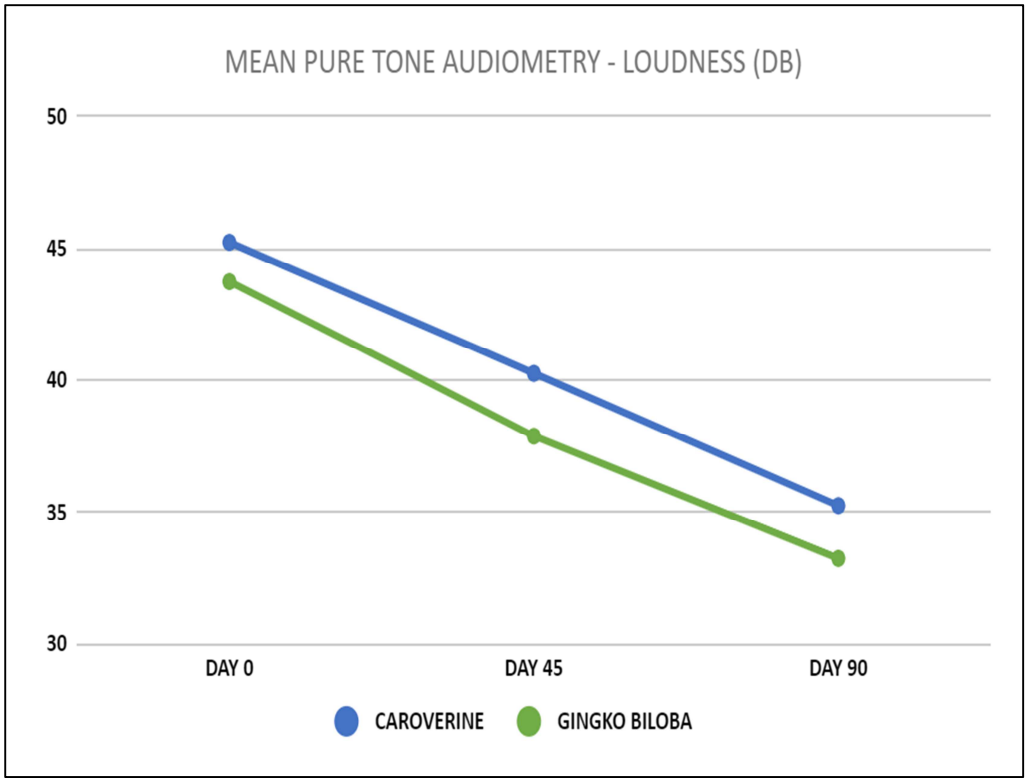
In group A the mean score of Pure tone audiometry - pitch matching(kHz) were 3.53 ,2.81,2.43 on day 0,45 and 90 respectively and in group B 3.26,2.7,2.31on day 0,45 and 90 respectively (table-4,5). Graph – 3 shows the comparison of mean pitch matching(kHz) between both groups on day 0,45 and 90.

Table – 6: Pure tone audiometry - loudness (dB)on day 0,45,90 on caroverine

	CAROVERINE					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	45.25	8.24	30	70	--	--
DAY 45	40.25	7.68	30	60	0.0031	VS
DAY 90	35.25	6.79	25	55	< 0.0001	HS

Table – 7: Pure tone audiometry - loudness (dB) on day 0,45,90 on gingko biloba

	GINGKO BILOBA					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	43.75	6.58	30	60	--	--
DAY 45	37.88	6.19	30	50	< 0.0001	HS
DAY 90	33.25	5.94	20	50	< 0.0001	HS



Graph-4: Pure tone audiometry - loudness (dB)on day 0,45,90 between both groups

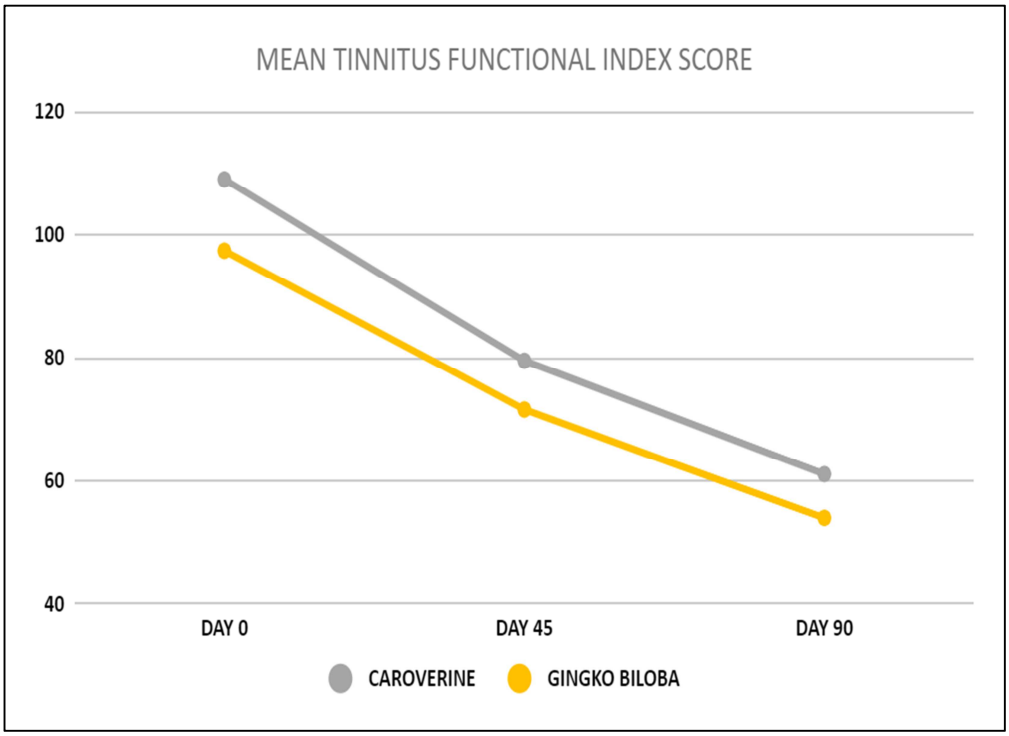
In group A the mean score of pure tone audiometry - loudness (dB)were 45.25,40.25,35.25 on day 0,45 and 90 respectively and in group B 43.75,37.88,33.25 on day 0,45 and 90 respectively (table-6,7). Graph – 4 shows the comparison of pure tone audiometry - loudness (dB) between both groups on day 0,45 and 90.

Table – 8: Mean TFI scores on day 0,45,90 on caroverine

	CAROVERINE					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	109.00	34.34	31	181	--	--
DAY 45	79.48	25.24	24	144	< 0.0001	HS
DAY 90	61.05	22.63	20	108	< 0.0001	HS

Table – 9: Mean TFI scores on day 0,45,90 on gingko biloba

	GINGKO BILOBA					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	97.43	28.31	45	161	--	--
DAY 45	71.55	19.79	40	129	< 0.0001	HS
DAY 90	53.93	16.91	28	90	< 0.0001	HS



Graph – 5: Mean TFI score on day 0,45,90 between both groups

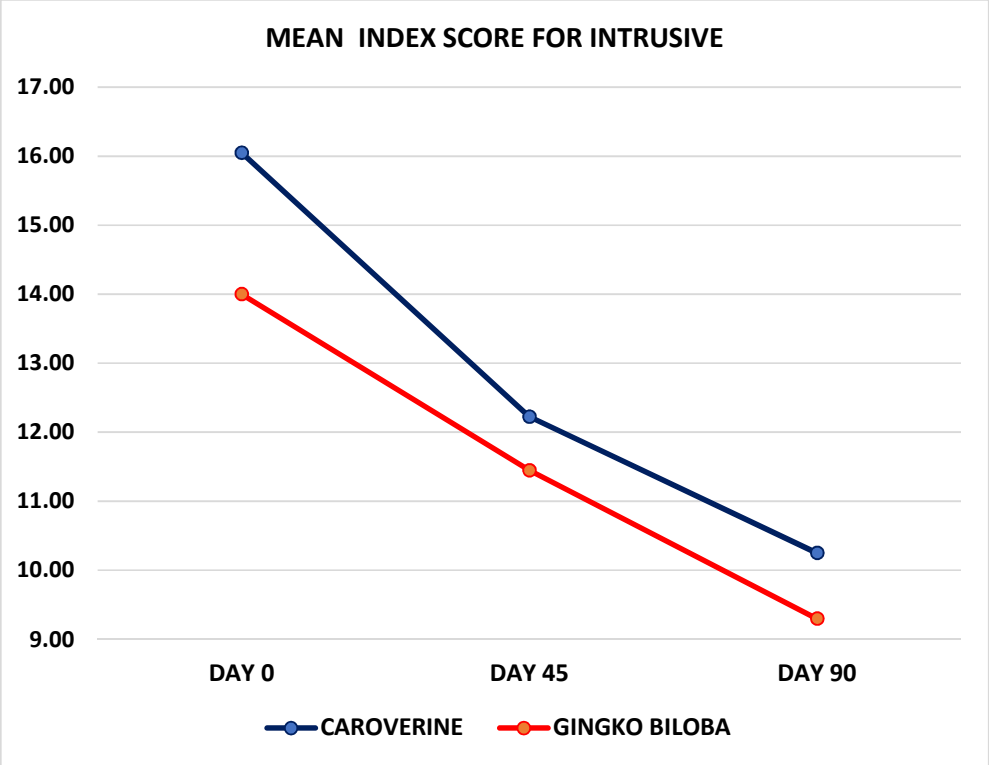
In group A the mean TFI score were 109,79.48,61.05 on day 0,45 and 90 respectively and in group B 97.43,71.55,53.93 on day 0,45 and 90 respectively (table-8,9). Graph – 5 shows the comparison of mean TFI score between both groups on day 0,45 and 90.

Table - 10: Mean TFI intrusive score on day 0,45,90 on caroverine

	INTRUSIVE					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	16.05	3.71	10	24	--	--
DAY 45	12.23	3.31	7	22	< 0.0001	HS
DAY 90	10.25	3.33	5	20	< 0.0001	HS

Table - 11: Mean TFI intrusive score on day 0,45,90 on gingko biloba

	INTRUSIVE					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	14.00	3.31	6	20	--	--
DAY 45	11.45	3.26	5	21	0.0004	HS
DAY 90	9.30	2.56	6	18	< 0.0001	HS



Graph – 6: Mean TFI intrusive score on day 0,45,90 between both groups

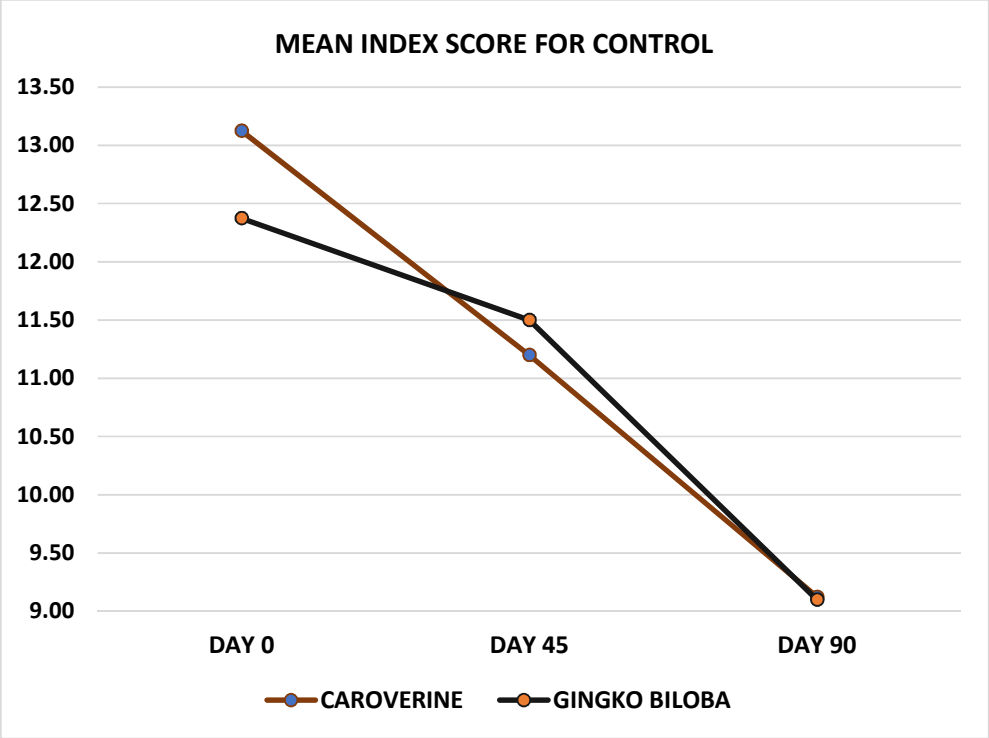
In group A the mean TFI intrusive score were 16.05,12.23,10.25 on day 0,45 and 90 respectively and in group B 14.00,11.45,9.30 on day 0,45 and 90 respectively (table-10,11). Graph – 6 shows the comparison of mean TFI intrusive score between both groups on day 0,45 and 90.

Table - 12: Mean TFI control score on day 0,45,90 on caroverine

	CONTROL					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	13.13	4.60	0	22	--	--
DAY 45	11.20	3.69	0	22	0.0212	S
DAY 90	9.13	3.52	0	20	< 0.0001	HS

Table - 13: Mean TFI control score on day 0,45,90 on gingko biloba

	CONTROL					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	12.38	3.22	5	18	--	--
DAY 45	11.50	3.25	5	20	0.1152	NS
DAY 90	9.10	2.89	5	18	< 0.0001	HS



Graph – 7: Mean TFI control score on day 0,45,90 between both groups

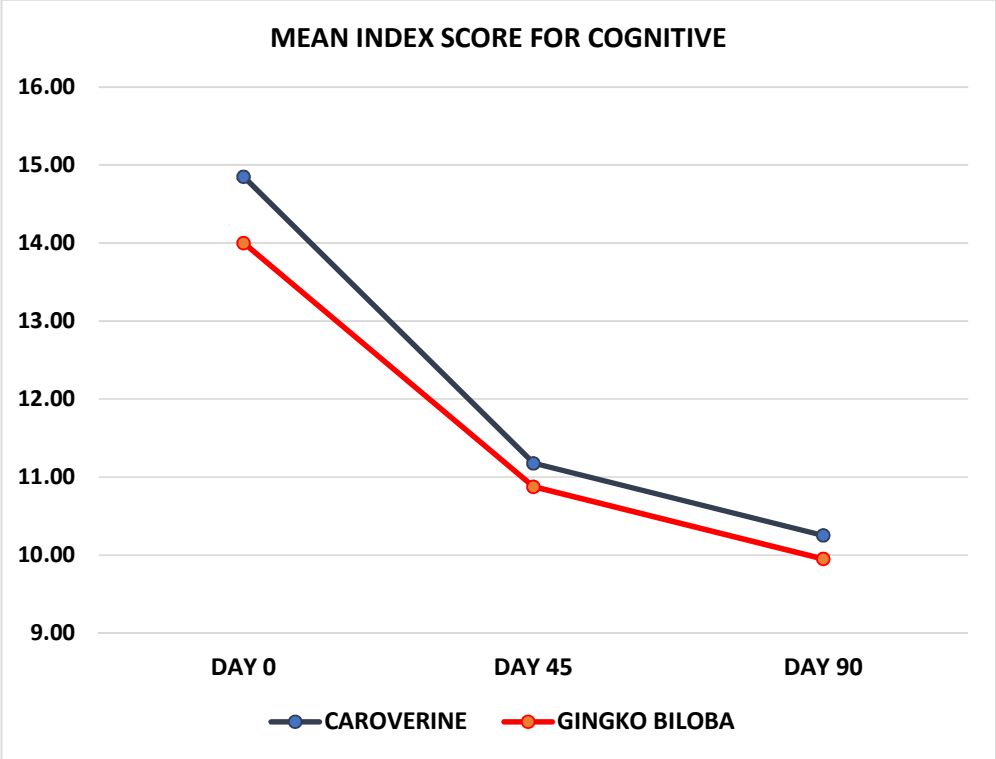
In group A the mean TFI control score were 13.13,11.20,9.13 on day 0,45 and 90 respectively and in group B 12.38,11.50,9.10 on day 0,45 and 90 respectively (table-12,13). Graph – 7 shows the comparison of mean TFI control score between both groups on day 0,45 and 90.

Table - 14: Mean TFI cognitive score on day 0,45,90 on caroverine

	COGNITIVE					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	14.85	4.00	0	22	--	--
DAY 45	11.18	2.88	0	17	< 0.0001	HS
DAY 90	10.25	2.94	1	16	< 0.0001	HS

Table - 15: Mean TFI cognitive score on day 0,45,90 on gingko biloba

	COGNITIVE					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	14.00	2.48	9	20	--	--
DAY 45	10.88	2.02	7	15	< 0.0001	HS
DAY 90	9.95	2.19	7	15	< 0.0001	HS



Graph – 8: Mean TFI cognitive score on day 0,45,90 between both groups

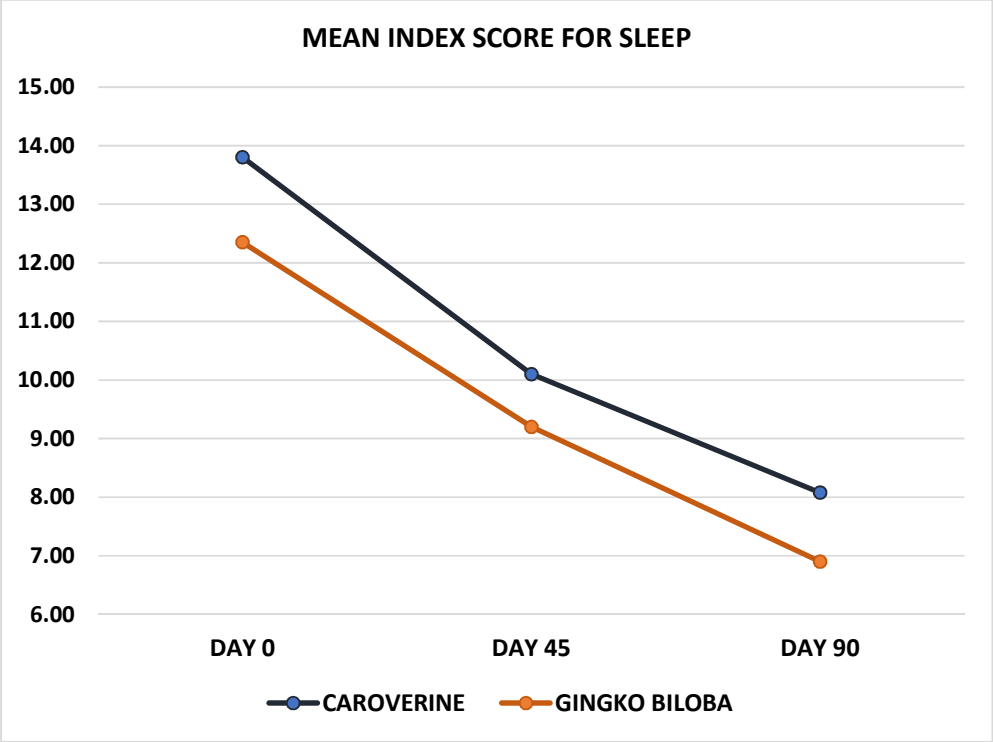
In group A the mean TFI cognitive score were 14.85,11.18,10.25 on day 0,45 and 90 respectively and in group B 14.00,10.88,9.95 on day 0,45 and 90 respectively (table-14,15). Graph – 8 shows the comparison of mean TFI cognitive score between both groups on day 0,45 and 90.

Table - 16: Mean TFI sleep score on day 0,45,90 on caroverine

	SLEEP					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	13.80	4.14	3	22	--	--
DAY 45	10.10	3.37	3	18	< 0.0001	HS
DAY 90	8.08	3.07	3	16	< 0.0001	HS

Table - 17: Mean TFI sleep score on day 0,45,90 on gingko biloba

	SLEEP					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	12.35	4.03	5	20	--	--
DAY 45	9.20	2.73	5	17	< 0.0001	HS
DAY 90	6.90	2.41	3	12	< 0.0001	HS



Graph – 9: Mean TFI sleep score on day 0,45,90 between both groups

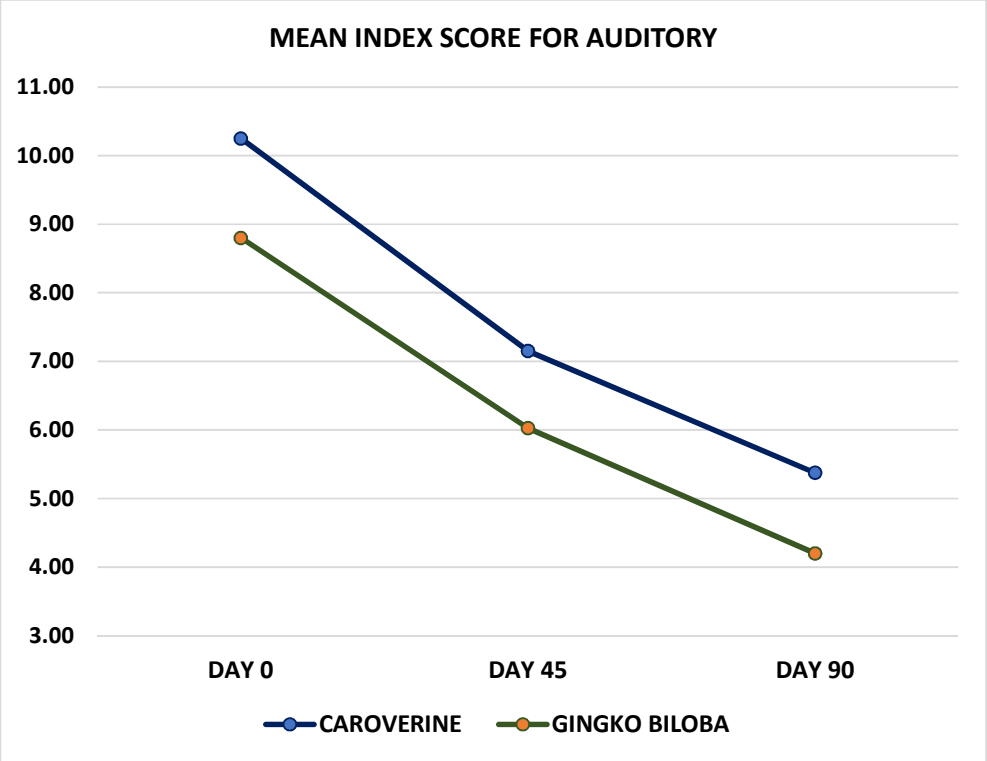
In group A the mean TFI sleep score were 13.80,10.10,8.08 on day 0,45 and 90 respectively and in group B 12.35,9.20,6.90 on day 0,45 and 90 respectively (table-16,17). Graph – 9 shows the comparison of mean TFI sleep score between both groups on day 0,45 and 90.

Table - 18: Mean TFI auditory score on day 0,45,90 on caroverine

	AUDITORY					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	10.25	5.58	0	21	--	--
DAY 45	7.15	4.19	0	17	0.0031	VS
DAY 90	5.38	4.02	0	13	< 0.0001	HS

Table - 19: Mean TFI auditory score on day 0,45,90 on gingko biloba

	AUDITORY					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	8.80	5.47	0	20	--	--
DAY 45	6.03	4.05	0	13	0.0059	VS
DAY 90	4.20	3.31	0	11	< 0.0001	HS



Graph – 10: Mean TFI auditory score on day 0,45,90 between both groups

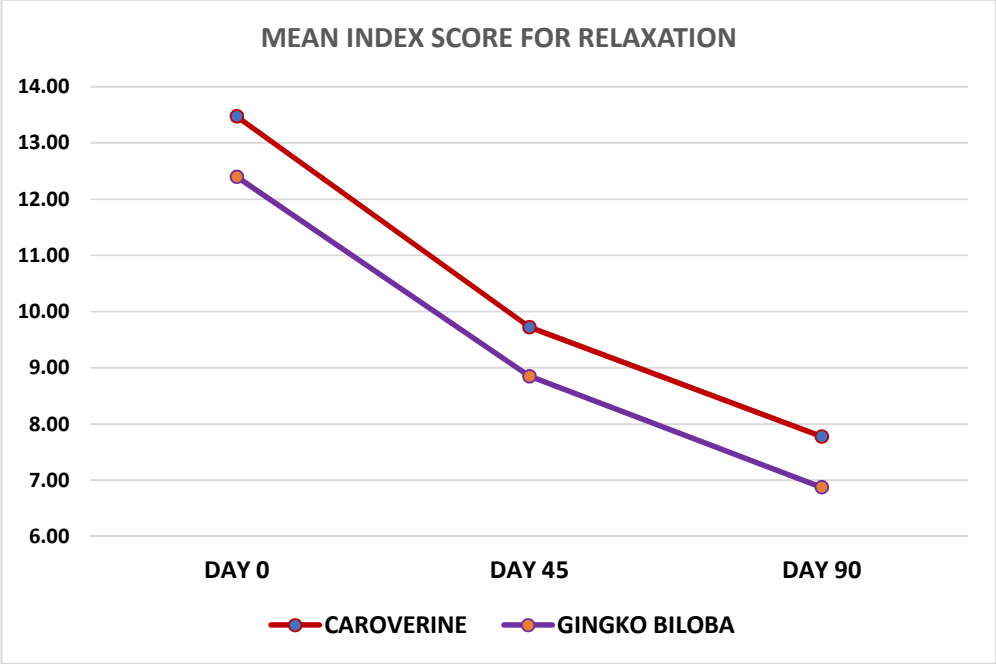
In group A the mean TFI auditory score were 10.25,7.15,5.38 on day 0,45 and 90 respectively and in group B 8.80,6.03,4.20 on day 0,45 and 90 respectively (table-18,19). Graph – 10 shows the comparison of mean TFI auditory score between both groups on day 0,45 and 90.

Table - 20: Mean TFI relaxation score on day 0,45,90 on caroverine

	RELAXATION					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	13.48	5.52	0	30	--	--
DAY 45	9.73	4.58	0	24	0.0007	HS
DAY 90	7.78	4.15	0	21	< 0.0001	HS

Table - 21: Mean TFI relaxation score on day 0,45,90 on gingko biloba

	RELAXATION					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	12.40	4.30	3	20	--	--
DAY 45	8.85	3.25	3	15	< 0.0001	HS
DAY 90	6.88	3.20	1	15	< 0.0001	HS



Graph –11: Mean TFI relaxation score on day 0,45,90 between both groups

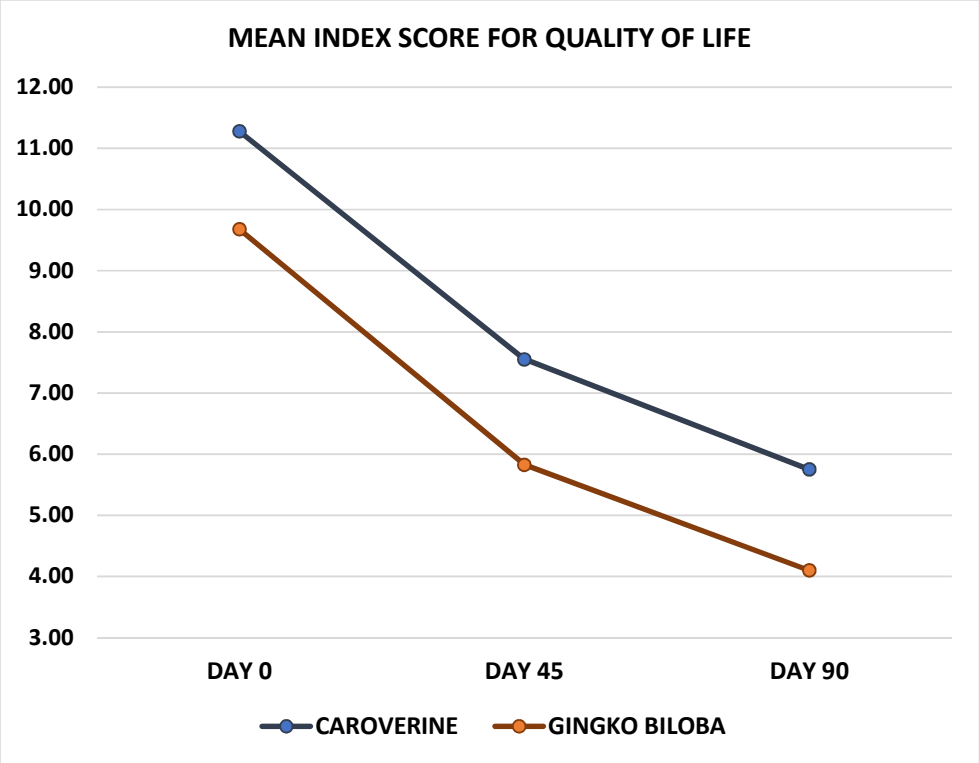
In group A the mean TFI relaxation score were 13.48,9.73,7.78 on day 0,45 and 90 respectively and in group B 12.40,8.85,6.88 on day 0,45 and 90 respectively (table-20,21). Graph – 11 shows the comparison of mean TFI relaxation score between both groups on day 0,45 and 90.

Table - 22: Mean TFI quality of life score on day 0,45,90 on caroverine

	QUALITY OF LIFE					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	11.28	8.81	0	29	--	--
DAY 45	7.55	6.72	0	23	0.0183	S
DAY 90	5.75	6.10	0	19	0.0008	HS

Table - 23: Mean TFI quality of life score on day 0,45,90 on gingko biloba

	QUALITY OF LIFE					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	9.68	8.07	0	27	--	--
DAY 45	5.83	5.95	0	17	0.0087	VS
DAY 90	4.10	4.65	0	14	0.0002	HS



Graph – 12: Mean TFI quality of life score on day 0,45,90 between both groups

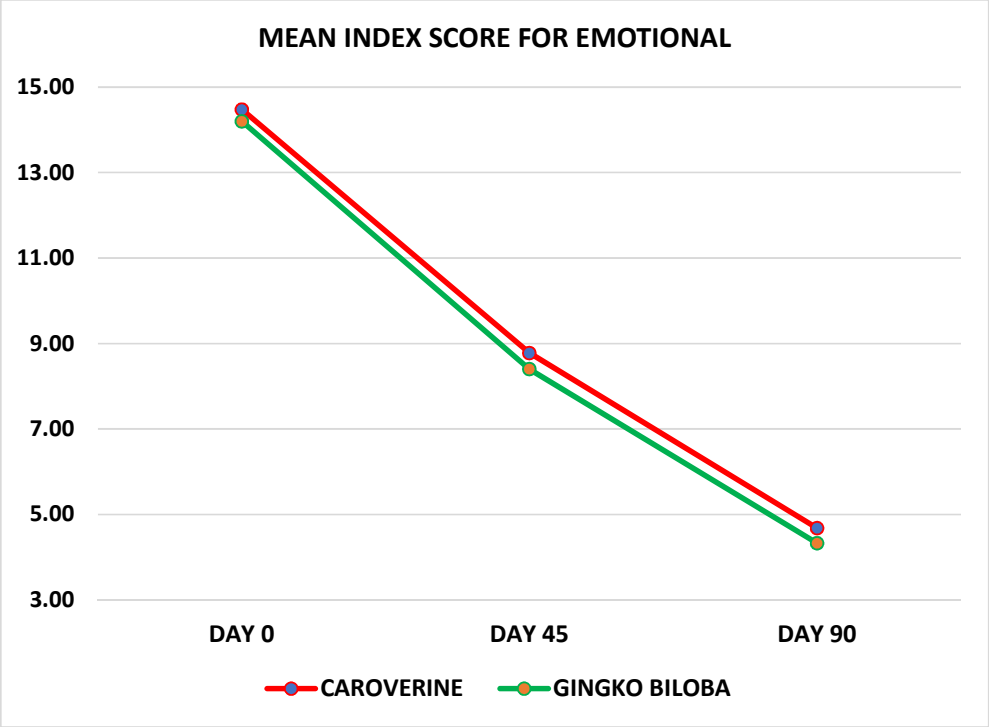
In group A the mean TFI quality of life score were 11.28,7.55,5.75 on day 0,45 and 90 respectively and in group B 9.68,5.83,4.10 on day 0,45 and 90 respectively (table-22,23). Graph – 12 shows the comparison of mean TFI quality of life score between both groups on day 0,45 and 90.

Table - 24: Mean TFI emotional score on day 0,45,90 on caroverine

	EMOTIONAL					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	14.48	4.72	2	24	--	--
DAY 45	8.78	3.96	0	16	< 0.0001	HS
DAY 90	4.68	3.98	0	13	< 0.0001	HS

Table - 25: Mean TFI emotional score on day 0,45,90 on gingko biloba

	EMOTIONAL					
	MEAN	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
DAY 0	14.20	4.30	7	23	--	--
DAY 45	8.40	3.66	1	16	< 0.0001	HS
DAY 90	4.33	3.32	0	13	< 0.0001	HS



Graph – 13: Mean TFI emotional score on day 0,45,90 between both groups

In group A the mean TFI emotional score were 14.48,8.78,4.68 on day 0,45 and 90 respectively and in group B 14.20,8.40,4.33 on day 0,45 and 90 respectively (table-24,25). Graph – 13 shows the comparison of mean TFI emotional score between both groups on day 0,45 and 90.

DISCUSSION:

Tinnitus is the perception of sound in the absence of an external acoustic stimulus or electrical stimulation of the ear. Tinnitus is a common and occasionally debilitating medical condition. The severity of tinnitus can range from arbitrary to completely disabling. Tinnitus being a common illness, does not have a standardized and effective treatment plan.

The aim of this study is to study the effect of gingko biloba versus caroverine in the treatment of tinnitus. The study was conducted at department of otorhinolaryngology and head and neck surgery, tertiary care centre, Belagavi from January 2021 to December 2021. 80 patients were included in the study and the patients were confirmed cases of tinnitus above 18 years of age.

In this study, subjects were allocated into 2 group. Group A was receiving received 60 mg caroverine per day and group B received 120 mg gingko biloba per day, for a period of 3 months.

Group A consisted of 16 females and 24 males (range: 18 – 75 years) and their mean age was 43.3 ± 13.7 years. There were 11 females and 29 males in group B, and their mean age ranged from min to max at 43.9 ± 13.74 years. Out of total 80 cases, showed statistical gender preponderance among males between both the groups. Likewise, in a study Sachin Jain et al,[3] The majority of the 48 patients with tinnitus who were chosen were between the ages of 30 and 40 (41.67%), followed by 50 and 60 (18.75%). With a male to female ratio of 1.82:1, it was discovered that males had greater rates of tinnitus. This stands in contrast to population statistics, which show that females outnumber males (53.1% to 46.9%).However, in a study conducted by

Jan Skutil et al,[37] in the 197 cases, 117(59.3%) were female showing a female preponderance and the majority age group being between 50-60 years. In the study conducted by Abha kumari et al,[6] out of 50 patients, maximum number were in age group of 41-50 years with a preponderance for males. In the study conducted by Nishad et al,[38] among 86 patients suffering from tinnitus, most of the patients were between 50-60 years (40.69%) followed by 40-50 years (22.09%) with the male to female ratio 2.07:1 showing male preponderance.

In our study, left ear was the most involved with 30 patients (37.5%). However, in a study conducted by Sachin Jain et al,[3] of 48 patients, bilateral ear involvement was most common (35.42%) followed closely by that of right ear (33.33%) and left ear (31.25%).

In our study, improvement in symptoms of tinnitus was objectively measured with pure tone audiometry pitch matching(kHz) and loudness(dB) on day 0,45 and 90. On day 0, the mean value of loudness in patients on gingko biloba was 43.75 ± 6.58 dB, which improved on day 45 to 37.88 ± 6.19 dB and on day 90 to 33.25 ± 5.94 dB showing significant improvement in the loudness in the gingko biloba group with a p value <0.0001. Similarly in a study conducted by Morgenstern and Biermann[39] with 99 patients, 50 of them received gingko biloba and 49 placebo over 12 weeks. Over the period of 12 weeks the loudness improved from a mean value of 42.2 dB to 39 dB in the gingko biloba group and 44.3 dB to 45.1 dB in the placebo group with a p value of 0.015. In a study conducted by Sachin Jain et al,[3] Before starting treatment, out of 48 patients, 24 (50%) had tinnitus that matched a pure tone sound between 41 and 60 decibels, and 20 (41.67%) had a match between 21 and 40 decibels. Three patients (6.25%) experienced tinnitus matching between 61 and 80 dB, while only single

patient had tinnitus matching between 0 and 20 dB. After three months of therapy, six patients in the caroverine group (26.09%) had tinnitus that matched a pure tone sound between 41 and 60 decibels, and seven (30.33%) had a match between 21 and 40 decibels. 9 patients (or 39.13%) had tinnitus that matched with 0-20 dB, while 1 patient (or 4.35%) had tinnitus that matched with 61-80 dB whereas in gingko biloba group, 5(20%) patients experienced tinnitus that matched with a pure tone sound of 41-60 dB, 11 (44 %) had a tinnitus match of 21-40 dB. 9(36%) patients had a tinnitus that matched with 0-20 dB and 0 had a tinnitus matching of 61-80 dB. In a study conducted by Peter Franz et al,[40] of 60 patients, 30 received caroverine and 30 placebo, whose mean value of tinnitus matching was 60dB and 45dB respectively before treatment, which changed to 50dB and 50dB after treatment.

In our study, for subjective assessment of tinnitus, tinnitus functional index questionnaire was used, which contained a total of 25 questions with 8 subscales and adding to a total score of 250. This questionnaire has not been used in any similar studies. The questionnaire was filled on day 0,45 and 90. In the caroverine group, the mean TFI scores on day 0,45 and 90 were 109.00 ± 34.34, 79.48 ± 25.24 and 61.05 ± 22.63 respectively, showing an improvement over 3 months with a significant p value <0.0001. In the gingko biloba group, the mean TFI scores on day 0,45 and 90 were 97.43 ± 28.31,71.55 ± 19.79 and 53.93 ± 16.91 respectively, showing an improvement over 3 months with a significant p value <0.0001. The subscales of the questionnaire comprise of intrusive, control, cognitive, sleep, auditory, relaxation, quality of life, emotional. The mean scores showed improvement across all subscales between both groups. In a study conducted by Sachin Jain et al,[3] of 48 patients, before initiation of treatment mean tinnitus grading scores were 5.08 in caroverine group and 4.48 in

gingko biloba group whereas after 3 months the mean tinnitus grading scores reduced to 4.04 and 3.20 respectively.

In a study conducted by Peter Franz et al,[40] of 60 patients, 30 received caroverine and 30 placebo, were subjectively rated on a five-point scale. Before initiation of treatment a score of 2,3 and 4 was reported by 5,12 and 2 cases respectively. 1 week after treatment a score of 1 and 2 was reported by 4 and 10 cases respectively, showing an improvement in the caroverine group.

In a study conducted by Basha Shaik F et al,[5] of 90 patients,30 received gingko biloba,30 caroverine and 30 multivitamin and were assessed by tinnitus case history questionnaire. In the caroverine group, before treatment 9 were mild,16 moderate and 5 severe whereas after treatment it improved to 13 mild,14 moderate and 3 severe. In the gingko biloba group, before treatment 2 were mild,22 moderate and 6 severe whereas after treatment it improved to 21 mild,9 moderate and 0 severe. In the multivitamin group, before treatment 11 were mild,16 moderate and 3 severe whereas after treatment it improved to 12 mild,5 moderate and 3 severe. Tchq score post-treatment with Gingko biloba showed statistically reduction with a value less than 0.001.

In a study conducted by Radhika Sodadasu et al,[41] of 60 patients,30 received caroverine and intratympanic steroid injection and 30 received placebo, were assessed by Tinntus handicap inventory questionnaire. In the study group, pretreatment mean score was 58.33±24.9 which improved to 46.13±28.79 after 6 months of treatment. Whereas in the control group no significant improvement in THI score was seen.

In a study conducted by Davies E et al,[42] of 909 patients, 448 received gingko biloba and 461 placebos, were assessed by a questionnaire with 3 subscales. In the study group, baseline loudness, awareness of or ability to ignore tinnitus, impact and variability of tinnitus scores were 443,453,458 and 478 respectively which improved to 302,315,302 and 338 respectively after 14 weeks of treatment which is significant.

In our study, in the caroverine group, the mean intrusive scores on day 0,45,90 were 16.05 ± 3.71, 12.23 ± 3.31, 10.25 ± 3.33 respectively and in the gingko biloba group the mean intrusive scores on day 0,45,90 were 14 ± 3.31, 11.45 ± 3.26, 9.30 ± 2.56 respectively which were significant with a p value <0.0001. In the caroverine group, the mean control scores on day 0,45,90 were 13.13 ± 4.60, 11.20 ± 3.69, 9.13 ± 3.52 respectively and in the gingko biloba group the mean control scores on day 0,45,90 were 12.38 ± 3.22, 11.50 ± 3.25, 9.1 ± 2.89 respectively which were significant with a p value <0.0001. In the caroverine group, the mean cognitive scores on day 0,45,90 were 14.85 ± 4, 11.18 ± 2.88, 10.25 ± 2.94respectively and in the gingko biloba group the mean cognitive scores on day 0,45,90 were 14 ± 2.48, 10.88 ± 2.02, 9.95 ± 2.19 respectively which were significant with a p value <0.0001. In the caroverine group, the mean sleep scores on day 0,45,90 were 13.8 ± 4.14, 10.1 ± 3.37, 8.08 ± 3.07 respectively and in the gingko biloba group the mean sleep scores on day 0,45,90 were 12.35 ± 4.03, 9.2±2.73, 6.9 ± 2.41 respectively which were significant with a p value <0.0001. In the caroverine group, the mean auditory scores on day 0,45,90 were 10.25 ± 5.58, 7.15 ± 4.19, 5.38 ± 4.02 respectively and in the gingko biloba group the mean auditory scores on day 0,45,90 were 8.8± 5.47, 6.03 ± 4.05, 4.2 ± 3.31 respectively which were significant with a p value <0.0001. In the caroverine group, the mean relaxation scores on day 0,45,90 were 13.48 ± 5.52, 9.73 ± 4.58, 7.78 ± 4.15 respectively and in the gingko biloba group the mean relaxation scores on day

0,45,90 were 12.4 ± 4.3, 8.85 ± 3.25, 6.88 ± 3.2 respectively which were significant with a p value <0.0001. In the caroverine group, the mean quality of life scores on day 0,45,90 was 11.28 ± 8.81, 7.55 ± 6.72, 5.75 ± 6.1 respectively and in the gingko biloba group the mean quality of life scores on day 0,45,90 was 9.68 ± 8.07, 5.83 ± 5.95, 4.1 ± 4.65 respectively which were significant with a p value <0.0001. In the caroverine group, the mean emotional scores on day 0,45,90 were 14.48 ± 4.72, 8.78 ± 3.96, 4.68 ± 3.98 respectively and in the gingko biloba group the mean emotional scores on day 0,45,90 were 14.2 ± 4.3, 8.4 ± 3.66, 4.33 ± 3.32 respectively which were significant with a p value <0.0001. Improvement in scores was seen across all subscales (intrusive, control, cognitive, sleep, auditory, relaxation, quality of life, emotional) over 3 months which were significant.

CONCLUSION:

Tinnitus is the perception of sound in the absence of any external acoustical or electrical stimulation of the ear. Tinnitus lasting longer than 3 months is considered as chronic tinnitus.

The result of this study implies that the drugs ginkgo biloba and caroverine given orally helped alleviate tinnitus. Improvement was seen in pitch matching and loudness on pure tone audiogram at the end of the study period of 3 months. Improvement was seen in tinnitus functional index scores at the end of 3 months. Improvement was across all subscales of TFI i.e., intrusive (unpleasantness, intrusiveness, persistence), sense of control (reduced sense of control), cognitive (cognitive interference), sleep (sleep disturbance), auditory (auditory difficulties attributed to tinnitus), relaxation (interference with relaxation), quality of life (quality of life reduced), emotional (emotional distress) at the end of 3 months.

Hence, from the observations in this study, we can conclude that ginkgo biloba and caroverine are both effective in alleviating tinnitus and can be administered as an effective mode of treatment as it is widely available, inexpensive, and without any negative side effects on the market.

SUMMARY

This study was conducted in "KLES Dr Prabhakar Kore Hospital, Belagavi during a study period of one year on patients aged between 18 and 65 years with Tinnitus attending ENT & HNS outpatient department".

All patients underwent thorough history taking and clinical examination. These patients were subjected to Pure Tone Audiometry for objective assessment and Tinnitus functional index questionnaire for subjective assessment of tinnitus.

The following results were noted-

- Male predominance was observed in the study, with a surge noted mostly in age demographics of 25-44 years.
- In this study, left ear was most commonly involved.
- Both groups showed statistically significant improvement in tinnitus.
- Both groups showed significant improvement across all subscales of TFI.

According to literature, there is no standardized treatment for tinnitus, hence research is ongoing to alleviate these symptoms for a better quality of life.

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ANNEXURE I – CONSENT FORM

"EFFECT OF GINGKO BILOBA VERSUS CAROVERINE IN THE TREATMENT OF TINNITUS"-A ONE YEAR RANDOMIZED CONTROL STUDY

PRINCIPAL INVESTIGATOR: **REG. NO: BE0120003**
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CO-INVESTIGATOR : _____
Professor,
Department of Otorhinolaryngology and Head and Neck Surgery.

INTRODUCTION AND PURPOSE:

The purpose of the study is to compare the effect of gingko biloba versus caroverine in the treatment of cochlear tinnitus-a one year randomized control study.

PROCEDURE:

If you agree to participate in this study, the relevant data will be collected as per the proforma and the final diagnosis will be confirmed.

After getting inducted in the study, you will be evaluated tinnitus on clinical examination. Patient will then have to undergo pure tone audiometry and will be evaluated.

BENEFITS:

Patient will not be eligible for any kind of monetary benefits or any free services.

RISKS:

Methods applied to do the study are safe.

COST OF PARTICIPATION:

The cost of the Investigation will be borne by the Study Subject. The other indirect expenses will be borne by the Investigator.

PRIVACY AND CONFIDENTIALITY:

The results of the study may be published in journals for scientific purposes. However, your identity will not be revealed. All information collected will be coded so that no one other than the investigator will know your identity.

WITHDRAWAL FROM THE STUDY:

You can withdraw from the study at any time if you wish to do so.

AUTHORIZATION TO PUBLISH THE RESULTS:

The researcher may use the information gathered from this study for presentation in scientific meetings. However, your identity will not be revealed.

QUERIES AND CONTACT:

If you have any questions about rights as a research participant you can contact **Dr. Harsha Hegde**, Chairperson, J.N. Medical college institutional Ethical Committee for Human Subjects Research, scientist, ICMR, National Institute of Traditional Medicine, Belagavi .

CONSENT SUMMARY:

I have been explained all the contents of this consent form in my local language and having understood and clarified all my queries about the study to the best of my knowledge, I hereby give my voluntary consent for participation in the study. I do sign the informed consent form in front of an eyewitness whom I recognize.

Name and Signature/ left thumb impression of the participant:

Name and Signature of the interviewer:

Name and Signature/ left thumb impression of the eyewitness (Relative):

Signature of the guide: **Date:**

ANNEXURE I – PROFORMA

"EFFECT OF GINGKO BILOBA VERSUS CAROVERINE IN THE TREATMENT OF TINNITUS"-A ONE YEAR RANDOMIZED CONTROL STUDY

Date:

O.P. No:

Name: Age:

Sex: Occupation:

Address: Phone No:

CLINICAL PROFILE:

Chief Complaint:

History of Present Illness

Past History:

Personal History:

Family History:

I) General Physical Examination -

Blood Pressure: Pulse: Respiratory Rate:

Pallor Icterus Clubbing Cyanosis Lymphadenopathy Oedema

II) ENT Examination

1. EAR EXAMINATION:

	Right	Left
Pinna		
Pre auricular area		
Post auricular area		
External auditory canal		
Tympanic membrane		

TUNING FORK TESTS:

Rinne's test	256 Hz	
	512 Hz	
	1024 Hz	

Weber's test:

Absolute Bone Conduction test:

2.NOSE EXAMINATION

External appearance		
Root		
Bridge		
Dorsum		
Alae		
Tip		
Columella		

Cold spatula test

Anterior Rhinoscopy

Posterior Rhinoscopy

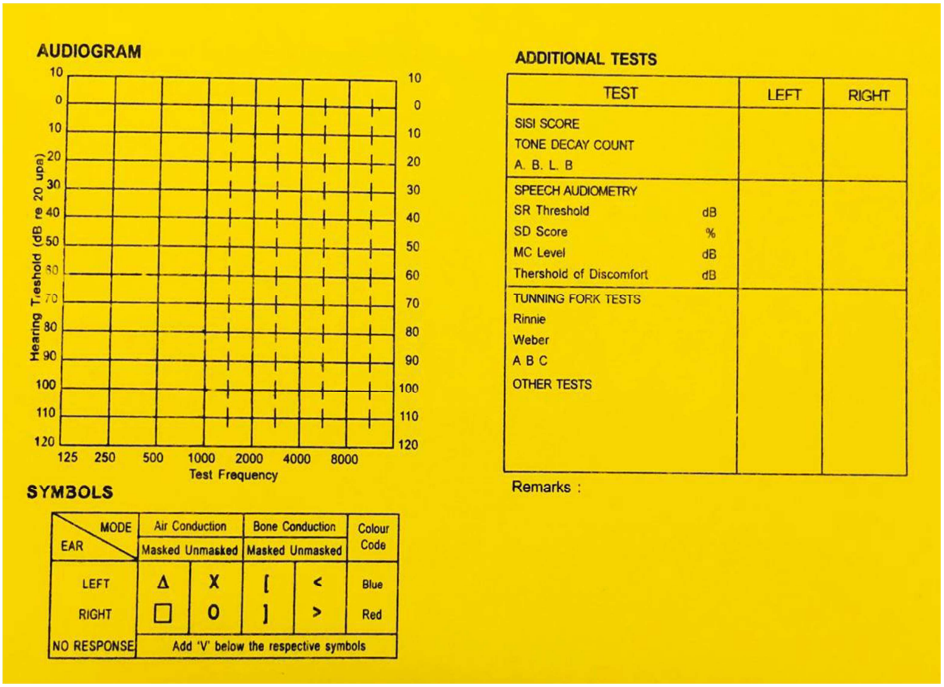
Paranasal Sinus Examination

3 THROAT EXAMINATION :

4. NECK EXAMINATION

Diagnosis:

PURE TONE AUDIOMETRY:



ANNEXURE III – PHOTOGRAPHS

Photograph 1- MAICO MA53 Audiometer

ANNEXURE IV: MASTER CHART

Patient Number	Name	Age	Gender	Ear	Duration	Drug	Pure Tone Audiometry - Pitch Matching (kHz)			Pure Tone Audiometry - Loudness (dB)			Tinnitus Functional Index score																												
							Day 0	Day 45	Day 90	Day 0	Day 45	Day 90	Day 0									Day 45									Day 90									
													Intrusive	Control	Cognitive	Sleep	Auditory	Relaxation	Quality of life	Emotional	Total(out of 250)	Intrusive	Control	Cognitive	Sleep	Auditory	Relaxation	Quality of life	Emotional	Total(out of 250)	Intrusive	Control	Cognitive	Sleep	Auditory	Relaxation	Quality of life	Emotional	Total(out of 250)
1	yallappa	34	male	right	6 months	gingko biloba	5	5	5	60	50	50	15	11	15	16	3	3	5	21	89	13	11	13	12	2	3	5	16	75	13	10	14	12	2	3	5	13	72
2	komal	35	female	left	6 months	caroverine	5	5	4.5	50	50	45	19	22	12	20	0	30	0	20	123	17	22	11	18	0	24	0	16	108	15	20	11	16	0	21	0	13	96
3	shobha	28	female	right	6 months	gingko biloba	5	5	4	40	40	35	18	17	9	12	0	12	0	13	81	17	17	8	12	0	9	0	10	73	14	14	8	10	0	7	0	6	59
4	humavan	59	male	right	7 months	caroverine	2.5	2.5	2	45	45	40	10	0	0	10	9	0	0	2	31	10	0	0	8	6	0	0	0	24	10	0	1	6	5	0	0	0	20
5	dundesh	75	male	left	1 year	gingko biloba	3.5	3.5	3	50	50	40	20	18	13	12	0	17	0	16	96	19	19	12	12	0	15	0	12	90	18	18	13	11	0	15	0	10	85
6	sagar	16	male	right	6 months	caroverine	5	4	4	60	60	50	24	12	18	12	0	24	0	20	110	22	13	17	10	0	23	1	15	101	20	12	16	8	0	19	1	10	86
7	anil	25	male	left	8 years	gingko biloba	3.5	3.5	3	40	35	35	12	13	9	8	0	8	0	15	65	12	13	9	7	0	6	0	12	59	10	10	10	6	0	5	0	6	37
8	jakappa	55	male	both	6 months	caroverine	3.5	3.5	3	40	40	30	21	16	15	15	0	15	0	18	100	19	18	14	14	0	12	0	14	91	17	16	13	12	0	9	0	8	75
9	mahaning	55	male	both	8 months	gingko biloba	2	2	2	30	30	25	10	12	17	6	0	11	1	10	68	8	12	15	6	0	9	0	7	56	9	11	15	5	0	8	0	4	52
10	kempanna	40	male	both	9 months	gingko biloba	2.5	2.5	2.5	30	30	25	7	13	12	8	2	9	0	10	61	6	14	11	7	1	8	0	7	54	6	12	10	7	0	6	0	4	45
11	nagappa	55	male	left	1 year	gingko biloba	3	3	2.5	40	40	35	13	12	15	7	1	7	0	9	64	12	14	13	7	1	6	0	7	62	12	13	14	7	0	3	0	4	53
12	pradeep	30	male	right	1 year	caroverine	2	2	1.5	35	35	30	12	6	11	3	0	10	1	7	50	10	8	11	3	0	9	1	5	49	10	8	11	3	0	8	1	3	44
13	sunita	55	female	both	1 year	gingko biloba	1.5	1.5	1	40	40	40	6	6	11	5	1	9	0	11	45	6	8	11	5	0	8	0	8	40	7	6	11	5	0	6	0	5	40
14	priyanka kamble	25	female	left	6 months	caroverine	3	2.5	2.5	40	40	35	14	10	14	11	1	12	0	11	73	13	11	13	10	0	8	0	8	61	13	10	13	10	0	7	0	5	68
15	sadashiv gopal	60	male	right	8 months	caroverine	2.5	2	2	35	35	30	10	9	11	7	3	9	0	8	80	10	9	9	7	2	6	0	4	68	9	7	10	6	1	4	0	0	58
16	rakesh jakappa	32	male	both	6 months	gingko biloba	3	2.5	2	45	40	40	15	14	13	7	0	17	0	14	65	13	15	11	7	0	12	0	10	56	11	14	11	6	0	9	0	7	41
17	basavaraj subrao	60	male	both	8 months	gingko biloba	2.5	2	2	45	40	35	10	11	13	8	5	11	2	7	65	9	12	10	7	4	9	1	4	56	7	9	9	6	2	7	1	1	42
18	laxman arjun	37	male	right	6 months	gingko biloba	2	1	1	35	30	20	11	15	15	9	1	16	1	16	84	10	15	13	6	0	14	0	12	70	9	11	12	4	0	12	0	9	57
19	lakkavva yallappa	49	female	left	6 months	caroverine	2	2	1.5	35	30	30	10	10	11	7	2	10	0	8	58	9	11	10	6	1	9	0	6	61	9	9	10	6	0	7	0	2	43
20	shobha vishwanath	43	female	right	8 months	gingko biloba	3	2	2	45	40	40	14	15	12	15	15	15	14	15	115	12	13	9	14	12	12	12	11	95	11	12	9	11	11	9	9	5	77
21	saraswati irappa	50	female	right	1 year	caroverine	5	4	3.5	50	40	35	14	13	13	14	11	14	16	13	108	12	13	12	13	9	12	14	8	91	12	11	11	10	8	9	13	5	79

22	samina asif	32	female	left	1 year	caroverine	3.5	2.5	2	50	50	40	17	16	16	17	15	16	19	17	133	15	16	13	14	13	13	17	13	114	13	13	11	11	10	10	13	8	89
23	nagavva	40	female	right	1 year	caroverine	3	2.5	2	40	40	30	16	17	19	16	14	14	17	19	132	14	16	16	15	12	13	13	15	115	12	13	14	12	11	10	11	9	92
24	suresh bhistappa	27	male	both	2 years	gingko biloba	2.5	2	1.5	40	30	30	13	13	14	15	13	15	17	17	117	12	13	12	13	10	14	13	14	101	10	9	11	10	7	11	10	9	78
25	yallappa ningappa	38	male	right	10 months	gingko biloba	3	2.5	2	40	30	30	17	16	17	15	13	14	17	17	126	14	16	15	13	12	11	13	12	106	13	13	13	10	9	8	9	6	81
26	basavaraj patil	27	male	both	1 year	gingko biloba	2	1.5	1.5	50	50	45	15	11	16	17	14	13	18	16	120	11	11	11	13	12	9	17	8	92	6	5	9	5	4	9	7	3	48
27	abubakar ghopdav	40	male	left	1 year	caroverine	3	2	2	40	30	30	17	15	13	17	11	12	16	18	119	9	10	10	9	8	8	10	7	71	7	7	9	8	5	7	8	3	54
28	reshma abubakar	34	female	left	1 year	gingko biloba	3	2	2	30	30	25	15	15	13	20	12	17	16	16	124	11	11	11	10	9	13	12	8	85	9	8	9	7	7	7	7	1	55
29	khatakahmed jamadar	61	male	left	1 year	gingko biloba	2	2	1.5	40	35	30	12	12	12	16	10	14	15	20	113	10	12	10	7	7	9	8	7	70	8	8	8	4	4	7	7	5	51
30	subash tippanna	45	male	both	2 years	gingko biloba	1.5	1.5	1	40	35	30	14	14	14	15	12	14	22	19	124	5	5	8	7	4	8	6	5	48	6	5	8	6	3	5	8	5	46
31	rushikesh gawade	36	male	right	1.5 years	gingko biloba	2.5	2	2	40	35	35	15	15	17	17	16	18	19	22	139	9	10	11	10	7	9	8	8	72	7	7	10	7	6	9	7	2	54
32	dundesh hosmani	75	male	both	1 year	caroverine	2	1.5	1.5	45	40	40	16	15	16	13	13	17	7	15	122	7	6	8	6	7	11	11	7	63	6	5	8	5	4	8	7	2	45
33	pooja yallappa	18	female	left	6 months	gingko biloba	2.5	2	2	40	35	35	14	14	14	10	10	14	15	14	105	11	13	11	8	7	11	11	6	78	9	11	9	6	4	9	8	1	57
34	humayan dilawar	59	male	right	6 months	caroverine	1.5	1	1	40	35	35	18	18	18	14	14	17	20	19	138	12	11	12	9	10	9	10	10	83	10	9	9	4	6	8	7	2	55
35	sunita darendra	55	female	right	1 year	gingko biloba	3	2	1	50	40	35	14	14	13	11	10	14	14	9	99	11	12	10	7	6	9	7	3	66	9	9	9	4	5	6	6	2	50
36	priyanka kamble	26	female	left	1 year	caroverine	2	1.5	1.5	40	40	30	15	11	13	12	10	12	13	11	97	9	10	10	7	4	7	9	3	59	6	6	6	7	3	6	5	1	40
37	shobha hugar	28	female	right	1 year	gingko biloba	2	1.5	1.5	50	40	35	15	14	15	16	11	17	18	15	121	9	10	11	10	7	11	13	8	80	7	8	9	7	4	8	8	3	54
38	sadashiv gopal	63	male	right	8 months	caroverine	2.5	2	1.5	40	40	30	16	11	16	13	11	17	16	15	115	11	10	10	8	7	7	10	6	105	8	9	8	5	3	6	6	3	48
39	fakiragauda	38	male	left	8 months	caroverine	2	1.5	1	30	30	25	15	19	15	13	12	17	16	16	123	12	14	10	7	9	9	10	6	77	8	10	11	8	8	7	7	1	60
40	mahaning lakappa	55	male	both	8 months	gingko biloba	3	2.5	2	50	45	40	9	15	14	11	10	17	15	12	107	8	9	9	7	6	11	9	6	65	6	8	11	5	5	6	6	0	47
41	mallikarjun patil	35	male	both	10 months	caroverine	2	1.5	1	50	45	40	15	15	16	16	11	16	16	15	121	13	14	13	13	8	13	12	10	96	9	10	9	7	3	8	7	2	55
42	laleeta krishnappa	37	female	left	3 years	caroverine	2	1.5	1	50	50	40	15	13	16	13	13	17	20	13	156	10	11	11	10	9	14	12	9	85	6	6	10	7	4	9	8	2	52
43	laxmi halagi	26	female	left	1 year	caroverine	2	2	1.5	40	35	35	19	15	19	19	15	17	19	16	139	15	14	12	7	9	10	13	7	87	5	9	9	4	4	7	6	2	48
44	irangowda goudar	21	male	both	6 months	caroverine	3	2.5	2	50	50	50	17	15	15	10	11	14	16	14	112	12	10	10	7	6	7	8	5	65	6	6	8	6	4	7	5	0	42
45	laxmibhai mahadev	65	female	right	6 months	gingko biloba	3	3	2	50	45	40	19	14	14	13	11	17	18	13	118	15	9	9	6	7	9	9	5	73	7	6	8	7	5	9	7	1	50
46	shobha maruti	47	female	left	6 months	caroverine	2.5	2	2	40	30	30	15	15	14	13	14	16	14	14	107	9	9	11	14	5	7	7	5	63	7	7	10	6	4	6	6	3	49
47	mallappa dundappa	56	male	left	6 months	gingko biloba	2	1.5	1.5	50	40	30	18	10	16	13	7	12	9	17	102	16	14	15	12	6	9	8	14	86	13	9	13	7	4	7	6	7	66
48	jagadish baburao	42	male	both	8 years	gingko biloba	3	2	1.5	50	40	35	19	11	18	15	12	14	6	16	111	13	12	11	10	9	12	6	9	82	10	9	9	7	6	8	1	2	52
49	arun yellappa	47	male	right	1.5 years	gingko biloba	6	5	4	55	50	40	15	8	15	15	12	15	8	15	103	12	7	12	9	12	10	4	10	76	10	6	8	5	10	7	0	4	51
50	padma deshpande	70	female	right	6 months	caroverine	6	4	3	70	60	55	20	12	17	18	12	10	8	14	112	15	11	14	15	9	8	1	9	57	12	7	10	9	5	6	0	2	52
51	raghavendra	63	male	both	6 months	gingko biloba	5	4	3.5	50	40	35	16	10	15	12	9	6	5	11	84	13	9	11	9	6	3	1	6	58	10	9	9	6	2	2	0	1	39
52	sandeep kanuga	45	male	both	6 months	gingko biloba	4	3	2.5	45	40	30	13	8	12	7	9	6	5	8	68	10	9	7	6	6	3	1	4	46	8	6	7	4	3	1	0	0	28
53	gayatri rohan	33	female	left	6 months	caroverine	4	3	2.5	50	40	30	15	12	15	12	9	12	8	14	97	10	10	13	9	6	9	4	9	70	8	9	11	6	3	4	0	3	44
54	rahul danesh	33	male	right	2 years	gingko	3.5	3	2	50	40	30	11	5	12	12	9	7	7	13	76	8	6	9	10	4	4	0	6	48	7	6	7	7	1	3	0	0	30

						biloba																																	
55	ramesh vittal	40	male	left	8 months	caroverine	3	2	1	40	30	30	10	5	9	9	6	9	4	11	63	7	6	6	6	3	6	3	6	43	5	3	4	3	0	3	0	2	20
56	sanjana viresh	41	female	both	6 months	gingko biloba	5	4	3	40	30	25	15	12	13	12	10	9	4	10	85	12	12	10	9	7	6	0	6	62	10	9	8	6	4	4	0	2	43
57	kavita kamble	40	female	both	9 months	caroverine	4	3	2.5	50	40	30	12	9	10	12	9	6	4	11	73	9	8	9	10	6	4	0	6	52	8	6	8	7	4	3	0	2	36
58	maruti nagale	47	male	left	6 months	gingko biloba	5	4	3	40	30	30	12	10	12	12	9	9	8	11	83	9	9	9	9	6	6	3	6	57	7	6	10	6	4	3	0	4	40
59	kavita karadi	40	female	right	2 years	gingko biloba	4	3	3	40	30	30	12	10	12	9	10	7	4	8	72	9	9	9	6	6	4	0	1	54	8	6	7	3	6	4	0	0	33
60	raghav vinay	49	male	left	8 months	caroverine	4	3	3	60	50	45	13	10	12	12	9	6	8	11	81	10	9	9	6	7	6	4	6	57	10	9	10	6	6	3	0	0	43
61	mallesh goudar	34	male	left	7 months	gingko biloba	3	2	2	50	40	30	13	10	12	9	9	6	4	8	71	10	9	9	7	6	6	0	3	44	8	9	7	4	3	3	0	0	33
62	shivappa more	52	male	left	7 months	caroverine	4	3	2	40	30	30	12	7	12	9	9	6	7	11	73	9	9	9	9	6	3	0	6	51	8	6	8	7	4	3	0	1	37
63	suresh more	47	male	right	10 months	gingko biloba	3	2.5	2	40	30	30	13	7	12	7	9	12	5	11	76	12	10	12	10	6	6	3	6	58	8	6	10	6	4	6	0	6	46
64	vinod patil	39	male	left	6 months	caroverine	5	4	3.5	50	40	35	16	10	15	12	9	8	5	11	86	12	10	12	10	6	6	3	6	65	10	9	10	7	4	3	0	0	45
65	yallappa maradi	34	male	right	8 months	gingko biloba	4	3	2.5	40	30	30	12	7	12	11	9	6	4	11	72	11	7	9	9	7	4	0	6	53	10	6	7	6	6	1	0	2	35
66	mahesh mali	33	male	left	6 months	caroverine	4	3	3	40	40	35	15	15	16	17	16	14	21	15	130	12	10	10	11	10	10	11	7	81	9	7	8	7	8	7	10	8	64
67	nagesh hanji	34	male	right	10 months	gingko biloba	5	4	4	45	40	35	19	17	18	18	17	17	23	20	149	13	12	13	12	11	11	15	11	98	11	10	13	11	10	12	13	8	88
68	malan patil	38	female	left	1 year	caroverine	4.5	4	3	50	40	35	20	17	20	19	19	20	27	24	166	14	13	14	12	13	12	18	13	109	11	10	12	11	10	11	15	9	89
69	vasant karadi	33	male	both	2 years	gingko biloba	3	2	2	45	40	30	20	18	19	19	17	17	22	23	155	13	10	10	10	11	11	15	13	93	11	11	12	12	9	11	14	10	90
70	parisa surendra	73	female	left	6 months	gingko biloba	5.5	5	4	45	40	30	17	15	20	20	20	20	27	22	161	21	20	15	17	13	13	17	13	129	10	11	12	10	10	11	14	9	87
71	shivaraj	59	male	right	2 years	gingko biloba	3	2	2	45	40	30	12	13	15	14	14	14	19	17	118	13	11	11	10	11	11	16	16	96	7	8	9	8	8	8	11	6	65
72	vijay ningappa	24	male	left	6 months	caroverine	4	3	2	40	40	30	23	20	22	22	21	21	29	23	181	19	18	16	18	17	17	23	16	144	12	10	13	10	11	11	14	9	91
73	sundharavva	44	female	left	8 months	caroverine	6	5	4.5	60	50	45	21	17	20	20	20	20	27	23	168	16	14	13	14	11	11	15	11	105	10	9	12	10	11	11	14	10	87
74	radha patil	60	female	right	8 months	caroverine	5	4	4	50	40	35	19	18	19	18	15	14	19	17	139	14	12	13	12	13	13	16	14	110	13	13	15	12	13	13	19	12	108
75	mohan goudar	40	male	both	2 years	caroverine	3	2	2	40	35	35	12	10	13	12	12	11	15	14	99	9	10	11	9	11	11	15	15	98	14	12	14	11	12	10	15	10	91
76	maruti kallappa	47	male	right	9 months	caroverine	5	4	4	50	40	35	15	11	15	12	9	7	4	11	85	13	10	12	9	9	6	0	7	66	11	9	10	7	7	3	0	4	51
77	narayan powar	51	male	both	8 months	caroverine	5	4	3	55	40	35	15	10	15	12	7	9	1	11	80	12	10	12	10	6	6	0	6	56	10	7	8	7	3	5	0	2	42
78	basavaraj nagappa	60	male	both	1 year	caroverine	4	3	2.5	40	30	30	15	10	12	12	6	9	1	14	79	12	10	9	9	6	8	0	10	64	13	10	10	8	6	8	0	7	59
79	malikarjun allappa	53	male	left	6 months	caroverine	4	3	3	40	35	30	21	18	20	20	18	17	22	23	162	15	11	11	11	11	11	15	12	100	15	12	14	13	12	10	13	11	92
80	veerbadrappa kadakal	41	male	right	1 year	caroverine	5	4	4	40	40	30	23	21	21	19	14	14	15	12	139	11	11	11	9	11	11	16	13	114	13	14	15	15	13	14	19	11	93
													1202	1020	1154	1046	762	1035	838	1147	8257	947	908	882	772	527	743	535	687	6041	782	729	808	599	383	586	394	360	4599