

ANTIOXIDANT THERAPY IN THE ELDERLY WITH TINNITUS: SYSTEMATICS REVIEW

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Abstract

Tinnitus is one of the most prevalent and annoying disorders that affect the ear and the auditory system. It is one of the most important symptoms in neurootology, along with hearing loss, vertigo, dizziness, and nausea. It can cause a variety of somatic and psychological disorders that interfere with a person's quality of life. There is a correlation between oxidative stress and tinnitus. Hair cell apoptosis, cochlear degeneration, alterations to supporting structures and stria vascularis, changes to the nerve fibers of the acoustic nerve, irregular neuronal activity in the auditory pathway, and malfunction in the central cortex are all possible outcomes of oxidative stress. Animal models of aging, noise damage, and ototoxicity have been used to investigate the relationship between oxidative stress and the death of hair cells. Antioxidants are substances that can take on a wide variety of chemical structures, but they are categorized as a single class because they share the ability to neutralize the effects of highly reactive and potentially damaging free radicals. These radicals are produced when foods undergo the necessary oxidation reactions that are a natural part of the digestion process. Antioxidant supplementation with vitamins, minerals, phytochemicals, and alpha-lipoic acid (ALA) might have therapeutic effects on tinnitus by reducing the subjective discomfort and the level of severity caused by the ringing in the ears.

Keyword: *Antioxidant; Elderly; Hearing; Inflammation; Tinnitus*

INTRODUCTION

Tinnitus is one of the most prevalent and distressing otology disorders. It affects between 10 and 30 percent of the population, with roughly 3 to 4 percent of people reporting having it at least once in their lifetime. Tinnitus is one of the most common and distressing otology diseases. Along with hearing loss, vertigo, dizziness, and nausea, it is one of the most important symptoms in neurootology, and it can cause a variety of somatic and psychological illnesses that interfere with one's quality of life.¹⁻³

Tinnitus can be brought on by a wide variety of factors, such as cardiovascular pathologies, otic pathologies, head injuries, electric shocks, otic barotraumas, and it can also be a side effect of a number of different medications.¹⁻³ In addition to this, because of the effect it has on the functionality of those who are affected, it is a substantial contributor to morbidity in the aged.² In the senior population, tinnitus can be caused by a wide variety of diseases, such as those related to otology, metabolism, the nervous system, or the cardiovascular system.⁴

Tinnitus has no recognized etiology, and the pathogenic mechanisms underlying the condition are only partially understood. At this time, there is no medication treatment that is successful; nonetheless, the treatment modalities mentioned in the literature provide varying levels of success.⁵ It has been hypothesized that oxidative stress plays an important part in the pathogenesis of tinnitus.^{6,7}

This is due to the fact that it has the potential to bring about cellular changes in hair cells, hair cell apoptosis, cochlear degeneration, changes in supporting structures and stria vascularis, changes in nerve fibers of the acoustic nerve, irregular neural activity in the auditory pathway, and dysfunction of the central cortex.^{6,7} Another study found that individuals with tinnitus had greater plasma concentrations of oxidative stress biomarkers and lower antioxidant activity than healthy people did. This was in contrast to the results of the control group.^{8,9}

The purpose of this study is to demonstrate the effectiveness of antioxidant therapy in the treatment of tinnitus in older adults using a systematic review.

METHODS

By adhering to the guidelines outlined in Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author made certain that the study was carried out in the acceptable manner and that the results were reliable. The research was carried out in a manner consistent with these guidelines, which ensured its quality. This is done to ensure that the conclusions of this study are true, and it is done in order to guarantee this. The goal of this literature review is to comprehend antioxidant therapy in the elderly with tinnitus: a systematics review by evaluating or analyzing the research that has been done in the past on the subject.

The primary purpose of this article is to stress how vital it is to give some thought to the problems that have been raised, which is the paper's overarching goal. The researchers that took part in the study had to demonstrate that they met one or more of the following criteria: 1) The paper needs to be written in English in order for it to be considered for publication, and the primary focus of the research needs to be on the cause or factor that contributes to patients dropping out of infertility treatment. This requirement must be met in order for the paper to be accepted. 2) This evaluation takes into consideration articles that were produced after 2018 but before the time period that is the primary focus of this systematic investigation. Editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are substantially identical to already published journal publications are some examples of studies that are not permitted.

We used "antioxidant therapy", "elderly", and "tinnitus" as keywords. The search for studies to be included in the systematic review was carried out from February, 18th 2023 using the PubMed and SagePub databases by inputting the words: (*"antioxidant s"[All Fields] OR "antioxidants"[Pharmacological Action] OR "antioxidants"[MeSH Terms] OR "antioxidants"[All Fields] OR "antioxidant"[All Fields] OR "antioxidating"[All Fields] OR "antioxidation"[All Fields] OR "antioxidative"[All Fields] OR "antioxidatively"[All Fields] OR "antioxidatives"[All Fields] OR "antioxidizing"[All Fields]*) AND (*"therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "therapies"[All Fields] OR "therapy"[MeSH Subheading] OR "therapy"[All Fields] OR "therapy s"[All Fields] OR "therapys"[All Fields]*) AND (*"aged"[MeSH Terms] OR "aged"[All Fields] OR "elderly"[All Fields] OR "elderlies"[All Fields] OR "elderly s"[All Fields] OR "elderlys"[All Fields]*) AND (*"tinnitus"[MeSH Terms] OR "tinnitus"[All Fields]*) used in searching the literature.

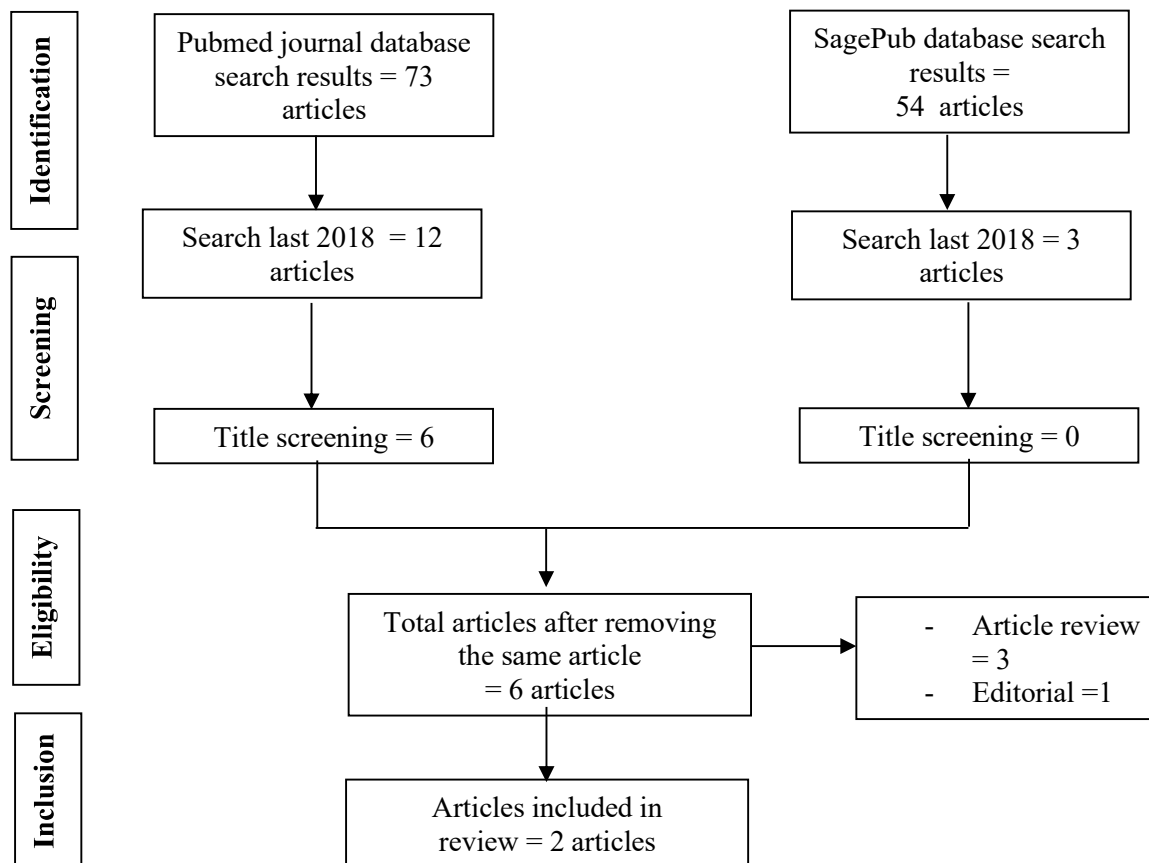


Figure 1. Article search flowchart

The writers used the abstract and title of each study to determine whether or not it qualified for inclusion. After then, the authors chose previous studies to use for this article. Analysis of a large number of publications following the same pattern led to the discovery of this result. All English contributions are required to be previously unpublished. Only those studies were considered for inclusion in the systematic review that fulfilled all of the criteria.

The search only delivers results that are helpful to the user. We don't consider research that doesn't meet our standards. Following that, the research will be analyzed. The names of people, the authors of the study, the publication date, the location, the study activities, and the parameters were found in this study. Each author conducted their own investigation into the research that was outlined in the publication's title and abstract before making a decision regarding which publications to examine in greater detail.

The next step will be to examine all of the articles that are qualified for inclusion in the review because they fulfill the requirements outlined in the review's inclusion criteria. Following that, we will select the papers that will be discussed in the review depending on what we have discovered. Based on this criterion, certain manuscripts are selected to undergo an evaluation. In order to simplify the process of selecting papers for further evaluation as much as is humanly practicable.

RESULT

Petridou, et al (2019)¹⁰ showed serum total antioxidant capacity (TAC), oxidized LDL (oxLDL), and superoxide dismutase (SOD), tinnitus loudness, frequency, and minimum masking level (MML), as well as Tinnitus Handicap Inventory questionnaire (THI), Tinnitus Functional Index (TFI), and Visual Analogue Scale (VAS) scores, were evaluated at baseline and follow-up. Only in the antioxidant group did tinnitus loudness and MML decrease substantially from baseline to post-measure (p <0.001), with the overall change being significantly different between the two groups post-intervention (p <0.001). THI and VAS were only reduced in the antioxidant group. The differences in serum TAC, SOD, and oxLDL modifications following an intervention were insignificant.

Table 1. The literature include in this study

Author	Origin	Method	Sample Size	Result
Petridou, 2019 ¹⁰	Greece	Randomized, double-blind, placebo-controlled clinical trial	70 patients	Tinnitus patients who receive antioxidant therapy appear to experience a reduction in the subjective discomfort as well as the intensity of their tinnitus.

Procházková, 2018	Czech Republic	Randomized clinical trial	197 patients	EGB 761® and pentoxifylline were similarly effective in reducing the loudness and annoyance of tinnitus as well as overall suffering of the patients. The incidence of adverse events was lower in the EGB 761® group.
Radunz, 2020 ¹¹	Brazil	Randomized clinical trial	35 patients	

Second study conducted with sub-chronic or chronic tinnitus patients were enrolled in double-blind trial and randomized to receive 120 mg EGB 761® or 600 mg pentoxifylline. For both treatment groups, significant improvements were observed in the Mini-TQ, the 11-Point Box Scales for tinnitus loudness and annoyance, the HADS anxiety score and the SDS. There was no relevant difference with regard to tinnitus-related outcomes between the two treatment groups. 20 adverse events were documented in EGB 761® group and 36 adverse events were reported for pentoxifylline group. No serious adverse event was reported during the study.¹²

Radunz, et al (2020)¹¹ found a substantial association between the tinnitus handicap inventory and the visual analogue scale. After 90 days of treatment with Ginkgo biloba extract EGB 761 and/or hearing aids, we noticed a considerable improvement in the patient's own perception of the loudness and intensity of their tinnitus. There was found to be no association between the moment at which tinnitus first appeared and the degree to which an individual perceived its loudness and intensity. Hearing aids worked better for individuals whose tinnitus had been present for a shorter period of time, whereas the effectiveness of Ginkgo biloba extract was not dependent on the length of time the condition had been present.

DISCUSSION

Tinnitus is a common and debilitating otology illness. It is one of neurootology's most critical symptoms, along with hearing loss, vertigo, dizziness, and nausea, and it can cause many somatic and psychological disorders that affect quality of life. Oxidative stress may cause tinnitus. Oxidative stress can cause hair cell apoptosis, cochlear degeneration, supporting structures and stria vascularis changes, acoustic nerve nerve fiber changes, irregular neural activity in the auditory pathway, and central cortex dysfunction. Oxidative stress-related hair cell apoptosis has been studied in animal models of aging, noise damage, and ototoxicity.^{6,10}

The mitogen-activated protein kinase/c-Jun N-terminal kinase (MAPK/JNK) pathway is activated by oxidative stress, which then leads to the release of cytochrome c from mitochondria. Damage to the mitochondrial membrane and activation of the caspase pathway, both of which promote apoptosis, are both caused by cytochrome c. It has been demonstrated that mild doses of oxidative stress can produce mitochondrial DNA (mtDNA) deletions in hair cells in organ of Corti preparations, which makes the hair cells more susceptible to additional damage. In addition, there is a possibility that oxidative stress is connected to endothelial damage inside the cochlear microcirculation.¹³

Tinnitus sufferers have higher plasma oxidative stress indicators and reduced antioxidant activity than healthy people. However, tinnitus research on antioxidant supplementation is scarce and inconsistent. Oxidative stress indicators are rarely measured. Flavonoid-rich Ginkgo Biloba reduces tinnitus discomfort. Antioxidants and phospholipids treatment for 18 weeks reduced oxidative stress and tinnitus intensity. Other studies found no advantage. Animal studies have revealed antioxidants' cochlea-protective mechanisms. ALA protects animal models against noise-induced hearing loss.^{14,15}

Antioxidants are compounds of many different chemical forms, grouped together because they all have the property of counteracting the effects of the highly reactive harmful free radicals that are formed as a result of essential oxidation reactions that normally occur in foods.^{16,17} The possible mechanism of antioxidant action was first explored when it was recognized that a substance with anti-oxidative activity tends to be a substance that is easily oxidized. Utilization of oxygen to produce energy through the metabolism of food nutrients acts as a prerequisite for the survival of all living things.¹⁸

The overall changes were significantly different between the two groups at the frequencies of 250 Hz, 2000 Hz, 4000 Hz, 10,000 Hz, and 12,000 Hz. The study that Petridou conducted indicated antioxidant supplementation led to significant improvements of hearing thresholds across all frequencies. Tinnitus patients could benefit from a better understanding of speech and language if improved thresholds at frequencies between 250 Hz and 8000 Hz are developed. These are the frequencies that are employed for speech recognition, and as a result, improved thresholds at these frequencies are of considerable importance.¹⁰

The researchers believe that the therapeutic effect on tinnitus that they found in this study can be linked to the protective mechanisms of antioxidants present in the supplements, which protect the cochlear hair cells from damage caused by reactive oxygen species (ROS). Experiments conducted with animal models, in-vitro assays, or auditory cell lines in situations of ototoxicity, age-related hearing loss, or noise-induced hearing loss have proven this to be the case. In a recent study that used cochlea explant culture from mice, researchers found that resveratrol, DL- α -lipoic acid, and a-tocopherol protected against the loss of hair cells caused by gentamicin.^{19,20}

Reactive oxygen species (ROS) produced in the presence of O₂ by mitochondria, phagocytic cells, peroxisomes, and cytochrome P450 enzymes under physiological conditions can have multiple functions in the human organism. On the one hand, they participate in the cell signal transduction cascade leading to the activation of several transcription factors responsible for regulating the expression of genes relevant for cell growth and differentiation.²¹

Antioxidants serve as hydrogen donors and are able to cut out the propagation phase of the reaction. Antioxidants often eliminate free radicals by oxidizing themselves and acting as reducing agents like thiols, ascorbic acid, or polyphenols. This process renders the free radicals harmless. In most cases, the most widely used antioxidants are hydroxyphenol molecules that have been modified with a variety of different ring substitutions.²¹

Antioxidant radicals are stabilized by delocalizing the electrons that are locally bound to them; as a result, antioxidant free radicals do not readily promote the formation of new free radicals. They react even further with the free radicals in lipids to generate molecules that are both stable and complicated. The ability of phenolic antioxidants is directly proportional to the amount of phenol groups that occupy positions 1,2 or 1,4 in the aromatic ring, in addition to the volume and electronic properties of the ring substituents that are present.²¹

Other systematic review showed inflammation and oxidative stress, which are both associated with aging, play a role in the development and progression of audio-vestibular dysfunction. It has been suggested that diets that include anti-inflammatory and antioxidant benefits could help ease the symptoms of this sickness. The elderly are more likely to experience hearing discomfort if they have a poor protein intake, which is linked to both oxidative stress and a diet high in fat.²²

A higher consumption of carbohydrates and sugar has been shown to have a positive correlation with the occurrence of audio-vestibular dysfunction. On the other hand, consuming a diet more typical of the Mediterranean region has been shown to protect against the condition. It is also beneficial to consume antioxidants in the form of vitamins A, C, and E; engage in physical exercise; get a sufficient amount of quality sleep; refrain from smoking; drink alcohol in moderation; and limit exposure to loud noise.²²

Antioxidants can be made by our bodies, and they can also be absorbed through the elements of food, namely in the form of fruits and vegetables. We can eliminate the necessity for taking antioxidant supplements if we increase our consumption of foods that naturally contain antioxidants. As a result, in order to maintain our health, we need consume a variety of vegetables and fruits that serve as a source of antioxidants because they are rich in vitamins A, C, and E as well as other minerals.

CONCLUSION

Tinnitus is a symptom. It can cause hearing loss, tension, ear damage, blood pressure, tumors, and atherosclerosis. Loud noise damages the fragile inner ear hair cells that convert sound into nerve impulses, causing tinnitus. Antioxidant supplementation with vitamins, minerals, phytochemicals, and alpha-lipoic acid (ALA) could have beneficial benefits on tinnitus by lowering the subjective discomfort and the intensity of the ringing in the ears.

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