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Effect of zinc on hearing

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ABSTRACT

Zinc is an essential element that is essential for our body and has both antioxidant and anti-inflammatory properties. It plays a major role in the physiological functions of body systems, and naturally takes place in the physiological processes that make up hearing. Especially as the role of zinc in inner ear physiology and auditory neural connections is investigated, researches related to the use of zinc in addition to the treatment of hearing loss caused by pathologies in the inner ear and/or neural pathways have increased recently. In this study, studies on the usability of zinc to support the treatment of hearing loss and tinnitus were summarized and compiled. It was concluded that most of the studies evaluating the effectiveness of zinc in sudden sensorineural hearing loss and otitis media did not show any benefit. On the other hand, in studies investigating the relationship between presbycusis and zinc, the opinion that low serum zinc values may lead to presbycusis is dominant. In most of the studies evaluating the effectiveness of zinc on tinnitus, no significant improvement was found. More studies with a high level of evidence are needed in this area.

Keywords: zinc, tinnitus, otitis media, presbycusis, sudden sensorineural hearing loss

ÖZ

Çinkonun işitme üzerine etkisi

Çinko vücudumuz için gerekli olan ve hem bir antioksidan hem de antienflamatuvar olma özelliği taşıyan önemli bir elementtir. Vücut sistemlerinin fizyolojik fonksiyonlarında büyük rol oynar, doğal olarak işitmeyi oluşturan fizyolojik süreçlerin içerisinde de yer almaktadır. Özellikle çinkonun iç kulak fizyolojisindeki ve işitsel nöral bağlantılardaki rolü araştırıldıkça iç kulak ve/veya nöral yollardaki patolojiler sebebiyle oluşan işitme kayıplarının tedavisinde çinkonun ek olarak kullanılabileceği ile alakalı araştırmalar son dönemde daha da artmıştır. Bu araştırma ile işitme kayıplarının ve tinnitusun tedavisine destek amacıyla çinkonun kullanılabilirliğine yönelik çalışmalar özetlenerek derlenmiştir. Ani sensörinöral işitme kaybında, otitis media hastalığında ve tinnitus üzerindeki çinkonun etkinliğinin değerlendirildiği araştırmaların çoğunda fayda göstermediği sonucuna varılmıştır. Diğer yandan, presbiakuzi ve çinko ilişkisinin araştırıldığı çalışmalarda serum çinko değerlerinin düşük olmasının presbiakuziye yol açabileceği görüşü baskındır. Bu alanda, daha fazla kanıt düzeyi yüksek çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: çinko, tinnitus, otitis media, presbiakuzi, ani sensörinöral işitme kaybı

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INTRODUCTION

Hearing loss, which is frequently seen in ear diseases, is caused by the dysfunction of all or a part of the auditory pathway between the outer ear and the primary auditory cortex (Jung, Kim, & Yeo, 2019).

Types of hearing loss may vary according to the anatomical region from which it originates. Types of hearing loss; it can be conductive type, sensorineural type, mixed type, functional type, as well as central auditory processing disorders.

Sensorineural hearing loss (SNHL) is a type of hearing loss resulting from dysfunction of all or part of the structures in the inner ear and/or auditory neural pathways. Among the factors causing SNHL are; factors such as noise, toxicity and aging. Acute otitis media (AOM) is inflammation of the middle ear. It is frequently observed in young children, but people of all ages can get this disease (Gulani & Sachdev, 2012). If AOM is left untreated, it causes sensorineural hearing loss. In the chronic state (Chronic otitis media), the neural pathways of hearing may also be damaged. Oral antibiotics are included in the treatment of AOM ~~(Yang, R. et al., 2016)~~.

Sudden sensorineural hearing loss (SSNHL) is defined as rapid/sudden onset hearing loss either unilateral (one-sided) or bilaterally (on both sides). Sudden SNHL is sensorineural in nature and provides certain audiometric criteria. Sudden SNHL treatment options may vary, they are usually shaped according to the region of the pathology. Auditory amplifications may be recommended. Idiopathic sudden sensorineural hearing loss (ISSNHL) is expressed as sudden sensorineural hearing loss without an exact cause (Chandrasekhar, et al., 2019).

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Presbycusis (age-related hearing loss) occurs as a result of the degeneration of cochlear cells and is a sensorineural hearing loss (Keithley, Canto, Zheng, Wang, Fischel-Ghodsian, & Johnson, 2005). The conditions that cause presbycusis are not fully known. Presbycusis is already known to be caused by various physiological degenerations, however, long-term exposure to noise, pathological factors, ototoxicity and genetic predisposition are thought to be the effects (Huang & Tang, 2010). Personal amplification (hearing aids) has positive effects as a treatment/rehabilitation option in patients with presbycusis (Gates & Mills, 2005).

Tinnitus is defined as the auditory perception (sound) felt in the ear or in the head when there is no auditory stimulus in the environment. Tinnitus can be seen in individuals with hearing loss as well as in normal individuals (Seidman & Ahsan, 2015). The cause of tinnitus may be oncological (hearing loss, noise trauma, Meniere's disease, acoustic neuroma, ototoxic drugs or substances, etc.), neurological (multiple sclerosis or head injury), metabolic (thyroid disorder, hyperlipidemia or vitamin B12 deficiency) or psychogenic (e.g., depression, anxiety, or fibromyalgia). Although many factors are suspected to be involved in this problem, the pathophysiology of tinnitus has not been adequately defined. However**,** zinc deficiency is considered a possible etiology (Berkiten, Kumral, Yıldırım, Salturk, Uyar, & Atar, 2014). Treatment of tinnitus may include multidimensional approaches. These may be cognitive-behavioral therapy, TRT (Tinnitus retraining therapy), hearing aids and cochlear implants, sound therapy, auditory perception training, and pharmacological treatment (Langguth, 2015).

Zinc is an essential trace element that has an important role in body metabolism (Soylu Özler, Dündar, Saylam, Çadallı Tatar, Özdek, & Korkmaz, 2014). It is an antioxidant that facilitates toxin excretion and is also a co-factor in many enzymes (Berkiten, et al., 2014). It also has basic functions in reproduction, bone formation, growth, wound healing, signaling in the nervous system, and behavioral responses (Coelho, Tyler, & Hansen, 2007). Zinc deficiency, on the other hand, can be associated with conditions such as impaired immune response, delayed wound healing, deficiencies in taste, olfactory function, and neurophysiological responses, and delayed motor development (Berkiten, et al., 2014).

Zinc ions are widely distributed in the central nervous system. Zinc-containing neurons are a subgroup of glutaminergic neurons (Soylu Özler, et al., 2014). Specifically, zinc has been shown to modulate synaptic function in the cochlear nucleus through its involvement with glutamate receptors (Coelho, C. B. et al., 2007). It has been reported that its deficiency activates NMDA (N-methyl-D-aspartate) receptors, one of the glutamate receptor families, and has an important role in inducing epileptic discharges (Soylu Özler, et al., 2014).

Copper/zinc superoxide dismutase (SOD1) contains copper and zinc as cofactors. It is believed to play a dominant role in the first step of antioxidant defense (Aydogan, Aydin, Tastan, Arslan, Senes, Unlu, & Kavuzlu, 2013). SOD1 is a cytosolic enzyme that converts the superoxide radical to hydrogen peroxide and oxygen, thereby protecting cells from the harmful effects of superoxide and hydroxyl radicals (Keithley, et al., 2005).

SOD1 is common in cochlear tissues. It is found in the spiral ligament, stria vascularis, spiral limbus, cells of the organ of Corti, and spiral ganglion cells (Keithley, et al., 2005).

In this study, the studies conducted in the last 10 years on zinc supplementation in the treatment processes of hearing loss and tinnitus, which are briefly described above, are summarized and compiled.

HEARING AND ZINC

Many studies have been conducted in the literature from past to present regarding the effect of zinc on hearing. In this review, the effect of zinc on hearing has been specifically examined under sub-titles.

Sudden Sensorineural Hearing Loss and Zinc

Sudden sensorineural hearing loss (SSNHL) is an otological condition defined as sensorineural hearing loss (SNHL) of 30 dB and above at least three consecutive frequencies that developed in the last 72 hours (Arslan & Çanakçı, 2021). In most cases, sudden sensorineural hearing loss is a symptom of an as yet undefined pathophysiology (O'Malley & Haynes, 2008).

Sudden hearing loss can be due to many different causes. Targeted audiological, neurotological, imaging, and further diagnostics are important following the foundations of the differential diagnostic decision tree, the patient's history (obtained by a third party if necessary), otoscope, diapason tests according to Weber and Rinne, and pure tone audiometry (Plontke, 2017).

Different therapeutic approaches are based on the pathophysiological mechanisms hypothesized to be responsible for inner ear dysfunction (Marx, Younes, Chandrasekhar, Ito, Plontke, O'Leary, & Sterkers, 2017).

In sudden sensorineural hearing loss (SSNHL), in addition to steroids, various treatments such as anti-inflammatory agents, antioxidants, calcium antagonists, vasodilators, vitamins, trace elements, plasma expanders are frequently preferred by physicians (Ibrahim, Zeitouni, & da Silva, 2018).

Being both an anti-inflammatory and an antioxidant, zinc is involved in very important neurophysiological and pathological processes occurring in the body (Sensi, Paoletti, Bush, & Sekler, 2009). Since the inner ear is rich in zinc, it has been suggested that zinc deficiency may be related to hearing loss and imbalance

(Yang, Tse Ko, Peng, & Hwang, 2011). It is important in terms of hearing physiology, especially because it is effective in synapses in the auditory system (8th cranial nerve) and more importantly, it is found in high concentration in the cochlear tissue in the form of (SOD1), which constitutes the first line of defense against reactive oxygen species (Rarey & Yao, 1996). For this reason, studies have been carried out on the effect of zinc on the physiology of hearing and on the fact that it will also affect the SNHL. Below is a list of the studies carried out in this field in the last 10 years.

In a study investigating the therapeutic effects of zinc in patients with sudden sensorineural hearing loss, 82 of 143 patients diagnosed with SSNHL were given corticosteroid therapy, and 61 were given zinc therapy in addition to corticosteroids. As a result of the study, significant hearing gains were observed in the zinc group at 2 kHz and 8 kHz in the pure tone average of the patients (Kim & Kim, 2015).

In another study investigating the efficacy of zinc in the treatment of SSNHL, patients aged 18–65 years, who used systemic steroids and systemic steroids for the treatment of sudden hearing loss, were included. There was no statistically significant change in the healing parameters of the zinc group (Arslan, et al., 2021).

Idiopathic Sudden Sensorineural Hearing Loss (ISSNHL) and Zinc

Sudden hearing loss is a sudden onset, usually unilateral, cochlear-derived hearing loss of unknown cause (idiopathic) and expresses varying degrees of severity, ranging from complete hearing loss (anacusia) (Plontke, 2017).

Various treatments have been used for ISSNHL, including steroids, vasodilators, antiviral agents, diuretics, and low-salt diets. However, approximately 30% to 60% of patients have been reported to recover spontaneously, usually within two weeks of onset (Hunchaisri, Chantapant, & Sirirattanapan, 2015). The studies on the relationship between zinc and idiopathic SSNHL in the last 10 years are listed below.

Yang et al. demonstrated that the recovery of ISSNHL can be enhanced by zinc supplementation in conjunction with steroid administration. In the study, a better hearing gain (33%-9%) and an increased successful recovery were observed in the zinc group compared to the control group. A significant correlation was observed between serum zinc level changes and post-treatment hearing thresholds. It has also been suggested that zinc may increase hearing recovery with its antioxidant and anti-inflammatory effects, which may reduce the oxidative stress of the cochlea in ISSNHL (Yang, et al., 2011).

In another study on idiopathic sudden sensorineural hearing loss (ISSNHL), no statistical difference was found between the zinc and control groups in terms of pure tone average (PTA) values and speech discrimination (SD) scores (Hunchaisri, et al., 2015).

Acute Otitis Media (AOM) and Zinc

AOM is usually a sequelae of a viral upper respiratory tract infection. Streptococcus pneumoniae, nontypeable Haemophilus influenza, Streptococcus pyogenes, and Moraxella catarrhalis are the most common bacteria causing AOM (Atkinson, Wallis, & Coatesworth, 2015).

It is known that AOM causes conductive hearing loss in the acute phase of the disease (Park, Park, Kim, & Park, 2013). Although conductive hearing loss in patients with acute otitis media is well known, its relationship with sudden sensorineural hearing loss is still considered controversial. Adults with acute otitis media should be evaluated for hearing loss and the risk of sudden sensorineural hearing loss should be considered. This may be especially true if the patient has tinnitus or if bacterial infection is suspected (Smith, Gutteridge, Elliott, & Cronin, 2017).

Sensorineural hearing loss (SNHL) occurs in various types of otitis media. Both chronic and acute otitis media (AOM) can affect cochlear function. Paparella et al. reported cases of transient or permanent sensorineural high-frequency hearing loss during and after AOM (Park, et al., 2013).

Zinc is an essential micronutrient important for immune function and resistance to infection (Walker & Black, 2004). It affects both innate and acquired immune systems (Ibs, Gabriel, & Rink, 2003). There have been a number of successful trials using zinc supplements for the prevention and treatment of pneumonia and other respiratory infections (Lassi, Moin, & Bhutta, 2016). In this context, the studies of the last 10 years on otitis media and zinc are listed below.

Twelve trials with a total of 6820 participants (3191 participants had a definitive otitis media episode) were reviewed. No significant difference was shown between the zinc and placebo groups. Another study showed a significantly lower rate of otitis media (0.69, 95%) in the zinc group. A small study in which 39 infants were treated for malnutrition showed the benefit of zinc for the number of episodes of otitis media. In 10 studies that contributed to the results, no significant difference was shown between the control group and the study group (Gulani, et al., 2012).

In a study investigating the efficacy of zinc in the treatment of acute otitis media in children, 94 children aged 6 months to 6 years with acute otitis media were studied. As a result, it has been shown that zinc does not make a significant difference when used with standard treatment, while it can reduce the complications of the disease (Rahmati, Mojdeh, & Behboodi, 2020).

Presbycusis and Zinc

Age-related hearing loss is termed presbycusis, which is characterized by a progressive decrease in hearing sensitivity, reduced speech recognition, and decreased processing of acoustic impulses. Speech comprehension in a noisy environment is poor in individuals with presbycusis. Hearing loss is usually bilateral, involving high frequencies, and may be associated with tinnitus (Taneja, 2021).

Four predominant types of pathological presbycusis have been identified: sensory, strial, neural, and cochlear conductive presbycusis (Schuknecht & Gacek, 1993). Schuknecht and Gacek concluded that sudden high frequency hearing loss indicates sensory presbycusis, a flat configuration threshold pattern is indicative of strial presbycusis, and the loss of speech discrimination is characteristic of neural presbyacusis. In cochlear conductive presbycusis, there is a flat type audiogram model that gradually decreases in the audiometric scale without a pathological correlation (Mazelova, Popelar, & Syka, 2002).

Inner ear tissue cells with the SOD1 complex have a large number of mitochondria and are therefore vulnerable to oxidative damage from respiration (Keithley, et al., 2005). The absence of SOD1 greatly causes degeneration (Le & Keithley, 2007). The SOD1 complex has been shown to protect the cochlea from damage from noise exposure, ototoxicity, and ischemia. In addition, it has been shown that elimination of the Cu/Zn SOD1 complex increases age-related cochlear hair cell loss (presbycusis) (McFadden, Ding, Burkard, Jiang, Reaume, Flood, & Salvi, 1999).

There are few studies reporting the effect of zinc supplementation in preventing or treating cochlear damage (Ahmadzai, et al., 2016). In this context, the study investigating the relationship between presbycusis and zinc is given below.

One hundred and twenty-six people with a mean age of 67 participated in a study in which serum zinc values of patients with presbycusis were correlated with hearing thresholds. As a result, serum zinc values of individuals with hearing loss at high frequencies were found to be significantly lower (Lasisi & Lasisi, 2014).

Tinnitus and Zinc

Tinnitus is the perception of a sound that has no external source. This sensitivity is often described as ringing in the ears, but the sound may be perceived inside or outside the head, predominantly in one or both ears. Tinnitus can be categorized as subjective and objective. Objective tinnitus, produced by blood flow in the body, muscle contractions, or spontaneous cochlear emissions, can be detected and measured by an external observer, and is rarely observed (Bauer, 2018). Subjective tinnitus is the perception of sound in the absence of an identifiable acoustic source and is heard only by the patient. Subjective tinnitus constitutes most of the cases (Chari & Limb, 2018). People with severe tinnitus often experience psychological changes and a decrease in their quality of life (Person, Es Puga, da Silva, & Torloni, 2016).

In humans, the zinc content in the inner ear is quite high, leading to speculation about the role of zinc in inner ear function. A correlation between low zinc levels and tinnitus has been reported (Seidman, et al., 2015).

Zinc modulates both excitatory and inhibitory neurotransmission and may therefore affect tinnitus. Some types of tinnitus are likely to result from an increase in spontaneous neural activity, and thus zinc deficiency, which can lead to increased neural firing, may be involved in tinnitus formation (Coelho, et al., 2007).

It has been shown that zinc's contribution to Na, KATPase (ion-carrying enzyme, Na+, K+ adenosine triphosphate) integrity and activity and its general stabilizing effect on cochlear biochemistry can reduce some tinnitus (Coelho, et al., 2007). The studies investigating the effect of zinc on tinnitus are briefly mentioned below.

Ochi et al. showed that there was a significant reduction in zinc levels in patients with tinnitus, and administration of doses of 34–68 mg of zinc for 2 weeks significantly reduced tinnitus (Seidman, et al., 2015).

In another study, 60 male factory workers with exposure to noise were evaluated. Zinc supplementation was given to the patients in addition to the systemic treatment. As a result of the study, it was observed that tinnitus symptoms decreased from pre-treatment to post-treatment (Dinarvand, Ziaei, Hoseini, Moosapoor, & Shangol, 2015).

In another study evaluating the use of zinc supplements, zinc was proven to be effective in the treatment of tinnitus compared to the control group in a randomized controlled study among elderly patients with tinnitus (Coelho, et al., 2016).

Three studies involving a total of 209 participants were included in a randomized controlled trial comparing zinc supplementation in adults aged 18 years and older with subjective tinnitus. In the first study, no significant difference was found between the zinc group (5%) who reported improvement after four months and the placebo group (2%). In another study, tinnitus highness was measured on a 0–100-point scale, it was reported that there was no significant difference between the zinc and placebo groups after four months (Scale difference: 0.50). In a study of 50 participants using an unconfirmed scale, no significant difference in subjective tinnitus scores was found between the zinc and placebo groups after eight weeks of follow-up. In conclusion; no evidence was found that zinc supplementation improves adults with tinnitus (Person, et al., 2016).

CONCLUSION

The important role of zinc in inner ear and auditory synaptic connections is known, but it cannot be said that this role shows a definite improvement in hearing loss and/or tinnitus. In studies on the effect of zinc on sudden hearing loss, the opinion that zinc supplementation does not provide a significant benefit, especially when used in addition to standard medical treatment, is dominant. Similarly, in studies examining the effect of zinc on otitis media, it was concluded that zinc did not show any improvement. In studies conducted with individuals with presbycusis, the low serum zinc levels of these individuals may

be an indication that zinc has a physiopathological role in the development of presbycusis. In studies examining the effects of zinc supplementation on tinnitus, it was reported that there was no significant benefit in individuals with normal serum zinc levels, but the tinnitus-reducing effect of zinc was observed in study groups with low serum zinc levels (especially in the geriatric population). There is a need for more well-designed and high-evidence studies on this subject.

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