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Effects of serum zinc level on tinnitus

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ABSTRACT

Objective: The aim of this study was to assess zinc levels in tinnitus patients, and to evaluate the effects of zinc deficiency on tinnitus and hearing loss.

Methods: One-hundred patients, who presented to an outpatient clinic with tinnitus between June 2009 and 2014, were included in the study. Patients were divided into three groups according to age: Group I (patients between 18 and 30 years of age); Group II (patients between 31 and 60 years of age); and Group III (patients between 61 and 78 years of age). Following a complete ear, nose and throat examination, serum zinc levels were measured and the severity of tinnitus was quantified using the Tinnitus Severity Index Questionnaire (TSIQ). Patients were subsequently asked to provide a subjective judgment regarding the loudness of their tinnitus. The hearing status of patients was evaluated by audiometry and high-frequency audiometry. An average hearing sensitivity was calculated as the mean value of hearing thresholds between 250 and 20,000 Hz. Serum zinc levels between 70 and 120 μg/dl were considered normal. The severity and loudness of tinnitus, and the hearing thresholds of the normal zinc level and zinc-deficient groups, were compared.

Results: Twelve of 100 (12%) patients exhibited low zinc levels. The mean age of the zinc-deficient group was 65.41 ± 12.77 years. Serum zinc levels were significantly lower in group III ($p < 0.01$). The severity and loudness of tinnitus were greater in zinc-deficient patients ($p = 0.011$ and $p = 0.015$, respectively). Moreover, the mean thresholds of air conduction were significantly higher in zinc-deficient patients ($p = 0.000$).

Conclusion: We observed that zinc levels decrease as age increases. In addition, there was a significant correlation between zinc level and the severity and loudness of tinnitus. Zinc deficiency was also associated with impairments in hearing thresholds.

1. Introduction

Tinnitus refers to the sensation of hearing sounds without any external source. It affects 17% of the general population, and 33% of older adults [1,2]. Although tinnitus can manifest at any age, it is more common in adults between 40 and 80 years of age [1,2]. Tinnitus is usually accompanied by hyperacousis or hearing loss. The cause of tinnitus may be oncological (e.g., hearing loss, noise trauma, Meniere's disease, acoustic neurinoma, or ototoxic medications or substances), neurological (e.g., multiple sclerosis or head injury), metabolic (e.g., thyroid disorder, hyperlipidemia, or

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vitamin B12 deficiency), or psychogenic (e.g., depression, anxiety, or fibromyalgia) [3,4]. Despite the suspected involvement of many factors, the physiopathology of tinnitus remains poorly characterized. Zinc deficiency is considered as a possible etiology [1,2,5].

Zinc is a trace element with an important role in metabolism. It is an antioxidant which facilitates toxin elimination, and is also a co-factor in many enzymes. Zinc deficiency is associated with impaired immune response, delayed wound healing, deficiencies in taste, olfactory function and neurophysiological responses, and retarded motor development [6]. Levels of zinc in the cochlea are higher compared with other areas: zinc has a role in cochlear function in the cochlear nucleus, in addition to neuronal function, such that zinc deficiency could cause tinnitus and hearing loss [7,8].

This study aims to assess the prevalence of zinc deficiency in patients with tinnitus, and evaluate its effects on tinnitus and hearing.

2. Material and methods

2.1. Study population

Ethical approval for the study was granted by the Ethics Committee of the Okmeydani Training and Research Hospital. One-hundred patients, who presented to an outpatient clinic with tinnitus between June 2009 and 2014 were included. The age of all patients, and the duration of, and any fluctuations in, their tinnitus, and their noise exposure and drug use histories, were obtained.

All patients underwent complete otorhinolaryngologic and audiometric evaluations, complete blood count assessment, and thyroid function and biochemical tests. Patients who had experienced tinnitus for at least 6 months were included. Presbycusis, neurological disease, acoustic neuromas or glomus tumors, chronic otitis media, otosclerosis, active Meniere's disease, and sudden idiopathic hearing loss were the exclusionary criteria, in addition to the use of psychotropic drugs, antidepressants, anticonvulsants and tranquilizers. Patients who were above 65 years and had symmetrical increase in hearing threshold was accepted presbycusis. Patients were divided into three groups according to age, as follows: Group I (patients between 18 and 30 years of age); Group II (patients between 31 and 60 years of age); and Group III (patients between 61 and 78 years of age).

2.2. Assessment of tinnitus severity

To assess tinnitus severity, the 12-item Tinnitus Severity Index Questionnaire (TSIQ) was applied [9]. The TSIQ employs Likert scales for questions pertaining to perceived tinnitus discomfort. The side of the head in which tinnitus was experienced (i.e., unilateral, bilateral or central), and its subjective loudness, were assessed.

Patients rated the loudness of their tinnitus on a scale ranging from 1 (*very quiet*) to 7 (*very loud*) [9]. They were also asked whether their tinnitus was intermittent or continuous.

2.3. Serum zinc level assessment

Atomic absorption spectrophotometry was used to measure serum zinc levels. Levels between 70 and 120 μg/dl were considered normal.

2.4. Hearing level examination

Audiology and high-frequency audiology were applied to all patients. Audiometric evaluation was performed in a sound-proof AC 40 audiometric cabin, calibrated according to ISO 9001 standards. Frequencies between 250 and 20,000 Hz were tested for air and bone conduction, at frequencies between 500 and 4000 Hz [10]. The mean hearing threshold levels, in both ears of patients with and without zinc deficiency, were compared for frequencies between 250 Hz and 20,000 Hz.

2.5. Statistics

The data of this study were assessed for statistical analysis with SPSS 17.O V. Descriptive statistical methods (mean, standard deviation), as well as student-t test were used for the comparison of quantitative data showing the parameters of the normal distribution. Analysis of the variances (ANOVA) and post hoc Tukey as the comparison test were used to compare between the age groups for serum zinc levels. Significance level was set as $p < 0.05$.

3. Results

3.1. Study population

The mean age of the patients was 50.2 ± 13.57 years (range: 17–80 years). Fifty-eight of the 100 (58%) patients were female, and 42 (42%) were male; 37% of the patients described a "whistling"-type tinnitus, and 32% described a bell sound. The remaining patients indicated that their tinnitus was of a mixed-type. The duration of patients' experience of tinnitus ranged between 6 and 120 months (mean = 17.59 months). Twelve patients (12%) had low serum zinc levels; the other 88 patients (88%) were characterized by normal zinc levels (Table 1).

The mean age of the patients with lower zinc levels was 65.41 ± 12.77 years, compared with 48.13 ± 12.36 years in patients with normal zinc levels. The mean serum zinc level was 64.00 ± 3.36 05 in zinc-deficient patients while it was 96.89 ± 15.11 in patients with normal zinc levels (Table 2).

Table 1 – Demographic data of tinnitus patients.

Age (year)	17–78	Mean (50.2 ± 13.57)
Tinnitus side	Right ear	22 (22%)
	Left ear	21 (21%)
	Bilaterally	57 (57%)
Sex	Female	58 (58%)
	Male	42 (42%)
Tinnitus duration (month)	6–120	Mean 17.59
Zinc	Zinc deficiency	n = 12 (12%)
	Zinc normal	n = 88 (88%)

Table 2 – Analysis of tinnitus patients.

	Zinc deficiency (n = 12)	Zinc normal (n = 88)
	Mean ± SD	Mean ± SD
Age	48.13 ± 12.36	65.41 ± 12.77
Zinc levels	64.00 ± 3.36	96.89 ± 15.11

Analysis of zinc levels according to age revealed a significant group difference ($p < 0.001$). A post-hoc Tukey test revealed that there was no difference between groups I and II ($p = 0.703$), but that group III had significantly lower levels of zinc compared with both groups I and II (p =0.000; $p = 0.000$; Tables 3–4 and Fig. 1).

The mean thresholds of air conduction (at 500, 1000, 2000, 4000 Hz) were significantly higher in zinc-deficient patients ($p = 0.000$; $p = 0.000$; Table 5 and Figs. 2–3).

Mean TSIQ scores were 31.33 ± 8.05 in zinc-deficient patients, *vs.* 24.59 ± 8.47 in patients with normal zinc levels. This difference was statistically significant ($p = 0.011$; Table 5).

Tinnitus loudness scores were significantly higher in zinc-deficient patients, at 2.83 ± 0.94, *vs.* 2.17 ± 0.86 in patients with normal zinc levels ($p = 0.015$; Table 5).

Table 6 describes the air conduction thresholds (expressed as means ± *SD*) for each frequency in the pure-tone audiometry of zinc-deficient and normal zinc level patients, between 250 and 20,000 Hz. Increased hearing loss was observed at frequencies between 250 and 8000 Hz (both ears; $p < 0.005$). No increase in hearing loss was observed at any other frequency, in either the right (Fig. 2) or the left ear (Fig. 3).

4. Discussion

Tinnitus can impact upon quality of life, although it is usually well-tolerated [11]. Despite the common perception that tinnitus relates to anatomical and functional changes, its physiopathology remains poorly understood [6]. Therefore, studies are being performed pertaining to the etiology and treatment of tinnitus. The relationship between zinc deficiency and tinnitus, cochlear damage, and hearing damage has been studied in both humans [8,12] and animals [13–16]. These studies suggest that zinc deficiency is among the etiological factors involved in tinnitus [8]. We therefore aimed to assess the effects of zinc deficiency on tinnitus and hearing levels.

The reported prevalence of zinc deficiency in tinnitus varies between 2% and 69% [17–21]. Gersdorff et al. [20] detected zinc deficiencies in 68.7% of 115 tinnitus patients; Paaske et al. [21] reported deficiencies in only 1 of 48 patients. Arda [18] reported a zinc deficiency prevalence of 38% ($n = 41$); Ochi [22] reported a prevalence of 49% ($n = 74$). In our sample, the prevalence was 12% ($n = 12$).

Table 3 – Zinc levels according to age groups.

Age Range	Serum zinc levels		P
	N	Mean ± SD	
18–30 age (Group I)	8	102.37 ± 17.80	0.000
31–60 age (Group II)	67	97.78 ± 15.56	
61–78 age (Group III)	25	76.94 ± 13.70	
Total	100	92.94 ± 17.80	

ANOVA p < 0.01.

Table 4 – Evaluation of zinc levels between each groups.

Serum zinc levels	*p*
Grup I–Grup II	0.703
Grup I–Grup III	0.000
Grup II–Grup III	0.000

Post Hoc (Tukey HSD) p < 0.01.

Although apparently subjective, tinnitus loudness scores are considered an accurate and quick method of measuring the discomfort caused by tinnitus [9]. The majority of previous studies have used an analog, subjective tinnitus rating scale, ranging between 0 and 7 or between 0 and 10, as the main outcome measure. One trial [18] employed loudness matching as an additional outcome measure. Coelho [23] reported that zinc deficiency increases both the severity and loudness of tinnitus. We used the TSIQ [9] to assess tinnitus severity, and observed that zinc deficiency increased both the severity and loudness of tinnitus.

Previous studies have demonstrated that the prevalence of tinnitus increases with age [24–27]. Zinc deficiency also increases with age, due either to the general effects of aging or to diminished intake [5]. Our results are consistent with studies suggesting that zinc deficiency is more common in individuals aged >60 years. The mean age of the zinc-deficit patients in our sample was 65.41 ± 12.77 years.

Although there are studies reporting positive correlations between tinnitus and zinc deficiency [8,17,18,20,22], several other studies do not report any such correlation [19,21]. Gersdorff [20] reported that zinc supplementation in tinnitus patients was effective in 52% of cases. Ochi [22] also reported that zinc levels were lower in a tinnitus group, in which zinc supplementation was associated with tinnitus improvement. Arda et al. [18] similarly reported a positive effect of zinc supplementation, independently of serum levels. Finally, Paaske [21] also indicated that zinc had a positive effect on perceived tinnitus severity.

A further objective of the current study was to analyze the relationship between zinc levels and hearing. Despite several previous studies reporting a relationship between zinc levels and tinnitus [5,7,8,14,24], others have emphasized the lack of

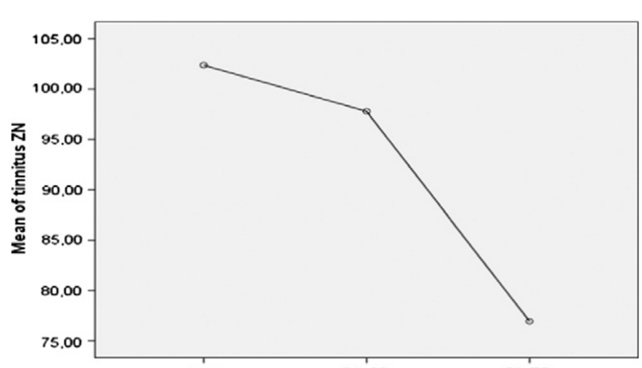

Fig. 1 – Change of zinc levels by age.

Table 5 – Hearing, tinnitus severity and loudness of usual tinnitus evaluation according to zinc levels.

	Zinc deficiency (n = 12)	Zinc normal (n = 88)	P
	Mean ± SD	Mean ± SD	
Hearing right	31.77 ± 7.10	23.93 ± 5.62	0.000
Hearing left	32.08 ± 6.22	24.26 ± 5.08	0.000
TSIQ	31.33 ± 8.05	24.59 ± 8.47	0.011
Loudness of usual tinnitus	2.83 ± 0.94	2.17 ± 0.86	0.015

Independent Samples t-test $p < 0.05$.

a relationship between zinc and hearing [13,22]. Schambaugh [5] reported that zinc was located in higher concentrations in the organ of Corti and vestibule, such that zinc deficiency might precipitate tinnitus, impaired balance and sensorineural hearing loss. It has also been suggested that zinc replacement could attenuate progressive hearing loss in older adults [28]. Hoeve [13] conducted an experimental study in which a zinc-deficient diet was maintained for 7 weeks; however, no morphological changes in the cochlea or hearing loss were observed. Ochi [22] reported that patients with tinnitus and hearing loss were characterized by normal zinc levels, but tinnitus patients without hearing loss had lower zinc levels. In contrast, Kang [14] conducted a study on mice in which a zinc-deficient diet was associated with hearing loss. However, following subsequent zinc supplementation, auditory brainstem response thresholds improved. Our study, in which hearing loss was observed in zinc-deficient patients, supports these results.

5. Conclusion

This study demonstrated that zinc levels decrease as age increases. In addition, hearing thresholds, and the loudness and severity of tinnitus, were also associated with lower levels of zinc. This study suggests that as the age increases; zinc level decreases, hearing thresholds increase and severity of tinnitus increases. More comprehensive and detailed studies are required to further validate the effects of zinc deficiency on hearing loss and tinnitus.

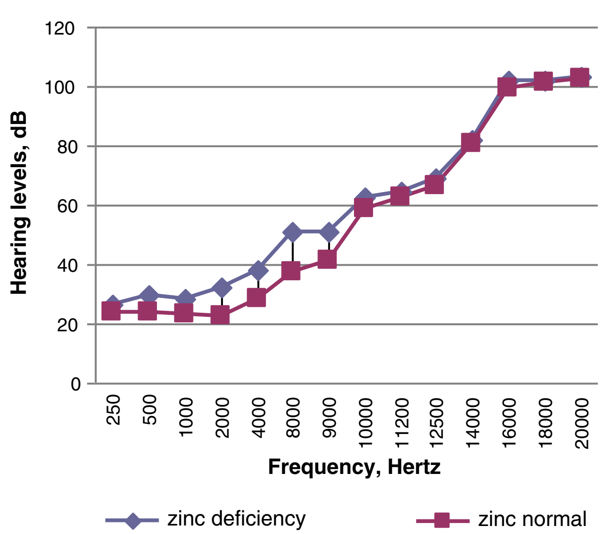

Fig. 2 – Hearing levels of tinnitus patients at right ear according to zinc levels between 250 and 20,000 Hz.

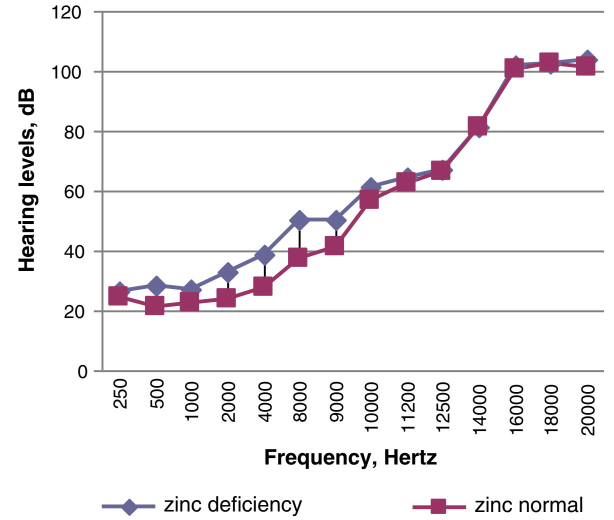

Fig. 3 – Hearing levels of tinnitus patients at left ear according to zinc levels between 250 and 20,000 Hz.

Table 6 – Pure tone air conduction thresholds (dB HL) in 100 patients (grand average).

Hz	Right hearing levels (patients with zinc deficiency) (dB)	Right ear hearing levels (patients with zinc normal) (dB)	Left ear hearing levels (patients with zinc deficiency) (dB)	Left ear hearing levels (patients with zinc normal) (dB)
250	26.66 (2.46 [a])	24.31 (4.68)	26.25 (3.10)	23.57 (4.96)
500	28.33 (8.61)	21.42 (10.30)	30.00 (8.25)	23.57 (7.35)
1000	27.08 (11.95)	22.44 (6.69)	28.33 (11.34)	23.01 (6.18)
2000	32.91 (10.10)	24.09 (5.17)	32.08 (8.90)	22.38 (7.07)
4000	38.75 (13.83)	27.78 (13.32)	37.91 (12.69)	28.12 (12.98)
8000	50.41 (16.16)	37.15 (20.45)	50.83 (12.76)	37.15 (20.45)
9000	61.25 (4.50)	41.42 (15.83)	51.25 (20.12)	41.42 (20.41)
10,000	64.58 (11.50)	56.87 (24.81)	62.50 (14.84)	58.75 (20.03)
11,200	64.58 (15.27)	62.38 (24.29)	64.58 (11.57)	62.38 (23.63)
12,500	67.08 (23.30)	66.13 (26.56)	69.16 (21.19)	66.25 (26.53)
14,000	81.25 (15.24)	81.07 (22.58)	82.08 (14.53)	80.73 (22.31)
16,000	102.08 (7.21)	100.45 (14.71)	101.66 (7.17)	99.54 (14.47)
18,000	102.5 (7.22)	102.44 (10.61)	102.08 (3.34)	101.02 (10.23)
20,000	103.75 (6.07)	101.02 (10.56)	102.91 (6.20)	102.78 (6.73)

SD: standard deviation, dB: decibel, Hz: Hertz.
[a] Values are means (SD).

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