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The Role of Trace Elements in Tinnitus

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Abstract In this study, we aimed to investigate the role of three trace elements, namely, zinc, copper, and lead, in tinnitus by analyzing the serum level of copper and lead and both the serum and tissue level of zinc. Eighty patients, who applied to outpatient otolaryngology clinic with the complaints of having tinnitus, and 28 healthy volunteers were included. High-frequency audiometry was performed, and participants who had hearing loss according to the pure tone average were excluded; tinnitus frequency and loudness were determined and tinnitus reaction questionnaire scores were obtained from the patients. Of all the participants, serum zinc, copper, and lead values were measured; moreover, zinc levels were examined in hair samples. The levels of trace elements were compared between tinnitus and control groups. The level of copper was found to be significantly lower in the tinnitus group ($p = 0.02$), but there was no significant difference between the groups in terms of the levels of zinc, neither in serum nor in hair, and lead in serum ($p > 0.05$). The lack of trace elements, especially that of "zinc," have been doubted for the etiopathogenesis of tinnitus in the literature; however, we only found copper levels to be low in patients having tinnitus.

Keywords Tinnitus · Trace elements · Copper · Zinc · Lead

Introduction

Tinnitus, which is one of the most frequent complaints among all auditory problems, is a sound that is heard by the individuals in the absence of any auditory stimulation. Whereas its prevalence increases after the age of 50, tinnitus can occur in any age [1], and its incidence is 10–30 % in the general population [2]. Tinnitus is classified into two classes, namely, objective and subjective tinnitus. Objective tinnitus is the form that the examiner can also hear the sound externally. Subjective tinnitus, which is the much more frequently seen form, is the one that no sound can be heard externally [3].

Etiology of the subjective tinnitus has not been clarified yet. The association between the etiology of tinnitus and the serum level of zinc (Zn) has been evaluated in some studies in the literature, and low level has been suggested as a factor in the etiology of tinnitus [4, 5]. However, the tissue level of zinc has never been studied yet, whereas it reflects Zn concentration of the last 3 months with high accuracy [6]. Zinc is an essential trace element and widely available in the central nervous system. In cochlea, it biochemically exists in synapses of the hearing pathway. In metabolic activities, zinc and copper (Cu) join in the structure of many enzymes such as copper-zinc superoxide dismutase (Cu-Zn-SOD), catalase, and glutathione peroxidase (GPx) [7]. That is why copper level should be considered as an involving factor in the pathophysiology of tinnitus. However, there is still no study in the literature examining the copper level particularly in patients with tinnitus. Lead (Pb) normally does not exist in the body,

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but its level can increase as a result of environmental pollution and occupational exposure. Lead exposure may lead to tinnitus, as well as peripheral nerve paralyzes and stroke [8].

In this study, we aimed to investigate the role of three trace elements, namely, Zn, Cu, and Pb, in tinnitus by analyzing the serum level of Cu and Pb and both the serum and tissue level of Zn.

Materials and Methods

After ethical approval was obtained from the Ethics Committee of Erciyes University, the study was carried out on 80 subjects having tinnitus and 28 healthy volunteers, with a total of 108 participants within the age range of 18–65 years, between June 2015 and January 2016. All the participants signed the consent form. The patients who applied to outpatient otolaryngology clinic with the complaint of having tinnitus lasting for at least 6 months underwent high-frequency audiometry, and those with normal hearing level in terms of pure tone average (PTA; average of hearing levels at 500, 1000, 2000 Hz) were included into the study. The medical and surgical histories of the participants were recorded. Considering ear pathologies and systemic diseases, which can cause tinnitus, physical examination, psychiatric assessment, complete blood count (CBC), biochemistry of the serum (including lipid profile), thyroid hormone levels, vit-B12 and folic acid levels, cervical radiography, and carotid and vertebral artery doppler ultrasonography were performed as routine examinations. As a result of those examinations, 36 of the patients with tinnitus were excluded because of having psychiatric disorders, such as anxiety and major depression (12 patients); any chronic disease (9 patients); any defined ear pathology (8 patients); and temporomandibular joint syndrome (7 patients). Besides the tinnitus patients, the 28 healthy volunteers, who had no complaints regarding hearing, underwent high-frequency audiometry as well, and those having normal hearing level according to PTA were also included into the study. The participants were then divided into two groups: the tinnitus group (n = 44) and the control group (n = 28) (Fig. 1).

Tinnitus frequency was determined by high-frequency audiometry (AC40 Diagnostic Audiometer; Interacoustics, Middelfart, Denmark) using narrow-band stimuli in the frequencies of 0.5, 1, 2, 4, 6, 8, and 10 kHz and asking the patient to match the most similar stimulus to his/her tinnitus. Tinnitus loudness was measured via masking method using ascending stimuli from 5 to 80 dB. The side (bilateral, right, left), characteristic (intermittent, continuous), and duration (years) of the tinnitus were questioned. The tinnitus reaction levels of the patients were measured via the Turkish version of the tinnitus reaction questionnaire (TRQ) [9]. Besides audiological evaluations of the patients in the study group, the serum copper, lead, and zinc levels of all of the participants were examined via atomic absorption spectrophotometry (Thermo Scientific™ iCE™ 3000 Series). Normal values were accepted to be 70–150 μg/dl for Zn, 50–155 μg/dl for Cu, and 0–25 μg/dl for Pb. In addition to that, the hair samples were taken from the occipital region, and then examined for zinc level (the normal range of Zn in hair is 100–280 μg/dl).

Localization, duration, loudness, and frequency of tinnitus as well as the TRQ scores were analyzed within the tinnitus group. Hearing thresholds and copper, zinc, and lead levels were compared between the tinnitus and the control group. Also, the correlations between the tinnitus loudness, TRQ scores, and the trace element levels were analyzed in the tinnitus group.

Statistical Analysis. Stata 14.0 software was used for statistical analyses. The normality of data distribution was analyzed with Shapiro-Wilk test. For the comparison of data having normal distribution, the Student's t test was used, while the Mann-Whitney U test was used for non-normally distributed data. Chi-square test was used for intergroup comparison of ratios. For the data having normal distribution in correlation analyses, the Pearson's test was used, and for the data having non-normal distribution, Spearman's test was used. $p < 0.05$ was the significance level.

Results

The mean ages of the participants were 43.75 ± 9.98 and 44.6 ± 10.79 years in the control group and the tinnitus group, respectively. The male to female ratio of was 14/14 in the control group while it was 16/28 in the tinnitus group. In terms of age and gender, the differences between the groups were not statistically significant (p = 0.56 and p = 0.25, respectively) (Table 1). Hearing levels in low and mid-frequencies were similar and within the normal limits in both groups; however, there was an obvious slope in the high-frequency region in the tinnitus group (Fig. 2). Speech discrimination scores were 97.12 ± 4.48 and 96.74 ± 4.96 in the tinnitus group and 97.57 ± 4.12 and 97.71 ± 4.41 in the control group, and the differences between the groups were insignificant in both ears (p = 0.6811 and p = 0.3238).

Twenty-eight of the patients in the tinnitus group had suffered from tinnitus for 2 years or less, 9 patients for 3–5 years, 4 patients for 6–10 years, and 3 patients for more than 10 years. The mean duration of tinnitus was 4.04 ± 7.08 years (Table 1).

The mean tinnitus loudness of the patients was 47.73 ± 18.38 dB (Table 1). Tinnitus loudness was 10 dB in 1 patient (2.27 %), 15–20 dB in 5 patients (11.36 %), 25–30 dB in 2 patients (4.55 %), 35–40 dB in 10 patients (22.73 %), 45–50 dB in 6 patients (13.64 %), 55–60 dB in 11 patients (25 %), 65–70 dB in 6 patients (13.64 %), and 75–80 dB in 3 patients (6.82 %).

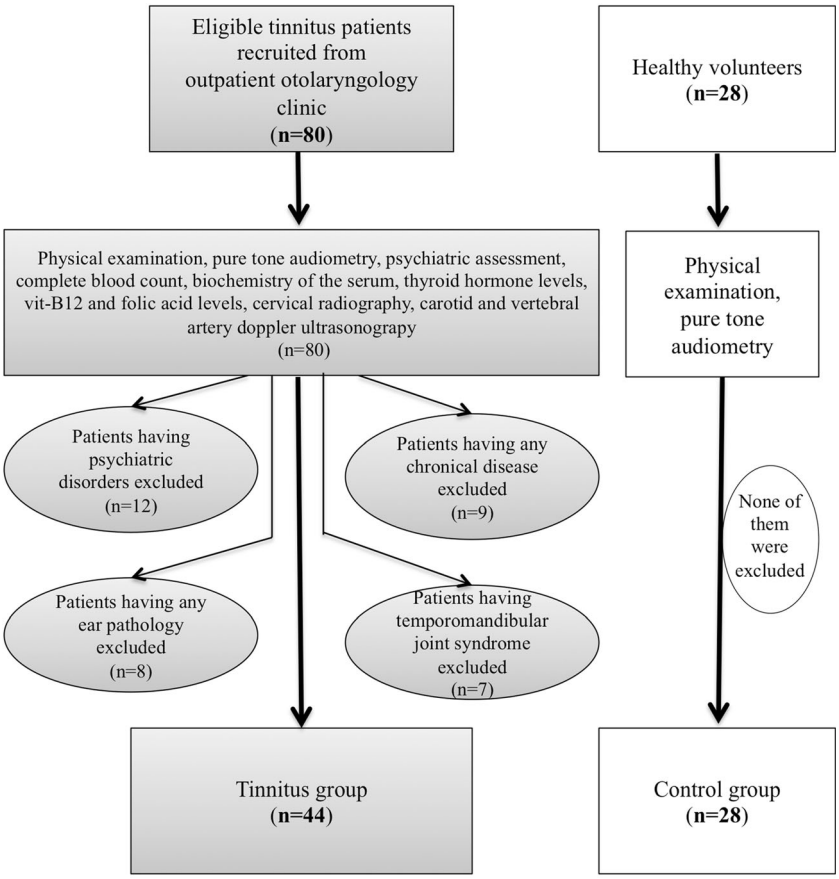

Fig. 1 Flowchart of the recruitment steps

In terms of tinnitus frequency, the mean of the tinnitus group was 6465.91 ± 3343.51 Hz, and it was lower than 4000 Hz in 7 patients (15.91 %) and 4000–8000 Hz in 27 patients (61.36 %) and higher than 8000 Hz in 10 patients (22.73 %) (Table 1).

Table 1 Baseline characteristics of the participants

	Tinnitus (*n* = 44)	Control (*n* = 28)
Age (years), mean ± SD (range)	44.66 ± 10.79 (21–65)	43.75 ± 9.98 (21–59)
Male gender, *n* (%)	16 (36)	14 (50)
Tinnitus localization, right, *n* (%)	18 (41)	
Tinnitus duration (years), mean ± SD (range)	4.045 ± 7.08 (0.5–40)	
Tinnitus loudness (dB), mean ± SD (range)	47.73 ± 18.38 (5–80)	
Tinnitus frequency, *n* (%)		
<4000 Hz	7 (15.9)	
4000–8000 Hz	27 (61.4)	
>8000 Hz	10 (22.7)	
Tinnitus character, *n* (%)		
Continuous	24 (55)	
Intermittent	20 (45)	
Tinnitus reaction questionnaire, *n* (%)		
Slight (0–16)	17 (38.6)	
Mild (18–36)	15 (34.1)	
Moderate (38–56)	7 (15.9)	
Severe (58–76)	4 (9.1)	
Catastrophic (78–100)	1 (2.3)	

SD standard deviation

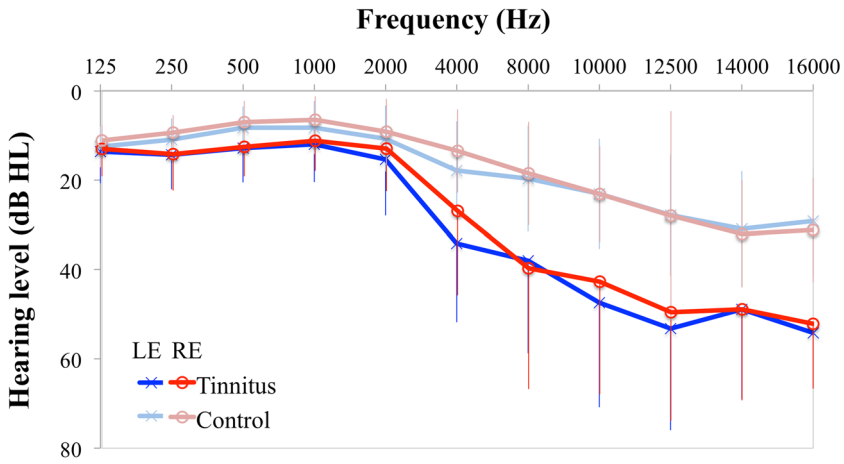

Fig. 2 Distribution of the hearing levels in the two groups

The mean TRQ score of the tinnitus group was 26.52 ± 19.73. According to the TRQ scores, 32 of the patients had slight or mild tinnitus, and 12 of them had moderate, severe, or catastrophic tinnitus (Table 1).

While there were 20 participants having intermittent tinnitus, the number of those having continuous tinnitus was 24 (Table 1). When the data of the patients in the tinnitus group were analyzed using subgroups according to having intermittent and continuous tinnitus, the mean age of the patients having continuous tinnitus (49.42 ± 1.86) was significantly higher than that of patients having intermittent tinnitus (40.25 ± 2.67) ($p = 0.0062$). However, no other variable including the level of the trace elements was significantly different from each other between the subgroups ($p > 0.05$).

Analyzing the levels of the trace elements, the only statistically significant difference between the two groups was found to be in the serum level of copper (Fig. 3). Whereas the serum level of copper was 105.80 ± 25.74 μg/dl in the control group, it was 92.18 ± 28.78 μg/dl in the tinnitus group ($p < 0.05$). There was no statistically significant difference between the tinnitus group and the control group in terms of zinc levels, neither in serum nor in tissue. The serum level of zinc in the control group was 83.47 ± 21.6 μg/dl and 79.01 ± 26.15 μg/dl in the tinnitus group ($p > 0.05$); the level of zinc in hair in the control group was 197.80 ± 72.23 μg/dl and 195.27 ± 78.45 μg/dl in the tinnitus group ($p > 0.05$). Serum lead level was determined to be 3.79 ± 4.98 μg/dl in the control group, while it was 5.02 ± 6.16 μg/dl in the tinnitus group, and the difference between the groups was statistically insignificant ($p > 0.05$). Considering the potential differences of the levels of trace elements between the two genders, we also compared the two groups according to gender and found no significant difference ($p > 0.05$); moreover, the analysis within the groups showed no significant difference between the two genders ($p > 0.05$) (Table 2).

When the numbers of participants whose level of trace elements were out of the normal ranges were compared between the two groups, no statistically significant difference was found (Table 3). Examination of the relationship between tinnitus loudness and the trace element levels showed that the only variable that has significant correlation with the tinnitus loudness was the serum level of lead ($p = 0.0291$; $r = -0.329$) (Fig. 4). The correlation analysis of the TRQ scores with the trace element levels also showed that only the serum level of lead has as significant relationship with the TRQ scores ($p = 0.0139$; $r = 0.3685$) (Fig. 5).

Discussion

Tinnitus, which affects millions of people all over the world, is a tremendous field of research in auditory science, since its pathophysiology has not been clarified yet. The level of trace elements, especially the deficiency of zinc, has been considered as a contributor to this phenomenon. However, controversial results have been reported in the literature so far [10–14]. Some studies reported that zinc deficiency exists more often in the tinnitus group than in healthy controls [4, 10, 13, 14], but some others reported no difference [11, 12]. Moreover, most of the studies, in which the effect of zinc replacement therapy on tinnitus was investigated, suggested no benefit [4, 11, 15].

Berkiten et al. [10] reported that 12 of 100 patients, who had suffered from tinnitus, exhibited low zinc levels, and zinc levels were significantly lower in elderly patients. Furthermore, the authors emphasized that the severity and loudness of tinnitus were greater in zinc-deficient patients [10]. Similarly, the findings of Yetiser et al. [4] showed that 13 out of 40 patients had decreased zinc levels and the tinnitus patients did not benefit from the 8 weeks of zinc therapy significantly, except the elderly patients, whose diet were found to be lacking zinc. Also, Arda et al. [16] have reported the frequency of zinc deficiency to be 31 % among the patients with tinnitus. The results of these studies do not confirm the previous report of Gersdorff et al. [17], who reported a very high prevalence (68.7 %) of zinc deficiency among the

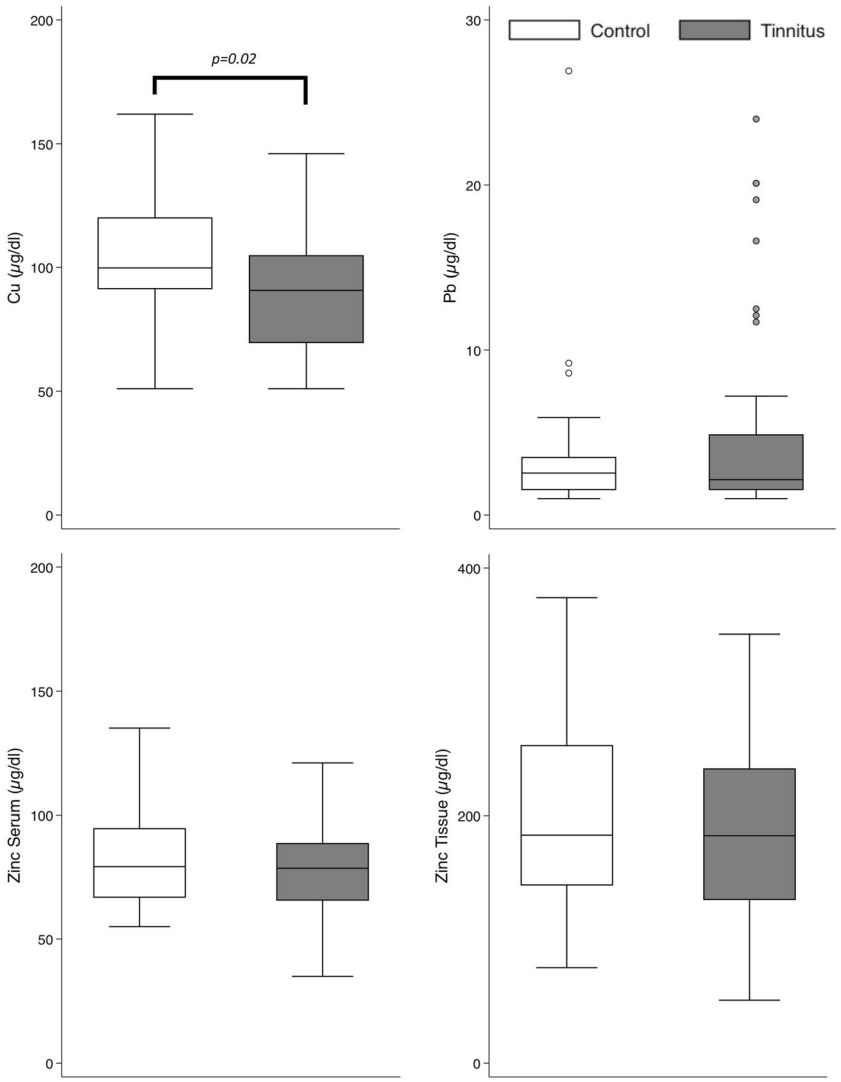

Fig. 3 Distribution of the serum levels of copper, lead, and zinc and the tissue concentration of zinc in the two groups

Table 2 Distribution of the levels of trace elements according to gender

	Tinnitus (n = 44)	Control (n = 28)	p value
Copper (µg/dl), mean ± SD (range)			
Female	102.31 ± 28.89 (62.8–146)	111.89 ± 24.49 (84–155)	0.2
Male	86.4 ± 27.5744 (51–161)	99.7 ± 26.38 (51–162)	0.1
p	0.09	0.22	
Lead (µg/dl), mean ± SD (range)			
Female	5.23 ± 5.71 (1.1–19.1)	4.75 ± 6.78 (1–26.9)	0.77
Male	4.89 ± 6.50 (1–24)	2.84 ± 1.92 (1–8.6)	0.9
p	0.65	0.87	
Zinc serum (µg/dl), mean ± SD (range)			
Female	76.24 ± 17.56 (42.6–99.7)	79.65 ± 15.25 (55–109)	0.58
Male	80.6 ± 30.18 (34.9–153)	87.3 ± 26.55 (62–140.2)	0.61
p	0.86	0.7	
Zinc hair (µg/dl), mean ± SD (range)			
Female	196.46 ± 92.36 (51–346.5)	199.83 ± 69.76 (77–320)	0.91
Male	194.59 ± 71.14 (104.8–399.8)	195.76 ± 77.20 (125.1–376)	0.72
p	0.96	0.65	

Table 3 Distribution of the number of participants whose level of trace elements are outside the reference ranges

	Tinnitus (n = 44)	Control (n = 28)	p value
Copper, n (%)			
Low (<50 μg/dl)	0	0	1
High (>155 μg/dl)	0	1	0.207
Lead, n (%)			
High (>25 μg/dl)	0	1	0.207
Zinc serum, n (%)			
Low (<70 μg/dl)	14 (31.8)	10 (35.7)	0.732
High (>150 μg/dl)	0	0	1
Zinc hair, n (%)			
Low (<100 μg/dl)	3 (6.8)	1 (3.6)	0.558
High (>280 μg/dl)	7 (15.9)	2 (7.1)	0.273

patients having tinnitus. Moreover, in a recent study [12], in which a large population of tinnitus patients and controls were included, investigators found that the serum zinc levels of the patients who have mild or moderate tinnitus were not significantly different from the controls. However, they reported that the zinc levels of the patients having severe tinnitus were significantly lower than those of the controls [12]. In this study, we found that the serum levels of zinc were similar between the groups. Furthermore, we also analyzed the zinc level in the hair, which also exhibited similarity between the groups. Nonetheless, excluding the patients having obvious hearing loss led to the formation of a relatively younger group with an average age of 44.6, whereas Berkiten et al. [10] reported that the mean age of zinc-deficient patients was 65.4. Moreover, patients having severe tinnitus had lower zinc levels, and their mean age was 60.61 in Jun et al.'s [12] study. The results of our study should be interpreted considering the age factor. On the other hand, our findings are only comparable with the studies in which the tinnitus patients having normal hearing are involved, since the other causes of cochlear pathologies can complicate the interpretation of the results. We only included the tinnitus patients whose hearing is normal at the low- and mid-frequency regions in order to compose a homogenous group of patients and get rid of other possible causes of tinnitus, such as noise trauma, which potentially affects hearing as well. However, our findings are not consistent with the study of Ochi et al. [13], in which the authors reported that the serum zinc levels of tinnitus patients whose hearing is normal are lower compared with those of the healthy controls.

As far as we know, this is the first study reporting the relationship between tinnitus and the serum levels of copper. However, investigating the effect of zinc treatment on tinnitus on an elderly group of patients, Coelho et al. [15] examined the copper levels initially in order to exclude the patients having copper deficiency and reported that 7 of the 116 (6 %) participants' serum levels of copper were low. Our results indicate that copper levels are lower in patients having tinnitus than those in the healthy volunteers overall. However, when we compared the two groups according to gender, we found no significant difference between the groups; the reason for this seems to be the small number of participants in the subgroups. Increasing the number of participants would potentially lead to obtaining a

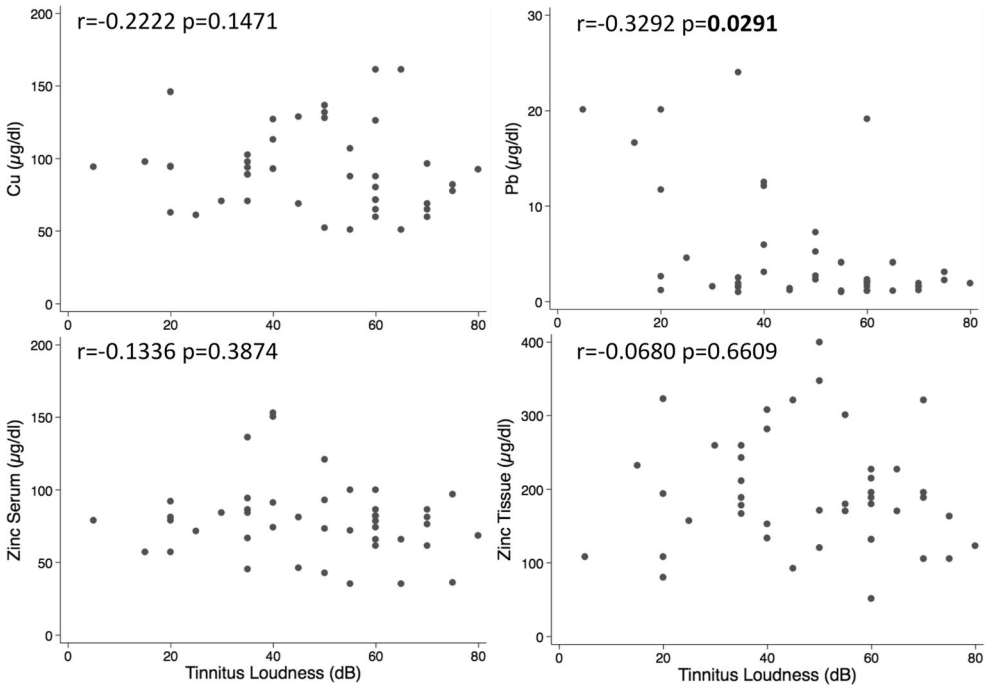

Fig. 4 Correlations between the tinnitus loudness and the levels of the trace elements

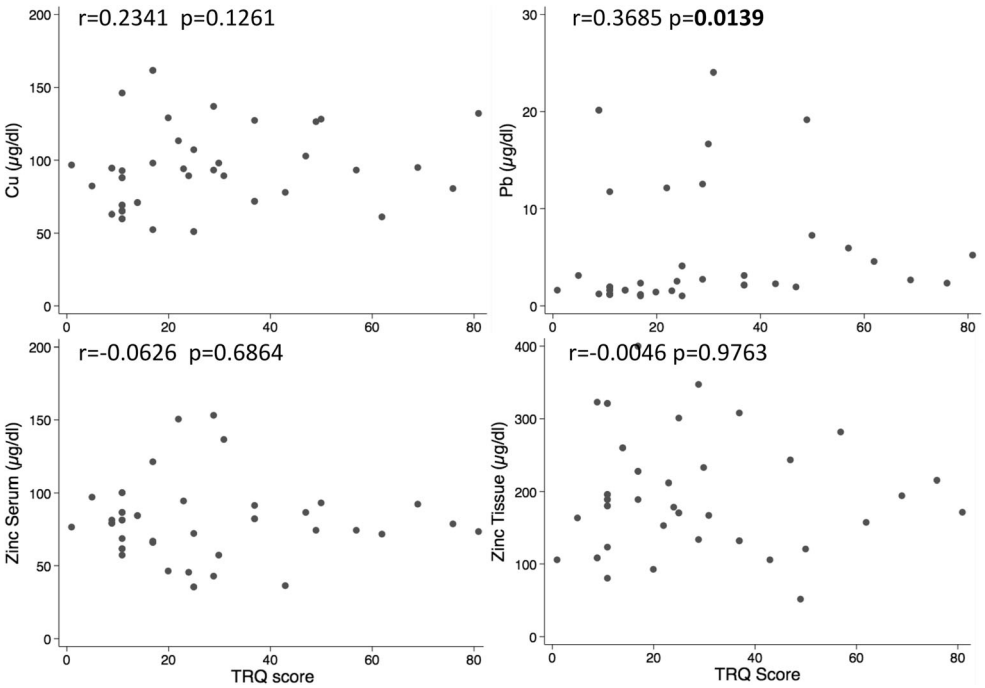

Fig. 5 Correlations between the tinnitus reaction questionnaire (TRQ) scores and the levels of the trace elements

statistically significant difference in the comparison according to gender as well. Copper is necessary in the production of neurotransmitters. Copper deficiency leads to problems in the nervous system [18]. Thus, in Wilson's disease, which is a genetic disorder with disrupted copper metabolism, tinnitus and hearing loss can be the components of the condition. In amyotrophic lateral sclerosis, it has been reported that copper level is significantly decreased in both cerebrospinal fluid and serum as opposed to healthy condition [19]. In the serum, copper and zinc are related with each other. There is a competitive correlation between them. Zinc is mainly present in the intracellular location. Hence, the serum zinc level is not a good indicator. That is why determining the zinc level in tissue provides better results. Zinc and copper are present in cochlea in the structure of the copper-zinc superoxide dismutase (Cu-Zn-SOD) enzyme especially in stria vascularis. The levels of these two trace elements are in relation with each other. These antioxidant enzymes remove the free oxygen radicals arising in the cochlea [20].

Especially in workers of pressing houses and battery factories, as a result of occupational exposure to lead, tinnitus, peripheral nerve paralysis, and stroke can occur. It is widely known that Goya, a well-known painter, had tinnitus, weakness, and unilateral paralysis due to lead exposure [7]. The reason for examining the lead levels in our study was to investigate if the lead levels increased in tinnitus. We have not seen any significant difference between the patients with tinnitus and healthy controls in terms of serum lead levels; however, correlation analyses showed the relationship between tinnitus loudness and lead level ($p = 0.0291$; $r = -0.329$).

Most of the studies in the literature were focused only on the level of zinc but not the other trace elements. From this aspect, our study aimed to better investigate the relationship of tinnitus with trace elements, by including the measurements of copper and lead besides zinc. As a result, the significant decrease was only found in the copper level of the tinnitus group ($p = 0.02$). The low level of copper may indicate a local damage of cochlea, which could lead to an increase in the Cu-Zn-SOD enzyme removing the free radicals. The limitation at this point is that antioxidant enzyme levels were not examined in blood.

In most of the studies on tinnitus, participants with any levels and patterns of hearing loss are included in the study groups; however, this makes the groups heterogeneous, because of the various etiologies of hearing loss. So, we investigated the role of trace elements in the etiology of tinnitus in a homogenous group of patients, all of which have normal hearing in the low- and middle-frequency region with no possible etiological factors other than presbycusis. One of the other advantages of our study is having examined also the tissue concentration of zinc, which provides more accurate results for the level of zinc.

Conclusion

We found that the serum copper levels of patients with tinnitus were lower than those of the healthy controls, whereas zinc and lead levels were alike. These results should be confirmed with studies on a large series of patients, as well as molecular studies, which can potentially clarify the reason of this phenomenon.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

References

1. Von Wedel H, Von Wedel UC, Zorowka P (1991) Tinnitus diagnosis and therapy in the aged. Acta Otolarygol Suppl 476:195–201
2. Moller AR (2010) Epidemiology of tinnitus in adults. In: Moller AR, Langguth B, DeRidder D, Kleinjung T (eds) Textbook of tinnitus: diagnosis and treatment, 1st edn. Springer, New York, pp. 29–38
3. Heller AJ (2003) Classification and epidemiology of tinnitus. Otolaryngol Clin N Am 36:239–248
4. Yetiser S, Tosun F, Satar B, Arslanhan M, Akcam T, Ozkaptan Y (2002) The role of zinc in management of tinnitus. Auris Nasus Larynx 29:329–333
5. Frederickson CJ, Moncrieff DW (1994) Zinc-containing neurons. Biol Signals 3:127–139
6. Combs DK, Goodrich RD, Meiske JC (1982) Mineral concentrations in hair as indicators of mineral status: a review. J Anim Sci 54:391–398
7. Akcıl E, Tug T, Doseyen Z (2000) Antioxidant enzyme activities and trace element concentrations in ischemia-reperfusion. Biol Trace Elem Res 76:13–17
8. Betlejewski S, Ossowski R (2009) Deafness and mentality in Francisco Goya's paintings. Otolaryngol Pol 63:186–190
9. Caner Mercan G, Ozturk K, Kirazlı T, Bilgen C, Kılıc MA, Ogut F (2013) Methodology of clinical trials on diagnosis and treatment of subjective tinnitus: proposal for a national protocol. Ege Journal of Medicine 52:125–130
10. Berkiten G, Kumral TL, Guven Y, Salturk Z, Uyar Y, Atar Y (2015) Effects of serum zinc level on tinnitus. Am J Otolaryngol 36:230–234
11. Paaske BP, Pederse CB, Kjems G, Sam IL (1991) Zinc in the management of tinnitus, placebo- controlled trial. Ann Otol Rhinol Laryngol 100:647–649
12. Jun HJ, Ok S, Tyler R, Hwang SY, Chae S (2015) Is hypozincemia related to tinnitus?: a population study using data from the Korea National Health and nutrition examination survey. Clinical and experimental otorhinolaryngology 8:335–338
13. Ochi K, Kinoshita H, Kenmochi M, Nishino H, Ohashi T (2003) Zinc deficiency and tinnitus. Auris, nasus, larynx 30 Suppl: S25–8.
14. Ochi K, Ohashi T, Kinoshita H, Akagi M, Kikuchi H, Mitsui M, et al. (1997) The serum zinc level in patients with tinnitus and the effect of zinc treatment. Nippon Jibiinkoka Gakkai Kaiho 100:915–919
15. Coelho C, Witt SA, Ji H, Hansen MR, Gantz B, Tyler R (2013) Zinc to treat tinnitus in the elderly: a randomized placebo controlled crossover trial. Otol Neurotol 34:1146–1154
16. Arda HN, Tuncel U, Akdogan O, Ozluoglu LN (2003) The role of zinc in the treatment of tinnitus. Otol Neurotol 24:86–89
17. Gersdorff M, Robillard T, Stein F, Declaye X, Vanderbem S (1987) A clinical correlation between hypozincemia and tinnitus. Arch Otorhinolaryngol 244:190–193
18. Hardin MF, Barker M, Neis P (2005) Rare auditory-electrophysiology finding in Wilson's disease. J Ark Med Soc 101:281–283
19. Kapaki E, Zournas C, Kanias G, Zambelis T, Kakami A, Papageorgiou C (1997) Essential trace element alterations in amyotrophic lateral sclerosis. J Neurol Sci 147:171–175
20. Rarey KE, Yao X (1996) Localization of Cu/Zn-SOD and Mn-SOD in the rat cochlea. Acta Otolaryngol 116:833–835