

# The Effect of Zinc Therapy on Tinnitus Symptoms Reduction

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## ABSTRACT

Tinnitus is a common complaint among noise-exposed workers. A dietary zinc supplementation is apparently beneficial in reducing symptoms in patients with tinnitus. Therefore, the present study aimed to investigate the prevalence of hypozincemia among patients with tinnitus and the effect of zinc therapy on the severity of symptoms. A total of 66 male workers afflicted with tinnitus were selected from industries in the Khuzestan Province, which yielded a final participant tally of 60 cases due to drop out. Serum zinc levels were measured for all the participants by flame atomic absorption spectrophotometry using non-diluted serum samples. Subsequently, 35 and 25 patients were randomly selected for zinc (60 mg/day) and placebo therapy, respectively, for two months. Moreover, the patients were categorized into two groups on the basis of serum zinc levels: group one (16 patients) with  $\leq 50$   $\mu\text{g/dl}$  and group two (19 patients) with  $> 50$   $\mu\text{g/dl}$  serum zinc level. Data analysis was conducted using SPSS software by paired *t*-test and one-way ANOVA. The age of the workers, represented as mean  $\pm$  standard deviation (SD), were  $34.9 \pm 5.1$ ,  $37.5 \pm 5.4$ , and  $36.1 \pm 5.5$  years for groups one, two, and placebo, respectively. The serum zinc levels before and after zinc/placebo therapy were found to be 47.7 and 77.3  $\mu\text{g/dl}$  respectively in group one, 86.6 and 98.2  $\mu\text{g/dl}$  respectively in group two, and 73.2 and 72.6  $\mu\text{g/dl}$  respectively in the placebo group. The tinnitus symptoms were observed to decrease from pre-treatment to the post-treatment condition in both groups, which received zinc therapy. Zinc therapy is likely to be beneficial for individuals with certain types of tinnitus and could relieve or possibly even prevent the condition. However, like other complex neurological disorders, one drug is unlikely to resolve tinnitus in all patients.

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## Introduction

Tinnitus is a common complaint among workers exposed to high levels of noise, and is even recognized as a work-related condition for compensation purposes in certain countries. Initiatives for the prevention of occupational hearing loss rarely focus on the prevention and management of tinnitus [1], which may affect the daily chores and sleep of nearly one to two percent of the population [2]. The significant risk factors for tinnitus include age, gender, various diseases (metabolic, neurological, and vascular alterations as well as dental conditions), hearing loss, and exposure to noise, ototoxic drugs, caffeine, nicotine, and alcohol [3-5]. In addition to the medical and audiological aspects of tinnitus, the psychosocial consequences are also significant, and have been previously investigated. Tinnitus has the potential to alter an individual's functional performance in professional, social, and leisure activities as well as in family relationships, hence affecting the quality of life.

Several theories have attempted to explain the physiopathology of tinnitus, including its cause and perception. The current consensus is that tinnitus results from aberrant neural activity in the auditory system, typically of an excitatory nature [6]. The subjective nature of tinnitus has led to lack of consensus on accepted outcomes for treatment, as well as a universally accepted classification or treatment strategy for tinnitus. The therapy is typically individualized, and ranges from placebo to surgery. Although surgery is effective, it is extremely resource-intensive, time-consuming, and requires specialized training; its widespread use for such a common problem is therefore unlikely and economically unfeasible. Thus, a safe and effective oral pharmacological intervention has the potential for offering an acceptable and widely accessible treatment for tinnitus [7].

Zinc is an essential trace metal with an important functional role in the auditory pathway; zinc therapy has therefore been proposed as a treatment for tinnitus, particularly for patients with hypozincemia. The serum zinc level is the most reliable, albeit not the best, parameter for assessing zinc balance in the body [8,9]. Three possible mechanisms linking zinc to tinnitus have been proposed: cochlear copper/zinc superoxide dismutase activity, synaptic transmission, and depression [10]. Several questionnaires purport to evaluate the impact of tinnitus on day-to-day life.

These questionnaires on tinnitus are not only beneficial for clinical applications, but are also valuable for understanding the relationship between personality and the psychopathology of tinnitus, its impact on the day-to-day life of afflicted individuals, the difficulties and perception associated with social support for the problem, and the incapacity and difficulties caused by tinnitus, which seriously impact the quality of life [11-13]. The present study was conducted to investigate the prevalence of hypozincemia in patients with tinnitus and the effect of zinc therapy on the severity of symptoms.

## Materials and Methods

A placebo-controlled, randomized, prospective investigation was conducted for assessing the possible beneficial effects of zinc therapy for tinnitus symptoms. A total of 66 male workers afflicted with tinnitus were selected from industries in Khuzestan Province, but the final tally of study participants was 60 cases as a result of drop out. Serum zinc levels were measured for all the participants by flame atomic absorption spectrophotometry using non-diluted serum samples obtained under fasting condition. Irrespective of the findings, 35 and 25 cases were randomly selected for the administration of zinc tablets (60 mg/day) or placebo (mint tablets), respectively, for two months. The patients were divided into two categories according to their serum zinc levels: group one (16 patients) with  $\leq 50 \mu\text{g/dl}$ , and group two (19 patients) with  $> 50 \mu\text{g/dl}$  serum zinc levels. The questionnaire presented five questions about tinnitus and its effects on sleep, work, or the activity of workers, and the responses were categorized into three ranks with relevant scores, as shown (Table 1). Data analysis was carried out using SPSS software by paired *t*-test and one-way ANOVA.

**Table 1.** The tinnitus questionnaire.

Questions	Rank		
	Always	Sometimes	Never
1 Do you have any sleep disturbance due to tinnitus?	1	0.5	0
2 Can you get to sleep easily?	0	0.5	1
3 Do you hear tinnitus sound in a quiet place?	1	0.5	0
4 Do you hear tinnitus during daily activities?	1	0.5	0
5 Do you forget tinnitus sound while working?	0	0.5	1

## Results

The age of the workers, represented as mean  $\pm$  standard deviation (SD), in groups one, two, and placebo were  $34.9 \pm 5.1$ ,  $37.5 \pm 5.4$ , and  $36.1 \pm 5.5$  years, respectively; significant difference was not observed between the groups. The serum zinc levels before and after zinc administration were found to be 47.7 and 77.3  $\mu\text{g/dl}$ , respectively, in group one, and 86.6 and 98.2  $\mu\text{g/dl}$ , respectively, in group two. The corresponding levels in the placebo group before and after the administration of mint tablets were found to be 73.2 and 72.6  $\mu\text{g/dl}$ , respectively. The results are summarized in **Table 2**. The subjective scoring derived from the questionnaire revealed the median scores in the two groups of workers receiving zinc therapy to be three and one before and after the treatment, respectively. The placebo group, on the other hand, exhibited similar scores before and after treatment, as shown (**Table 3**).

**Table 2.** Serum zinc levels ( $\mu\text{g/dl}$ ), as mean  $\pm$  SD.

Groups	Serum zinc level (M $\pm$ SD)		P-value
	Pre-treatment	Post-treatment	
Zinc group 1	47.7 $\pm$ 5.32	77.3 $\pm$ 6.16	0.02
Zinc group 2	86.6 $\pm$ 8.44	98.2 $\pm$ 11.48	< 0.001
Placebo group	73.2 $\pm$ 5.27	72.6 $\pm$ 5.63	0.87

**Table 3.** Median subjective scores derived from tinnitus questionnaire (ranges: 0–5).

Groups	Median of scores	
	Pre-treatment (range)	Post-treatment (range)
Zinc group 1	3 (2.3-4.2)	1 (0.1-1.8)
Zinc group 2	3 (2.2-4.2)	1 (0.4-2.1)
Placebo group	3 (2.1-4.1)	3 (1.9-4.8)

## Discussion

Currently, drugs approved for the treatment of tinnitus are not available. The alternative treatment strategies for tinnitus include the administration of zinc and magnesium or magnetic therapy. The general opinion among the medical establishment is that these alternate strategies provide little benefit, although this cannot be said with assurance in the absence of substantial research on several of these treatments. However, there is no doubt that good nutrition in general is important for recovery from any type of injury, including the injury that results in tinnitus. The reported results for zinc therapy for tinnitus show remarkable variability, as do the

epidemiological estimates of the prevalence of zinc deficiency, with the latter estimates ranging from 2% to 69% of the population. Further studies are therefore warranted [14].

Zinc is an oligoelement present in the auditory system, and is involved in glutamatergic excitation of synaptic networks by apparently acting on the postsynaptic receptors of certain glutamatergic synapses [15].

Thus, zinc could modulate the tinnitus perception in certain patients by modulating glutamatergic activity in the central auditory pathways. Additionally, the cochlear antioxidant effects of zinc could also play a role in the improvement of tinnitus perception in certain patients [16].

The present study revealed that serum zinc deficiency in group one prior to zinc therapy could be a causative factor for tinnitus, as also indicated in other studies [17, 18]. In contrast, other studies revealed little correlation between hypozincemia and tinnitus, and the absence of significant improvement in subjective tinnitus upon the administration of zinc supplements [19].

The administration of zinc at a dosage of 60 mg/day restored the serum levels of this metal in both groups one and two to the normal range observed with the daily intake of zinc. Statistically significant differences were observed in the serum zinc levels between the pre- and post-treatment conditions of both groups.

Similarly, dramatic decreases in the subjective scores of both groups were observed using a five-scale ranking, which is attributable to increase in serum zinc levels upon the administration of zinc tablets during the course of the study.

This observation is also reflected in certain other studies, including Gersdorff et al, where a 10–25 mg dose of zinc administered to a few patients with hypozincemia [20], and Ochi et al, where doses of 34–68 mg administered over a period of two weeks were found to significantly decrease tinnitus.

Excellent results have been reported using a combination of niacin and 25 mg zinc gluconate administered twice a day [18]. Seidman et al showed that supplementation with zinc at a dose of 90–150 mg/day is beneficial in certain cases [9]. The serum zinc levels in the placebo group showed a slight decrease subsequent to the administration of placebo, although the difference was not statistically significant. Apparently, the indoctrination created by the administration of placebo in this group did not

exert any effect on reducing the subjective symptoms of tinnitus among the workers, although serum zinc levels were within the normal range.

Given the critical role of zinc in several aspects of cochlear and neuronal functions of the auditory pathway, its deficiency is apparently implicated in tinnitus. The present as well as few other studies report positive effects of zinc supplementation on diminishing subjective symptoms among tinnitus patients [10, 21].

In addition, certain studies have shown that patients with tinnitus who had normal hearing had significantly lower serum zinc levels compared to control subjects. In contrast, significant differences in serum zinc levels were not observed between patients with tinnitus who exhibited hearing loss and control subjects in another study [17].

Moreover, a few studies have reported little or no improvement in tinnitus symptoms with zinc therapy, with the exception of a few patients with low serum zinc levels [7, 22].

Taken together, these findings support an important role for zinc in the pathophysiology of tinnitus, although little information is available on the subject. The participants of the present study are still under follow up in order to detect any recurrent episodes of tinnitus. Whether increasing the duration of treatment renders more significant benefits remains to be addressed.

Finally, zinc therapy is beneficial for individuals with certain forms of tinnitus and is likely to relieve tinnitus and possibly even prevent it [10]; however, like other complex neurological disorders, one drug is unlikely to resolve tinnitus in all patients.

Therapeutic strategies targeting specific subgroups [8] and increased duration of treatment are likely to yield greater rates of success. Of note, copper and zinc compete for intestinal absorption, such that chronic ingestion of zinc is likely to result in copper deficiency. Acute zinc toxicity is usually induced upon the ingestion of > 200 mg of zinc in a single day, and is characterized by epigastric pain, nausea, vomiting, and diarrhea.

## Conclusion

Zinc plays an important role in the functioning of the auditory system, with its deficiency apparently implicated in tinnitus. Zinc therapy is therefore likely to be beneficial for relieving tinnitus. A few studies have suggested that zinc supplementation is effective

in decreasing subjective disorders among tinnitus patients.

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