ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Investigation of the Relationship Between Serum Copper, Zinc, and Magnesium Levels and Benign Paroxysmal Positional Vertigo (BPPV)

Serum Bakır, Çinko, Magnezyum Düzeylerinin Benign Paroksismal Pozisyonel Vertigo (BPPV) Hastalığı İle İlişkisinin Araştırılması

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ABSTRACT

Aim: *This study examined the association between serum trace element concentrations (copper, magnesium, and zinc) and benign paroxysmal positional vertigo (BPPV), a common cause of vertigo.*

Materials and Methods: *This retrospective study was conducted by reviewing laboratory data recorded in the hospital automation system for patients who presented with vertigo at the Kafkas University Health Practice and Research Center between January 1, 2022, and April 1, 2024. A total of 119 individuals were included, comprising 81 (68.07%) patients diagnosed with BPPV and 38 (31.93%) in the control group. Participants had a mean age of 52 years; females accounted for 60.5% of the cohort, while males comprised 39.5%.*

Results: *Comparative analyses revealed distinct serum copper, magnesium, and zinc profiles between the BPPV and control groups ($p<0.05$). Higher copper and magnesium concentrations were observed in individuals with BPPV, whereas zinc levels were greater in the control group. Among the trace elements examined, magnesium demonstrated the strongest association with BPPV, with higher levels corresponding to a 9,709-fold increase in the odds of the disorder.*

Conclusion: *Alterations in serum trace element levels, particularly increased magnesium levels, may be related to the presence of BPPV. These findings suggest that mineral metabolism may play a contributory role in vestibular disorders and provide a foundation for further research in this field.*

Key words: *vertigo; magnesium; copper; zinc*

ÖZET

Amaç: *Bu çalışmada, serum eser element düzeyleri (bakır, magnezyum ve çinko) ile vertigonun en yaygın nedenlerinden biri olan benign Paroksismal Pozisyonel Vertigo (BPPV) varlığı arasındaki ilişkinin değerlendirilmesi amaçlanmıştır.*

Materyal ve Metot: *Bu retrospektif çalışma, 1 Ocak 2022 ile 1 Nisan 2024 tarihleri arasında Kafkas Üniversitesi Sağlık Uygulama ve Araştırma Merkezi'ne vertigo şikâyetiyle başvuran hastaların hastane otomasyon sisteminde kayıtlı laboratuvar verilerinin incelenmesiyle gerçekleştirildi. Çalışmaya BPPV tanısı konulan 81 (%68,07) hasta ile kontrol grubu olarak 38 (%31,93) kişi olmak üzere toplam 119 olgu dâhil edildi. Katılımcıların yaş ortalaması 52 olup, %60,5'i kadın ve %39,5'i erkekti.*

Bulgular: *BPPV ve kontrol grupları karşılaştırıldığında, serum bakır, magnezyum ve çinko düzeylerinin gruplar arasında farklı dağılım gösterdiği izlendi ($p<0,05$). Bakır ve magnezyum düzeylerinin BPPV grubunda daha yüksek olduğu, buna karşılık çinko düzeylerinin kontrol grubunda daha yüksek seyrettiği belirlendi. Değerlendirilen parametreler arasında magnezyumun BPPV ile daha belirgin bir ilişki gösterdiği ve magnezyum düzeylerindeki artışın BPPV olasılığını 9.709 kat artırdığı saptandı.*

Sonuç: *Serum eser element düzeylerindeki değişikliklerin, özellikle magnezyum düzeylerindeki artışın, BPPV varlığı ile ilişkili olabileceği düşünülmektedir. Bu bulgular, vestibüler bozukluklarda mineral metabolizmasının olası rolüne işaret etmekte olup, bu alanda yapılacak ileri çalışmalar için yol gösterici olabilir.*

Anahtar kelimeler: *vertigo; magnezyum; bakır; çinko*

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Introduction

Benign paroxysmal positional vertigo (BPPV) is a common peripheral vestibular disorder that presents with brief episodes of vertigo induced by positional head movements and is accompanied by characteristic nystagmus (1). Due to its clinical impact, BPPV significantly negatively affects daily living activities and quality of life, accounting for a significant proportion of patients presenting with vertigo complaints (2). Epidemiological evidence indicates that BPPV occurs more frequently with advancing age and is observed more often in women than in men (3).

The basic pathophysiological mechanism of BPPV is the abnormal stimulation of the vestibular system during head movements, due to the migration of calcium carbonate particles (otoconia) from the utricle into the semicircular canals (4). This process is explained by two main mechanisms: canalithiasis, in which free-floating otoconia affect endolymph flow, and cupulolithiasis, in which otoconia adhere to the cupula, causing continuous stimulation (5). Clinical evidence indicates that a large proportion of cases of BPPV have no identifiable cause. In contrast, secondary forms are most often reported in association with conditions such as head trauma, vestibular neuritis, Ménière's disease, migraine, and prior surgical interventions (6–8).

Although BPPV is primarily defined as a mechanistic vestibular disease, it is known that the structural integrity and function of the vestibular system are closely related to cellular ion balance, energy metabolism, and oxidative stress response (9). Elements such as magnesium play critical roles in neurotransmission, ion channel functions, and antioxidant defense mechanisms (10). It has been shown to have an important role in processes associated with oxidative stress (11). Furthermore, magnesium is reported to have clinical and prognostic importance in various systemic diseases and to be associated with cellular stress responses (12).

Emerging clinical evidence suggests reduced serum magnesium levels in patients with BPPV. It has raised the possibility that disturbances in trace element balance may be involved in the disease process (13). Nevertheless, the evidence linking serum copper, magnesium, and zinc levels to BPPV remains sparse, and existing results do not allow definitive conclusions.

This study compared serum copper, magnesium, and zinc levels between patients diagnosed with BPPV and individuals presenting with vertigo without a BPPV diagnosis.

Material and Method

Study Design

This retrospective observational study was conducted at Kafkas University Health Practice and Research Center in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Kafkas University Faculty of Medicine Clinical Research Ethics Committee (Approval No: 80576354-050-99/447; May 29, 2024). Patients presenting to the Ear, Nose, and Throat Clinic with vertigo between January 1, 2022, and April 1, 2024, were included. Laboratory data of patients with and without BPPV were retrieved from the hospital database and analyzed.

The control group consisted of patients with vertigo unrelated to BPPV, as obtaining biochemical data from asymptomatic individuals is not feasible or ethically justified in routine practice. This design ensured clinical comparability and minimized selection bias. Patients with vestibular, neurological, or systemic disorders affecting mineral metabolism were excluded from the control group.

Inclusion Criteria

The study population consisted of adults aged 18 years or older who presented with vertigo during the defined study period. Patients diagnosed with BPPV based on clinical assessment and positional testing were included, along with a control group of vertigo patients in whom BPPV was excluded.

Exclusion Criteria

Individuals under 18 years of age, those not evaluated at Kafkas University Health Practice and Research Center, and patients with Ménière's disease, vestibular neuritis, acoustic neuroma, sudden sensorineural hearing loss, head trauma, or prior otologic surgery were excluded.

Data Collection

Sociodemographic data and serum copper, magnesium, and zinc levels of all patients who did not meet the exclusion criteria were obtained from the hospital automation system. In addition, the patients' clinical diagnoses and records regarding BPPV were reviewed.

Statistical Analysis

Statistical analyses were performed using IBM Statistical Package for Social Sciences (SPSS) program software. Continuous variables were expressed as mean ± standard deviation or median (range), depending on distribution, assessed by the Shapiro-Wilk test. Between-group comparisons were conducted using the independent-samples t-test or the Mann-Whitney U-test, as appropriate. Categorical variables were analyzed with the chi-square or Fisher's exact test. Receiver operating characteristic (ROC) curve analysis evaluated the discriminatory performance of serum copper, magnesium, and zinc levels for BPPV (Fig. 1). Logistic regression analysis was used to identify factors associated with BPPV. A p-value <0.05 was considered statistically significant.

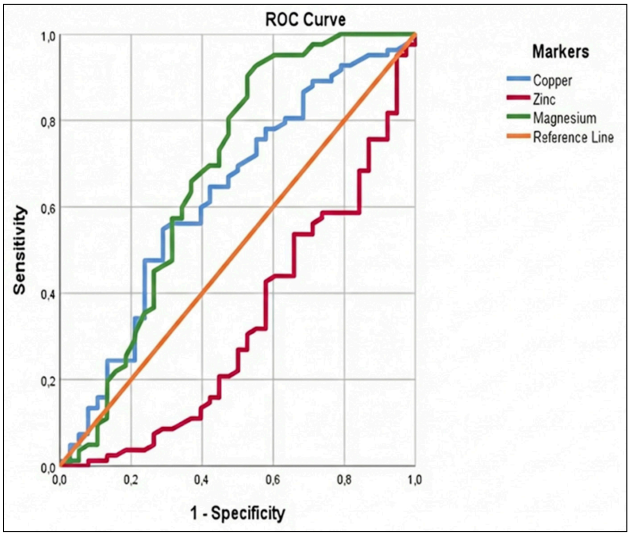

Figure 1. *The ROC curves for copper, zinc, and magnesium.*

Results

A total of 119 patients were included, comprising 81 with BPPV and 38 controls. Demographic characteristics and serum trace element levels are presented in Table 1. Serum copper, magnesium, and zinc levels differed significantly between groups (p<0.05).

Receiver operating characteristic analysis identified optimal cutoffs of >159.08 for copper (sensitivity 54.88%, specificity 71.05%), ≤109.6 for zinc (sensitivity 84.15%, specificity 44.74%), and >1.8 for magnesium (sensitivity 90.24%, specificity 47.37%). Cutoff values are summarized in Table 2.

Table 1. *Comparison of the study group with age, copper, zinc, and magnesium variables*

Variable	Total (n=119)	BPPV (n=81) Mean ± S. D. Median (min-max)	Control (n=38) Mean ± S. D. Median (min-max)	Test Stat.	p value
Gender. n (%)				4.058	0.044*
Female	72 (60.5)	44 (54.3)	28 (73.7)		
Male	47 (39.5)	37 (45.7)	10 (26.3)		
Age (years)	51.9±14.02	52.96±14.02 53(21–80)	49.61±13.92 51(23–79)	1.223	0.224‡
Copper (µg/dL)	160.39±34.32	163.98±32.87 161.64(94.93–260.72)	152.66±36.5	-2.212	0.027†
Zinc (µg/dL)	100.93±21.77	96.07±17.58 94(56.7–151.9)	111.41±26.12 104.55(63.3–167.95)	-3.001	0.003†
Magnesium (mg/dL)	1.94±0.2	1.98±0.16 1.96(1.65–2.66)	1.85±0.25 1.84 (1.38–2.48)	-3.124	0.002†

p<0.05; chi-square test; ‡: independent samples t-test; †: Mann-Whitney U test.

Table 2. *Cutoff scores, AUC values, sensitivities, specificities, and statistical significance of copper, zinc, and magnesium parameters by study group*

Variables	AUC-ROC (95% CI)	p	Cut-off	Sensitivity	Specificity	+LR	-LR	PP	NP
Copper	0.626(0.532–0.712)	0.026	>159.08	54.88	71.05	1.90	0.64	80.4	42.2
Zinc	0.70(0.579–0.753)	0.002	≤109.6	84.15	44.74	1.52	0.35	76.7	56.7
Magnesium	0.677(0.586–0.760)	0.003	>1.8	90.24	47.37	1.71	0.21	78.7	47.8

AUC: area under the curve; CI: confidence interval.

Table 3. *Evaluation of factors affecting BPPV using binary logistic regression analysis*

Regression coefficients							
						Odds ratio for 95% CI	
	β	Standard error	Wald statistics	p	Odds ratio	Lower limit	Upper limit
Constant	-2.095	0.627	11.177	0.001	0.123	0.958	6.808
Copper	0.938	0.500	3.512	0.061	2.554	0.999	7.373
Zinc	0.998	0.510	3.836	0.050	2.714	2.187	29.581
Magnesium	2.273	0.568	15.994	0.001	9.709		

Variables included in the model: copper, zinc, magnesium; β: regression coefficient; CI: confidence intervals.

Table 4. *Correlations between copper, zinc, and magnesium levels according to study groups*

Groups	Variables	Statistics	Copper	Zinc
Total (n=119)	Zinc	r	-0.103	
		p	0.263	
	Magnesium	r	0.066	-0.078
		p	0.473	0.398
Control (n=38)	Zinc	r	0.286	
		p	0.082	
	Magnesium	r	0.089	-0.056
		p	0.596	0.740
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BPPV (n=81)	Zinc	r	-0.205	
		p	0.064	
	Magnesium	r	-0.096	-0.005
		p	0.389	0.968

r: Spearman's correlation coefficient.

Logistic regression analysis assessed the association between serum copper, magnesium, and zinc levels and BPPV. Magnesium and zinc were significantly associated with BPPV, whereas copper showed a borderline, non-significant association. Odds ratios and confidence intervals are presented in Table 3.

In the BPPV group, no significant associations were found between otological findings and canal involvement, affected side, or comorbidities. Spearman correlation coefficients are shown in Table 4.

In the BPPV group, 54.32% were female, and 45.68% were male. Most patients (87.65%) had no otological findings; tinnitus and aural fullness were present in 9.88% and 2.47%, respectively (Table 5). No significant associations were found between BPPV and canal involvement, affected side, or comorbidities, whereas gender was significantly associated.

Discussion

In this study, the clinical characteristics and serum trace element levels of patients diagnosed with BPPV were evaluated. Posterior semicircular canal involvement was predominantly detected in our study. It has been reported that otoconia are more prone to accumulate in this canal due to the posterior canal's gravity-sensitive anatomical location, and that BPPV most frequently occurs in this form (13,14). The high rate of posterior canal involvement found in our study is consistent with the literature and supports the determining role of anatomical factors in the pathophysiology of BPPV.

Right-sided BPPV was observed more frequently compared to the left side. Predominant involvement of the right labyrinth has been previously reported, and it has been suggested that this may be related to sleeping position habits (15,16). The lateralization findings obtained in our study suggest that behavioral factors may influence otoconial displacement.

The average age of the patients was concentrated in the middle– and advanced-age groups. It is known that the incidence of BPPV increases with age and that age-related otoconial demineralization, weakening of connective tissue fibers, and changes in calcium metabolism contribute to this condition (17,18). Our findings support the negative effects of aging on the vestibular system.

Auditory symptoms accompanying BPPV have been observed infrequently. Tinnitus has been reported to be only weakly associated with BPPV and is therefore not a typical symptom of BPPV (19). The low incidence of tinnitus in our study supports this view. A feeling of fullness in the ear was also rarely detected. Although BPPV has been reported to occur in conjunction with other inner ear pathologies, such as Ménière's disease,

Table 5. *Comparison of gender, canal, side, and comorbidities in the BPPV group*

Variable	Total (n=81)	None (n=71)	Tinnitus (n=8)	Ear Fullness (n=2)	p value
Gender. n (%)					**0.024 η**
Female	44 (54.32)	35 (49.3)	8 (100)	1 (50.0)	
Male	37 (45.68)	36 (50.7)	0 (0)	1 (50.0)	
Canal. n (%)					**0.374 η**
Posterior	78 (96.3)	69 (97.2)	7 (87.5)	2 (100)	
Horizontal	3 (3.7)	2 (2.8)	1 (12.5)	0 (0)	
Side. n (%)					**0.397 η**
Right	51 (62.96)	43 (60.6)	6 (75.0)	2 (100)	
Left	30 (37.04)	28 (39.4)	2 (25.0)	0 (0)	
Comorbidity. n (%)					**0.205 η**
None	57 (70.37)	51 (71.8)	4 (50.0)	2 (100)	
Hypertension	14 (17.28)	13 (18.3)	1 (12.5)	0 (0)	
Diabetes	2 (2.47)	2 (2.8)	0 (0)	0 (0)	
HT + DM	8 (9.88)	5 (7.0)	3 (37.5)	0 (0)	

n: number of patients; %: column percentage; &: chi-square analysis; η: Fisher's exact test; HT: Hypertension; DM: Diabetes Mellitus

this association is limited (20,21). The low incidence of ear fullness observed in our study indicates that this symptom is not specific to BPPV.

Copper is an essential trace element for central nervous system function and plays a key role in fundamental biological processes such as iron metabolism and neurotransmitter synthesis. A previous study reported lower serum copper levels in patients with BPPV, suggesting that reduced copper levels may contribute to disease pathogenesis through mechanisms involving oxidative stress and calcium metabolism (22). In contrast, our findings showed higher serum copper concentrations in the patient group than in the control group. This discrepancy may be due to differences in population characteristics, methodological approaches, and study design, as well as to the complex, multifactorial interactions among trace elements within the vestibular system. Moreover, these findings suggest that alterations in copper levels, rather than absolute deficiency alone, may be relevant to vestibular dysfunction.

Zinc plays a key role in a wide range of biological functions, including enzymatic reactions, immune regulation, and antioxidant defense mechanisms. Elevated serum zinc levels in patients with BPPV have been reported previously; however, this observation has been considered contradictory to certain pathophysiological hypotheses suggesting a protective role of zinc in inner ear homeostasis (22). The discrepancy between the findings of the present study and those reported in the literature underscores the complex, tightly regulated nature of trace element metabolism in vestibular disorders. Variations in zinc levels may reflect differences in population characteristics, dietary habits, and methodological approaches, as well as potential interactions between zinc and copper that could influence vestibular function. Together, these factors underscore the need for a cautious interpretation of serum zinc alterations in the context of BPPV.

Magnesium is a fundamental mineral involved in hundreds of biochemical processes, contributing to neuromuscular function, cellular energy generation, and overall mineral homeostasis (23). Physiological otoconial function relies on a tightly regulated ionic environment within the endolymph, particularly on the balance between calcium and carbonate ions, maintained by calcium-channel–mediated transport in the inner ear. Ultrastructural analyses of human otoconia have demonstrated that both magnesium and calcium play critical roles in shaping otoconial size and structural properties (24). Earlier clinical investigations have noted higher average serum magnesium levels in individuals with BPPV than in control populations, although these differences have not consistently reached statistical significance (25,26).

When interpreted within standard reference ranges, the identified cut-off values for magnesium (1.8 mg/dL), copper (159.08 mcg/dL), and zinc (109.6 mcg/dL) fall within low-normal, upper-limit, and mildly elevated levels, respectively (27–29). These findings suggest that subtle variations within conventional reference intervals, rather than overt deficiencies or toxicities, may be associated with BPPV and highlight

the potential role of mineral homeostasis in vestibular function.

From a clinical perspective, assessment of serum trace elements may provide additional supportive information in selected patients with recurrent, bilateral, or treatment-resistant BPPV. Although canalith repositioning maneuvers remain the cornerstone of management (30), variability in recurrence and treatment response suggests that underlying metabolic or mineral-related factors may contribute to disease behavior. Evaluation of serum magnesium, copper, and zinc levels could therefore be considered as part of a broader clinical assessment in carefully selected cases. Nevertheless, current evidence does not justify routine screening or supplementation in all patients with BPPV. The potential diagnostic, prognostic, and preventive implications of trace element imbalance require confirmation in larger prospective studies before integration into routine clinical practice.

In our study, we found that higher serum magnesium levels significantly increased the incidence of BPPV, even though mean values were within the normal reference range. This finding suggests that even small, clinically insignificant changes in serum magnesium may affect inner ear physiology and BPPV pathogenesis. Furthermore, our results indicate that the ionic composition of the endolymph within which the otoconia are located may be more decisive for vestibular function than systemic serum levels, highlighting the need for more detailed studies in this area.

Conclusion

This study suggests that serum copper, zinc, and magnesium levels in patients presenting with vertigo may be associated with BPPV. The findings indicate that changes in mineral and trace element homeostasis, in particular, may affect the vestibular system. Even if serum levels are within normal reference ranges, relative differences in these elements should be considered potentially contributing to the pathophysiology of BPPV. From this perspective, the evaluation of serum trace elements can contribute to a better understanding of the clinical features of BPPV. Nonetheless, confirmation in larger, prospectively designed cohorts is required before this association can be translated into a diagnostic or predictive application in routine clinical settings.

Several limitations should be acknowledged. First, the control group consisted of vertigo patients without BPPV, which may introduce potential confounding effects related to other vestibular conditions. Second, the retrospective and single-center design limits causal inference and generalizability. Third, only serum copper, zinc, and magnesium levels were evaluated, without assessment of inner ear fluid composition, which may more directly influence otoconial stability. Finally, the lack of serial measurements prevented evaluation of temporal changes in trace element levels. Prospective, multicenter studies are needed to clarify these associations further.

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