ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Should We Look For Blood Parathormone in Patients with Vertigo?

Vertigo Hastalarında Kanda Parathormon Bakmalı mıyız?

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ABSTRACT

Aim: *Though vertigo is a symptom which is defined by an individual as spinning of themselves or an object, it is generally defined by the patients as the sensation of falling, disequilibrium, dizziness and fainting. The main problem on the patients is the determination of the underlying illness. Most of vertigos have peripheral causes and benign paroxysmal positional vertigo takes the first place. It is followed by peripheral and central causes. Patients usually consult the policlinics of Ear, Nose and Throat, internal medicine, neurology in addition to emergency departments with balance disorders. These patients undergo examinations, screening methods, audiology and balance tests and routine blood tests.*

Material and Method: *In this study in which 397 patients who consulted the hospital with complaints of vertigo between 2011 and 2017 evaluated retrospectively.*

Results: *In our study, first of all peripheral causes and 44.8% of these were benign paroxysmal positional vertigo. Hyperparathyroidism was detected in 4 (1%) of the cases in our patient groups that the only complaint was dizziness and there were no other characteristics in the examinations. Parathyroid adenoma was detected in three of them and hyperplasia was detected in the other. In the ones who had adenoma after parathyroidectomy and in the other case after bisphosphonate treatment, both parathormone levels decreased to normal and vertigo complaints totally disappeared.*

Conclusion: *It is recommended that parathormone values should be taken into account in the blood tests during the process of diagnosis in vertigo patients.*

Key words: *vertigo; dizziness; hyperparathyroidism*

ÖZET

Amaç: *Vertigo kişi tarafından etrafındaki objelerin veya kendisinin döndüğü şeklinde ifade edilen bir semptom olmasına karşın, hastalar tarafından genel olarak dengesizlik, sersemlik, düşme ve baygınlık hissi olarak tanımlanır. Hastalarda asıl sorun altta yatan hastalığın belirlenmesidir. Vertigoların çoğu periferik nedenlidir ve ilk sırada benign paroksimal pozisyonel vertigo yer alır. Bunu diğer periferik ve santral nedenler takip etmektedir. Hastalar denge sorunları nedeniyle akut dönemde çoğunlukla acil poliklinikler haricinde Kulak Burun Boğaz, iç hastalıkları, nöroloji polikliniklerine başvururlar. Bu hastalara muayene, görüntüleme yöntemleri, odyoloji ve denge testleri ile rutin kan testleri yapılmaktadır.*

Materyal ve Metot: *Hastanemize 2011–2017 yılları arasında vertigo yakınması ile başvuran 397 hasta retrospektif olarak değerlendirildi.*

Bulgular: *Çalışmamızda, ilk sırada periferik nedenler ve bunların başında da %44,8 oranında benign paroxysmal positional vertigo saptanmıştır. Hasta gruplarımızda tek yakınması baş dönmesi olan, diğer muayenelerinde özellik bulunmayan 4 (%1) olgumuzda hiperparotiroidi saptanmıştır. Bunların üçünde paratiroid adenomu, diğer olguda hiperplazi belirlenmiştir. Adenom saptananlarda paratiroidektomi sonrası, diğer olgumuzda bifosfonat tedavisi sonrası hem parathormon düzeyleri normale inmiş hem de vertigo yakınmaları tamamen kaybolmuştur.*

Sonuç: *Vertigo hastalarında tanı aşamasında kan testlerinde parathormon değerlerine de bakılması tavsiye edilmektedir.*

Anahtar kelimeler: *baş dönmesi; sersemlik; hiperparatiroidi*

Introduction

Vertigo is either a sensation of motion when there is no motion or an exaggerated sense of motion in response to movement[1]. Dizziness comes in many forms in each age group. In pediatric and adolescent the most common diagnosis is a migraine headache, as frequent causes of disequilibrium in adults is Benign Paroxysmal Positional Vertigo (BPPV) [2,3]. Along with that, a group which is defined as idiopathic vestibulopathy is discussed[4].

Primary hyperparathyroidism (PHPT) is a disease which occurs as a result of the fact that parathyroid glands overly release it and which generally appears with hypercalcemia and symptoms related to it. The recent prevalence of PHPT is approximately between 0.25% and 0.66% of the population. Women are more affected than men with a rate of 3:1. Incidence increases as the

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age go up, and it has a dramatic increase after the age of 50[5]. The most frequent cause (% 80–85) for PHPT is parathyroid adenoma[5–8]. The patients of hyperparathyroidism frequently consult doctors with complaints of bone pain, renal calculus, constipation, fatigue, drinking too much water, need to urinate and broken bones stories[9,10]. Asymptomatic pHPT has a prevalence of between 72.7% and 95%, and it becomes the dominant phenotype of pHPT in modern western societies[11,12]. In asymptomatic hyperparathyroidism patients, serum calcium may be slightly high; PTH may be 1.5–2 times higher than average or may be close to the upper limit of normal as a result of being incompatible with calcium level. When retrospectively questioned, symptoms such as depression, fatigue, and lethargy were detected with a maximum rate of 80% in the patients[13,14].

In this study, besides routine biochemical examinations, PTH levels were also checked in the patients who consulted the hospital with complaints of vertigo. Mainly the results of vertigo patients that etiology was not detected were presented with literature knowledge.

Material and Method

In this study in which 578 patients who consulted the hospital with complaints of vertigo between 2011 and 2017 evaluated retrospectively. One hundred eighty-one patients of whom neurological examinations were not completed, who did not have blood results and who were under 18 years old were not included in the study. The Anamnesis, applications and follow-ups, systemic and neurologic examinations, the information of age, sex and biography, the examinations carried out for diagnosis (laboratory results, neuroimaging, the screening of the vascular structure of neck, vestibular and audiological examinations) were recorded from the information obtained from the files. The study protocol was approved by the ethical board of the hospital (2019/02).

From biographic information of the patients, cerebrovascular disease, hypertension, diabetes mellitus, dyslipidemia, chronic obstructive pulmonary disease, atrial fibrillation, migraine, previous cerebrovascular disease, a disorder of thyroid, Parkinson disease, epilepsy, psychiatric story and the story of malignancy were taken under review. Sex and age distributions according to the main symptoms of the patients were determined. All the patients were divided into four groups of peripheral, central, psychogenic and metabolic concerning diagnosis information.

Routine ENT and head and neck examination, Head Thrust Test, dynamic positional tests (Dix-Hallpike and Roll), fistula test, Romberg test, Post-pointing test, walking test (Babinski-Weil) and Fukuda (Unterberger) test were applied on all of the patients.

As laboratory examinations, complete blood count, FT3, FT4, TSH, preprandial blood glucose, urea, creatinine, cholesterol, vitamin B12, vitamin D, PTH and blood calcium tests were carried out. Blood samples were taken at the hours between 08.00 and 09.00 after a night of fasting. Serum calcium and phosphor levels were measured via AU 2700 analyzer (Beckman Coulter, Tokyo, Japan) with the colorimetric method. The concentrations of vitamin D and PTH were measured via Coulter UniCel DxI 600 immunoanalyser (Beckman Coulter, CA, USA).

Neck ultrasonography and 99 mTc-MIBI parathyroid scintigraphy was carried out in order to diagnose and localize the pathologic gland on the patients on whom PHPT was detected. The existence of bone pathology which was caused by hyperparathyroidism was investigated via direct bone radiographic. Selective parathyroidectomy operation was carried out on three patients who possessed adenoma (Figure 1). Bisphosphonate treatment was provided to the case that was thought to be hyperplasia.

Figure 1. *Gross image of parathyroid adenoma.*

The sample size was not calculated for the present study due to the design of the present study, and all patients who treated at our clinic between 2011–2017 were included in the present study. Statistical analyses were carried out on IBM SPSS for Windows Version 22.0 package software program. Numeric variables were summarized with average ± standard deviation while categorical variables were summarized with number and percent. The fact that whether there were any differences in terms of categorical variables was investigated via chi-square test or Fisher exact test. The significance level was taken as $p<0.05$.

Results

In this study, 397 patients (between the ages of 18 and 82) were evaluated. 251 (63.2%) of the patients were female; 146 (36.8%) of them were male. The average age of the patients was 59.9±18.2. The patients were divided into four groups as peripheral, central, psychogenic and metabolic depending on their diagnosis. There were 210 (53%) patients in the peripheral group, 98 patients (24.6%) in central group, 56 patients (14.1%) in the psychogenic group and 33 patients (8.3%) in the metabolic group.

Age distribution of the patients according to their diagnosis related groups was determined. 144 (68.6%) of the peripheral group were female while 66 (31.4%) of them were male, 47 (47.9%) of the central group were female while 51 (52.1%) of them were male, 42 (75%) of the psychogenic group were female while 14 (25%) of them were male, 18 (54.5%) of the metabolic group were female while 15 (45.5%) of them were male. It was observed in the age distribution according to diagnosis-related groups that the women ratio was statistically significantly higher in the psychogenic group ($p<0.001$). The consultation time of the patients in the central group was statistically significantly different from the other groups ($p<0.001$). The patients in the central group had shorter consultation times.

Age distribution of the patients according to their diagnosis related groups was determined. The average age of the peripheral group was 59.1 (±17.7), the average age of the central group was 62.6 (±18.1), the average age of the psychogenic group was 50.7 (±16.1) and the average age of the metabolic group was 61.4 (±18.4). It was observed in the age distribution according to their diagnosis related groups that the average age in the psychogenic group was statistically significantly lower than the other groups ($p<0.001$). Clinical and demographic data of the patients are shown in Table 1.

In this study, the distribution of 210 (53%) patients who were in the peripheral group according to diagnosis-related groups (Table 2). In 178 (44.8%) of these patients, BBPV was detected as the cause, and in 153 of them, posterior canal involvement was detected while lateral canal involvement was detected in 25 of them. 21 of them (5.4%) were diagnosed with Meniere disease, 4 of them (1%) were diagnosed with vestibular neuritis, 4 of them (1%) were diagnosed with the usage of vestibulotoxic drugs, 2 of them (0.5%) were diagnosed with lateral semicircular canal fistula (LMCF) due to chronic otitis, 1 of the patients (0.3%) was diagnosed with superior semicircular canal dehiscence syndrome (SSCD). The patients who were diagnosed with BBPV were treated with canalith repositioning maneuvers (Modified Epley, Barbeque). The treatments of dieting, betahistine HCI and transtympanic steroid treatments were carried on the patients who were diagnosed with

Table 1. *Clinical and demographic data of the patients*

	Peripheral	Central	Psychogenic	Metabolic
Number of Cases	210	98	56	33
Average age	59.1±17.7	62.6±18.1	50.7±16.1*	61.4±18.4
Vertigo presentation duration (days)	6.7±9.8	3.5±6.3**	9.8±12.3	6.2±10.3
Sex		51	14	15
Male	66	47	42***	18
Female	144			
First vertigo attack	60%	72%	65%	80%

* $p<0.001$, ** $p<0.001$, *** $p<0.001$, Chi-square test/Fisher exact test.

Table 2. *The causes of peripheral vertigo*

	Number	All Cases (%)
BPPV	178	44.8
Meniere Disease	21	5.4
Vestibular Neuronitis	4	1.0
Vestibulotoxicity	4	1.0
LSCF	2	0.5
SSCD	1	0.3

BPPV, benign paroxysmal positional vertigo; LSCF, lateral semicircular canal fistula; SSCD, superior semicircular canal dehiscence syndrome.

Table 3. *The causes of central vertigo*

	Number	All Cases (%)
Migrainous Vertigo	33	8.4
VBI	27	6.8
Ischemic Stroke	14	3.5
TIA	9	2.3
SOL	6	1.5
Parkinson	3	0.7
Epilepsy	3	0.7
Demyelinating Disease	3	0.7

VBI, vertebrobasilar insufficiency; TIA, transient ischemic attack; SOL, space occupying lesion.

Meniere disease. The patients who were diagnosed with vestibular neuritis were treated with vestibule-static medications. Rehabilitation training was provided to the patients who were diagnosed with vestibulotoxicity. Mastoidectomy and fistula repair surgery was applied to the patients who had LSCF; symptomatic treatment was adequate on the patient who had SSCD.

The diagnosis distribution of 98 (24.6%) of the patients who were in the central group were determined (Table 3). 33 (8.4%) of the patients were diagnosed with migrainous vertigo, 27 (6.8%) of them were diagnosed with vertebrobasilar insufficiency (VBI), 14 (3.5%) of them were diagnosed with ischemic stroke, 9 (2.3%) of them were diagnosed with transient ischemic attack (TIA), 6 (1.5%) of them were diagnosed with space-occupying lesion (SOL), 3 (0.7%) of them were diagnosed with Parkinson disease, 3 (0.7%) of them were diagnosed with epilepsy, 3 (0.7) of them were diagnosed with demyelinating disease. The treatments of these diseases were carried out at neurology and neurosurgery clinics.

56 (14.1%) patients in the psychological group were diagnosed with a panic attack, depression, generalized anxiety disorder, obsessive personality disorder by the psychiatric clinic where they were directed, and they were treated in the same unit.

In 10 of 33 patients in the metabolic group, vitamin B12 deficiency was detected and its rate compared to the total patient number was 2.5%. It was followed by PHPT with 4 (1%) cases, by an antidepressant setback with 2 (0.5%) cases and by carbamazepine overdose with 1 (0.3%) case. Parathyroid adenoma was identified in three of the patients on whom PHPT was detected. Selective parathyroidectomy was applied to the patients who possessed adenoma. On the postoperative first day, PTH levels of all patients returned to normal, and in the next one-week period all their complaints disappeared. The case in which hyperplasia was detected was taken under bisphosphonate treatment, PTH levels returned to normal in a short time, and the complaints were gone. It was found in PHPT cases in which adenoma was detected that in the first case PTH level was 137pg/mL, in the second case it was 125pg/mL, in the third case it was 85pg/mL, in the fourth case it was 128pg/mL. Post-treatment PTH levels were valued as 12pg/mL, 10pg/mL, 5pg/mL and 8pg/mL respectively. The difference between the PTH levels of pre-treatment and post-treatment was statistically significant ($p<0.05$).

Discussion

Vertigo and balance disorders are significant health problems in every country in the world. Particularly, more than 30% of the people who are over 60 experience dizziness complaints in a period of their lives[3]. About 5% of primary clinic consultations consist of dizziness. This complaint can be limited within four groups concerning patient history: Vertigo, disequilibrium, presyncope, and lightheadedness (nonspecific dizziness). The leading causes of vertigo are benign proximal positional vertigo, Meniere disease, vestibular neuritis, and labyrinthitis. Presyncope mostly occurs as an adverse effect of medications; however, the consultation can be with a diagnosis of Parkinson disease and diabetic neuropathy disequilibrium. Psychiatric disorders such as depression, anxiety, and hyperventilation mostly define lightheadedness[15,16].

Etiologies migraine, migraine, paroxysmal vertigo, psychogenic, viral infections, chronic daily headache, trauma, and postural orthostatic tachycardia syndrome may be frequently seen in adolescence[2]. Dizziness caused by Peripheral is the most frequent complaint in middle-aged and older adults. Among all dizziness types in various studies, BPPV takes the first place with rates of 25–50%, and it was followed by Meniere syndrome, vestibular neuronitis, vestibular migraine, and psychogenic dizziness[2,3,15,19–21]. It was determined in this study that the most frequent cause of dizziness was BPPV in line with the literature. Furthermore, the psychogenic group was statistically more significant than the other groups, and it has consisted of predominantly young and female patients.

The series consisted of the patients who had chronic vertigo complaints. Age groups were in such a wide range as 18–82 years old, and most of them were the patients who were on the fifth and sixth decade. Peripheral causes were seen as the first cause with the rate of 53% in the cases investigated. The most frequent cause was BPPV with a rate of 44.8%, and it was followed by central dizziness with a rate of 26.6%. The total percentage of psychogenic (14.1%) and metabolic (8.3%) groups was as high as 24.4% in this study. When their symptomatology was investigated, it is remarkable that most of them were not specific and there were not significant characteristics in the findings of their examination. The fact that the patients who consulted hospitals with vertigo complaint are treated symptomatically not only in emergency clinics but also in other clinics caused the perception of "vertigo is untreatable" by the patients[3,15,16]. Particularly to the patients who did not possess any symptoms except balance disorder, drug use and quitting taking drugs were asked, neurologic, psychiatric and endocrinological consultations were carried out. Psychiatric and metabolic causes were determined in these cases which were defined as idiopathic vertigo. In the routine examinations which were recommended in this study, hemogram, glucose, thyroid, and lipid metabolism examinations are carried out, and folic acid, vitamin B12, vitamin D, and serum electrolytes levels are measured[16,19,20]. In this study, PTH levels of the cases were investigated in addition to these items.

Vitamin B12 deficiency affects multiple systems, and sequelae vary in severity from mild fatigue to severe neurologic impairment. Neurologic manifestations are caused by progressive demyelination and can include peripheral neuropathy, areflexia and the loss of proprioception and vibratory sense[22]. Hunt et al. reported asymptomatic vitamin B12 deficiencies with the rates which increase by age in several societies[23]. In this study, vitamin B12 deficiency with the rate of 2.5% was detected on the patients who consulted with the complaint of a balance disorder.

Even though there are several studies carried out on the links between hypercalcemia, vitamin D deficiency and disequilibrium, gait disorder and BPPV; there is no relationship reported between PHPT which continue with normal calcium and phosphates levels and vertigo[17,18]. PHPT is a clinical syndrome which leads to hypercalcemia (occasionally normocalcemia) and hypophosphatemia caused by excessive PHT release and continues with the diagnosis depending on this fact. It is generally defined as the disease of stones, bones, abdominal cavity, and psychogenic complaints. Besides typical symptoms, gait disorder, disequilibrium, and psychiatric disorders, as well as nonspecific symptoms such as cervical and mediastinal hemorrhaging which occurs due to spontaneous laceration of parathyroid adenoma, may appear[6,24–28].

Recently, primary HPT means the HPT table on which there are no complaints of skeletal, renal and neuromuscular systems[7–10]. Despite being asymptomatic during preoperative evaluations, patients often report post-operative retrospective amelioration of unreported preoperative sign and symptom of hyperparathyroidism[29]. Frequent non-specific symptoms in the general population might be partly responsible for that, as they often make the diagnosis difficult and interdisciplinary[30].

PTH levels which increased with normal serum calcium are less occasionally seen in the cases of asymptomatic hyperparathyroidism. The diagnosis of this case is provided with the fact that there are no causes to increase secondary parathormone and the level of serum 25-hydroxyvitamin D remains normal level. In the countries where vitamin D deficiency is widely seen, the occurrence frequency of normocalcemic hyperparathyroidism increases depending on the fact that vitamin D deficiency masks the increase in the serum calcium concentration which is linked to PHPT[14]. The fact that most of the dizziness does not have any typical symptomatology and vitamin D deficiency prevalence is high in Turkey lowered the PHPT probability. As a result of this fact, PTH levels of the patients who consulted the hospital with vertigo complaint were

checked routinely. In the ones who had high PTH, the existence of parathyroid adenoma was investigated. In the ones in whom adenoma was detected, the adenoma was surgically removed. In another patient who did not possess adenoma and diagnosed with hyperplasia, symptoms dramatically disappeared with bisphosphonate treatment. These two cases strengthened the hypothesis of this study.

The relationship between hyperparathyroidism and vertigo is not clear. Wu et al. and Guler et al. remarked that the relationship between BPPV and hypercalcemia and asserted that the calcium increase in canalith might be caused by this[17,18]. Vosnakidis et al. detected hypercalcemia and HPT as the cause of atrioventricular block on a patient who consulted with the complaints of dizziness and headache. They related this fact to calcium cumulating in the heart of the patient[31]. It is thought that, in some of HPT cases, the tables such as metabolic syndrome, pancreatitis, cardiovascular diseases, and autoimmune gastritis may be related to asymptomatic calcium depositions on these organs10. Lundberg et al. stated in their experimental studies that calcium depositions may occur on membranous labyrinth endolymph which is deficient in calcium ions[32].

As a conclusion, it is recommended that in the patients who consult with complaints of balance disorder, all the symptoms which are nonspecifically evaluated in their history should be evaluated carefully and algorithms regarding the etiology should be constituted. It is also recommended that parathormone values in blood should be investigated as hyperparathyroidism was detected as a cause of vertigo with a rate of 1% in this study.

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