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Original Article / Çalışma - Araştırma

The relationship of homocysteine, vitamin B12, folic acid levels with vertigo

Homosistein, B12 vitamini ve folik asit düzeylerinin vertigo ile ilişkisi

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Objectives: In this study the relationship of serum homocysteine, vitamin B12, folic acid levels and peripheral vestibular dysfunction (PVD) was investigated.

Patients and Methods: Forty-one patients (31 females, 10 males; mean age 57.3±14.3 years; range 12 to 80 years) who admitted to Baskent University Hospital Ear Nose and Throat Department between the dates of April 2005 - December 2007 with complaint of vertigo were prospectively analyzed and diagnosed using audio-vestibular test, at the same time serum homocysteine, vitamin B12, folic acid measurements was done from the blood samples of patients. The patients were divided into three groups as Meniere's disease, vestibular neurinitis, and benign paroxismal positional vertigo (BPPV) according to the diagnoses and serum homocysteine, vitamin B12, folic acid levels of patients were compared to normal values in and between groups.

Results: Of the patients, 29.3% (n=12) were diagnosed with Meniere's disease, 36.6% (n=15) with vestibular neurinitis, and 34.1% (n=14) with BPPV. Serum homocysteine leves of patients were 12.42±3.56 umol/L, 11.32±4.14 umol/L and 10.72±2.95 umol/L (p>0.05) in Meniere's disease, vestibular neurinitis, and BPPV respectively; vitamin B12 levels were 371.58±141.35 pg/ml, 288.13±139.51 pg/ml, 352.14±150.41 pg/ml (p>0.05) respectively and folic acid levels were 8.76±3.2 umol/L, 10.63±6.59 umol/L, 8.8±3.18 umol/L (p>0.05) respectively. The values were similar in all patients. No statistically significant difference was found in and between groups comparing with normal values.

Conclusion: This is the first prospective study investigating the relationship of serum homocystein, vitamin B12 and folic acid levels with PVD. We found that there is no relationship of homocysteine, vitamin B12, folic acid levels with PVD.

Key Words: Folic acid; homocysteine; vertigo; vitamin B12.

Amaç: Bu çalışmada serum homosistein, vitamin B12, folik asit düzeyleri ile periferal vestibüler disfonksiyon (PVD) arasındaki ilişki incelendi.

Hastalar ve Yöntemler: Baş dönmesi yakınması ile Nisan 2005 - Aralık 2007 tarihleri arasında Başkent Üniversitesi Hastanesi Kulak Burun Boğaz Anabilim Dalı'na başvuran 41 hasta (31 kadın, 10 erkek; ort. yaş 57.3±14.3 yıl; dağılım 12-80 yıl) odyovestibüler testler ile prospektif olarak incelendi ve tanıları konuldu, aynı zamanda hastalardan alınan kan örneğinden serum homosistein, vitamin B12 ve folik asit düzeylerinin ölçümü yapıldı. Hastalar konulan tanı doğrultusunda Meniere hastalığı, vestibüler nörinit ve benign paroksismal pozisyonel vertigo (BPPV) üç gruba ayrıldı. Hastaların serum homosistein, vitamin B12, folik asit düzeyleri gruplar arasında ve grup içinde normal değerlere oranlanarak karşılaştırıldı.

Bulgular: Hastaların %29.3'üne (n=12) Meniere hastalığı, %36.6'sına (n=15) vestibüler nörinitis ve %34.1'ine (n=14) BPPV tanısı konuldu. Serum homosistein düzeyleri sırasıyla Meniere hastalığı, vestibüler nörinit ve BPPV grubunda 12.42±3.56 umol/L, 11.32±4.14 umol/L ve 10.72±2.95 umol/L (p>0.05); vitamin B12 düzeyleri sırasıyla 371.58±141.35 pg/ml, 288.13±139.51 pg/ml, 352.14±150.41 pg/ml (p>0.05) ve folik asit düzeyleri sırasıyla 8.76±3.2 umol/L, 10.63±6.59 umol/L, 8.8±3.18 umol/L (p>0.05) olarak hastaların tümünde benzer bulundu. İstatistiksel olarak normal değerlere oranla grup içinde ve gruplar arasında anlamlı bir farklılık bulunmadı.

Sonuç: Bu çalışma serum homosistein, vitamin B12, folik asit düzeyleri ile PVD arasındaki ilişkiyi inceleyen ilk prospektif çalışmadır. Homosistein, vitamin B12 ve folik asit düzeyleri ile PVD arasında bir ilişki bulunmadı.

Anahtar Sözcükler: Folik asit; homosistein; vertigo; vitamin B12.

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The inner ear is a sensitive organ that has a blood-labyrinth barrier separating its blood supply from circulating blood in the body. Nevertheless, vestibular function is sometimes affected by metabolic changes.[1] When the vestibular function is affected in any way, we encounter a patient with vertigo. The assessment of these patients is based on the differentiation between central and peripheral vestibular dysfunction,[2] but not all of the reasons that cause vertigo are adequately known. Vascular damage in the labyrinth is another possible pathophysiologic reason for vertigo. There have been very few studies investigating the blood parameters related to hemostasis in vertigo. A lot of blood tests have been developed for determining hereditary or acquired thrombosis.[3] Hyperhomocysteinemia, vitamin B12 and folic acid deficiency are risk factors for both arterial and venous thrombosis.

There is a complex pathway related with the metabolism of the amino acid methionine to cysteine. Homocysteine plays an important role in this pathway which depends on vitamin B12, B6, and folic acid.[4] Homocysteinemia may increase the risk of vascular damage in labyrinth by factors such as toxic damage to the endothelium, simulation of proliferation of smooth muscle cells, enhanced low density lipoprotein peroxidation, increased platelet aggregation, effects on coagulation system.[4]

There have been very few studies performed to detect the vascular damage or alteration on hemostasis in patients with vertigo.[2,3,5-9] The aim of this study to evaluate the role of serum homocysteine, vitamin B12 and folic acid levels in patients with vertigo who were referred to our department because of peripheral vestibular dysfunction.

PATIENTS AND METHODS

A total of 41 patients (31 females, 10 males; mean age 57.3±14.3 years; range 12 to 80 years) referred to the Başkent University Hospital, Department of Otorhinolaryngology with peripheral vertigo included in this study. This study was performed with the permission of the ethics committee of the Başkent University Hospital (07.12.2004; 04/178).

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The anamnesis of all patients was acquired and then all patients underwent audio-vestibular tests according to the possible diagnosis of vertigo. Informed consent forms were obtained from the patients after explanation of the study, than a single 5-ml venous sample for serum homocysteine, vitamin B12, and folic acid detection was collected. Vitamin B12 and folic acid were measured using immunoassay procedure (Immunolite 2000-BIODPC, USA); homocysteine were measured using Fluoresence Polarization Immunoassay procedure (AxSYM Systems, ABBOTT, IL, USA).

These data were evaluated to the normal values of homocysteine, vitamin B12 and folic acid according to the manufacturer's instructions. The normal serum values of homocysteine, folic acid, and vitamin B12 were 3.36-20.44 umol/L, 3-17 umol/L, 193-982 pg/ml respectively.

After audiological and electronystagmographic or videonystagmographic tests 29.3% (n=12) of patients were diagnosed with Meniere's disease according to the guidelines of the Committee on Hearing and Equilibrium of the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS); 36.6% (n=15) were diagnosed with vestibular neurinitis; and according to the vestibular positional tests 34.1% (n=14) were diagnosed with benign paroxysmal positional vertigo (BPPV). All patients were treated according to their diagnosis.

Kruskal-Wallis test was used to detect the differences among the three vertigo groups (Meniere's disease, vestibular neurinitis, and BPPV). P value <0.05 was considered statistically significant.

RESULTS

In this study 29.3%, 36.6%, and 34.1% of the patients were diagnosed with Meniere's disease, vestibular neurinitis, and BPPV respectively.

There were no significant differences in age between the three groups (Meniere's disease, vestibular neurinitis, and BPPV). The ages and number of patients are shown in Table 1.

Table 1. Age and number of the patients in three groups of patients

	n	%	Mean±SD
Meniere's disease	12	29.3	55.5±10.8
Vestibular neurinitis	15	36.6	59.5±15.9
BPPV	14	34.1	56.6±15.8

SD: Standard deviation; BPPV: Benign paroxysmal positional vertigo.

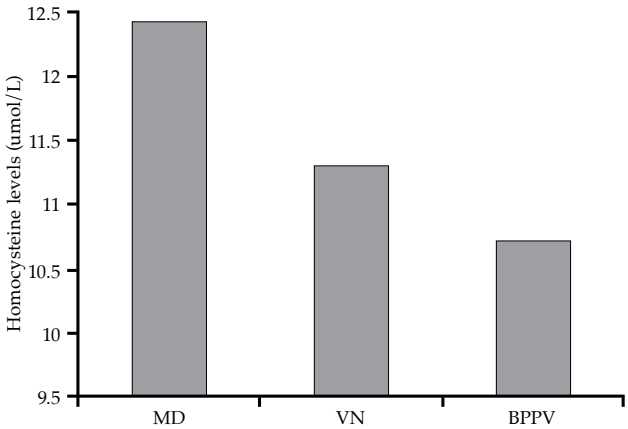

Figure 1. *Serum homocysteine levels in three groups. MD: Meniere's disease; VN: Vestibular neurinitis; BPPV: Benign paroxysmal positional vertigo.*

The mean ± SD of serum homocysteine levels were 12.42±3.56, 11.32±4.14, and 10.72±2.95 umol/L in the groups of Meniere's disease, vestibular neurinitis, BPPV. There were no statistical differences between these groups (p>0.05; Figure 1).

The mean ± SD of vitamin B12 levels were 371.58±141.35, 288.13±139.51, and 352.14±150.41 pg/ml in the groups of Meniere's disease, vestibular neurinitis, BPPV. There were no statistical differences between these groups (p>0.05; Figure 2).

The mean ± SD of serum folic acid levels were 8.76±3.2, 10.63±6.59, and 8.8±3.18 umol/L in the groups of Meniere's disease, vestibular neurinitis, BPPV. There were no statistical differences between these groups (p>0.05; Figure 3).

There were 19 patients (46.3%) with hypertension, two (4.9%) with hyperlipidemia, four (9.8%) with hypothyroidism, one (2.4%) with hyperthyroidism, and four (9.8%) with diabetes mellitus. The serum levels of homocysteine, vitamin B12, and folic acid were within normal.

DISCUSSION

Homocysteine which induces vascular oxidative stress, is one of the vasoconstrictive factors. It was described as a sulfur-containing amino acid and intermediary product of methionine metabolism in 1932 by de Vigneaud.[10] Hyperhomocysteinemia disrupts endothelium dependent vasodilatation and it is also known that homocysteine is a risk factor for atherosclerosis.[4] Atherosclerosis causes damage in organs perfused especially by end-arterial systems as the cochlea.[11] It may also stimulate proliferation of vascular smooth cells and is also a risk factor for arterial and venous thrombosis.[12] The cause of these effects is related to inhibition of endothelial NO (nitric oxide) synthesis and overproduction of oxidative radicals. Nitric oxide has antiplatelet activity and is known to prevent vasoconstriction.[13] These produced radicals such as hydrogen peroxide, superoxide anion, hydroxyl anion may impair the endothelium dependent activation of protein C which predisposes to thrombosis, and cause intimal damage.[4,12,14] In other terms elevated levels of homocysteine lead to increased vascular accumulation of reactive oxygen species which is mediated by increased superoxide output in vascular cells via mechanisms involving nitric oxide synthase and increased homocysteine oxidation.[14]

Hyperhomocysteinemia has been estimated to be 5% in the general population.[11] Hyperhomocysteinemia occurs in two ways. In one way it occurs by the inability of homocysteine to remethylate to methionine and in the other by transsulfuration of methionine to cysteine.

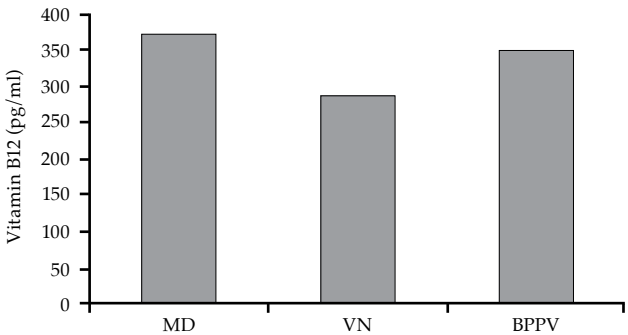

Figure 2. *Serum vitamin B12 levels in three groups. MD: Meniere's disease; VN: Vestibular neurinitis; BPPV: Benign paroxysmal positional vertigo.*

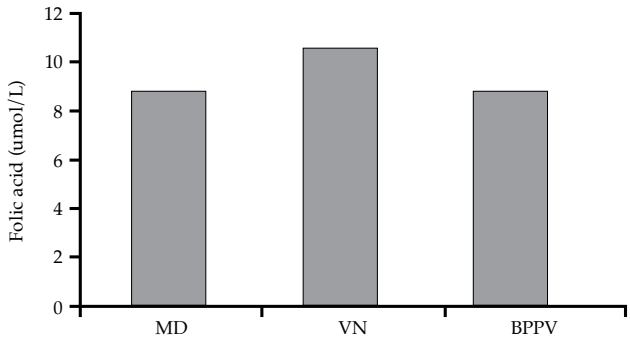

Figure 3. *Serum folic acid levels in three groups. MD: Meniere's disease; VN: Vestibular neurinitis; BPPV: Benign paroxysmal positional vertigo.*

Folic acid, vitamin B6, and vitamin B12 are important factors in these two processes.[12] Because homocysteine metabolism requires folate and vitamin B6.[15] Due to folic acid, vitamin B12, and vitamin B6 are important dietary determinants of homocysteine. In some studies, it was shown that daily folic acid, vitamin B12, vitamin B6 supplementation lower homocysteine levels.[10,16-18] In spite of this in other studies researchers did not find beneficial effects on major vascular events.[19,20]

It is known that the frequent causes of peripheral vertigo are BPPV, vestibular neurinitis and Meniere's disease. However the pathophysiology of peripheral vertigo is not exactly clear. A possible pathophysiologic factor may be an ischemic condition of the labyrinth. The inner ear is protected from abnormalities in the circulating blood by the blood-labyrinth barrier but vestibular function can be affected by metabolic disorders.[1] On the other hand the labyrinthine branches are small and receive less collateral flow from the internal carotid artery so that it becomes a target of the effects of atherosclerosis.[2] There are not a lot of studies related for this possible factor. Fattori et al.[3] showed that most patients with acute unilateral peripheral vestibular dysfunction had multiple important alterations in hemostasis. Scaramella[12] published a case report and postulated that hyperhomocysteinemia predisposed a patient to clot formation in the left internal jugular vein and to develop Meniere's symptoms. The author considered that the clot in the jugular vein caused an increase in venous pressure that resulted in venous insufficiency in the vestibular organs. Couloigner et al.[21] showed that surgical lowering of the high jugular bulb improved symptoms of Meniere's disease and pulsatile tinnitus. Gomez et al.[2] indicated in their studies that isolated vertigo could be a manifestation of vertebrobasilar ischemia. The authors showed that focal atherosclerotic narrowing or widespread narrowing of the vertebrobasilar system could cause vertigo, and reported successful management of most of their patients with anticoagulation therapy.[2] Grad and Baloh[22] postulated that isolated episodes of vertigo could be explained on the basis of transient ischemia to the vestibular labyrinth. Mahmud et al.[23] reported a patient with vitamin B12 deficiency who developed paroxysmal positional vertigo which disappeared with cyanocobalamin therapy.

In this prospective study, we found that there is no correlation between homocysteine, vitamin B12, folic acid levels and peripheral vestibular dysfunction. Thus it may be claimed that vascular effects due to hyperhomocysteinemia and folic acid, vitamin B12 deficiency may play only a minor role in peripheral vertigo. In our study we had a limited number of patients so that additional studies are required to explain the effects of homocysteine, folic acid, and vitamin B12.

In conclusion, this is the first prospective study investigating the relation between serum homocysteine, Vitamin B12 and folic acid levels with vertigo. In this study we found that there is no correlation between homocysteine, vitamin B12, folic acid levels and peripheral vestibular dysfunction.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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