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Evaluation of biochemical variables in patients with trigeminal neuralgia

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Abstract

The aim of this study was to evaluate the calcium, sodium, potassium, serum iron, vitamin B12, and albumin concentrations, and alkaline phosphatase (ALP) activity, in samples of serum from patients with primary trigeminal neuralgia (TN), and investigate the associations between them. Results from 73 patients who had been diagnosed with primary TN between December 2015 and 2017 were compared with those of 70 healthy subjects. Calcium ($p = 0.013$), iron ($p = 0.004$), and albumin ($p = 0.001$) concentrations in the primary TN group were significantly lower than those in the control group, whereas the ALP activity was significantly higher in the TN group than in the control group ($p = 0.007$). However, there was no significant difference in the sodium, potassium, or vitamin B12 concentrations. Biochemical variables have a role in the pathogenesis and treatment of primary TN, but there are few studies that characterise the relations between the condition and the biochemical changes. Further studies are therefore necessary to gain more information.

Keywords: Primary Trigeminal Neuralgia; Biochemical Parameters; Serum Biochemistry

Introduction

Primary trigeminal neuralgia (TN) is a chronic disease that is characterised by episodes of sudden, severe, paroxysmal pain in the face.[1] The incidence is between 4 and 27/100 000 people and it is more common in women and elderly people. The pain can be initiated either by certain stimuli or spontaneously, and the duration of these episodes ranges from seconds to minutes.[2–4] Although it is argued that vascular pressure on the trigeminal nerve is its most common cause, there is no consensus.[5–7] As the pathogenesis of primary TN is not fully understood, various treatments have been recommended.

In many systemic diseases, there is a correlation between the biochemical variables and the disease, and their regulation influences the treatment. A recent study examined the relations between primary TN and some biochemical variables and found that they were altered in affected patients.[8] We measured biochemical variables in our patients, and analysed the associations between them and primary TN.

Patients and methods

Between December 2015 and December 2017, 91 patients in the Department of Neurology at Adıyaman University Fac-

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ulty of Medicine were diagnosed with primary TN, based on the diagnostic criteria of the American Academy of Neurology (AAN) and the European Federation of Neurological Societies (EFNS).[9,10] The criteria were:

the presence of paroxysmal pain in the area reached by the trigeminal nerve; assessment of the symptoms of primary TN; and the presence of demyelination or vascular malformations on neurological examination with magnetic resonance imaging.

Blood biochemistry values of 73 out of 91 patients were included as the study group, while the remaining 18 patients were excluded because of deficiencies in the biochemical variables; systemic diseases; smoking; and the use of alcohol, narcotics or medicinal drugs.

The control group comprised the biochemistry values of 70 healthy people who did not have TN or any systemic disease, and who did not use cigarettes, alcohol, narcotics, or medicinal drugs. We compared the concentrations of calcium, sodium, potassium, serum iron, vitamin B12, and albumin, and the activity of alkaline phosphatase (ALP), in the two groups. This was a retrospective study and was approved by the University Ethics Committee with approval number 2017/5-13.

Statistical analysis

The data were analysed with the help of IBM SPSS Statistics (version 22, IBM Corp). The ShapiroWilk test for normality was used to assess the normality of the sample, and the Mann Whitney *U* test was used to calculate the significance of differences between the groups as the variables were not normally distributed. The chi squared test was used to compare associations between groups of nominal variables. Probabilities of less than 0.05 were accepted as significant.

Results

There were 54 female and 19 male patients in the TN group, mean (SD) age 58 (18) years (range 24-90). This compared with 49 women and 21 men in the control group, mean (SD) age 54 (15) years (range 27-90).There was no significant difference between the groups and the distributions were homogeneous. The biochemical results are shown in Table 1.

Table 1
Results of comparisons of biochemical results between patients with primary trigeminal neuralgia (TN, n = 73) and controls (n = 70).

Variable	Mean (SD)	Range	p value
Calcium (mmol/L):			0.013
TN	2.25 (0.44)	2.1-2.6	
Control	2.3 (0.1)	2.1-2.57	
Potassium (mmol/L):			0.709
TN	4.38 (0.41)	3.2-6.1	
Control	4.37 (0.42)	3.4-5.4	
Sodium (mmol/L):			0.092
TN	138.12 (3.59)	125-149	
Control	138.78 (2.25)	132-143	
Iron (μmol/L):			0.004
TN	12.6 (4.6)	2.1-27.2	
Control	14.2 (4.9)	1.9-31.3	
Vitamin B12 (pmol/L):			0.274
TN	177.9 (115.9)	36.9-708.2	
Control	172.6 (62.6)	58.3-405.1	
Alkaline phosphatase (U/L):			0.007
TN	82.45 (22.47)	37-174	
Control	73.03 (16.74)	25.127	
Albumin (g/L):			0.001
TN	35.8 (4.8)	21-50	
Control	39 (2.6)	34-46	

Discussion

Primary TN is characterised by sudden, sharp, attacks of pain in one or two branches of the trigeminal nerve that can last from a few seconds to a few minutes. TN is usually diagnosed in the 4th-6th decades of life and often among women. The mean age of our patients was 58 years and TN was about three times more prevalent among women than men. These findings are in agreement with those given in other publications.

Although the pathogenesis is not well known, it is hypothesised that microvascular decompression, autoimmune disorders, anatomical variations, and biochemical effects all have roles in it.[6–8] The most popular of these hypotheses is decompression of microvessels, where it has been suggested that vascular compression near the nerve roots may cause segmental demyelination of the nerves that results in TN. The microvasculature decompression is thought to be caused by the neovascular decompression of the trigeminal nerve at the posterior cranial fossa. Although there may be an additional symptomatic cause such as multiple sclerosis, tumour, or arteriovascular malformation in some patients, the pathogenesis of these conditions is not fully understood. Neurovascular structures are affected by malformations in the vascular structure, atherosclerotic changes, oedema, or a tumour in the vascular zone.[11]

It has recently been suggested that there may be a relation between blood biochemistry and TN, as some of the underlying causes of changes in these biochemical variables are thought to be changes in the systemic and vascular structures. We therefore aimed to investigate this.

Although most of the calcium in the body is found in bone as calcium phosphate, it has many other vital functions. One of these is modulating neuronal conductance, and low concentrations of calcium may cause spontaneous uncontrolled neurotransmission, resulting in inflammation of nerve fibres.[12] In a recent study by Zhao et al calcium concentrations in patients with TN were reported to be lower than those in healthy subjects.[8] In the present study calcium concentrations were also lower in the patients than in the control group. Calcium may therefore cause changes in nerve conduction in patients with TN.

Sodium and potassium are vital for cellular metabolism, are used in the transport of ions between cells, and are regulated by the sodium and potassium pumps.[13] In our study, the concentrations of these two elements were similar in the two groups, which suggests that in primary TN they fulfill functions similar to those in healthy people.

The increase in the serum concentration of iron has been suggested as a cause of atherosclerosis through arterial thickening, and atherosclerosis in the patients with TN may be involved in its pathogenesis by compressing the branches of the trigeminal nerve. However, serum concentrations of iron in our patients were lower than those in the control group.[14,15] In contrast, a recent study found that they were higher in patients than in healthy controls.[8] As the results of this study do not correlate with ours, further research is necessary to find out the associations between primary TN and the serum concentration of iron.

Vitamin B12 is closely associated with nervous tissue, and vitamin B12 deficiency has been reported to cause demyelination in the spinal nerves.[12] Although vitamin B12 concentrations in patients with TN were reported to be low in other previous studies, and patients were treated with vitamin B12 supplements, this treatment has now been abandoned.[16,17] In our study, concentrations of vitamin B12 in patients were similar to those in the control group, indicating that TN is not associated with vitamin B12, and suggesting that it cannot be treated with vitamin B12 supplements.

ALP is an enzyme that is linked to the cell membrane and is made of glycoproteins. It causes vascular calcification by reducing pyrophosphate, which is an effective inhibitor of vascular calcification. Increased vascular calcification, in turn, causes atherosclerosis in the vascular structures.[18–20] In the present study, ALP activity in blood in patients was higher than in the control group, which suggests that the increase in ALP activity may cause vascular decompression as a result of calcification. As a result, the trigeminal nerve may be affected by the atherosclerotic changes in the vascular structure, which is thought to be a cause of TN.

Albumin is the most common protein found in human plasma, and a decreased albumin concentration is the main reason for increased oedema in the body. A decrease in albumin can also indicate infection.[21,22] Albumin concentrations in our patients were significantly lower than those in the control group, so the risk of oedema could be higher in the patients, which would adversely affect the trigeminal nerves.

For the treatment of primary TN, the AAN and EFNS suggested that carbamazepine or oxcarbazepine should be the primary choice, with baclofen or lamotrigine as the second choices, and levetiracetam, gabapentin, pregabalin, topiramate, and Botox® as the third choices, and they proposed surgical treatment only after the exhaustion of the first three therapeutic approaches.[9,10] However, these are used to treat the symptoms, rather than the cause of the disease.

The difficulty in the treatment of TN is a lack of understanding of its pathogenesis. Among previously published studies, only one investigated the calcium, phosphorus, magnesium, and iron concentrations in affected patients,[8] and older studies examined the associations between it and vitamin B12 concentrations.[16,17] We found that, in addition to calcium, iron, and vitamin B12 concentrations, there were also associations with sodium, potassium, and albumin concentrations, and ALP activity. Our results might suggest that regulation of biochemical abnormalities through supplements might provide an alternative treatment for primary TN. However, further studies are needed to confirm and clarify this.

We conclude that these results suggest that the biochemical variables may have a role in the pathogenesis and regulation of TN, and may be effective in its treatment. Further studies with extended numbers, and studies that analyse the use of these variables for the treatment of TN, are necessary to better understand these associations.

Conflict of interest

We have no conflicts of interest.

Ethics statement/confirmation of patients' permission

This study has been approved by the University Ethics Committee with approval number 2017/5-13. Patients' permission was obtained.

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