

Serum level of ionized calcium in patients with migraine during a migraine attack and times without migraine

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Abstract

Introduction: Migraine is known as a debilitating headache. The aim of this study was to compare the level of serum ionized calcium in patients with headache attack and in normal subjects. To assess and compare the serum ionized calcium, which is the active form of this ion level during the migraine attack and in the normal subject (with no headache).

Material and Methods: The study was performed on 50 patients who were referred to the Jahrom, Honari Clinic. Migrainous patients were selected according to the Criteria of International Headache Society (IHS). Serum ionized calcium level was measured by Ion Selective Electrode (ISE) method.

Results: Seventy- six percent of all patients who participated in this study were women, the rest of them were men. Mean age for women was 34.8 years old and for men 37. Mean serum level of ionized Ca²⁺ was 3.5 mmol/L and 4.5 mmol/L in women during the headache attacks and normal subjects respectively and Mean serum level of ionized Ca²⁺ was 3.7 mmol/L and 4.3 mmol/L in men during the

headache attacks and normal condition (with no headaches) respectively. There was a significant difference in serum Ca²⁺ level during migraine attacks which decreased significantly compared with normal mode in women and men (P<0.05).

Conclusion: According to the results obtained in this study, serum levels of Ca²⁺during migraine attacks decreased significantly compared with normal subjects, which indicates Ca²⁺ has an impact on these attacks. However, more research in this area appears to be needed.

Key words: Serum ionized calcium, migraine, headache attack

Introduction

Migraine is a common headache that may be accompanied by symptoms such as nausea, vomiting and increased sensitivity to light and sound, which is called migraine with aura (MA) (1). The main symptom of a migraine is usually an intense headache on one side of the head (2, 3). This debilitating progressive and chronic neurovascular disorder affects approximately 6% of males and 18% of females worldwide (4). Migraine is more frequent in midlife with 3- fold more prevalence in women. The prevalence of migraine in European adults is 14.7% and in Asian countries is 3% in men and 10% in women (5, 6).

In Iran, migraine is of the most common types of headache. Evidence shows that migraine prevalence is 95% in south of Iran, which is considered high (3). Regarding the high incidence and prevalence of migraine and its disabling nature, it seems crucial to detect the exact mechanism. This can guide us through better plans for disease management. Extensive research has been done on the role of minerals and many studies have been made on the role of magnesium and calcium in the pathophysiology of migraine (6).

Previous studies described that neuromuscular disorders may be due to changes in amount of active form of calcium (7) and also calcium-phosphate metabolism disturbance was seen in relapsing-remitting multiple sclerosis (RRMS) patients, which increases during disease progression (8).

In addition, some probable mechanisms have described the relationship between calcium level and migraine headache attacks (9). For example, studies have shown that serum magnesium levels in migraine patients compared to healthy controls is slightly lower and the level of serum calcium is higher (3). Overall most research has been done on the effect of magnesium on migraine attacks and less research has been done in the case of calcium. Calcium is known to have anti-spasmodic action, which helps alleviate headaches and migraines (10).

However, studies have shown that when calcium is administered along with Vitamin D, it reduces the frequency of migraines in a considerable number of patients (11). Magnesium and calcium interact with each other. If blood has overly high calcium levels, the body may excrete the extra calcium (1). This can trigger a loss of magnesium, which is expelled along with the calcium, leaving a magnesium deficiency and conflicting results have been reported in association with calcium levels in patients with migraine (1, 5).

Due to the high prevalence of migraine, complications, medical and psychological comorbidities and effective symptoms on patient quality of life, limitations on the use of appropriate treatment and the need to prevent attacks of the disease (12), doing research on this disease is essential to evaluate the hypothesis that serum ionized calcium is a causal risk factor for migraine headache.

The aim of this study was to assess and compare the level of serum ionized calcium, which is the active form of this ion, during the migraine attack and in normal subjects (those with no headache).

Materials and Methods

This cross sectional and analytical study has been done on 50 patients with headache referred to Honari Neurology Clinic of Jahrom, Iran, who had inclusion criteria for migraine (13).

Patients completed a questionnaire containing information such as age, sex, history of trauma, smoking, family history of migraine or a history of mental disorder.

In this study 5 mL of blood sample was taken from each patient during the migraine attack and when they were in a normal condition (no headaches at the time of blood sampling). The blood samples were centrifuged at 3000 rpm for 10 minutes. After separation of the serum, 300 microliters serum were collected from patients to determine serum level of Ca²⁺ by Ion Selective Electrode (ISE) method using ISE analyzer (14).

An ion-selective electrode is a transducer (or sensor) that converts the activity of a specific ion dissolved in a solution into an electrical potential. The voltage is theoretically dependent on the logarithm of the ionic activity, according to the Nernst equation. Ion-selective electrodes are used in analytical chemistry and biochemical/biophysical research, where measurements of ionic concentration in an aqueous solution are required (15, 16).

Prior ethical approval was obtained, and in using these human tissues, safety and ethical guidelines were conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent before entry, and the research study was approved by the Human Ethics Committee of the Jahrom University of Medical Sciences with ethics research committee number: JUMS. ERC.1392-1125.

Results were reported as mean \pm Standard deviation (SD). The groups were compared using t tests (and non-parametric tests) comparisons using Graph pad prism (version 6) software. P values < 0.05 were considered as significant difference between groups.

Results

The patients were aged 21-60 years who were 76% women and the rest = men, with a mean age of 34.8 years for women and 37 years for men.

Mean serum level of Ca²⁺ was 3.5 mmol/L and 4.5 mmol/L in women during the headache attacks and normal respectively and Mean serum level of ionized Ca²⁺ was 3.7 mmol/L and 4.3 mmol/L in men during the headache attacks and normal condition (with no headaches) respectively. There was a significant difference on serum Ca²⁺ level during migraine attacks decreased significantly compared with normal mode in women and men (P values <0.05).

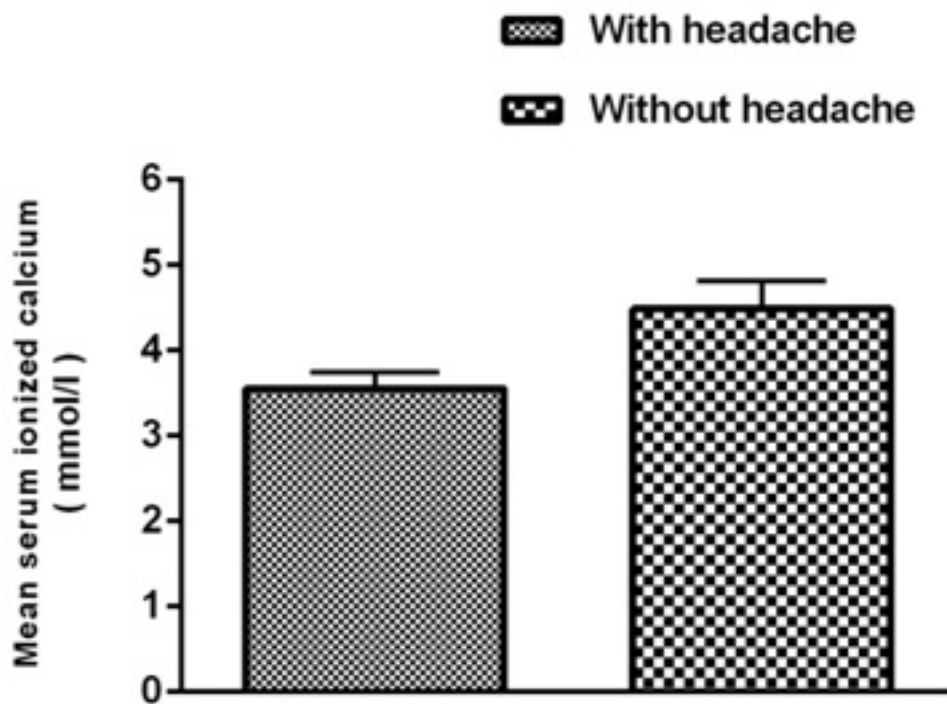


Figure 1: Decreasing ionized calcium level during migraine headache

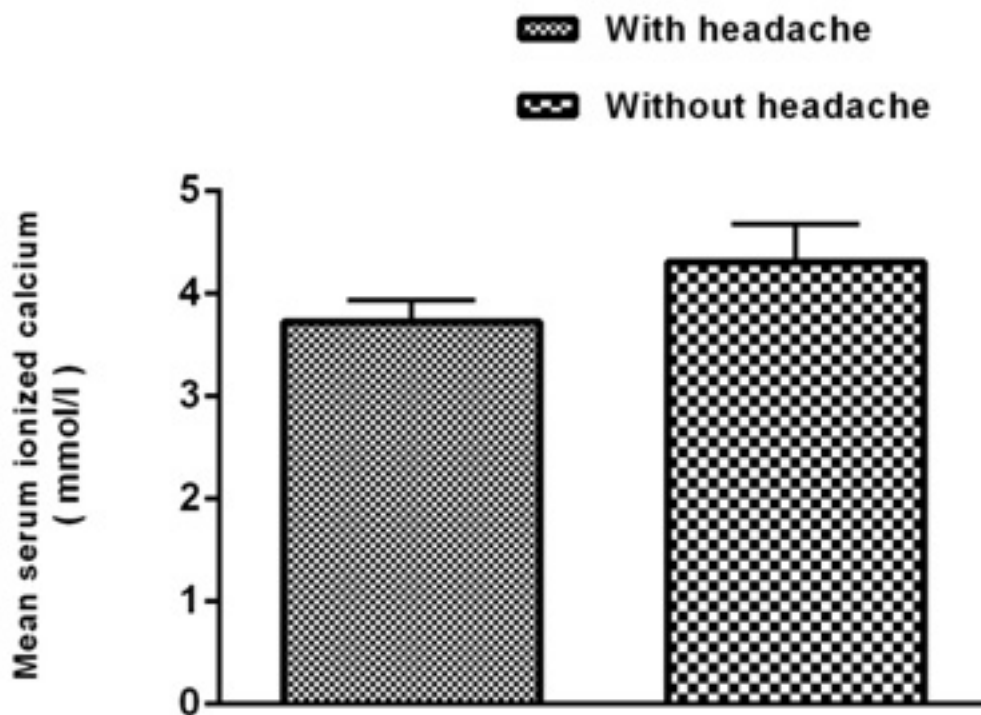


Figure 2: Mean serum ionized calcium level reduced significantly during migraine headache in women

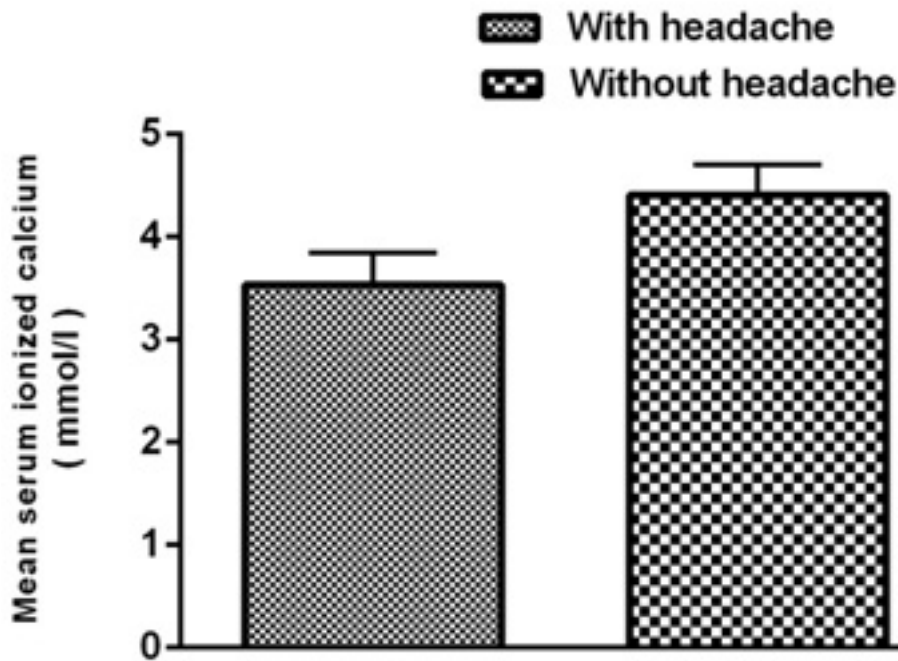


Figure 3: Mean serum ionized calcium level decreased significantly during migraine headaches in men

Discussion

Migraine seems to have a complex pathogenesis (2). Several theories have been suggested to explain the mechanism of migraine. A phosphorylation oxidative defect, malfunction of intra neuronal voltage gated calcium channels, intracellular magnesium (Mg) deficiency or a combination of these may make the cells susceptible to spontaneous depolarization (17).

Many patients with familial hemiplegic migraine have a missense mutation in the P/Q calcium channel, so that this form of migraine, at least, is associated with a demonstrable calcium channelopathy. In menstrual migraine, ionized Mg level is decreased and the ratio of Ca/Mg level is increased. Therefore, serum Mg level may have a role in pathogenesis of menstrual migraine (18).

The results of the present study showed serum ionized calcium level decreased substantially in migraine headaches compared to normal subjects. Also examining the ionized calcium level in men and women separately showed that the ion level in both genders reduced significantly in migraine headaches than normal subjects.

Findings may also add to the growing evidence for involvement of magnesium in migraine pathophysiology (1). Other studies show that Ca²⁺ and other ion channels are important in the mechanism of cortical spreading depression, which is believed to initiate migraine attacks (2). Thus, impaired function of cerebral Ca²⁺ channels may facilitate the initiation of attacks (10). Recent studies have also concluded that abnormalities in the channels within the cells that transport calcium, magnesium, sodium and potassium contribute to the onset of migraines (3). The calcium channels are known to regulate the release

of serotonin. with impaired functioning of the channels, serotonin may not effectively be released or may be released in low quantities (2). As a consequence of this dip, a range of migraine symptoms begin to occur (19).

Previous study suggests that the abnormality of glucose level, insulin resistance, and β -cell function have significant correlation with alteration of serum calcium homeostasis (20). As these factors were not adjusted in our study, this is a limitation for the present study.

Conclusion

Based on the results obtained in the present study, there was a significantly decreased serum ionized calcium level in patients during migraine attack in males and females compared to in normal subjects (those with no headaches).

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