



Clinical assessment of serum parameters in patients with migraine

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Abstract

Objective: The objective of our study is to clinically assess alterations in various serum parameters (Magnesium, Bilirubin, C-reactive protein) in patients with migraine and compared with controls.

Methods: A prospective study was conducted in Pushpagiri Medical College Hospital comprised of 50 migraine patients and equal number of healthy controls. Migraine Patients with or without aura are selected. Serum parameters such as magnesium, bilirubin and C-reactive protein is measured in patients who are willing to participate. These parameters are then quantitatively estimated using semi auto analyser. The results were analysed using t test and Chi square statistical analysis.

Results: There were 50 migraine patients with a mean age group of 32.5 ± 5 years and 50 healthy individuals with a mean age group of 30.46 ± 5 years. The serum magnesium levels were found to be low in patients with migraine. It was also found that patients with migraine had a decreased levels of bilirubin and an increase in CRP. This shows that there is significant relation with the serum parameters in patients with migraine

Conclusion: It is clear from our study that the serum parameters like CRP, Magnesium and bilirubin have specific role in the genesis of migraine and these parameters can be used as biomarker for diagnosis of migraine and also magnesium supplements can be used for the treatment of migraine.

Keywords: migraine, CRP, magnesium, bilirubin

1. Introduction

Migraine is a widespread neurovascular brain disorder. The prevalence of this disease in women is 3-18 % and in men is 4-6 %. (talebi) It is typically characterised by recurrent attacks of disabling headaches and associated symptoms, such as vomiting, nausea and sensitivity to light, sound and head movements. Headaches are generally characterised by unilateral throbbing pain. (hayriye). Migraine attacks are of two types: migraine with aura and without aura. Migraine headaches result from activation of trigeminal nerve branches. Cerebral vasodilation of brain nerves following nerve stimulation resulting from pain may be the main two causes of inflammatory process of migraine headaches. Various vasodilators in cerebral nerves include Vasoactive Intestinal Peptide (VIP), Peptide Histidine Isoleucine (PHI), Neuropeptide Y (Nry), Substance P (sp) and Calcitonin Gene Related Protein (CGRP) (hossenali) these materials are blocked by with anti-migraine drugs. Recently some macro minerals and trace elements have gained recognition as important for the treatment and diagnosis of migraine. There are numerous articles on heavy metals and macro minerals in migraine but there are few studies on serum parameters in migraine patients. Therefore this study is to clinically assess serum parameters in migraine patients in comparison with healthy control group.

2. Patients and Methods

This prospective study was conducted in Pushpagiri Medical College Hospital, Thiruvalla, Kerala from January 2017 to June 2017 and comprised of 50 migraine patients and equal number of healthy controls. The entire study was carried out

after getting approval from Institutional Ethics Committee. All patients were provided with a brief introduction regarding the study and the confidentiality of the data was assured. A written Informed Consent was obtained from the patient or care giver. Patients diagnosed with migraine were identified and their medical records in the department was studied. Both female and male patients, patients with and without aura, patients willing to give the informed consent and patients with age between 18 and 55 years were enrolled into the study. All the subjects were non-smokers. The study objectives were described to patients and they entered the study consciously and voluntarily. Patients who are not willing to give the consent, psychiatric patients, patients with other types of headache, patients having other comorbidities or medications which alter the levels of serum parameters are excluded from the study. For control group, all the above consideration was taken into account too. The healthy volunteers comprised of students and faculties of Pushpagiri College of Pharmacy. After obtaining the hospital number, name and other demographic details of patients, residual blood was collected from the biochemistry lab. The serum samples were then separated by centrifugation and used to analyse Magnesium (Mg), C Reactive protein (CRP), Bilirubin levels. Determination of serum concentrations was done by using Semiautoanalyser.

The data was analysed using SPSS and independent t-test was used to comparing means and Chi-square test for multiple comparisons among populations. Descriptive statistics for studies variables were presented as mean, standard deviation, minimum and maximum values. Level of significance was considered as $p \leq 0.05$.

3. Results

Of the 100 subjects in study, there were 50 cases and 50 controls. Among the cases, 36 were females and 14 were males with a mean age of 32.5 ± 0.5 years. Among the controls, there were 29 females and 21 males with an overall mean age of 30.46 ± 0.5 years.

Serum levels of CRP (<0.0001) were elevated and Mg (<0.0001), Bilirubin (<0.0001) levels were significantly lower in patients with migraine compared to the controls. Investigating CRP levels in population showed that its mean level was 17.93 mg/dL in migraine patients and 0.96 mg/dL in control group. ($p = <0.0001$) and maximum level was 29.01 mg/dL and its minimum level was 8.30 mg/dL. These differences were reported significant statistically. CRP levels also show a relationship with age of the patients as it increases as the age increases. The average magnesium levels were 0.43 mmol/L in migraine patients and 0.83 mmol/L in the control group ($p = 0.0001$). The maximum and minimum level of magnesium was 0.74 mmol/L and 0.15 mmol/L respectively. The magnesium levels was significantly lowered in patient population compared to control group. The mean bilirubin values were 0.22 mg/dL in patient population and 0.73 mg/dL in control population. The maximum and minimum levels were 0.40 mg/dL and 0.01 mg/dL respectively. Magnesium and bilirubin levels are not significantly related to the age of the subjects. Eighteen percent of patients taking flunarizine drug showed weight gain and drowsiness as ADR. During our study we monitored the medication adherence using MARS questionnaire. No major drug interactions were found during our study period.

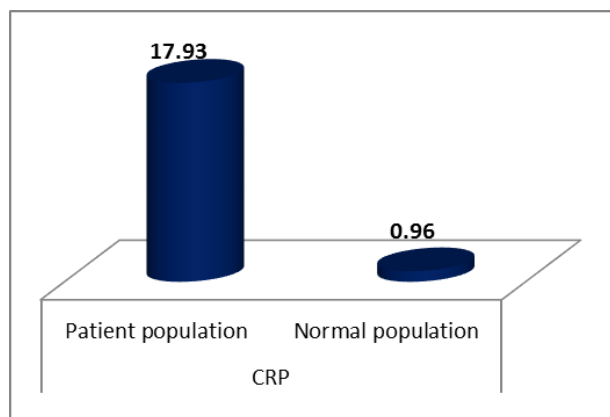


Fig 1: Comparison of CRP in Normal and Patient Population

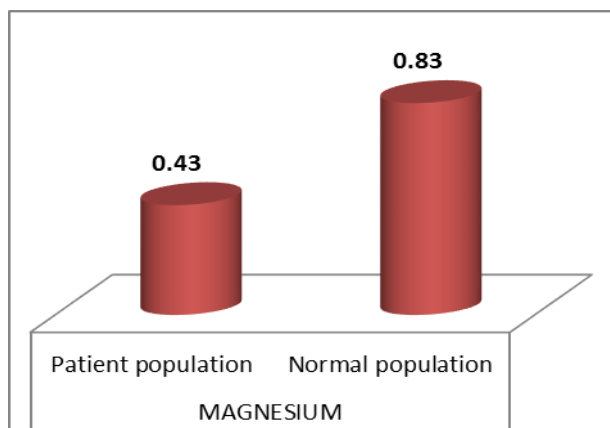


Fig 2: Comparison of Magnesium in Normal and Patient Population

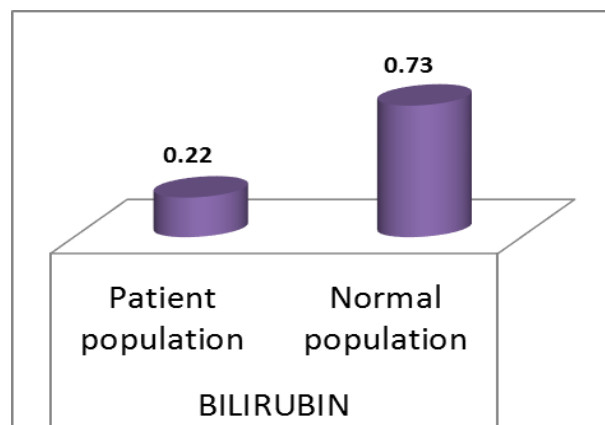


Fig 3: Comparison of Bilirubin in Normal and Patient Population

Table 1

Parameters	Control Group		Patient Group	
	Mean	St.Dev	Mean	St.Dev
CRP	0.958	0.298	17.934	6.54
Mg	0.428	0.151	0.827	0.137
Bilirubin	0.218	0.066	0.725	0.307

4. Discussion

The study investigated the serum levels of parameters like bilirubin CRP and magnesium in patients with migraine. From our results it can be said that alterations in these parameters can be used for the early diagnosis and treatment of migraine. Although many studies seeking to understand the pathophysiology of migraine have been conducted, but the exact aetiology remains unknown. However, it is thought that migraines are a neurovascular response, and the factors causing migraine include genetics, Mg deficiency, excitatory amino acids, neurophysiological changes, monoamines, the hypothalamic-pituitary adrenal axis, opioids and endogenous pain control systems. Recently, some minerals and trace elements have started to gain recognition as biological parameters in the pathogenesis of migraine. However, relatively little research has been performed regarding their role in various diseases. In migraine patients increased levels of CRP have been considered as a marker in assessing neurogenic inflammation. In various disease an inverse relationship between serum bilirubin and CRP has been observed. CRP is considered as an important regulator of the innate immune system and also as a paramount mediator of the acute-phase response. It is associated with other various chronic inflammatory processes, such as rheumatologic conditions, cancer, and CVD.

Magnesium is the second most abundant intra-cellular cation which is essential in many intracellular processes and plays an important role in migraine pathogenesis. Only 2% of the total magnesium is in the measurable extracellular space, 67% is in the bone and 31 % is located intracellularly, so routine blood test do not reflect true body magnesium. Magnesium deficiency may promote cortical spreading depression, hyperaggregation of platelets, affect function of serotonin receptor, and influence synthesis and release of a variety of neurotransmitters.

Bilirubin has been seen as a toxic waste product since it is product of heme metabolism. Recent studies have demonstrated that bilirubin possess cytoprotective and strong antioxidant properties. Several studies have shown that

inflammation plays a significant role in the pathogenesis of migraine, wherein largely pro inflammatory cytokines are released and involved in sensitization of nerve endings during migraine. The existence of neurogenic inflammation and oxidative stress during migraine may lead to the lower serum bilirubin concentration.

5. Conclusion

In our study we investigated the serum levels of certain parameters in patients with migraine. We found that serum levels of CRP was significantly higher but serum levels of bilirubin and Mg were significantly lower in patients with migraine. In the light of our results, it can be said that disturbances in these parameters might predispose people to migraine attacks. Therefore these parameters can be used for early diagnosis and treatment of migraine.

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