



## CLINICAL ASSESSMENT OF SERUM PARAMETERS IN PATIENTS WITH MIGRAINE

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### ABSTRACT

Migraine is a widespread neurovascular brain disorder. Macro minerals and trace elements have gained recognition as important for the treatment and diagnosis of migraine. 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:** We are planning to conduct our prospective study in Pushpagiri Medical College Hospital comprised of 100 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 analyzer. The results obtained from our study is compared with the healthy individuals. From our study we may prove that serum parameters has a significant role in the diagnosis and treatment of migraine.

**KEYWORDS:** Migraine, CRP, Magnesium, Bilirubin.

### INTRODUCTION

Migraine is a widespread neurovascular brain disorder. It is typically characterized by recurrent attacks of disabling headaches and associated symptoms such as vomiting, nausea and sensitivity to light, sound and head movements. Headaches are generally characterized by unilateral throbbing and one of most commonly reported complaints among the adult population. Recently some macro minerals and trace elements has gain recognition as important for the treatment and diagnosis of migraine.

### PATHOPHYSIOLOGY

It is believed that ischemia induced by intracranial vasoconstriction is responsible for the aura of migraine and the subsequent rebound vasodilation and activation of perivascular nociceptive nerve resulted in headache. Migraine headache results from activation of trigeminal nerve branches. Cerebral vasodilatation of brain nerves following nerve stimulation resulting from pain may be the main two causes of inflammatory process of migraine headaches. Various nerve vasodilators in cerebral nerves include: Vasoactive Intestinal Peptide (VIP), Peptide

Histidine Isoleucine (PHI), Neuropeptide Y (Nry), Substance p (sp) and Calcitonin Gene Related Peptide (CGRP). These materials would be blocked with anti-migraine drugs. These materials lead to dilation of Dora vessels and increase blood flow and cause buildup of fluid in tissues and localized edema. Finally it should be mentioned that source of migraine pains are inflammation and inflammatory response.

### SYMPTOMS

#### AURA

These may occur before or during migraines. This can be sensory symptoms, movement or speech, visual disturbances such as flashes of light or wavy, zig zag vision. Examples of aura includes vision loss, weakness or numbness in the face, difficulty speaking, uncontrollable jerking. Migraine can be accompanied by gastrointestinal symptoms such as nausea and vomiting

### TREATMENT

The treatment of an individual migraine attack once it has occurred, or acute treatment, is commonly referred to as "abortive therapy." Four major medications are used

for abortive therapy: (1) Triptans; (2) Ergotamine; (3) Dihydroergotamine and (4) Midrin, a combination of Isometheptene mucate, Dichloralphenazone, and Acetaminophen.

Other medications include CGRP receptor antagonists and among herbals feverfew. For relatively mild migraine symptoms, over-the-counter pain medications such as aspirin, acetaminophen, or nonsteroidal anti-inflammatory drugs (NSAIDs) like ibuprofen, may be sufficient. The patient needs to understand that taking migraine medications more than 3 days a week may lead to rebound headaches-headaches that keep coming back, in part because of the medications.

Anti-nausea medications, sedatives, narcotic pain relievers, muscle relaxants are used as rescue medications and antidepressants, antihypertensives, calcium channel blockers, anticonvulsants are used as preventive therapy.

### ROLE OF VARIOUS SERUM PARAMETERS IN MIGRAINE

**CRP (C reactive protein)** is one of the known inflammatory markers in the body. It is a substance produced by liver in response to inflammation. Increased levels of CRP have been considered as a marker in assessing neurogenic inflammation of migraine patients. An inverse relationship between serum bilirubin and CRP has been observed in various diseases.

Magnesium is an important intercellular element that involved in numerous cellular functions. Deficiencies in magnesium play an important role in pathogenesis of migraine by promoting cortical spreading depression, alteration of neurotransmitter release and the hyper aggregation of platelets. Magnesium helps to maintain normal nerve and muscle function, supports a healthy immune system keeps the heart steady and helps bones remain strong.

Bilirubin is produced when liver breakdowns old RBCs. It circulates in the body as conjugated and unconjugated forms and excreted in bile and urine.

### REVIEW ARTICLES

1. **HOSSEINALI SALEHI *et al.***, (2011); conducted a STUDY ON COMPARISON OF SERUM CRP IN MIGRAINE SUFFERERS AND NORMAL POPULATION. Migraine has two clinical manifestations: migraine with aura and without aura. Diagnosis of migraine was based upon the criteria of International Headache Society (IHS). These criteria for migraine headache include prevalence, length of one day, unilateral nature of it, nausea, vomiting and severe disability. This study was done as a case control study on migraine patients who visited Basat hospital between migraine attacks in 2011 among 50 normal people. Sample size of the study was determined by simple statistical relationship and

considering maximum amount for variance of trait distribution in a population consisted of about 49 people for each group. People who were under 18 and over 35 years old, persons with BMI <18, BMI >30, patients with hypercholesterolemia, diabetes, Hypertension, pregnant women, history of cardiovascular disease and use of drugs other than OCP were excluded from the sample. For control group all above consideration was taken into account too. Methodology of this research was as follows: Patients who complained from headache were examined and interviewed till essential sample size were collected. Those patients, whose migraine diagnosis was confirmed, by considering criteria for excluding from the study, were entered in the study. For these patients CRP level was measured between migraine attacks or at least after 72 hours passed from the last attack. For control group, after interviewing and examining, 50 individuals were selected among present healthy ones in the hospital, persons with the patients or those people who were under general health screening. Then they were entered in the study. Data collection was done as field data collection including interviews and examinations of patients, measuring CRP serum levels and registering them in a checklist. Finally obtained results were analyzed using SPSS 16 software and independent t test was used for comparing means. Finding level of significance was considered as  $p \leq 0.05$ . Comparing CRP levels in two groups of control and case study showed that this material in case study group was 16.4 mg/dL and in control group was 9.76 mg/dL. The present study demonstrated that CRP inflammatory marker was higher at migraine sufferers in comparison with normal general population and could explain the role of inflammation in creation and progression of this type of headache.

2. **Hayriye Gonllulu *et al.***, (2013); conducted a study on the LEVELS OF TRACE ELEMENTS AND HEAVY METALS IN PATIENTS WITH ACUTE MIGRAINE HEADACHE. They compared the levels of trace elements and heavy metals in patients with acute migraine and healthy controls. This prospective study was conducted at YuzuncuYil University, Turkey from May to July 2013 and comprised migraine patients and an equal number of healthy controls who were enrolled using a simple random sampling method. IHS classification was used to make diagnosis of migraine. The control group comprised of healthy volunteers working in the hospital. None of the subjects in either group had been taking antioxidants, vitamin supplements. All the subjects were non smokers. Blood samples were collected from both the groups, placed into empty tubes and immediately stored at 4 degree Celsius. The serum samples were then separated from the self by centrifugation at 3000 rpm for 10 minutes and the parameters were analyzed using Atomic

absorption spectro photometry. Data was analyzed using SPSS 13. Serum levels of copper, cadmium, zinc, lead, iron, cobalt, manganese and magnesium were measured in both groups and were assessed by atomic absorption spectrophotometry. Cadmium, Iron, Manganese and Lead levels were significantly elevated in migraine patients compared to controls while Copper, Magnesium and Zinc were decreased and cobalt demonstrated no change. Trace elements and heavy metals may have a role in the genesis of considerable oxidative stress in patients with acute migraine headache.

- 3. LING CAO *et al.*, (2015);** conducted a study on LOWER SERUM BILIRUBIN CONCENTRATION IN PATIENTS WITH MIGRAINE. Bilirubin has been seen as a toxic waste product since it is product of heme metabolism. However, recent studies have demonstrated that bilirubin possess cytoprotective and strong antioxidant properties.<sup>[4,5]</sup> In addition, Vtvicka V *et al*<sup>[6]</sup> indicated that bilirubin contributes to influence the expression of Fc receptors in macrophages, which indicates underlying immunomodulatory properties of bilirubin.<sup>[7]</sup> Of note, bilirubin can reduce production of interleukin-2 in human lymphocytes.<sup>[8]</sup> Obviously, bilirubin may be an important antioxidant and anti-inflammatory agent. It has been recently shown that serum total bilirubin level can be used to stratify arterial stiffness in patients with coronary artery disease.<sup>[9]</sup> Moreover, serum bilirubin is associated with glomerular filtration rate, and lower serum bilirubin is considered to be a potential risk factor to determine reduction of kidney function in the general population. Serum samples were collected from 120 patients with migraine and 128 healthy individuals. Fasting blood was used to measure serum total bilirubin (Tbil) concentration (normal range: 5.5-27.5 mmol/L), serum direct bilirubin (Dbil) concentration (normal range: 0-8.6 mmol/L) and serum indirect bilirubin (Ibil) concentration (normal range: 5.5-18.9 mmol/L). The diagnosis of all migraineurs was made on the basis of international criteria.<sup>[13]</sup> Individuals with following diseases and/or situations were excluded in our study: cardia-cerebrovascular diseases, hypertension, diabetes, presence of known chronic liver and kidney diseases, infectious diseases, malignant tumor, metabolic syndrome and other diseases that may influence the measure of serum Tbil concentration. The normal range for alanine aminotransferase (ALT) and aspartate aminotransferase (AST) is 9-50 U/L and 15 -40 U/L, respectively. Hence, individuals with abnormal ALT and AST concentration were also excluded in this study. Tbil, Dbil, Ibil, ALT and AST concentration were measured using Roche 8000 automatic biochemical analyzer. Tbil, Dbil and Ibil

concentration were significantly lower in patients with migraine than healthy controls

- 4. OZEROL E *et al* (2003);** conducted a study on DETERMINATION OF COPPER ZINC AND MANGANESE IN THE NAIL AND SERUM IN PATIENTS WITH MIGRAINE. Metallo-enzymes contain trace elements in their molecular structure to be metabolically active. Manganese-superoxide dismutase (Mn SOD) contains Mn and copper, zinc-superoxide dismutase (Cu, Zn SOD) contains Cu and Zn as prosthetic groups. There have been some studies on the oxidant/antioxidant status of patients with migraine. In the present study, the levels of copper, zinc and manganese in nail and serum were investigated in 53 patients with migraine and 19 healthy subjects. Copper, Zn and Mn levels were measured by atomic absorption spectrophotometry and results obtained were statistically compared. The concentration of Mn in nail and serum was significantly higher in migraine patients than those of control subjects. Although Zn and Cu concentrations in nail were increased in migraine group compared to control group, the difference was not statistically significant. There was a statistically significant increase in Cu level ( $p < 0.02$ ) and decrease in Zn level in serum from patients with migraine compared to those of control group. The unchanged or increased levels of trace elements, which play important roles as prosthetic groups in SOD, in both nail and serum may suggest that the antioxidant enzyme activities are not negatively affected from the changes. The results obtained are discussed in the light of the literature on the relationship between migraine and trace elements plus antioxidant systems.

- 5. YOU-FAN PENG *et al.*, (2016);** conducted a study on SERUM BILIRUBIN AND THEIR ASSOCIATION WITH C-REACTIVE PROTEIN IN PATIENTS WITH MIGRAINE.

Increased levels of C-reactive protein (CRP) have been considered as a marker in assessing neurogenic inflammation of migraine patients. An inverse relationship between serum bilirubin and CRP has been observed in various diseases. Therefore, we analyzed serum bilirubin levels in migraine patients, and investigated the relationship between serum bilirubin and CRP in migraineurs. A total of 86 newly diagnosed migraine patients were consecutively recruited to this study. Significantly lower median serum total bilirubin, conjugated bilirubin (CB) and unconjugated bilirubin were found in patients with migraine than healthy controls, and the levels of CRP were significantly higher in migraine patients than healthy controls. A negative correlation between CRP and CB was observed in patients with migraine ( $r = -0.255$ ,  $P = 0.018$ ). In a multiple linear regression model, the concentrations of CRP remained negatively correlated with CB. study demonstrates that serum bilirubin concentrations are

decreased in migraineurs and CB levels were found to be positively correlated with CRP in migraine patients.

## CONCLUSION

Serum parameters have shown role in the pathophysiology of migraine. From our study, serum parameters can be used in future for further diagnosis and treatment of migraine.

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