ORIGINAL ARTICLE

SERUM proBRAIN NATRIURETIC PEPTIDE IN MIGRAINE PATIENTS

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Background: Migraine is one of the commonest of primary headache syndromes rated by WHO to be as disabling as a day with quadriplegia, psychosis and dementia. Migraine has been found to be associated with increased levels of pro BNP that may indicate preclinical cardiac involvement in patients with migraine. Objectives were to compare the levels of serum proBNP among migraineurs and healthy controls and to find out whether proBNP measurement could represent as a potential biomarker of identifying asymptomatic migraineurs. **Methods:** This was a cross sectional comparative study in which serum proBNP levels were measured and compared between 35 migraine patients (24 females and 11 males) and 16 healthy controls (13 males and 3 females). **Results:** Serum proBNP levels were raised in migraine group than the healthy controls and the results were significant (p=0.00). Serum proBNP levels were 32.0±11.5 ηg/L in migraine group and 21.63±8.7 ηg/L in healthy controls. **Conclusion:** Raised serum proBNP levels indicate that the patient is prone to develop migraine.

Keywords: Migraine, proBNP, Cardiovascular Disease

Pak J Physiol 2016;12(4):21–3

INTRODUCTION

Headaches or Cephalagias are defined as a diffuse pain in the various parts of the head not confined to the area of distribution of a nerve.[1] According to IHS criteria, headaches are broadly classified as Primary and Secondary headaches.[2,3] Primary headaches by definition are idiopathic and account for more than 90% of all headache complaints.[3–5] Secondary headaches are DE novo headaches that occur with another disorder capable of causing it. These headaches are always secondary to some underlying clinical disorder.[5]

Migraine is one of the most common primary headaches after tension type headaches.[6] Migraine is defined as a "recurrent incapacitating neurovascular disorder with attacks of headaches for 4 to 72 hours characterized by unilateral location, pulsating quality, and moderate to severe intensity of debilitating pain and aggravation by movements and associated with photophobia, phonophobia, nausea and vomiting.[7,8]

Migraine is a global disorder affecting all races, cultures and geographical locations. The overall prevalence of migraine is 6–8% in men and 15–25% in women.[7,9]

Migraine has been shown in studies to be a major risk factor for CVD.[10] The mechanisms that link migraine to CVD and ischemic vascular events are uncertain and complex.[11] Continuing attacks of migraine lead to changes in peripheral vasculature which increases the susceptibility to atherosclerotic changes and IHD. Shared environmental and genetic factors and Shared comorbidities like hyperlipidemia, diabetes, and hypertension may also explain the relationship between migraine and coronary disorder.[12–15]

The pro-BNP levels increase in correlation with ventricular wall stress and severity of heart failure. pro-BNP serves as an important prognostic marker of mortality in cardiovascular events especially heart failure. There is a linear correlation between rising BNP levels and worse prognosis in patients with heart failure.[16]

Migraine has been found to be associated with increased levels of proBNP in a recently published report that may indicate cardiac involvement in patients with migraine.[10]

Very little is known about the risk of migraine in South Asia[17] so the objective of this study was the early recognition of South Asian migraineurs and to find out whether proBNP measurement could represent as a potential biomarker of identifying asymptomatic at risk migraineurs.

MATERIAL AND METHODS

The study was conducted in Departments of Physiology and Neurology, Sheikh Zayed Postgraduate Medical Institute, Sharif Medical City Hospital, and Lahore General Hospital, Lahore after taking permission from the respective Heads of Departments. Male and female patients of 20–45 years age fulfilling the International Headache Society criteria for migraine[18] were included in the study.

Patients with known history of acute pulmonary embolism, pulmonary hypertension, sepsis, chronic obstructive pulmonary disease, hyperthyroidism or renal failure were excluded from the study as all these conditions are associated with raised levels of proBNP.[19] Sixteen healthy controls with no known history of migraine, CVD or history of any other factor increasing serum proBNP levels were included in the study. A comparison of serum proBNP levels was studied between the migraine group and healthy controls.

A 3 ml blood sample was drawn after aseptic measures using venipuncture method and disposable

syringe and allowed to clot for 30 minutes. The sample was then centrifuged at 10,000 RPM for 10 minutes. Serum was transferred to a secondary tube, labelled and stored at -20 ºC. proBNP levels were estimated in serum by ELISA using Human proBNP kit.

Patients from outdoor and hospital admission fulfilling the inclusion criteria were included in this study after taking a written informed consent. Detailed history and examination of the patients was performed. Data was recorded in the form of a questionnaire, entered and analysed using SPSS-21. Data for serum proBNP was described as Mean±SD. Serum proBNP levels were compared in migraine group by using Independent sample *t*-test. Comparison of serum proBNP levels between groups was done using One-Way ANOVA, and $p<0.05$ was taken as significant.

RESULTS

In our study, 80% of the patients in migraine group were of 0–30 years age, 17.1% of the migraine patients were 31–40 years old, and 2.9% of the patients were >40 years. In the control group, 56.25% of the patients were between the ages of 0–30 years and 43.75% were of 31–40 years age. In migraine group, out of 35 patients, 11 were males and 24 were females. In control group 13 were males and 3 were females (Table-1).

Serum proBNP levels were raised in migraine group compared to healthy controls (32.0±11.5 ηg/L vs. 21.63±8.7 ηg/L), (p=0.00). Serum proBNP levels were raised in migraine group. In migraine group the mean proBNP level in males was 32.04±9.8 ηg/L and in females it was 31.98±8.5 ηg/L. There were no significant differences in the levels of proBNP in migraine groups by gender (p=0.990).

Table-1: Distribution of participants in 2 groups by age and gender

Parameter		Migraine	Controls
Age Groups	≤30 Year	28 (80%)	9 (56.25%)
	31–40 Year	6 (17.1%)	7 (43.75%)
	>40 Year	1 (2.9%)	0 (0.00%)
Gender	Male	11 (31.4%)	13 (81.3%)
	Female	24 (68.6%)	3 (18.8%)
	Total	35 (100%)	16 (100%)

Table-2: Comparison of serum proBNP levels between healthy subjects and migraineurs

Groups		Serum proBNP	*p*
Control	Total (n=16)	21.63±8.7	0.000*
Migraine	Total (n=35)	32.0±11.5	
	Male (n=11)	32.04±9.8	0.990
	Female (n=24)	31.98±8.5	

*significant

DISCUSSION

Only scanty data from South Asian region[17] is available on the subject and our study is one of the pioneer studies in South Asian migraineurs.

Migraine has been found to be associated with increased levels of proBNP that may indicate cardiac involvement in patients with migraine. Migraine has been shown in studies to be a major risk factor for CVD; increased proBNP levels can indicate preclinical cardiac involvement in migraine patients.[10,12]

Serum proBNP is an established diagnostic and prognostic cardiac marker. Normal serum proBNP level has been shown in studies to be between 0.5–30 ρg/ml (1 ρg/ml=1 ηg/L).[20] Some studies have reported significant rise in proBNP level shown that serum proBNP level of 80 ηg/L is significant for heart failure.[16,19–21]

In our study it was found out that serum proBNP level was raised in migraineurs than the healthy controls. So raised serum proBNP levels not only indicate cardiac dysfunction but also indicate that the patient is prone to develop migraine. Also because of high prevalence of migraine and CVD, raised serum proBNP levels can represent as a useful tool in early recognition of not only the cardiac dysfunction but also the patients who are prone to develop migraine.

CONCLUSION

Raised Serum proBNP levels can prove to be very useful tool in early recognition of cardiac disease and migraine. Also early initiation of treatment can result in better clinical outcomes in migraine patients. However, further large scales studies should be conducted particularly in South Asian migraineurs so that precise and comprehensive results regarding raised levels of proBNP in migraineurs can be obtained.

ACKNOWLEDGEMENTS

The author is grateful to Professor Dr. Sibgha Zulfiqar, Head of Physiology Department, Shaikh Zayed Medical Institute, Lahore who endlessly encouraged and facilitated me to carry out this research. The author is highly obliged to Professor Dr. Muhammad Aslam, Vice Chancellor, University of Health Sciences, Lahore for providing me the laboratory facility for sample analyses. The author is highly grateful to the entire Department of Physiology, Sharif Medical and Dental College for their full cooperation.

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Received: 24 Aug 2016 Reviewed: 15 Oct 2016 Accepted: 6 Nov 2016