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CORRELATION OF B TYPE NATRIURETIC PEPTIDE AND ITS 7TH DAY OUTCOME IN STROKE PATIENTS ADMITTED TO A TERTIARY CARE HOSPITAL OF EAST SIKKIM.

Physiology

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ABSTRACT

Introduction: BNP (B – type Natriuretic Peptide) is an established cardio-vascular and cardio–renal biomarker. Studies show increase in levels of BNP in acute stroke patients independent of heart disease. Stroke has a high morbidity, Socio-economic burden and mortality. High BNP levels in acute phase of stroke have shown to predict post stroke mortality and morbidity.BNP can therefore be used to guide management of stroke patients.

Aims and Objectives: To find the correlation between the biomarker BNP levels in acute stroke patients and their 7th day outcome in terms of morbidity and mortality.

Materials and Methods: A prospective study on 50 acute stroke patients fulfilling the inclusion criteria attending the Central Referral Hospital, East Sikkim was undertaken. Data regarding age, sex, type of stroke, BNP levels on the 1st morning after admission and the 7th day outcome was noted in excel sheet. Data was then statistically analyzed and p value of ≤0.05 was considered significant.

Result: Majority of the patients were male. 25% patients improved & 28% worsened by the 7th day. 54% patients had ischemic stroke. BNP levels rose significantly more in ischemic (mean = 455.115±715.030 pq/ml) than that in hemorrhagic (mean = 147.265±142.441 pq/ml) stroke. Even though the higher BNP levels could predict the type of stroke, we found them to be a poor predictor of the 7th day outcome (r = 0.021, P = 0.884).

Conclusion: BNP levels can be a biomarker to assess the outcome of patients with acute stroke. The results of this study were not found significant. Small sample size and one week outcome maybe the reason which can be avoided with a larger sample size and a longer follow up.

KEYWORDS

BNP, stroke

INTRODUCTION:

Stroke according to WHO is defined as "Rapidly developing clinical signs of focal or global disturbance of cerebral function, with symptoms lasting for more than 24 hours or leading to death and with no apparent cause other than of vascular origin"(WHO Monica Project Principal Investigators 1988)[1]. In both developed and developing countries of the world, stroke remains the major cause of morbidity, mortality and serious socio-economic burden. Outcome of stroke patients mostly depends on the clinical assessment and neuroimaging studies. Blood biomarkers can play an important role in the management of such patients by aiding in decision making. Biomarkers are chemicals, its metabolites, or the products of an interaction between a chemicals and some target molecules or cell that is measured in the human body[2]. In human body fluids or tissues, the measurement of biomarkers can help to predict physiological states, diseased states, increased disease risks and pharmacologic responses to therapy [3]. Biomarkers in stroke patients can be used effectively in giving a more personalized care keeping in mind the heterogenous pathophysiologies and mechanism of stroke [3]. Blood biomarkers which gives a rapid result, is cheap and is specific & sensitive can be of use in day to day practice in the management of stroke patients. However, the role of biomarkers in the management of stroke patients is yet to become a standard protocol as there is a relative dearth of research in this field. Brain natriuretic peptide (BNP) is a neurohormone mainly synthesized by cardiomyocytes in a short period of time and in large quantities, as a response to volume or pressure overload[4]. BNP is also known to be secreted in the brain, primarily by the hypothalamus induced by cerebral ischaemia[4]. BNP is an established cardio-vascular and cardio–renal biomarker. Studies have shown an increase in levels of BNP in acute stroke patients independent of heart disease as BNP production may be stimulated by change in catecholamine levels because of neuro-hormonal disturbances and hypoxia inducible factor induced in strokes[5]. BNP level increases with age, in women, renal dysfunction, diuretics and decreases with angiotensin receptor blockers. Limited study has been done on the physiological and pathological role of BNP in human brain. BNP levels are found to increase in ischemic stroke more than in hemorrhagic stroke. High BNP levels in acute phase of stroke have shown to predict post stroke mortality and morbidity.

MATERIALS AND METHODS:

This prospective hospital based study was conducted for oneyear in the Department of Medicine, Central Referral Hospital (CRH), a tertiary care hospital in East Sikkim associated hospital of Sikkim Manipal Institute Of Medical Sciences, Gangtok, after obtaining ethical clearance from Institutional Ethics Committee. After obtaining a written informed consent from the patient or legally accepted representative all adult stroke patients presenting to CRH, fulfilling the inclusion criteria were enrolled for the study. Inclusion criteria included all patients of stroke diagnosed by neuroimaging and presenting within 6 hours of onset of symptoms. Patients with history of previous stroke, Subarachnoid Hemorrhage, Transient Ischemic Attack, cardiac failure, malignancy and end stage renal disease were excluded from the study. The demographic profile of the enrolled patients were noted and stroke severity was assessed using Rankin Scale (Code 0 to Code 6) on admission and on the 7th day to compare the outcome. The outcome was assessed as either improved, worsened, status quo or death by comparing the score on both the days. The BNP was measured on the first morning of admission of all patients using "Alert Heart check meter SBAS 80044G"by finger prick. Other routine biochemical tests were done as per the stroke management protocol of the hospital.Data was collected and stored in Microsoft© Office©Excel©2013 and analysed using IBM©SPSS© - version21 and p value of ≤0.05 was considered significant.

RESULTS:

A total of 50 patients participated in the study. Male patient (74%) outnumbered female patients (26%). Most of the patients (78%) had crossed the age of 50 years and majority of them (48%) were in the age range of 51 to 70 years. Mean age of the study group was 62.62±14.79 years (male patients= 62±13.92, female patients= 64.38±17.53, F=0.246, df=1, p=0.622).

Ischaemic and haemorrhagic stroke was a diagnosis in 54% and 46% patients respectively. Male patients suffered equally with ischaemic and haemorrhagic stroke (18 and 19, respectively out of 37), while ischaemic stroke was almost twice as common compared to haemorrhagic in female patients (9 and 4, respectively out of 13) (χ^2= 1.641, df=1, p=0.170). More (20/27, 74%) of elderly patients (age of 60 years or more) suffered from an ischaemic stroke while the patients who had a haemorrhagic stroke were more (19/23, 82.6%) in early age group (less than 60 years of age), however the finding was not significant statistically (χ^2=10.578, df=5, p=0.060).

Half of the patients (50%) showed improvement, 32% remained in the state as they were at the time of presentation. Eighteen (28%) patients worsened over the course of the treatment and 2 (4%) of them died. The improvement or worsening of the patients was age independent as we didn't find any association between age and outcome (χ^2= 11.438, df=15, p=0.721). Outcome also didn't seem to be dependent on gender of the patients (18.9% male patients and 15.4% female patients worsened at the end of 7th day, χ2= 1.379, df= 3, p=0.710).

Mean BNP level of the study population was 313.504±551.739 U/L Maximum BNP levels were found to be in age group of 81-90 years (817±1095.766 U/L) while the patients in 61-70 years had the least level of BNP (135.5±160.242 U/L). The differences in BNP level among various age group was not significant (F=1.535, df=5, p=0.199). BNP level of male and female patients were also not significantly different (male patients= 290.7±568.157 U/L, female patients= 378.4±518.122 U/L, F=0.240, df=1, p=0.627). However, the difference in BNP levels in ischaemic and haemorrhagic stroke was significant (ischaemic= 455.115±715.030 U/L, haemorrhagic= 147.265±142.441 U/L, F=4.112, df=1, p=0.048). A regression analysis to correlate BNP levels to 7th day outcome didn't find a significant association between the two (R=0.021, F=0.022, df=1, p=0.884).

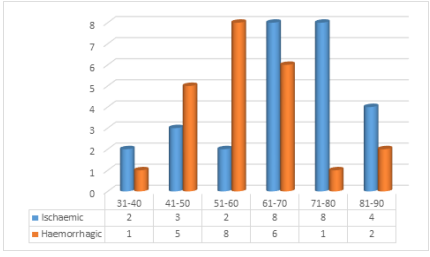

Figure 1 – Distribution of type of stroke in the various age groups

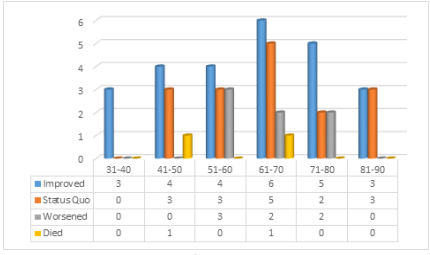

Figure 2 –Distribution of the 7th day outcome (Rankin Scale) in the various age groups

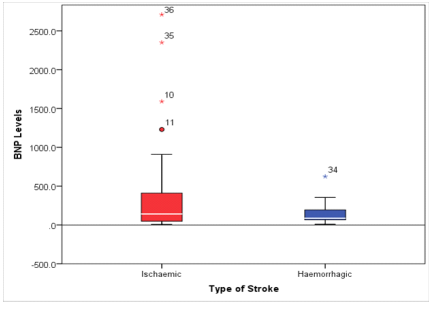

Figure 3 –Box plotting of BNP levels in Ischemic and Haemorrhagic stroke

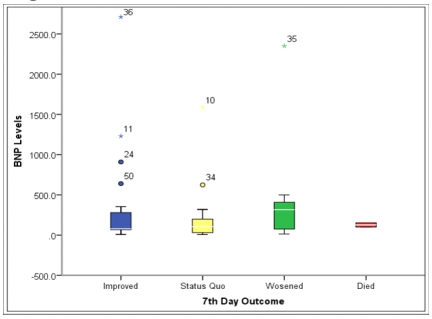

Figure 4 –Box plotting of the BNP levels and the 7th day outcome (Rankin Scale)

DISCUSSION:

Stroke is considered as one of the leading disability causingillness and also the 4th commonest cause of mortality worldwide. Apart from the standardised diagnostic and prognostic tools available for the management of acute stroke patients, role of biomarkers cannot be ignored. Time restriction associated with imaging have made the researchers to explore more possible methods which will be reliable, specific, cheap and fast and biomarkers are thought to have a major role to play. Plasma biomarker BNP levels in acute phase of stroke have found to have a prognostic value in the management of acute stroke patients. Montaner J etal. did a study on 896 stroke patients and concluded that patients with high plasma BNP levels had a bad prognosis seen either as a detoriation in the stroke score or have died [6]. In another study by Natalia S Rost etal. they studied 569 ischaemic stroke patients and found that high level of plasma BNP levels have a strong association with ischaemic (cardioembolic) stroke and poor functional outcome at 6 months [7]. Our study showed that the patients with ischaemic stroke had a higher level of BNP than the patients with haemorrhagic stroke. The seventh day outcome in our study also showed a bad prognosis in patients with high levels of BNP but it was not statistically significant. In a systematic review and meta-analysis conducted by Teresa Garcia- Berrocoso et al. titled "B- type natriureticpeptides and mortality after stroke", 3498 stroke patients from 16 studies were analysed and found that patients with high BNP levels, mortality rate was high. They also concluded that the association of BNP with mortality was not affected by aetiology of stroke and the time from onset of stroke to death of the patients[8]. Association of BNP with mortality of stroke is independent of age, sex and stroke scale score. In a study conducted in India by Bindu Menon et al. on 100 acute ischaemic stroke patients they observed that plasma BNP levels had increased in ischemic stroke involving the large anterior circulation and had a poor functional outcome at the end of 3 months on assessment by NIHSS[5]. Michael L. James et al. in their study to predict neurological outcome after Intracranial Haemorrhage using S100 and BNP levels on 28 adult haemorrhagic stroke patients also found that the two biomarkers were independently highly predictive of functional neurological outcome at time of discharge using modified Rankin score[9]. We analysed the 7th day outcome of the patients included in the study by Rankin scale and tried to correlate it with the plasma BNP levels however using a regression analysis we did not find a significant association between the two. Most of the studies done in terms to evaluate the prognosis in relation to the level of BNP in acute stroke patients were done at either 3 months or later after stroke but in this study it was evaluated on the 7th day hence providing a short term prognosis.

CONCLUSION:

BNP levels can be used as a biomarker to assess the outcome of patients with acute stroke. The results of this study were not found to be statistically significant and a small sample size could be the reason, which can be avoided with a larger sample size. Since a short term prognosis depends on various other factors other than BNP levels so a long term follow up with a detailed statistical analysis may be considered to establish a relationship between BNP and the prognosis in stroke patients. The heterogeneity in age distribution, the size of infract and hemorrhage which was not evaluated in this study, is also a limitation.

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