Short Communication

C - Reactive Protien Assay: A Risk Marker in Ischemic Stroke

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Abstract: Plasma C - reactive protein (CRP), an inflammatory plasma marker, is an independent predictor of future stroke. Hence, an estimation of CRP in patients with ischemic stroke was carried out in Mamata General Hospital, Khammam, as a prospective study and to establish C- reactive protein as an independent risk factor in ischemic stroke. CRP value of CT evaluated ischemic stroke patients within 6hrs after admission showed CRP <6mg/L. Females shows high risk than males with high baseline CRP values. C - reactive protein was significantly elevated in patients with ischemic stroke. It is nonspecific highly sensitive and independent risk factor for prediction of ischemic stroke in patients without other risk factors for atherosclerosis.

Keywords: Plasma CRP levels, Ischemic Stroke, Cerebrovascular disease

INTRODUCTION

Stroke is the major consequence of Cerebrovascular disease and remains as a common cause of human morbidity and mortality. Plasma CRP levels in ischemic stroke suggest that this inflammatory plasma marker is an independent predictor of future stroke [1]. The high CRP value was not related to acute ischemic episode but might be due to chronic underlying systemic inflammatory process [2]. Risk of ischemic stroke is more common in women, with high baseline CRP values. Addition of CRP to standard lipid screening may improve risk prediction among patients with either high or low cholesterol levels.

Stroke is defined as the rapidly developing clinical sign of focal disturbance of cerebral function with symptoms lasting for more than 24hrs or leading to death with no apparent cause other than vascular origin. As proposed by Ophlus [3], infection could be the causal factor in pathogenesis of atherosclerosis and now it is accepted as an inflammatory disease. Possible infections include *Clamydia, H. Pylori, Herpes* CMV etc. Ridker [4] found that a protein (C- reactive protein) is elevated several years in advance of first heart attack or stroke. It is synthesized exclusively by hepatocytes and the rate of synthesis and secretion is increased within hours of acute onset of inflammation either infectious or non infectious aetiology [5]. The normal value of C-Protein is <3mg/l and it may rise to 30mg/l within 24-48 hrs after inflammation. Apparently measuring C-reactive protein might provide novel method to detect worrisome levels of atherosclerosis in otherwise healthy persons.

An estimation of C - reactive protein in ischemic stroke was carried out in Mamata General Hospital, Khammam, to find out positive relation between levels of C - reactive protein (within 6hrs of onset of stroke) and ischemic stroke and to establish C- reactive protein as an independent risk factor in ischemic stroke.

MATERIALSAND METHODS

A prospective comparative study was carried out in Mamata General Hospital, Khammam, during 2012-2013 to find out positive relation between levels of C - reactive protein (within 6hrs of onset of stroke) and first attack of ischemic stroke. Sample size with a study group of 50 patients (CT proved infarcts) and 40 age and sex matched control subjects.

Patients with less than 75 years of age, history of hypertension, diabetes, heart disease, tuberculosis, hyperlipidemia, arteritis, renal failure, hepatic disease, previous history of stroke or TIA or seizure, obesity (BMI> $30/m^2$), using NSAIDS and statin, haemorrhagic stroke, tumour, subarachnoid haemorrhage, head injury (within 3 months), CT negative stroke, meningitis, brain abscess, or any chronic infection that affects CRP value, recent infection (<3wks) and fever (>100f) at the time of presentation were excluded from this study.

A detailed clinical history was taken with emphasis on presence or absence of vomiting, head

ache and convulsions within 24 hours of onset of stroke and past history for other associated diseases. Routine investigations like CBP, CUE, FBS, Lipid profile, ECG, LFT, X-ray CT scan were done, Blood was collected within 6 hours after onset of stroke to avoid confounding factor i.e. ischemic injury which can raise CRP levels. Estimation of CRP was done in 50 patients with ischemic stroke and in 40 controls.

CRP was done with latex agglutination slide test Immunostat CRP (Ranbaxy) which is qualitative and semi quantitative rapid slide test. This test is based on immunological reaction between CRP of sample and latex particles coated with specific antibody to human CRP which sensitized to detect levels greater than 6mg/L CRP.

RESULTS

Maximum ischemic stroke patients without any traditional risk factors for atherosclerotic disease were seen in more than 60 years of age in males and 51-60 years in females with a male to female ratio is 2.2:1.

CT scans showed MCA territory infarcts were more common with 67% followed by PCA territory infarct (25%) and ACA territory infarct (8%). Mean body mass index (BMI) among the stroke patients was 21.24 ± 1.03 kg/m^2 and in control group it was 21.01±1.27kg/m2. BMI in stroke patients ranged between 20.1 and 23.0kg/m^2 where as in control group it was 19.1 and 22.0kg/m^2. CRP value was >6mg/L in 40 out of 50 study group patients and only 16 patients showed CRP value <6mg/L this was statistically significant Where as only 4 patients in control group had CRP value >6mg/L. CRP value was increased in 26 out of 35 men (74%) and 13 out of 15 females which means risk of ischemic stroke is more in case of females than men with high baseline CRP values.

DISCUSSION

Stroke is the major consequence of the cerebro vascular disease. The incidence of stroke is increasing in India even in younger individuals. The incidence is increasing in the individuals even in the absence of traditional risk factors for atherosclerotic vascular diseases like hypertension, diabetes, obesity etc. It is paramount importance to identify the new risk markers and strategies to prevent ischemic cerebro vascular diseases.

Although the proximate cause of most brain infarcts is thrombus formation atherosclerosis as suggested by Ross [6], there is an increasing evidence to link inflammation with the pathogenesis of arthrosclerosis and thrombosis. Earlier studies [7,8] suggested that C- reactive protein, an acute phase reactant, is an indicator of underlying systemic inflammation and a novel plasma marker for atheroembolic disease. Though plasma CRP level is an independent predictor of the risk of future stroke, it is not a disease specific but sensitive marker produced in response to tissue injury, inflammation, immunological stimuli. Survey reports of Ford [9] showed CRP concentration was higher in patients with stroke after adjusting for smoking, HDL cholesterol and systolic BP.

In this study Stroke constituted 15% of all admission in Mamata General Hospital. Out of 50 ischemic stroke patients 40 patients had high baseline CRP values. Increased CRP levels are seen in 26 out of 35 men (74%) and 13 out of 15 women (86%) indicating clear risk for ischemic stroke and more in case of women than in men with high baseline CRP values. These observations are similar to the reports of Rost [10] and Ridker [5] showing. CRP levels were two fold higher in stroke than in control groups and three times higher risk in women with the highest CRP quartile whereas men had two times the risk of ischemic stroke /TIA with a p value of p<0.003.

Ridker et al. [5] and Ford et al [9] showed men with highest quartile of base line CRP value having twice the risk of future ischemic stroke (relative risk1.9) and independent of lipid profile, FBS and Blood pressure. In the study of Rost et al [10] men and women with mean age of 69.7,were estimated for C-reactive protein using immunoassay and during 12 to 14yrs follow up in ischemic stroke and TIA men had 2 times risk and women had 3times risk. Ridker et al. [5] reported that CRP is a better predictor of vascular risk than IL-6 and it was not subjected to diurnal variation. The high CRP value was not related to acute ischemic episode but might be due to chronic underlying systemic inflammatory process.

Study by Gussekloo et al [1] showed that C - reactive protein is a strong but nonspecific risk factor of fatal stroke and risk of death from stroke increased linearly up to 10 fold in subjects with highest levels of C-reactive protein at base line (p<0.001). In another study by Horne et al [2] showed the combination of lipid profile and CRP as more powerful predictors of stroke and cardiovascular diseases.

CONCLUSIONS

The C- reactive protein was significantly elevated in patients with ischemic stroke. The raise of CRP may not be due to ischemic stroke may be secondary to underlying chronic inflammatory process which is the mechanism for atherosclerosis. Elevated CRP is nonspecific highly sensitive and an independent risk factor for prediction of ischemic stroke in patients without other risk factors for atherosclerosis thus the elevated CRP provide method of predicting the risk of future ischemic stroke in patients at risk and in general population.

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