Original Research Article

A study on High Sensitivity C – Reactive Protein as a determinant in the outcome of acute ischemic stroke

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Abstract

Background: In recent years, there has been increasing evidence which shows strong links between inflammation and the pathogenesis of atherothrombotic stroke. Acute phase proteins have been implicated to play roles both during acute and chronic inflammatory processes in different diseases including ischemic stroke. Even low grade infections may cause elevation of various acute phase reactants which may partly be responsible for the inflammatory process observed in atherosclerotic lesions, which may in turn relate to occurrence of ischemic symptoms.
Aim of the study: To evaluate the predictive value of hs-CRP in relation to the ultimate functional outcome in first ever ischemic stroke after 4 weeks.
Materials and methods: A total of 50 patients who presented with acute ischemic stroke confirmed by CT scan were enrolled into the study. As soon as the patients were admitted within 48 hours of onset of stroke, serum samples were taken for hs-CRP estimation. The serum hs-CRP level was correlated with the functional recovery of patients after 4 weeks using the GOS. Patients with score of 4 and 5 were included in the good outcome and patients with score of 1, 2, 3 were included in the poor outcome category.
Results: Mean age of individuals in this study was 60.32 years ± 7.44. Male patients were 48% (24) and female patients were 52% (26). Patients with GOS score of 4 or 5, i.e. those with favorable outcome (34%) 30% had CRP < 10.1 mg/L and 4% had CRP $\geq$ 10.1 mg/L. All the remaining 66% cases with GOS score of 1, 2 or 3, (i.e. unfavorable outcome) had hs-CRP $\geq$ 10.1 mg/L.

Conclusion: Patients with elevated hs-CRP had a poorer outcome when compared to patients with lower levels of CRP, four weeks after the onset of ischemic stroke.

Key words

Acute ischemic stroke, High sensitivity C-reactive protein, Outcome.

Introduction

Inflammatory factors play an important role in the pathogenesis of ischemic stroke. Acute phase proteins level such as a fibrinogen, CRP, ferritin increase after acute ischemic stroke. These findings support a possible role of an inflammatory stimulus in the acute ischemic stroke. High levels of hs-CRP are associated with adverse cardiovascular and cerebrovascular events. High CRP predicts the risk of carotid stenosis; first stroke and post stroke mortality. Elevated plasma CRP concentrations are also associated with an increased risk of cerebrovascular events and an increased risk of fatal and nonfatal cardiovascular events in ischemic stroke patients. Determination of plasma CRP concentrations could be used as an adjunct for risk assessment in primary and secondary prevention of cerebrovascular disease and be of prognostic value. CRP is as an independent predictor of cerebrovascular events in at-risk individuals and ischemic stroke patients [1].

Materials and methods

Inclusion criteria

All patients who presented within 48 hours of onset of stroke and who gave informed consent to participate in the study were included.

Exclusion criteria

- Subarachnoid hemorrhage, subdural hemorrhage and intracerebral hemorrhage were excluded with the aid of CT scan.
- Patients above 70 years of age were excluded.
- Patients with evidence of active infection and neoplastic conditions at the time of study were excluded.
- Patients with rheumatic heart disease and collagen vascular disease were excluded.
- Patients who were actively smoking at the time of study were excluded.
- Patients with previous history of transient ischemic attack or reversible ischemic neurological deficit were excluded.

Study method

A total of 50 patients who presented with acute ischemic stroke confirmed by CT scan were enrolled into the study. As soon as the patients were admitted within 48 hours of onset of stroke, serum samples were taken for hs-CRP estimation. Serum hs-CRP levels were also estimated in fifty normal patients (without any evidence of acute infection, neoplasm, rheumatic heart disease, collagen vascular disease, hypertension, DM, IHD) and was found to be within normal limits. Standard guidelines for the treatment of acute ischemic stroke were followed. None of the patients received any thrombolytic treatment. They were treated only with antiedema measures and antiplatelets such as aspirin alone and with good nursing care and physiotherapy.

The patients were reviewed after 4 weeks after onset of stroke and were stratified using the Glasgow Outcome Scale (GOS). The serum hs-CRP level was correlated with the functional recovery of patients after 4 weeks using the GOS. Patients with score of 4 and 5 were included in the good outcome and patients with score of 1, 2, 3 were included in the poor outcome category.

The statistical methods used for analysis were

- Chi- Square test
- Sensitivity/Specificity test

All analysis was done using Windows-based SPSS statistical package (Version 11.5).

Results

Mean age of individuals in this study was 60.32 years ± 7.44. Male patients were 48% (24) and female patients were 52% (26). Patients with GOS score of 4 or 5, i.e. those with favorable outcome (34%) 30% had CRP < 10.1 mg/L and 4% had CRP ≥ 10.1 mg/L. All the remaining 66% cases with GOS score of 1, 2 or 3, (i.e. unfavorable outcome) had hs-CRP ≥ 10.1 mg/L (**Table – 1 to 4**).

Table - 1: Age of individuals.

	Number of cases	Mean	SD	Std Error Mean
Age	50	60.32	7.44350	1.05267

Mean age of individuals studied = 60.32 years ± 7.44.

Table - 2: Gender Distribution.

	Male	Female	Total
Number of Cases	24 (48%)	26 (52%)	50 (100%)

Table - 3: hs-CRP Vs GOS Score.

GOS	hs-CRP (mg/L)		Total
	< 10.1	≥10.1	
1	0(0%)	2(4%)	2(4%)
2	0(0%)	13(26%)	13(26%)
3	0(0%)	17(34%)	17(34%)
4	7(14%)	3(6%)	10(20%)
5	8(16%)	0(0%)	8(16%)
Total	15(30%)	35(70%)	50(100%)

Table - 4: hs-CRP Vs GOS Group.

GOS group	hs-CRP (mg/L)		Total
	< 10.1	≥ 10.1	
Favorable	15(30%)	2(4%)	17(34%)
Unfavorable	0(0%)	33(66%)	33(66%)
Total	15(30%)	35(70%)	50(100%)

P= 0.000 significant

Thus there was significant statistical correlation between hs-CRP levels and functional outcome of the patient at the end of 4 weeks based on GOS score.

Discussion

CRP formerly considered solely an excellent biomarker of inflammation, is now viewed as a direct contributor in atherosclerosis. Recent evidences have emerged implicating CRP directly in atherogenesis. CRP has been found in human atherosclerotic plaque and CRP has been shown to cause endothelial cell dysfunction, oxidant stress and intimal hypertrophy in experimental models. There is growing evidence of the prognostic importance of C-reactive protein in ischemic stroke. However, the independent value of CRP at different stages after stroke has not been established. Higher CRP concentration was an independent predictor of mortality together with age and the severity of the stroke on the National Institute of Health Stroke Scale [2].

Age and gender

The correlation of hs-CRP levels with age and gender was studied. There was no statistically significant correlation between age and gender of the patient with the hs-CRP levels. This may be because of the small sample size of our study group. But in a study conducted by So Yeon Ryu et al in 2005, age had an independent association with plasma hs-CRP whereas gender showed no significant association with plasma hs-CRP [3]. Also another study conducted by Rohde Lep et al in 1999 concluded that hs-CRP levels were statistically significant with age [4].

Hs-CRP vs TOS group

The correlation between hs-CRP levels measured within 48 hours of onset of stroke to that of the functional outcome of the patient at the end of 4 weeks (using GOS) was carried out.

Out of the 50 cases enrolled in the study, 35 cases (70%) had CRP values $\geq$ 10.1 mg/L and 15 cases (30%) had CRP < 10.1 mg/L. Out of the 35 cases with CRP $\geq$ 10.1 mg/L, 4% had GOS score of 1, 26% cases had GOS score of 2, 34% cases had GOS score of 3. On the other hand, of the remaining 15 cases with CRP < 10.1 mg/L, none had a GOS score of 1, 2 or 3. 14% cases had a GOS score of 4 and 16% cases had a GOS score of 5.

Out of the 50 patients, 2 died. Both of them had very high hs-CRP levels. Thus patients with CRP levels < 10.1 mg/L had a relatively favourable outcome (GOS score of 1, 2 or 3) when compared to patients with levels $\geq$ 10.1 mg/L (GOS score of 4 and 5).

So, in our study, the correlation between hs-CRP levels within 48 hours of onset of ischemic stroke and the prognosis of the cases at the end of 4 weeks was statistically significant, the p value for hs-CRP being 0.000.

This is consistent with the various studies conducted using hs-CRP as a prognostic indicator of acute ischemic stroke [5-10].

Conclusion

Patients with elevated hs-CRP had a poorer outcome when compared to patients with lower levels of CRP, four weeks after the onset of ischemic stroke. Knowledge of the prognostic influence of the levels of CRP in the outcome of stroke of atherothrombotic etiology helps the clinician to offer realistic expectations to the families of stroke victims

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