

ROLE OF CRP LEVELS IN ACUTE ISCHEMIC STROKE

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Abstract

Use of serum diagnostic levels has been an established practice in medicine. CRP levels are known to provide an approximation of the extent of inflammation. The present study was formulated to ascertain if levels of CRP in acute ischaemic stroke cases can be a prognostic or diagnostic marker for the condition. The study was a prospective case control format and utilized a subject pool of 50 subjects as case and control each. The study observed a significantly elevated level of CRP in cases with an acute ischaemic stroke. The study concluded that use of CRP can be an effective modality in clinical practice in managing such cases.

Keywords: CRP, Acute Ischaemic Stroke, TOAST

Introduction

C-Reactive protein is a plasma protein present homogeneously in all vertebrates and some invertebrate species. The CRP plays a role in inflammatory responses to stimuli on a systemic level rather than a local site-based reaction. (1)The molecule of CRP binds to a specific site of action which are revealed in the process of cell death or on the cell walls of certain infective pathogenic organisms. Thereafter, it causes a cascade in which the circulating levels of CRP are essentially elevated indicating that an acute inflammatory immune response is active.(2)The elevated levels of CRP in the system can also provide a stimulus for endothelial cells to promote the migration and activation of various adhesion molecules which allow the transport of mononuclear cells and T cells inside the vessel wall. This migration promotes the formation of atherosclerotic plaques. (3-4)Additionally it was determined that CRP plays a pivotal role in superoxide ions formation and stimulation of tissue necrosis factors in the system while causing fibrinolysis, endothelial cell lysis and eventually plaque erosion. These are due to its acute inflammatory activity but can lead to an ischemic stroke (4-5)Stroke can be defined as a syndrome characterized by a rapid onset of local or complete loss of brain function for a duration of more than 24 hours or death with no apparent cause apart from vascular origin.(6)In the Indian context, stroke is a disease which has a high mortality rate and in cases where death has not occurred, the disability is long and arduous. Studies have hypothesized that the pathophysiology of stroke is an inflammatory one associated with

atherosclerosis. This led to the opinions that a severe stroke will have an elevation of inflammatory markers which if detected can aid in prognostic and diagnostic marking (7-8)With this in mind, the present study was conducted to ascertain if high sensitivity C-reactive protein can be used as a marker for acute ischemic events.

Material and Methods: The present study was a double-blind randomized control study conducted over a period of 12 months from June 2019 to June 2020 in a tertiary care hospital in Dhule Maharashtra. Institutional ethical clearance was obtained prior to commencement of study. The study entailed the inclusion of 50 subjects who fulfilled the inclusion criteria. Inclusion was done of individuals who had suffered an ischemic stroke, were between 30-70 years of age and were brought to the hospital within 24 hours of event. The subjects were individuals who had no co-morbidities that could alter CRP levels, nor were using steroids for any ailments. If found so, the subjects were excluded from the study. The subjects were individuals who had only a single event of stroke and subjects with a prior h/o stroke or ischemic event were excluded from the study. The study pool also included a pool of age and gender-matched controls. These individuals were apparently healthy subjects who had never been in a stroke-like condition or had any infective pathology / steroid usage. Stroke diagnosis was made by radiological methods (CT/MRI), as well as history, clinical examination and specific neurological examination. The severity scoring was based on NIHSS criteria (9) while etiological classification was done as per TOAST criteria

(10) Serum samples for determination of hsCRP level were taken within 24 hours of hospital arrival. hsCRP level was measured using the highly sensitive near-infrared particle immunoassay method which classified hsCRP levels in low risk (< 1 mg/L), moderate risk (1–3 mg/L) and high risk (> 3 mg/L) groups according to American Heart Association and Centers for Disease Control and Prevention criteria (11). The demographic details, medical and personal history as well as examination findings were recorded in pre-designed tabular format. The tabulations were analyzed in consultation with institutional statistician using SPSS ver 12 software.

Observations:

The results revealed that the mean age of the patients is 58.57 ± 10.24 years, while the mean age of the controls was 58.22 ± 9.87 years. The gender distribution and age of the case and control group was comparable

Among the selected study subjects, in the patients group, the commonest risk factor was elevated BP. Hypertension was seen in 66% (n=33) subjects. The second commonest factor was dyslipidemia which comprised of 60 % cases (n=30). Other risk factors were smoking, diabetes and LV dysfunction. Among the patients, occlusion was dominantly in small vessels and comprised 36 cases (72 %). Cardio-embolic etiology was commonest among the subjects comprising of 58 % (n=29) cases. Majority of the subjects had a stroke in their anterior circulation territory composed of 88 % (n=44) cases. Based on NIHSS grading, the commonest condition at time of admission was moderate (66% , n=33), followed by mild grade (20%, n=10). The mean hsCRP levels were found to be higher in subjects with hypertension. Based on serum levels, high hsCRP was found in 84 % cases (n=42) as compared to only 6 % in control subjects. Statistical analysis using chi square test revealed a p value of <0.001 between elevated hsCRP and stroke severity.

Discussion:

In the present study, we determined that the commonest etiological risk factor for stroke was hypertension. This is in concurrence with studies by various authors in India and abroad. (12-14) Hypertension has been the most common and important treatable risk factor for stroke in most of the other epidemiology studies including ICASS and the INTERSTROKE study. (13,14) Among our 50 patients with ischemic stroke, the most common TOAST class was small-vessel occlusion followed by large-artery atherosclerosis. Our findings are consistent with findings from a study by Sharma *et al.* (15), who observed in their study that lacunar stroke was the most frequent stroke subtype. However our results are not in concurrence with Kaul *et al.* (16) who performed a study, in which 392 patients with ischemic stroke, consisting of 282 men and 110 women, aged 54 (range 2–97 years) years were included. They found that majority of patients had large-artery atherosclerosis. Among patients included in this

study, most of them had anterior circulation stroke, In a study by Sivanandy *et al.* (16) it was found anterior circulation involvement in 73.9% of studied patients was seen. This is in concurrence with our study. Melakea *et al.* (17) found anterior circulation involvement in 75% of studied patients in similar picture to our study. The serum hsCRP levels in patients with ischemic stroke had high hsCRP (≥ 1 mg/L) levels compared to 6% healthy controls. Chaudhuri *et al.* in their study found that hsCRP level was significantly higher in stroke patients than in controls. Other studies have shown varying prevalence. Rajput *et al.* performed a study in stroke patients from Pakistan and found that 132 (88%) patients had elevated CRP level (> 10 mg/L). (7,18)

Conclusion:

Significantly high hsCRP prevalence among patients in our study suggests the important role of inflammation in ischemic stroke pathogenesis. It needs to be further evaluated whether some infectious agents trigger a pro-inflammatory response besides the conventional risk factors in patients with ischemic stroke. High hsCRP level may be a marker to initiate primary and secondary preventive strategies. The study is limited by a small sample size and further large scale studies can be conducted to effectively analyse the efficacy of using CRP as a standard prognostic tool in acute ischaemic events.

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