

HIGH SERUM C-REACTIVE PROTEIN AS PREDICTOR OF SYSTEMIC INFLAMMATORY RESPONSE SYNDROME IN SEVERE HEAD INJURY PATIENTS

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Objectives: Despite the fact that many studies have shown that the role of high sensitivity C-reactive protein (Hs-CRP) in inflammation diseases, the role of this molecule in severe head injury (SHI) has not been understood clearly. Severe head injury was defined as a trauma to the head frequently found in Emergency Units where some cases result in mortality. Severe head injury was defined as Glasgow Coma Scale (GCS) score between 3 and 8. Based on this data, we felt that it was important to determine the role of Hs-CRP as a predictor of SIRS in SHI patients. **Method:** This was a Cohort prospective study about the role of serum Hs-CRP as a predictor for Systemic inflammatory response syndrome (SIRS) in SHI patients at Sanglah General Hospital, Bali-Indonesia from August 2012 to February 2013. A number of 60 patients fulfilled the inclusive criteria. The data were analyzed descriptively to show the characteristics of the samples and was analyzed using univariate and multivariate analysis to determine the predictor factors for SIRS in SHI patients. A confidence interval of 95% ($p < 0.05$) was applied. **Results:** From 60 samples collected, there were 43 males (71.7%) and 17 females (28.3%), the majority age of the samples were 20-40 years old (21 samples, 35%). On the first day 49 samples (81.6%) had elevated serum Hs-CRP levels. Fifty seven samples (95%) had SIRS, and only 3 samples (5%) did not have SIRS. Bivariate analysis between Hs-CRP level and SIRS was significant ($p = 0.001$). Multivariate analysis showed that pneumonia and high Hs-CRP serum levels were significant predictor factors for SIRS in SHI patients. **Conclusion:** High serum Hs-CRP levels could be used as a reliable predictor factor for SIRS in SHI patients.

Keywords: Severe head injury, Glasgow coma scale, high sensitive C-reactive protein, Systemic inflammatory response syndrome.

INTRODUCTION

Head injury has been a global issue as a result of industry and transportation development that cause a large number of work accident victims. Head injury still constitutes a serious health problem nowadays. The number of incidents, level of disability and mortality rate are still high 75-80% of the total number of head injury are classified as mild and the rest as moderate and severe.^{1,4}

Head injury incident continue to increase annually. In general, mortality rate was high, 3-8%, and approximately 6,17-12,22% from, 2002-2006, at Dr. Soetomo General Hospital in Surabaya. At Sanglah General hospital in Denpasar, over 2000 cases a year of head injury incident on average more than 70% of which is dominated by patients

with mild head injury.²⁹ The increase of inflammation reaction in patients with head trauma involved cytokine, chemokine, and APR (Acute Phase Reactant) found in serum and cerebrospinal fluid. APR is activated during serum trauma on the head. In Sogut's previous research in Turkey (2010), he discovered a significant increase of CRP (C-Reactive Protein) in patients with head trauma in accordance with level of trauma where patients with $GCS \leq 8$ is 103.41 ± 50.76 mg/l compared with patients with $GCS \geq 8$ as much as 22.05 ± 26.0 mg/l with $p < 0.001$.³⁵

Both CRP and Hs-CRP are tests to measure the same molecule in blood. Hs-CRP is a test to determine the risk of cardiovascular disease in healthy people with level < 10 mg/dl whereas CRP test is used for patients facing the risk of infection/inflammation caused by virus germs or bacteria in patients with inflammation disease caused by chronic inflammation (such as arthritis rheumatic) with CRP level > 10 mg/dl. In this research, the researcher wants to know CRP level

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in patients with severe head trauma based on CGS value on the assumption that the more severe the head injury is, the higher is the CRP level in blood circulation.

Systemic Inflammatory Response Syndrome (SIRS) is a spectrum of clinical conditions which are resulted from a series of inflammatory mechanisms induced by multiple pathways. This response can occur due to burn injury, trauma (it can be due to head trauma), pancreatitis, and so on.^{15,26}

MATERIALS AND METHOD

A Cohort prospective study is used in this research to learn about high level Hs-CRP in blood as a predictor for SIRS in SHI patients. This study is conducted at Sanglah General Hospital, Bali-Indonesia from August 2012 to February 2013 with 60 patients who fulfilled the inclusive criteria. This research was approved with an ethical clearance from Locally Ethical Issue Board Sanglah General Hospital/Faculty of Medicine Udayana University. Informed concerns were obtained for all patients. Data is presented in tables and is analyzed using Chi Square Test to CI 95% ($p < 0.05$).

RESULTS

This research is conducted on severe head injury patients with GCS 3-8 who visited Sanglah General Hospital emergency unit for medical treatment between August 2012 and February 2013.

This research observed 60 patients each group of whom consisted of 17 female patients (28.3%) and 43 male patients (71.7%). The level of serum Hs-CRP was measured on the first day, where we discovered 10 samples of low level Hs-CRP (16.7%), 1 normal sample (1.7%), and 49 samples of high level Hs-CRP (81.6%). Then on the third day, we evaluated the occurrence of SIRS to the whole samples in which we found 57 (95%) had SIRS and 3 (5%) samples showed no sign of SIRS as can be seen in Table 1.

Table 1
Subject Characteristics

Variable	SIRS on 3 rd day		Total	p
	SIRS (+)	SIRS (-)		
Sex				
Male	41	2	43	0.844
Female	16	1	17	
Age				
0-10 years	3	1	4	0.204
20-20 years	6	0	6	
20-40 years	20	2	22	
40-60 years	19	0	19	
>60 years	9	0	9	
Hs-CRP level				
Low	7	3	10	0.001*
Normal	1	0	1	
High	49	0	49	

*significant at $p < 0.05$

Table 2
Order of Hs-CRP Level for all Subjects

Variable	Hs-CRP level on 1st day			p
	Low	Normal	High	
Hypertension				
Yes	1	0	18	0.200
No	9	1	31	
Smoking				
Yes	2	0	27	0.080
No	8	1	22	
Diabetes Mellitus				
Yes	1	0	10	0.661
No	9	1	39	
Dyslipidemia				
Yes	0	0	10	0.260
No	10	1	39	
Contraceptive				
Yes	1	0	8	0.802
No	9	1	41	
Gingivitis				
Yes	1	0	0	0.079
No	9	1	49	
Pneumonia				
Yes	2	0	34	0.007*
No	8	1	15	
Rheumatoid Arthritis				
Yes	0	0	1	0.892
No	10	1	48	
Alcohol				
Yes	2	1	12	0.208
No	8	0	37	
Workouts				
Yes	1	1	19	0.086
No	9	0	30	
Weight Loss				
Yes	0	0	2	0.793
No	10	1	47	
Cardiovascular disease				
Yes	0	0	6	0.473
No	10	1	43	
Treatment (Statin, Fibrates, Niacin)				
Yes	0	0	8	0.355
No	10	1	41	

*significant at $p < 0.05$

DISCUSSION

Sixty subjects actively participated till the final stage of the research. Hs-CRP examination was done on the first day and SIRS examination on the third day. Hs-CRP level reached its peak after the first 24 hours and remained stable during the existence of stimulant IL-6 for 7-12 days.

Hs-CRP level in blood was found significantly higher in cohort group with GCS 3-8 on the first day ($p < 0.05$). This is in accordance with the result of Kalabalikis research (1999), in which they observed 45 severe head injury patients who showed the increase of Hs-CRP level in blood where the highest point was on the first and second days. Average level of CRP blood in severe head injury patients is significantly higher than that of mild head injury patients. It is found in this research there is an increase of Hs-CRP level in severe head injury patients on the first day in 49

samples (81.6%). Concentration increase of Hs-CRP in blood is known in patients with infection, burn injury post surgery. The most significant increase on the first and second days and is related with the level of trauma severity.

In this research it is also found low level Hs-CRP 10 (16.7%) and normal 1 (1.7%). This is due to the difference in level of trauma severity, pathology and location of pathology in intracranial brain injury besides the insufficient number of research samples. Massive bleeding in silent area such as in frontal lobus and occipital areas will not influence the decrease of GCS as much as the same bleeding that occurs in lobus temporal, parietal of fossa posterior areas. Taupin V (1993) obtained the result of research in animals in which there is a meaningful difference of cytokine level in cortex contra lateral and hippocampus ipsilateral area and brain contra lateral that experience injury.

Systemic Inflammation Response Syndrome is defined as systemic inflammation response because of inflammation response. It happens due to microorganism invasion into tissues that can cause sepsis. In this study, out of 60 severe head injury samples we find low level CRP in 10 samples (16.7%) and SIRS occurs in 7 of them whereas SIRS fails to occur in 3 samples. Normal level Hs-CRP 1 sample (1.7%) and become SIRS and high level Hs-CRP is found in 49 samples (81.6%) where all 49 samples become SIRS.

In this research we find a significant correlation between Hs-CRP mainly in the increase of Hs-CRP in blood with incident rate of SIRS in severe head injury patients. A number of 57 samples out of 60 samples of severe head injury patients became SIRS and only 3 samples fail to become SIRS with $p = 0.001$. This reality is in conformity with the theory that has been widely accepted that the increase of neuro inflammation response will occur in severe head injury patients as indicated by activation of microglia and astrosit cells, damage of brain blood barrier, an increase in production of proinflammatory cytokine and free radical it damages cell membrane, cytokine (IL1, IL6 and TNF- α) that cause damage of brain blood barrier which eventually results in neuron damage. A condition of hyper metabolism and hyper catabolism is also found in severe head injury that constitutes acute phase response which, with help of cytokine will produce acute phase protein especially Hs-CRP in serum. The severe brain injury is the severe pathology occurs. The greater inflammation occurs, the greater SIRS occur in patients with head injury. Damaged brain tissue in de novo produces IL-6. This interleukin constitutes potential simulator for hepar cell in order to produce Hs-CRP (Hs-CRP in serum) then enter intracranial cavity through damaged brain blood barrier.^{12,26}

The main goal of handling SIRS is to prevent source of infection, repair and retrieve perfusion tissue, repair and maintain ventricle function and other supportive efforts.¹⁵

CONCLUSION

From 60 samples of Severe head injury, there were 49 (81.6%) whose Hs-CRP level in blood increased on the first day and 57 (95%) with SIRS on the third day when $p < 0.05$) so that high level Hs-CRP in blood can be used as predictor that causes SIRS to occur.

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