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Prognostic Value of the C-reactive Protein Levels in the Head Injury

Deok-Gu Lee, M.D., Kyeong-Seok Lee, M.D., Jai-Joon Shim, M.D., Seok-Mann Yoon, M.D., and Hack Gun Bae, M.D.

Department of Neurosurgery, Soonchunhyang University Chonan Hospital, Chonan, Korea

Objective: C-reactive protein (CRP) is an acute-phase protein, whose the blood levels increase rapidly in response to infection, trauma, and other inflammatory conditions. The relation of CRP levels to TBI is not well known. This study is to assess the association of early serum CRP concentrations, with the degree of the brain damage and the prognosis of the patients with the diffuse head injury.

Material & Method: From September 2004 to March 2004, we measured serum CRP at least twice, the first within 2 days (initial; CRPi) and the second between 3 to 7 days (early; CRPe) after the trauma. Serum CRP was measured by immunoturbidity method. In 187 patients, the relationship between the clinical features and serum CRP level was analyzed.

Results: The serum levels of CRPi were not significantly different according to the age, the initial Glasgow Coma Scale (GCS) score, the outcome, and the operative intervension. High serum levels (20 mg/l<) of CRPe were more common in patients with low GCS (3-12), in patients who underwent surgery, and in patients with poor outcome.

Conclusion: CRPe can be a useful adjuvant, especially in cases of diffuse brain injury where imaging studies are usually less optimal to reveal the severity of TBI.

Key Words: C-reactive protein · Biological markers · Diagnosis · Glasgow coma scale · Glasgow outcome scale · Craniocerebral trauma

INTRODUCTION

We can assess the severity of traumatic brain injuries(TBI) by the Glasgow coma scale(GCS) score[4], or radiological studies such as computed tomography(CT) or magnetic resonance imaging (MRI)[12]. The imaging studies are very useful to identify many focal hemorrhagic lesions. However, they are often inadequate, especially for the diffuse lesions or mild head injuries. There are some biochemical serum markers for TBI, such as creatine kinase isoenzyme BB(CK-BB)[8,9,13,21,24], neuron specific enolase (NSE)[17,24], prostaglandins[15], myelin basic protein[17], and S-100B protein[18,22]. To measure these serum markers, we usually need special kits for them.

C-reactive protein (CRP) is an acute-phase protein, the blood levels of which increase rapidly in response to infection, trauma, ischemia, burns, and other inflammatory conditions[5,14,19]. Most laboratories have a suitable equipment to measure the level of CRP. The cost for CRP measurement is relatively cheap. The relation of CRP levels to TBI is not well known. This study was done to assess the association of early serum CRP concentrations with the degree of the brain damage and the prognosis of the TBI patients.

Corresponding Author: **Kyeong-Seok Lee,** M.D.
Department of Neurosurgery, Soonchunhyang University Chonan Hospital, 23-20, Bongmyong-dong, Chonan, 330-721 Korea
Tel: 82-41-570-2182, Fax: 82-41-572-9297
E-mail: kslshl@schch.co.kr

MATERIALS AND METHODS

From September 2003 to March 2004, 341 consecutive patients were admitted after head injuries. We measured serum CRP at least twice, the first within 2 days (initial; CRPi) and the second between 3 to 7 days (early; CRPe) after the trauma. Serum CRP

Table 1. The serum level of the early CRPe(mg/L) and Glasgow coma score(GCS)

GCS score \ CRPe	<10	10~20	20<
3~12	14	10	43
13~15	55	21	44

P value = 0.001; GCS = Glasgow coma scale

Table 2. The serum level of the early CRPe(mg/L) and outcome

Outcome \ CRPe	<10	10~20	20<
Good	61	24	58
Poor	8	7	29

P value = 0.006; good = good recovery and moderate disability; poor = severe disability, persistant vegetative state and death

was measured by immunoturbidity method. We collect these data retrospectively. We could have data of 238 patients, in whom we measured serum CRP at least twice. We excluded 32 pediatric (not more than 15 years old) patients and 19 patients with chronic subdural hematomas. Finally in 187 patients, the relationship between the clinical features and serum CRP level was analyzed.

As the clinical features, we collect data on the age, GCS score, the outcome at discharge(Glasgow outcome score), and methods of treatment. The age was divided into two groups, the young (from 16 to 50) and the aged (over 50). The level of consciousness was grouped into either a low (3 to 12) or a high (13 to 15). The outcome was grouped into the good (good recovery and moderate disability) and the poor (from severe disability to death). The method of treatment was either conservative or operative.

Statistical significance was tested by the chi-square test. A two-tailed p value <0.05 was considered significant.

RESULTS

The high serum level (more than 20 mg/L)of CRPi was more common in the aged. However, this difference was not statistically significant(p=0.055, 3×2 chi-square test). There were no statistically significant differences according to the initial GCS, the outcome, or the method of treatment (p=0.743, p=0.490, p=0.242), repectively.

Table 3. The serum level of the early CRPe(mg/L) and methods of treatment

Treatment \ CRPe	<10	10~20	20<
Operative	53	20	49
Conservative	16	11	38

P value = 0.028

In CRPe, there were no statistically significant differences according the age (p=0.874). However, the high serum level of CRPe was more commonin patients with low GCS(Table 1), in patients with poor outcome(Table 2), and in patients who underwent surgery(Table 3). These differences were statistically significant(p<0.05).

DISCUSSION

CRPi tended to increase with age. Normally, CRP values marginally increase with age and increased body mass in adults, and are minimally higher in females and smokers[19]. The serum levels of CRPi were not significantly different according to the age, the initial GCS score, the outcome, and the operative intervention. However, high serum levels (20 mg/l<) of CRPe were more common in patients with low(3-12) GCS, in patients with poor outcome, and in patients who underwent surgery.

There are extensive studies on some biochemical markers for TBI. The sensitivity and specificity of CK-BB is inadequate for use as an indicator of TBI[10]. Serum levels of NSE do not correspond to the amount of TBI, probably because of its long (20 hours) half-life[10]. S-100B serum levels are correlated to both clinical measures of injury severity, neuroradiological findings and outcomes in several studies from different authors[7,18,22]. S-100B protein is the most promising marker for evaluation of TBI[10]. However, to measure levels of S-100B protein, a special kit for an immunoluminometric assay should be a must. In most hospital laboratories, they do not have such a kit for routine evaluation.

CRP is a relatively nonspecific marker of inflammation. However,

most laboratories can measure the levels of CRP with relatively cheap cost. CRP is secreted by the liver in response to a variety of inflammatory cytokines[5]. In the general population, CRP values range between 0.1 and 10 mg/L in adults[19]. Levels of CRP increase very rapidly in response to trauma, inflammation and infection, and decrease just as rapidly with the resolution of the condition. There was significant relation between peak levels and Abbreviated Injury Scale and Injury Severity scores[6]. Optimal time to measure CRP levels revealing tissue damage may be 3 days after trauma. In children with TBI, CRP was normal 4 hours after injury, then increased reaching peak levels in 48 hours[11]. Values are maximal at 24～48 hours and are persistently increased for approximately 5～7 days[19]. In severe TBI, data on certain enzyme activities and inflammation markers recorded at 72 hours best discriminated between survivors and nonsurvivors[3]. Serum CRP levels also increase in muscle damage[1], organ failure[14], neurosurgical procedures[2], or even in hypertension[20], lumbar disc herniation[23], and post-traumatic stress disorders[16]. Thus, the measurement of CRP can be used not only to monitor various inflammatory states and many different disorders, but also to assess the severity of tissue damage.

CONCLUSION

In TBI, CRP alone is not adequate to assess the severity of TBI due to its poor specificity. However, it can be useful in cases of diffuse brain injury, in which imaging studies are usually less optimal to reveal the severity of TBI. To test sensitivity and specificity of CRP in diffuse brain injuries, further studies are more needed.

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