We measured the serum concentration of C-reactive protein (CRP) by a high-sensitive method in patients with lumbar disc herniation. There were 48 patients in the study group and 53 normal controls. The level and type of herniation were evaluated. The clinical data including the neurological findings, the angle of straight leg raising and post-operative recovery as measured by the Japanese Orthopaedic Association (JOA) score, were recorded. The high-sensitive CRP (hs-CRP) was measured by an ultrasensitive latex-enhanced immunoassay. The mean hs-CRP concentration was 0.056 ± 0.076 mg/dl in the patient group and 0.017 ± 0.021 mg/dl in the control group. The difference was statistically significant (p = 0.006). There was no other correlation between the hs-CRP concentration and the level and type of herniation, or the pre-operative clinical data. A positive correlation was found between the concentration of hs-CRP before operation and the JOA score after. Those with a higher concentration of hs-CRP before operation showed a poorer recovery after. The significantly high concentration of serum hs-CRP might indicate a systemic inflammatory response to impingement of the nerve root caused by disc herniation and might be a predictor of recovery after operation.

Lumbar disc herniation (LDH) induces an inflammatory reaction around the nerve roots which may cause radicular pain.1-21 In histological studies, inflammatory cells, predominantly macrophages, have been found in herniated disc tissue harvested during surgery.2,3,6,8-10,12,14-17,19-21 These cells spontaneously produce inflammatory mediators such as interleukin-1 (IL-1),5 interleukin-6 (IL-6),4,5 tumour necrosis factor (TNF)-α,5 intercellular adhesion molecule-1 (ICAM-1),9 lymphocyte function-associated antigen (LFA-1),9 basic fibroblast growth factor (bFGF),9 prostaglandin E2 (PGE2),4,5,7 leukotriene B4 (LTB4),11 thromboxane B2 (TxB2),11 phospholipase A2,1 nitric oxide (NO)4 and matrix metalloproteinases (MMPs).4 These cytokines, especially IL-6, might increase the serum C-reactive protein (CRP) concentration,22 but when this is measured by the conventional method, it is within normal limits in most of these patients. Such assessment of the serum CRP might not detect the local inflammatory reaction which occurs in the small area surrounding the disc herniation. The CRP is typically measured in clinical laboratories by either immunonephelometric or immunoturbidimetric assays which have a limit of detection of 0.3 to 0.5 mg/dl.

Recently, an ultrasensitive latex-enhanced immunoassay (Latex) for high-sensitivity CRP (hs-CRP) concentration analysis has become available23 and has been found useful in predicting future myocardial infarction and stroke.24-27 It was felt that the method might be able to detect small areas of inflammation around disc herniation in the lumbar spine. The present study was undertaken to determine whether or not the serum CRP concentration is increased in patients with LDH and, if it is increased, to evaluate any correlation between the concentration and the clinical signs.

Patients and Methods

A total of 48 patients with herniation of a lumbar intervertebral disc were assessed. There were 22 men and 26 women with an average age of 26.4 years (16 to 39). Fifty-three normal volunteers comprised the control group which included 10 men and 43 woman with an average age of 21.4 years (21 to 28). All participants had appropriate MRI. In the patient group, a conventional neurological examination was carried out. The level and side of the herniation were confirmed through MRI. CT and/or myelography. The type of herniation was evaluated by MacNab’s classification.28 After taking the blood samples, posterior discectomy was carried out in 17 patients with the rest having conservative
treatment. The clinical data were evaluated according to the Japanese Orthopaedic Association (JOA) score (Table I). In the patients who underwent posterior discectomy, the post-operative recovery from six months to one year after surgery was evaluated according to the post-operative JOA score.

 Patients were excluded who were older than 40 years or had a history of lumbar disc surgery, infection, chronic inflammatory disease or malignancy. The MRI confirmed the absence of disc herniation in the control group to whom the same exclusion criteria were applied. Informed consent was obtained from all of the participants before they joined the study.

For each patient and control subject, 2 ml of serum was obtained and stored at –80˚C. The pre-operative blood samples were analysed to assess the hs-CRP concentration as measured by an ultrasensitive latex-enhanced immunoassay (N-Latex CRP II) employing the BNProSpec nephelometer (Dade Behring, Newark, New Jersey). This assay is capable of measuring hs-CRP at a concentration of 0.00095 mg/dl.

**Statistical analysis.** The concentrations of hs-CRP in the serum were expressed as mean ± SD. Differences between groups were analysed for statistical significance using the Student’s t-test (unpaired). A p value of less than 0.05 was considered statistically significant.

**Results**

Twelve disc herniations were at L4-5, 22 were at L5-S1 and 14 were at both L4-5 and L5-S1. A protrusion type of herniation was observed in 34 patients and an extrusion pattern in seven. We did not confirm the pattern of the herniation in the remainder. Five patients had severe limitation of straight leg raising of less than 30˚, 21 had moderate limitation of between 30˚ and 70˚ and 18 had slight limitation. The mean pre-operative JOA score was 15.8 ± 4.6 points and it recovered to 26.0 ± 2.6 points after operation. The recovery rate was 77.3 ± 20.5%.

The mean serum hs-CRP concentration was 0.056 ± 0.076 mg/dl in the patient group and 0.017 ± 0.021 mg/dl in the controls. There was a statistical difference between the two groups (Fig. 1) (p = 0.006). In the patient group, there was no other correlation between the hs-CRP concentration and the level and type of herniation, the angle of straight leg raising or the pre-operative JOA score (Table II). However, a positive correlation was found between the pre-operative hs-CRP concentration and the post-operative JOA score. The patients with a higher pre-operative hs-CRP concentration showed a lower score after operation (Fig. 2).

**Discussion**

CRP is among the most useful of acute phase proteins as a marker since its serum concentration increases several times.
hundredfold within 24 to 48 hours after tissue injury. It is the most sensitive parameter for monitoring infection after surgery. The serum CRP concentration often increases to over 1 mg/dl in cases of post-operative infection. However, the present study showed that while the increase in patients with disc herniation was significant, it was small, of the order of $10^{-2}$ mg/dl.

Le Gars et al compared the CRP analysed by an ultrasensitive method in 35 patients with sciatica due to disc herniation and age- and sex-matched controls. They showed that the concentration was significantly higher in the patients than in the controls. They used an enzyme-linked immunosorbert assay with a limit detection of 0.0005 mg/dl. Although they used a different method from that in the current study, both indicate that a systemic inflammatory response is found in patients with disc herniation using a highly sensitive analysis of CRP. This may be due to cytokines which are produced and released by inflammatory cells, including macrophages or monocytes, in response to tissue damage. Pro-inflammatory cytokines, such as IL-6 and IL-1, are largely responsible for the induction of CRP synthesis in the liver. Although we did not assay these cytokines or perform histological analysis, numerous studies have shown that inflammatory responses occur in the area surrounding the disc herniation. The response to such a reaction may stimulate the liver resulting in an increase in the concentration of CRP in the serum.

The current study did not reveal any correlation between the serum concentration of hs-CRP and the differing MRI and clinical findings. No correlation has been found between the histological evidence of macrophage infiltration around disc herniation and the clinical findings. However, a positive correlation between the pre-operative concentration of hs-CRP and the JOA score after operation might indicate that the patients with a higher pre-operative level of CRP showed poorer post-operative recovery. Ridker et al and Ridker found that the baseline concentration of CRP was higher among men and women who went on to have myocardial infarction or an ischaemic stroke, and concluded that the baseline concentration of CRP predicted the risk of future myocardial infarction and stroke.

The mechanism linking CRP concentration to atherothrombosis is unclear, although it has been speculated that chronic inflammation due to previous infections, such as Chlamidia pneumoniae, Helicobacter pylori, herpes simplex virus, or cytomegalovirus, might be associated with the development of an atherosclerotic plaque. If the increase of CRP concentration in the patients with LDH reflects chronic inflammation around the nerve root, recovery after operation may be prolonged in patients with higher levels.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

Table II. Correlation between the hs-CRP concentration and the level and type of herniation, the angle of straight leg raising and the JOA score before operation

<table>
<thead>
<tr>
<th>hs-CRP (mg/dl)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of herniation</td>
<td></td>
</tr>
<tr>
<td>L4-5</td>
<td>0.084 ± 0.084</td>
</tr>
<tr>
<td>L5-S</td>
<td>0.055 ± 0.086</td>
</tr>
<tr>
<td>L4-5 and L5-S</td>
<td>0.034 ± 0.038</td>
</tr>
<tr>
<td>Type of herniation</td>
<td></td>
</tr>
<tr>
<td>Protrusion</td>
<td>0.062 ± 0.085</td>
</tr>
<tr>
<td>Extrusion</td>
<td>0.041 ± 0.044</td>
</tr>
<tr>
<td>Angle of straight leg raising</td>
<td></td>
</tr>
<tr>
<td>&lt; 30°</td>
<td>0.054 ± 0.037</td>
</tr>
<tr>
<td>30° ≤ angle &lt; 70°</td>
<td>0.052 ± 0.042</td>
</tr>
<tr>
<td>≥ 70°</td>
<td>0.069 ± 0.027</td>
</tr>
<tr>
<td>JOA score before operation</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>0.0126 ± 0.010</td>
</tr>
<tr>
<td>10 ≤ score &lt; 20</td>
<td>0.057 ± 0.065</td>
</tr>
<tr>
<td>≥ 20</td>
<td>0.055 ± 0.098</td>
</tr>
</tbody>
</table>

Fig. 2

Correlation between pre-operative hs-CRP concentration and post-operative JOA score (r = -0.583).
References


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