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Prognostic Usefulness of High Sensitivity C-Reactive Protein for Transforaminal Epidural Steroid Injection in Patients with Radicular Pain

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Abstract

Objective. There are several types of lumbar stenosis, such as central, lateral recess, foraminal. The symptoms of lumbar stenosis are neurogenic claudication, numbness, tingling, etc. The treatment modality is medication, physical therapy, intervention, and surgery. The epidural steroid injection has been used for treatment of low back pain/radiculopathy. However, we could not predict what percent had pain relief after epidural steroid injection.

The purpose of this study was to evaluate the usefulness of high sensitivity C-reactive protein (hsCRP) as a marker for predicting the efficacy of lumbar transforaminal epidural steroid injection.

Design. A total of 55 patients with lumbar stenosis underwent lumbar transforaminal epidural steroid injection under fluoroscopic guidance. Prior to injection, all patients were examined and their visual analog scale (VAS) score and hsCRP score were recorded. They returned 4 weeks following their initial injection and repeat hsCRP, and VAS sores were obtained.

Results. The average pretreatment hsCRP and VAS score for all 55 patients were 3.2 ± 4.3 mg/L and 8.1 ± 1.1, respectively. Forty-two of 55 patients had 1.6 mg/L of hsCRP. After procedure, the VAS decreased from 8.0 ± 1.1 to 2.5 ± 1.1. In contrast, the averages of hsCRP and VAS scores of 13 patients were 9.4 ± 3.7 mg/L and 8.2 ± 0.9, respectively, at baseline, which decreased to 1.2 ± 0.9 mg/L and 2.5 ± 0.8 at 4 weeks later. At posttreatment, the VAS score difference between the two groups was not statistically significant. There was no correlation between hsCRP and VAS score ($P = 0.426$).

Conclusion. The results suggest that there was no correlation between pretreat hsCRP and posttreat VAS. Therefore, hsCRP may not be useful as predictor of response to TFESI in patients with spinal stenosis.

Key Words. Low Back Pain; hsCRP; Transforaminal Epidural Steroid Injection; Chronic

Introduction

Lumbar spinal stenosis results from degeneration of the facet joint, disc herniation, and hypertrophy of ligament flavum. Due to these circumstances, there is compression of neural element and their nutrient supply in the central canal, lateral recess, or neural foramen. The symptoms of lumbar stenosis are back pain, leg pain, and weakness [1]. Lower extremity neurogenic claudication presents in approximately 94% of cases and is bilateral in 69% [2].

Nonoperative treatments for lumbar stenosis consist of pharmacotherapy, exercise, physical therapy, and hormone replacement. In addition, epidural steroid injection represents an important therapeutic modality [3].

Epidural steroid injection is widely used for treatment of low back pain and lower extremity pain. Steroid is administered through the injections, and is thought to be integral in decreasing inflammation around the affected nerve tissue [4], hence leading to a reduction in pain. However, we are not aware of any prediction of effectiveness of lumbar transforaminal epidural steroid injection (TFESI).

Laboratory measurement of acute phase protein is a valuable indicator of the presence, extent, and response of

inflammation to treatment. Among acute phase protein, C-reactive protein (CRP) is the first acute phase protein and a sensitive systemic marker of inflammation and tissue damage [5], and it also appears 6–8 hours after infection.

Several studies in the literature have demonstrated that CRP can be used as a predictor and marker of the status of the disease [6–10]. In patients with peripheral vascular disease, CRP appears to be a strong predictor and marker of severity of peripheral vascular disease and also may predict the risk of restenosis after angioplsty [11]. Pain severity was associated with high sensitivity CRP (hsCRP) levels in patients with advanced osteoarthritis [12]. Also in lumbar disc herniation, patients with higher preoperative hsCRP showed poorer postoperative recovery [13,14]. Ackerman and Zhang [14] reported that in patients with higher hsCRP level prior to epidural steroid injection, less pain relief was achieved by the lumbar epidural steroid injection.

Even though the aforementioned studies have demonstrated the usefulness and validity of CRP as an aid establishing a prognostic marker, the question posed in the present study was different: whether or not hsCRP values in patients with lumbar spinal stenosis, who are being treated with lumbar epidural steroid injection, correlate with clinical improvement. Also there has been relatively little information in the literature regarding the role of hsCRP as marker for the prediction of effectiveness of lumbar epidural steroid injection.

The purpose of this study was to evaluate the usefulness of hsCRP as marker for predicting the efficacy of lumbar transforaminal epidural steroid injection in patients with lumbar spinal stenosis.

Materials and Methods

The study subjects consisted of 55 male patients with lumbar spinal stenosis who were suffering with leg pain. Their ages ranged from 30 to 77 years. The Institutional Review Board approved the review of this study. All patients had magnetic resonance imaging or computerized tomography (CT) scan and we performed conventional neurological examinations. Inclusion criteria were 1) unilateral radicular pain without pain in the back, together with radiographic signs of foraminal stenosis; 2) duration of symptom: 2–24 months; and 3) male. Exclusion criteria were 1) chronic oral steroid medication use; 2) oral, peripheral, or epidural steroid use in last 3 months; 3) systemic inflammatory disease, including rheumatoid arthritis, ankylosing spondylitis, Reiter's syndrome, etc.; 4) oral temperature >100.4; 5) cognitively impaired adults and patients unable to give consent; 6) aspirin, clopidogrel bisulfate, coumadin, or heparin use in the prior 2 weeks; or 7) a history of bleeding disorders; and 8) coxarthrosis, gonarthosis, and arterial insufficiency in the legs, polyneuropathy, concomitant serious disease, or previous surgery on the back.

The hsCRP was measured by a Hitachi 7080 (turbidimetric immunoassay method) before injection. The subjects were divided into two group according to pretreatment hsCRP values (group 1: hsCRP <4 mg/L, group 2: hsCRP >4 mg/L).

All patients performed single TFESI under fluoroscopic guidance, 40 mg triamcinolone acetonide (Triam®, Shinpoong, South Korea) injected along with 1% of lidocaine 1 mL to the level of each patient's stenotic site. All the injections were performed by the same anesthesiologist. The patient was placed in the prone position. Under fluoroscopic guidance, after sterile preparation, draping, and local anesthesia, a 23-gauge, 3.5-inch spinal needle was gently advanced on oblique view to the safe-triangle, which is composed of the pedicle, a tangential base that corresponds to the exiting nerve root, and the lateral border of the vertebral body. Both anteroposterior and lateral fluoroscopic projections confirmed proper needle placement. At each level, 0.5 mL of contrast medium (iohexol) was injected to confirm the position and no blood or cerebrospinal fluid was aspirated, the physician injected the steroid. The triamcinolone 1 mL (40 mg) was diluted with 1 mL of lidocaine 1%.

Patients were asked to fill out visual analog scale (VAS) at baseline (prior to procedure) and at 4 weeks following the procedure. The hsCRP was measured by a Hitachi 7080 (TIA method) at same interval. An hsCRP elevation was defined as a level above the normal range of 4 mg/dL (this is our hospital normal reference values).

The effect for injection was estimated as the change in pain score from before to after the infusion. The Mann–Whitney *U*-test was used for statistical analysis to compare between and within VAS and hsCRP. Type I error rate <0.05 was considered significant. The sample size of 20 was specified in advance to provide 75% power to detect a difference in the amount of change in pain score between treatments. All statistical analysis was performed on SPSS version 17.

Results

Fifty-five men patients were enrolled in this study (Table 1). The mean value of hsCRP at pretreatment was 3.2 ± 4.3 mg/L (range 0.2 to 17.8 mg/L). In 42 of 55 patients showed hsCRP <4 mg/L, whereas the hsCRP >4 mg/L group was 13 patients.

The mean VAS score at baseline, there was no statistically significant difference between patients with hsCRP <4 mg/L and that with >4 mg/L (Table 2).

Four weeks after receiving TFESI, marked reduction in the mean pain score were observed in the both group. The VAS of the hsCRP <4 mg/L patients (n = 42) at pretreatment was 8.0 ± 1.1, which decreased to 2.5 ± 1.1 after TFESI ($P = 0.000$). The reduction in mean pain severity score showed no difference between group 1 and group 2.

Table 1 Patient demographics

	hsCRP < 4 mg/L	hsCRP > 4 mg/L
N	42	13
Age (year)	61.7 ± 11.0	63.2 ± 10.4
Height (cm)	157.1 ± 8.2	156.3 ± 9.7
Weight (kg)	62.5 ± 5.1	61.5 ± 4.7
Duration of pain (month)	10.3 ± 5.2	10.7 ± 6.6
Involved level (no of patient)		
L3-4	9	0
L4-5	22	9
L5-S1	11	4

Table 2 Summary statistics for visual analog score and high sensitivity C-reactive protein

		<4 mg/L (n = 42)	>4 mg/L (n = 13)
VAS	Pretreatment	8.0 ± 1.1	8.2 ± 0.9
	Posttreatment	2.5 ± 1.1	2.5 ± 0.8
hsCRP (mg/L)	Pretreatment	1.6 ± 2.6	9.4 ± 3.7
	Posttreatment	0.5 ± 0.5	1.2 ± 0.9

In both groups, the hsCRP values were significantly reduced (P = 0.008) (Table 2). The reduction in mean hsCRP observed in group 2 was greater than those with group 1. In the hsCRP >4 mg/L patients (group 2), both VAS and hsCRP were significantly lower in the posttreatment than in the baseline (P = 0.000).

The hsCRP did not correlate with clinical improvement in the either group (Figures 1 and 2) (Figure 3, P = 0.842, r = 0.028).

Discussion

This study did not reveal any correlation between the hsCRP and VAS scores following epidural steroid injection in patients with lumbar spinal stenosis. Although group 2 demonstrated a greater reduction than group 1 in post-treatment hsCRP, posttreatment VAS did not significantly difference between both groups. Our results are different from those of Ackerman and Zhang, who studied systemic inflammatory maker and pain response to lumbar steroid injection in patients with lumbar disc herniation [14].

Only male patients were chosen for this study because it has been shown that gender affects hsCRP levels [15]. In our study, 13 of 55 patients with higher hsCRP levels prior to TFESI had good pain relief by the LESI. Among acute phase protein, CRP is the first acute phase protein and it also appears 6–8 hours after infection. CRP is response to inflammation, infection, malignancy, and tissue damage. Some studies have reported that hsCRP is increased in the acute phase of inflammation or during severe pain

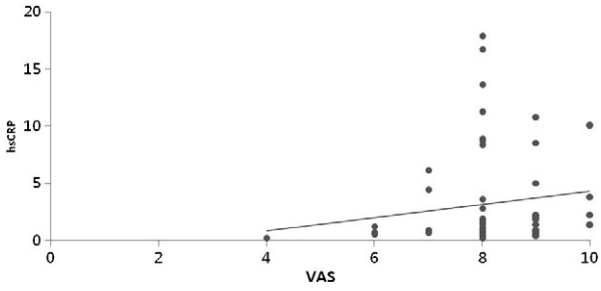

Figure 1 Correlation between baseline hsCRP and pretreat VAS (P = 0.298) (r = 0.143).

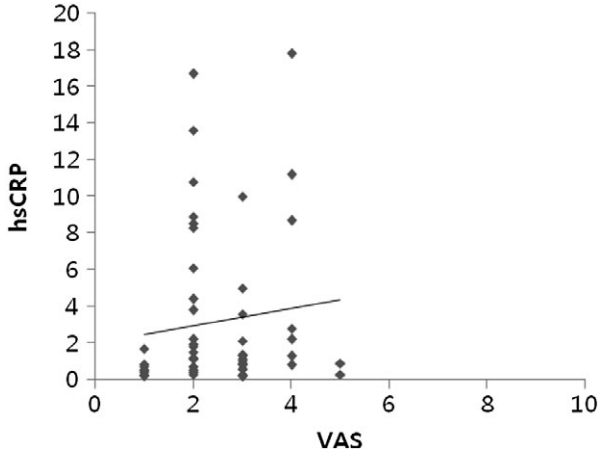

Figure 2 Correlation between baseline hsCRP and posttreat VAS (P = 0.091) (r = 0.230).

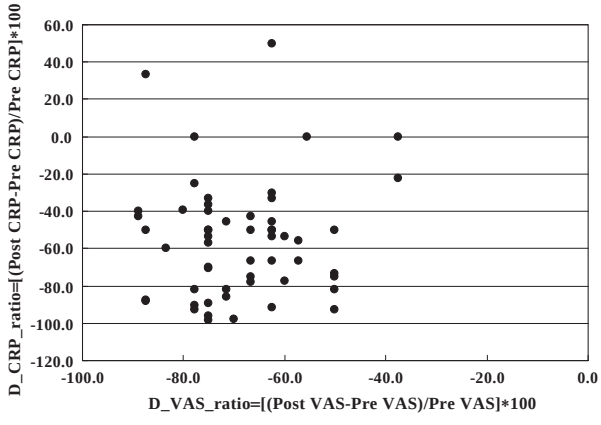

Figure 3 Correlation between the amount of change of VAS (Posttreatment–Pretreatment) and that of hsCRP (P = 0.842) (r = 0.028).

[5,16–18] with a trend toward ultrasensitive CRP higher levels in patients with severe nerve root symptoms [18]. In the current study, despite duration of their symptom of more than 2 months, hsCRP values were elevated in only13 patients. We consider that some patients with foraminal stenosis could have acute nerve root irritation (causing acute radicular pain) from increase activities, therefore hsCRP could be elevated.

Some authors have reported that the higher hsCRP levels are associated with less pain relief or poor outcome after treatment. Sugimori et al. [13] reported that patients with a higher concentration of hsCRP before posterior discectomy showed poor recovery after surgery. Moreover, there was a positive correlation between a higher preoperative hsCRP concentration and a lower score on the postoperative Japanese Orthopedic Association score [13]. Ackerman and Zhang reported that less pain relief was achieved by LESI in patients with higher hsCRP levels prior to lumbar epidural steroid injection (LESI) [14]. The authors explained that the reason for less pain relief after treatment was due to a more pronounced inflammatory response that occurred in disc extrusion and sequestered disc and suggested that the efficacy of lumbar epidural steroid injection is inversely related to hsCRP levels.

One possible explanation for our result was that patients with chronic sciatic pain were included in present study. Previous studies suggest that there is no correlation between hsCRP and pain in patients with chronic low back pain [12,19]. Sugimori et al. [13] reported that there was no correlation between the hsCRP concentration and the level and type of herniation, or the preoperative clinical data (the angle of straight leg rising, Japanese Orthopedic Association Score). Gebhardt et al. [19] reported that the level of hsCRP did not have major clinical relevance when evaluating chronic low back pain. In chronic low back pain patients, pain severity is more strongly related to being overweight and psychological factors than to pathophysiological changes in low grade systemic inflammation that would be the cause in patients with acute sciatic pain [12].

In the current study, 42 of the 55 patients had normal levels of pretreatment hsCRP. In those patients, the hsCRP values declined after TFESI. However, both pre- and posttreatment hsCRP values were within normal range. The chronic inflammatory process involved, induces CRP production that reaches levels not high enough to detect in baseline hsCRP values. Also, even in patients with acute lumbosacral pain, there was no corresponding course of CRP with pain or function after 3 weeks of treatment [19].

There were several limitations in present study. The outcome was measured only by the patient's pain score; there was no functional outcome measurement, psychological improvement, and medication reduction, etc. In addition, there was a lack of clear structure during long-term follow up.

In the present study, although significant reduction of hsCRP level among the group-II patients, no statistically significant difference on post-VAS between both groups. Despite pre-hsCRP was within normal reference level (1.6 mg/L) in group 1, VAS was decreased to 2.5 at 4 weeks later. It means that hsCRP did not predictor in patients with LSS.

In conclusion, the strength of this study is that it attempts to provide an objective laboratory marker for prognosticating a clinical process in lumbar spinal stenosis. In present study, all patients showed clinical improvement regardless of hsCRP levels. Therefore, the hsCRP did not represent useful marker for predicting of efficacy of TFESI.

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