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Original Article

The importance of C-reactive protein levels for surgical decision-making and determination of response to conservative therapy in patients with acute sciatica

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Abstract

Aim: We aimed to determine C-reactive protein (CRP) levels in patients with intervertebral disc disease (IDD) and to evaluate these patients' radiological and clinical characteristics.

Material and Methods: A total of 102 patients were divided into four groups according to lumbar MRI results using the Macnab classification: bulging, protrusion, extrusion-sequestration, and normal. Straight leg raising test (SLR) and visual analogue scale (VAS) were used for clinical evaluation. Patients with bulging and protrusion were treated with conservative therapy within 5-10 days and bed-rest. Blood samples, SLR values and VAS scores were obtained from these patients before and after conservative therapy. The extrusion-sequestration group underwent lumbar spinal surgery. Medical treatment was not applied to this group and blood samples were collected only preoperatively. Individuals with normal MRI findings and no spinal complaints were evaluated as controls.

Results: CRP levels were found to be 6.61 ± 7.78 in controls, 6.62 ± 5.28 in the bulging group, 11.50 ± 21.71 in the protrusion group and 17.18 ± 48.22 in the extruded-sequestration group (p=0.321). CRP levels were significantly decreased after treatment in the bulging group (p=0.001). Positive correlations were found between post-treatment VAS scores and pre-treatment WBC in the protrusion group, and with CRP levels in the bulging group.

Conclusion: Although no statistically significant difference was determined, we observed higher mean serum CRP levels in the surgical group (extrusion-sequestration). We believe that further studies must be performed to determine whether serum CRP levels can be used as a prognostic marker in surgical decision making.

Keywords: C-reactive protein; inflammation; intervertebral disc; sciatica

INTRODUCTION

A great amount of research has been performed for the evaluation of low back pain; as it has been demonstrated to be: "A very common condition in all populations", and continuing to quote the same study, "60–80% of people suffer from low back pain and 35% experience sciatica pain at least once throughout their lives. Surgical intervention may be required in 10% of patients with lumbar disc hernia (LDH)". Therefore, low back pain and LDH is a major problem for the community (1). Sciatica is a painful condition that begins in the lower back and radiates to the lower hip and downward to different regions depending on which spinal nerve is affected. The condition often causes disability and a significant decrease in quality of life. Many risk factors have been identified in sciatica, including aging, obesity, smoking, trauma, immobilization, working in an office environment, working as a machine operator, heavy-workers and carpenters (2). It is well known that the condition can result from compression of the sciatic nerve anywhere throughout its course due to underlying spinal or non-spinal causes. Although sciatica has several well-defined causes, spinal column disorders including herniated discs, osteoarthritis and spondylolisthesis constitute 85% of all sciatic cases (3).

The intervertebral disc (IVD) plays a significant role in maintaining the integrity of the spinal column and functions mechanically to absorb and distribute loads from body weight and muscle activity along the spinal column. Disc degeneration disrupts the load-bearing capability of discs by altering the architecture and biochemical configuration of the disc (4). Under the influence of factors such as aging, trauma, genetics and lifestyle, cells around the disc secrete catabolic factors that may change extracellular matrix deposition and could also trigger an inflammatory reaction (5). Clinical studies have shown that both inflammation and compression are important

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for the symptomatic nerve root and are associated with peripheral neuropathy, resulting in weakness, pain and numbness (6). Various biomarkers have been investigated in order to understand the effects of inflammation and its role in the pathogenesis of acute sciatica and disc pathologies, and to elucidate the choice of conservative or surgical intervention. However, their results are uncertain and inconsistent.

C-reactive protein (CRP), a member of the pentraxin family, is a well-known prototype acute phase reactant that has many important biological features, including the lack of diurnal variation, the lack of variations with age and sex, the possibility that it can increase thousands of folds its normal level within 24-48 hours of the acute phase response, and its rapid decrease to previous levels when inflammatory action has regressed (7). It is synthesized in the liver by induction of cytokines and other mediators and is used as a common indicator of infection and inflammation. In patients with sciatica and disc pathologies, it has been shown in a few studies that CRP levels could change slightly due to local inflammation.

The aim of this study was to determine the changes in CRP levels due to the inflammatory response in patients presenting to the neurosurgery outpatient clinic with complaints of acute sciatica and disc pathologies, and to evaluate our results together with radiological and clinical features. In addition, we aimed to investigate prospectively whether CRP levels could be employed as a prognostic marker in surgical decision making.

MATERIAL and METHODS

Study design

This prospective randomized controlled study was carried out from July 2013 to May 2014 at the Neurosurgery Department of Diskapi Beyazit Training and Research Hospital, Ankara, Turkey. A total of 102 patients, aged 14-88 years, who had complaints of acute sciatica not exceeding a duration of 3 months were included in the study. Anamnesis, physical examination and radiological imaging, including lumbar spinal magnetic resonance imagination (MRI), were performed in all patients. All lumbar spinal MRI findings were examined and reported by the same radiologist. Clinical data including age, gender, smoking, the status of physical exercise and occupation were obtained from patient files. Straight leg raising test (SLR) and visual analogue scale (VAS) scores were used in the clinical evaluation of patients.

The SLR, also called the Laseque test, is a widely used basic neurological maneuver during physical examination to evaluate the sciatic nerve in relation to lumbosacral nerve root irritation (8). Briefly, when the patient is in the supine position, the leg is gently raised straight by flexing the hip (with the knee in extension) until pain develops. The angle between the leg and the horizontal plane is measured at the point where the pain begins. The test is considered positive if the pain occurs below 60 degrees. In terms of VAS, it is the most frequently used psychometric response scale to measure pain intensity in chronic low-back pain patients (9). The severity of the pain was self-assessed by using a linear visual scale indicated with equal distances from 0 to 10. A score of 0 was identified as no pain whatsoever, while 10 was identified as the worst possible pain.

Patients with any systemic inflammatory diseases including colitis and rheumatoid arthritis, metabolic conditions including diabetes mellitus and thyroid diseases, history of spinal surgery, instability problems such as spondylolisthesis and spondylolysis, grade 3-4 spondyloarthrosis, acute or chronic infectious diseases, sensory disorders, cancers, fractures, those using corticosteroids, and patients with psychiatric disorders, ischemic heart disease or stroke were excluded from the study.

The patients were divided into four groups using the Macnab disc herniation classification: bulging group, protrusion group, extrusion-sequestration group, and the group with normal MRI findings (controls). Patients whose MRI findings did not conclusively fit any of these groups were excluded from the study. According to Macnab disc herniation classification; *Bulging:* dehydrated nucleus pulposus, with the annulus fibrosus remaining under the load on the disc but extends into the spinal column. The disc is defined as symmetrically exceeding the borders of the adjacent vertebral corpus (more than 2 mm). *Protrusion:* The intervertebral disc shows posterior herniation due to incomplete damage to the annulus fibrosus. The disc extends partially and asymmetrically towards the spinal column or foramen. *Extrusion:* The intervertebral disc shows posterior herniation due to complete damage to the annulus fibrosus. The nucleus pulposus is completely outside the annulus fibrosus and the herniated disc that ruptures the posterior longitudinal ligaments extends to the spinal column. *Sequestration:* A part of the nucleus pulposus is extruded due to complete damage to the annulus fibrosus and this fragment is no longer associated with the nucleus pulposus (10).

Patients in the bulging and protrusion groups were treated with standard conservative medical treatment (analgesics and myorelaxants) with duration of 5 to 10 days and bed rest was recommended. Blood samples, SLR values and VAS scores were obtained from these patients before and after medical treatment. Extrusion-sequestration group consisted of patients with lumbar disc herniation in a single lumbar region who were undergoing lumbar spinal surgery for the first time. These patients had neurological deficits. Medical treatment was not applied to this group and surgical intervention was performed. Blood samples were collected from the patients in this group only preoperatively and no blood was collected postoperatively. The group with normal lumbar spinal MRI findings was composed of patients who had no signs of infection and who had no spinal complaints. They had been admitted to our outpatient clinic with other neurosurgical complaints that warranted MRI evaluation but the results showed a lack of lumbar pathologies. Blood samples were obtained and no medical treatment was given to patients in this group.

The study was performed in accordance with the ethical standards specified in the Declaration of Helsinki and was approved by the Research Ethics Committee of Diskapi Yildirim Beyazit Training and Research Hospital. Written and verbal informed consent was obtained from individuals before participating in this study.

Biochemical Analyses

For blood counts, standard ethylene diaminetetraacetic acid (EDTA) containing tubes were used for sample acquisition. Complete blood count analyses, based on the technique of laser flow cytometry scatter grams, were performed in the central laboratory of our institution using the same analyzer (Sysmex XE-5000, Lincolnshire, IL, USA). Erythrocyte sedimentation rate (ESR) was determined using the Westergren method. It was considered elevated if ESR levels were greater than 20 mm / h.

To obtain serum, blood samples were drawn from the antecubital vein of all participants after overnight fasting. After clotting, blood samples were centrifuged at 4000×g for 10 min and serum was separated. Serum CRP levels were quantitatively measured by the nephelometric method using a commercial kit (Immage Reagent,Beckman Coulter Fullerton, California, US) calibrated with the WHO reference standard calibrator 5 plus on the Immage Immunochemistry System. CRP values greater than 0.8 mg / dL were evaluated as abnormal CRP values.

Statistical Analysis

Statistical analyses were performed using MedCalc Statistical Software version 12.7.7 (MedCalc Software, Ostend, Belgium; http://www.medcalc.org). Quantitative data were tested for normality using the Shapiro Wilk test and were expressed as mean ± standard deviation or frequency (percentage). Depending on normality, the Mann-Whitney U test or the Student t-test were used for the comparison of two groups for the independent group comparisons of continuous variables. The Wilcoxon Signed Rank test was used to compare paired measurements in the event of non-normal distribution. The ANOVA test was used to compare more than two continuous variables with independent and normal distribution. Correlations were calculated us-ing Spearman's correlation test. The results were within the 95% confidence interval and the level of statistical significance was set at p <0.05.

RESULTS

A total of 102 acute sciatica patients were included in the study. In the extrusion and sequestration group, there were 10 females and 15 males with a mean age of 44 ± 12 years. In the protrusion group, there were 7 females and 5 males with a mean age of 48 ± 10.6 years.

In the bulging group, 15 female patients and 6 male patients were included and these patients had a mean age of 43 ± 12.7 years. The control group consisted of 30 females and 14 males. No statistically significant differences were found between groups according to age. In our study group, 56 patients were housewives and 20 patients were heavy-workers. Clinical features are shown in Table 1.

Table 1. Clinical features of the patients

	Extruded-Sequestration	Protrusion	Bulging	Control	Total	p value
Number of patients	25 (43.1%)	12 (11.8%)	21 (20.6%)	44 (43.1%)	102 (100%)	
Gender						
Female	10	7	15	30	62	
Male	15	5	6	14	40	
Mean Age (years)	44 ± 12	48 ± 10.6	43 ± 12.7	42 ± 17.3	43 ± 14.6	0.623
The use of tobacco						
(+)	3	1	1	8	13	
(-)	22	11	20	36	89	
Daily sport activities						
(+)	0	1	1	1	3	
(-)	25	11	20	43	99	
Occupation						
Housewives	12	6	13	25	56	
Heavy-workers	8	3	6	3	20	
Others	5	3	2	16	16	

Others: Retired, student, office workers, p value is significant <0.05 level

No significant differences were found between the groups with regard to WBC and mean ESR levels, at the beginning of the study (Table 2). Post-treatment WBC levels were 6.53 ± 3.39 in the bulging group and 7.14 ± 1.99 in patients with protrusion. There were no significant differences in WBC and ESR levels between the bulging and protrusion groups after conservative therapy (p=0,576 and p=0,444, respectively). There were also no within-group differences in WBC and ESR levels when pre- and post-treatment values were compared in the bulging and protrusion groups (p>0,05) (Table 2).

Table 2. WBC and ESR levels in patients

	Pre-treatment WBC	Post-treatment WBC	p value	Pre-treatment ESR	Post-treatment ESR	p value
Bulging	8.08±2.68	6.53±3.39	0.159	21.3±12.5	21.2±14.3	0.549
Protrusion	7.40±1.33	7.14±1.99	0.556	18.7±16.2	20.3±21.2	0.423
Extruded-Sequestration	9.04±3.75			22.6±21.7		
Controls	8.17±2.00			16.8±9.3		
p value	0.313	0.576		0.456	0.444	

WBC: White blood cell count (shown as x 10^3xμL), ESR: Erythrocyte sedimentation rate (shown as millimeters/hours). p value is significant <0.05

CRP levels in patient groups are shown in Table 3. At the beginning of the study, CRP levels were found to be 6.61 ± 7.78 in controls, 6.62 ± 5.28 in the bulging group, 11.50 ± 21.71 in the protrusion group and 17.18 ± 48.22 in the extruded-sequestration group. No significant differences were shown in CRP levels between the groups (p=0.321). CRP levels were significantly decreased after the treatment in the bulging group (p=0.001). No significant differences were found in CRP levels in the protrusion group after the treatment (p=0.248).

Table 3. CRP levels of patients before and after treatment

	Pre-treatment CRP	Post-treatment CRP	p value
Bulging	6.62±5.28	5.17±3.65	**0.001**
Protrusion	11.50±21.71	11.76±24.90	0.248
Extruded-Sequestration	17.18±48.22		
Controls	6.61±7.78		
p value	0.321	0.970	

CRP: C-reactive protein. P value is significant <0.05.

Table 4. Correlations between SLR values and biochemical analyses in bulging and protrusion group

	Pre-treatment WBC	Post- treatment WBC	Pre-treatment CRP	Post- treatment CRP	Pre-treatment ESR	Post- treatment ESR
Pre-treatment SLR in bulging group	-0.02	0.068	-0.185	0.141	0.052	0.080
	p:0.993	p:0.788	p:0.463	p:0.647	p:0.842	p:0.795
Pre-treatment SLR in protrusion group	-0.538	-0.595	-0.519	-0.371	0.00	0.042
	p:0.109	p:0.070	p:0.152	p:0.291	p:1.000	p:0.915
Post-treatment SLR in bulging group	-0.013	0.008	-0.223	-0.254	0.445	0.370
	p:0.968	p:0.980	p:0.464	p:0.425	p:0.148	p:0.262
Post-treatment SLR in protrusion group	-0.446	-0.677	-0.020	-0.192	-0.192	-0.075
	p:0.268	p:0.065	p:0.967	p:0.650	p:0.650	p:0.873

WBC: White blood cell count, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, SLR: Straight leg raising test

Table 5. Correlations between VAS scores and biochemical analyses in bulging and protrusion group

	Pre-treatment VAS	Post-treatment VAS
Pre-treatment WBC in Bulging	0.075	0.090
	p:0.746	p:0.866
Pre-treatment SLR in protrusion group	0.280	**0.949**
	p:0.378	**p:0.014**
Post-treatment WBC in Bulging	-0.038	-0.294
	p:0.869	p:0.571
Post-treatment WBC in Protrusion	0.348	0.632
	p:0.267	p:0.252
Pre-treatment CRP in Bulging	-0.25	**0.883**
	p:0.914	**p:0.020**
Pre-treatment CRP in Protrusion	-0.569	0.527
	p:0.068	p:0.361
Post-treatment CRP in Bulging	0.379	0.975
	p:0.147	p:0.005

Post-treatment CRP in Protrusion	-0.483	0.527
	p:0.112	p:0.361
Pre-treatment ESR in Bulging	-0.059	0.677
	p:0.806	p:0.140
Pre-treatment ESR in Protrusion	-0.472	0.158
	p:0.121	p:0.800
Post-treatment ESR in Bulging	0.101	**0.912**
	p:0.711	**p:0.011**
Post-treatment ESR in Protrusion	-0.206	0.738
	p:0.543	p:0.155

WBC: White blood cell count, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, VAS: Visuel analogue score

No significant correlations were revealed between patients' SLR values and biochemical results (Table 4). Positive correlations were found between post-treatment VAS scores and pre-treatment WBC values in the protrusion group, and with CRP levels and post-treatment ESR levels in the bulging group (Table 5).

DISCUSSION

The current study aimed to investigate CRP levels in patients with sciatica and disc pathologies, with a view to determine the prognostic value of serum CRP levels for surgical decision making. We demonstrate decreased CRP levels after the conservative treatment in patients with bulging identified by MRI. Although statistical significance was not achieved, we also observed that mean serum CRP levels were higher than the normal reference value (<0.8 mg / dL) in the surgical group (extrusion-sequestration). Therefore, we believe that it may be possible to utilize serum CRP levels as a marker for surgical decision making.

Sciatica is a painful symptom of multiple diseases and originates in the lower back and radiates along the path of the sciatic nerve. Intervertebral disc disease is a strong cause of sciatic pain, leading to progressive molecular, structural and biomechanical changes in the disc. It may result from mechanical compression of the nerve roots by the herniated nucleus pulposus. Further, as a result of prolonged compressions in the nerves that develop mechanically, the condition may also trigger a mild but significant inflammatory response. It has also been revealed in studies that IDD also includes an underlying inflammatory component around the nerve root, which may cause radicular pain and could be responsible for pain perception (11). Histological examinations have demonstrated that inflammatory cells including macrophages and monocytes are at large around the herniated disc tissue (12). Local inflammation around the nerves is associated with the release of cytokines from macrophage and monocytes in response to nerve root inflammation. These pro-inflammatory cytokines are interleukin-1 (IL-1), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), intercellular adhesion molecule-1, lymphocyte-associated antigen-1, basic fibroblast growth factor, prostaglandin E2, leukotriene B4, thromboxane B2, phospholipase A2, nitric oxide and matrix metalloproteinases (11,13). With the effect of mediators released by inflammatory response, nerve tissue becomes more sensitive to compression compared to other peripheral nerves, causing pain with the slightest manipulation or stress (14). High levels of inflammatory mediators, especially IL-1 and IL-6, may induce of CRP synthesis in the liver, leading to an increase in serum CRP levels. CRP is a sensitive marker of inflammation and tissue damage.

A few studies have been conducted in patients with sciatica and disc pathologies to evaluate the alterations in CRP levels throughout the disease, and to compare its relationship with clinical parameters such as pain and SLR (15-19). However, the results of these studies were inconsistent. Gebhardt et al. examined the course of hs-CRP levels over a period of 6 months and found that hs-CRP remained at constant levels in patients with chronic low back pain, suggesting no significant systemic inflammatory reactions occurred in patients with chronic low back pain (15). In a study conducted by Park et al., it was shown that CRP and ESR values did not rise in patients with low back pain due to inflammatory reactions (16). In contrast to these studies, Le Gars et al. found higher CRP levels in 35 patients with sciatica due to disc herniation (compared to controls) by an ultrasensitive method (17). Talghini et al. demonstrated higher hs-CRP levels in patients with extrusion compared to a group with only bulging, suggesting a cut-off point of 2.6 for the identification of extrusion (18). Ackerman and Zhang reported that hs-CRP levels of patients with lumbar disc protrusion, prolapse, extrusion and sequestration groups increased by 0%, 20%, 80% and 73%, respectively (19). They also revealed less pain relief following lumbar epidural steroid injection in patients with higher hs-CRP levels before treatment, and suggested that the reason for less pain relief after treatment was due to the higher inflammatory response occurring in extruded and sequestrated discs. In contrast to that study, Park and Lee showed no correlation between hs-CRP and VAS score following steroid injection in lumbar disc disease patients (20). Sugimori et al. revealed increased hs-CRP levels in 48 lumbar disc herniation patients compared to controls

and no correlation between serum hs-CRP concentration and preoperative MRI and clinical data, including type of herniation, the angle of straight leg rising and Japanese Orthopedic Association score (13). They also showed a negative correlation between preoperative hs-CRP and postoperative recovery, demonstrating the predictive value of CRP for clinical course. Although not statistically significant, we observed an increase in CRP values between groups with the progression of disease. Our results indicate that disc pathologies result in subclinical systemic inflammatory response. This may suggest that patients with a higher CRP level could in fact have worse clinical condition or progression. In addition, Gebhart et al. also demonstrated that, during the first 3 weeks of in-patient treatment, there was a corresponding significant decrease in hs-CRP and pain levels, and also a significant improvement in SLR (15). They also showed that, after the initial period, CRP levels returned to initial levels; indicating a close relationship. Consistent with this study, we found a significantly decreased CRP level with conservative medical treatment (analgesics and myorelaxants) in the bulging group –but not in the protrusion group. This demonstrates that the inflammatory activity may decrease as a response to conservative therapy during the initial degeneration stages of disc herniation.

In our study, CRP levels of the individuals in the surgical group (extruded-sequestrated) were higher compared to other groups before conservative medical treatment. Rathod et al. showed increased hs-CRP levels in 50 lumbar disc disease patients compared to 50 normal subjects (21). They also found a relationship between preoperative hs-CRP level and postoperative disability score and suggested that hs-CRP could serve as a marker for treatment decisions. Consistent with this study, our results show that CRP levels may be used to identify patients that are candidates for surgical treatment in the presence of acute sciatica with increased CRP level (<0.8 mg / dL). Therefore, instead of performing lumbar spinal MRI in every patient suffering from acute sciatica, it will be more effective to perform MRI in patients with higher CRP levels, contributing to the reduction of high costs with imaging.

Many studies have reported that the incidence of sciatica and disc pathologies begin at adolescence and the incidence of this condition gradually increases and peaks in the period between 35-55 years of age (22). Similarly, the mean age of the participants in our study was 43 ± 14.6 years. Besides, in our study, the majority of patients were housewives and workers. In a large study of 1120 Turkish patients with chronic low back pain, it was observed that the majority of patients were women and housewives, and it was emphasized that women who were housewives represented an important risk group because of their limited activity (23). The majority of the workers who participated in our study were working in heavy industrial jobs such as construction work. In the etiology of low back pain, factors such as exposure to vibration affecting the whole body, frequent repetition of lifting-rotating movement, rapid work and monotonous work life have been reported (24). Our study adds evidence to the literature that being a housewife or a heavy worker are risk factors for sciatica.

Inflammation causes pain in lumbar disc diseases. Stürmer et al. also showed that higher VAS score was found to be independently associated with high levels of hs-CRP in patients with acute sciatica, but not in patients with chronic low back pain (7). Consistent with this study, we found a statistically significant correlation between pre-treatment CRP levels and post-treatment VAS scores. Besides, the mean VAS score values of the patients in the bulging group before medical treatment were higher than those in the protrusion group. This supports the hypothesis that the severity of pain may be an independent predictor of subclinical inflammation in disc diseases. However, no statistically significant correlations were found between CRP levels before and after medical treatment and SLR values in the bulging and protrusion groups. This indicates that CRP levels did not correspond with the clinical examination as evaluated with the SLR.

There were some limitations in our study. In addition to acute infections and systemic inflammatory conditions, body mass index and obesity are known to affect CRP levels (7). We did not record body mass index values in our patients. Secondly, we used the VAS and SLR values to assess the participants' clinical status, which was based on the patient's self-report on the assumption that they could respond correctly. Thirdly, the study included what could be identified as a small sample size relative to the number of groups. Further studies with larger samples are recommended.

CONCLUSION

CRP levels are altered with medical treatment in patients with bulging. In our study, CRP levels were higher in the surgical group (extruded-sequestrated) compared to reference values, although no statistically significant difference was found when groups were compared. Nevertheless, this result may suggest that the patient may be a surgical candidate if CRP levels are higher than the normal reference value (<0.8 mg / dL) in patients presenting with acute sciatica. Therefore, we believe CRP levels can be used as a prognostic marker in surgical decision making. However, further prospective studies with a larger number of patients are needed to support our suggestions.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: The studywas performed in accordancewith the ethical standards specified in the Declaration of Helsinki and was approved by the Research Ethics Committee of Diskapi Yildirim Beyazit Training and Research Hospital. (09/03).

REFERENCES

1. Ozger O, Kaplan N. Evaluation of clinical outcomes of 271 patients undergoing lumbar microdiscectomy in the light of literature. Ann Med Res 2020;27:664-9.
2. Seyithanoglu H, Aydin T, Taşpınar O, et al. Association between nutritional status and Modic classification in degenerative disc disease. J Phys Ther Sci 2016;28:1250-4.
3. Baloh RW. Sciatica and Chronic Pain: Past, Present and Future. In: Springer. 1st edition. Springer International Publishing, Los Angeles, 2018.
4. Khan AN, Jacobsen HE, Khan J, et al. Inflammatory biomarkers of low back pain and disc degeneration: a review. Ann N Y Acad Sci 2017;1410:68-84.
5. Schol J, Sakai D. Cell therapy for intervertebral disc herniation and degenerative disc disease: clinical trials. Int Orthop 2019;43:1011-25.
6. Valat J-P, Genevay S, Marty M, et al. Sciatica. Best Pract Res Clin Rheumatol 2010;24:241-52.
7. Meier-Ewert HK, Ridker PM, Rifai N, et al. Absence of diurnal variation of C-reactive protein concentrations in healthy human subjects. Clin Chem 2001;47:426-30.
8. Ekedahl H, Jönsson B, Annertz M, et al. Accuracy of Clinical Tests in Detecting Disk Herniation and Nerve Root Compression in Subjects With Lumbar Radicular Symptoms. Arch Phys Med Rehabil 2018;99:726-35.
9. Chiarotto A, Maxwell LJ, Ostelo RW, et al. Measurement properties of visual analogue scale, numeric rating scale, and pain severity subscale of the brief pain inventory in patients with low back pain: a systematic review. J Pain 2019;20:245-63.
10. Masaryk TJ, Ross JS, Modic MT, et al. High-resolution MR imaging of sequestered lumbar intervertebral disks. Am J Roentgenol 1988;150:1155-62.
11. Jungen MJ, Ter Meulen BC, Van Osch T, et al. Inflammatory biomarkers in patients with sciatica: a systematic review. BMC Musculoskelet Disord 2019;20:156.
12. Cunha C, Silva AJ, Pereira P, et al. The inflammatory response in the regression of lumbar disc herniation. Arthritis Res Ther 2018;20:251.
13. Sugimori K, Kawaguchi Y, Morita M, et al. High-sensitivity analysis of serum C-reactive protein in young patients with lumbar disc herniation. J Bone Joint Surg Am. British volume 2003;85:1151-4.
14. De Geer CM. Cytokine Involvement in Biological Inflammation Related to Degenerative Disorders of the Intervertebral Disk: A Narrative Review. J Chiropr Med 2018;17:54-62.
15. Gebhardt K, Brenner H, Stürmer T, et al. The course of high-sensitive C-reactive protein in correlation with pain and clinical function in patients with acute lumbosciatic pain and chronic low back pain—a 6 months prospective longitudinal study. Eur J Pain 2006;10:711-9.
16. Park CH, Lee SH. Investigation of high-sensitivity C-reactive protein and erythrocyte sedimentation rate in low back pain patients. Korean J Pain 2010;23:147.
17. Le LG, Borderie D, Kaplan G, et al. Systemic inflammatory response with plasma C-reactive protein elevation in disk-related lumbosciatic syndrome. Joint Bone Spine: Revue du rhumatisme 2000;67:452-5.
18. Talghini S, Vahedi A, Lotfinia I. Discriminating extrusive and bulging disk herniations by using serum hs-CRP. Pakistan journal of biological sciences: PJBS 2013;16:1411-4.
19. Zhang J. Serum hs-CRP as a useful marker for predicting the efficacy of lumbar epidural steroid injections on pain relief in patients with lumbar disc herniations. J Ky Med Assoc 2006;104:295-9.
20. Park CH, Lee SH. Prognostic usefulness of high sensitivity C-reactive protein for transforaminal epidural steroid injection in patients with radicular pain. Pain Med 2011;12:219-23.
21. Rathod TN, Chandanwale A, Ladkat KM, et al. High sensitive C-reactive protein-Effective tool in determining postoperative recovery in lumbar disc disease. Indian J Orthop 2014;48:354.
22. Mostofi K, Peyravi M, Moghaddam BG. A comparison of sciatica in young subjects and elderly person. J Clin Orthop Trauma 2019.
23. Ketenci A, Yildiz E, Muslumanoglu L, et al. Kronik mekanik bel ağrılı 1120 hastanın özellikleri. Turk J Phys Med Rehab 1998;1:60-4.
24. Kopec JA, Sayre EC, Esdaile JM. Predictors of back pain in a general population cohort. Spine 2004;29:70-7.