The Effect of Body Mass Index on the Outcome of Lumbar Epidural Steroid Injections: Six-Month Follow-Up

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Received: 28 Sep. 2019; Accepted: 11 Mar. 2020

Abstract- Obesity is a risk factor for severe, radicular, and debilitating lumbosacral pain. The use of non-surgical treatment methods in obese patients is important. Epidural steroid injection (ESI) is a common procedure that helps patients with low back pain and radicular symptoms. So far, using ESI in patients with lumbar herniated discs remains to be controversial among physicians. Thus, the current study was carried out to compare the therapeutic effects of ESI's in obese and non-obese patients with spinal disc herniation. This prospective, clinical trial study was conducted among 124 patients (58=non-obese, 66=obese) with low back pain caused by a lumbar herniated disc, who referred to our Pain Clinic from 2017 to 2018. The ESI was done using the parasagittal inter-laminar approach. The severity of pain was measured by the patients' self-report of pain and using the visual analog scale (VAS) before the treatment and two and six weeks after the treatment. The Oswestry Disability Index (ODI) was also measured in the treatment groups. Patients were followed for 6 weeks (IRCT20131124015515N3). Overall, 58 (46.8%) patients had a BMI of 20-25 kg/m^2, 38 (30.6%) had a BMI of 25-30 kg/m^2, and 28 (22.6%) patients had a BMI of >30 kg/m^2. The changes in the pain scores and ODI at different time periods showed no statistically significant differences in the two groups (P=0.685, P=0.995), respectively. The ESI is an effective, safe, minimally invasive, and cost-effective method that can result in pain relief and improvements in patients' function after a short period of time. Hence, we suggested that this treatment be considered for all patients with acute/chronic low back pain as well as radiculopathy.

Acta Med Iran 2020;58(7):322-331.

Keywords: Epidural steroid injections; Lumbar disc herniation; Body mass index; Outcome

Introduction

Morbid obesity and weight gain are among the factors that increase the risk of developing low back pain (1). Excessive pressure on the spinal cord (2), systemic inflammation (3), and a degenerative disc (4) are considered possible mechanisms by which obesity may lead to low back pain.

Obesity is considered an epidemic and is highly associated with low back pain. However, it is not clearly known yet as to whether obesity directly causes low back pain or not? (5-7).

A large number of studies have identified obesity as a risk factor for developing lumbosacral radicular pain (6-10). Thus, a high number of patients who begin treatment for low back pain are obese because obesity is a risk factor for severe, radicular, and debilitating lumbosacral pain (11).

A herniated disc can mainly be controlled by conservative therapies such as resting, oral steroids, anti-inflammatory medicine, and physical therapy. The success rate of conservative treatments is high in these patients and results in significant improvements in symptoms, which reduces the need for surgical interventions.

In the event of failure of conservative treatments, considering the increased postoperative complications as a result of a high BMI, the use of non-surgical treatment methods in this group of patients becomes significant (12).

An epidural steroid injection (ESI) is a common procedure that helps patients with low back pain and radicular symptoms (13). ESI can help relieve the pain, improving function, and preventing spinal surgery,

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particularly in patients with acute and subacute herniated disc and radicular pain (14-22).

Reducing inflammation and nerve edema and the neuroprotective properties against nerve damage are among the benefits of ESI (23-25). ESI is a common treatment for neurogenic claudication caused by spinal stenosis (23,25-27), spinal pain, and radicular pain (26-31). Some studies have shown that symptomatic herniated disc, failed back surgery syndrome, and symptomatic spinal stenosis could be treated with ESI's (32-33). Based on previous literature, ESI relieves radicular pain in the short term (34). Some studies have also demonstrated that ESI was effective in reducing radicular pain secondary to spinal stenosis (29,31,35-38).

Some previous studies have reported contradictory results regarding the effect of ESI on patients with lumbar herniated disc (30-33). Others also indicated that interlaminar ESI helped to reduce the pain caused by spinal stenosis over a short period of time (35).

In a number of studies, depths of epidural space from the skin of the injection site were examined in interlaminar lumbar (39-44), thoracic (45-47), and cervical (48-49) procedures. Depths of lumbar epidural space in patients admitted to midwifery (41-43,44,50), and non-midwifery (39,40,43) wards were also investigated in several studies.

Moreover, several studies reported a relationship between BMI and depths of epidural space (42-44,50). Nowadays, obesity is a growing issue that affects clinical outcomes of treatments (51).

So far, using ESI in patients with lumbar herniated discs is still a controversial subject between physicians, pain specialists, and neurosurgeons.

Considering the existing conflicts regarding the use of ESI in patients with lumbar herniated discs and considering that limited studies have been conducted to assess the issue, the current study was carried out to compare the therapeutic effect of ESI in obese and non-obese patients with lumbar disc herniation.

Materials and Methods

This is a clinical trial study (IRCT20131124015515N3) conducted among 124 patients with low back pain caused by a lumbar herniated disc, who referred to a pain clinic of a tertiary health care center during 2017-2018. Patients older than 18-year-old, with herniated discs, spinal stenosis <30% diagnosed by clinical examinations and CT scan or MRI, foot pain, bilateral radiculopathy, and lumbar disc (disc bulging, and disc herniation in one or two levels) as well as candidates for ESI were included in the present study after obtaining an informed and written consent to enter the study. Patients with central disk herniation with extrusion pain or progressive or severe sensory symptoms or disorders, degenerative herniated disc, history of ESI over the past six months, history of opioid abuse, recent abuse of long-acting opioids with radicular pain for more than a year, more than two herniated discs at different sites of the spinal cord, coagulation disorders, sensitivity to steroids, malignancy, psychiatric problems (and lack of compliance), speech problems, pregnancy, indications for surgery, local skin infections at the surgical area, spinal deformity, history of lumbar spine surgery, cauda-equina syndrome, vertebral fractures, tumor or infection in the spine, inflammatory spondylopathy, neurological defects and those who did not give their informed consent, were excluded from the study. In this regard, until reaching the desired sample size, the study subjects were selected among those who referred to the hospital and met the inclusion criteria.

After obtaining the IV line, a non-invasive pulse oximetry monitoring system was set for all the patients in the operating room, and their blood pressure and heart rate were measured and recorded.

To carry out the surgical procedure, the patient was placed on a fluoroscopy bed, and a pillow was put under the abdomen in the prone position. The patient's vital signs were monitored during the procedure. The ESI was carried out using a parasagittal interlaminar approach under the guidance of the fluoroscopy at the pathology level and at the proper dermatome for injection, which was determined by the patient's site of pain and according to MRI findings. After skin preparation with betadine, local anesthesia was administered using 1% lidocaine injections into the subcutaneous space. The ESI was carried out using the parasagittal interlaminar approach and using an 18-gauge epidural needle (9-cm long). Proper placement of the needle under the guidance of the fluoroscopy at the pathology level of the disc was confirmed by 1-2 ml injection of a contrast material under the fluoroscopy view. At the lateral point, the interlaminar opening to the midline was directly visualized under the anteroposterior (AP) fluoroscopy guide. The needle was inserted directly from paramedian to the skin in an AP direction using the loss of resistance (LOR) technique to locate the epidural space. Using the parasagittal approach, the needle was maintained throughout the procedure. In order to control the non-distribution of contrast material in intravascular, subarachnoid, and subdural space, consistent imaging was performed. At the target space, 1-2 ml of contrast

material was injected, and the results of the epidurogram were recorded. In the case that the contrast material did not flow through the disk space, the needle would be repositioned. After confirming its proper position as well as the flow rate of the contrast material (visipaque 320 mg/ml) with the epidurogram, the epidural injection of a mixture containing 2% ropivacaine (2 ml), normal saline (6 ml), and triamcinolone40 mg/ml (8 ml) was administered. After this, patients were transferred to the recovery room.

The severity of pain was measured by the patients' self-report of pain and using the visual analog scale (VAS) criteria (0: no pain at all, 1-3: mild pain, 4-7: moderate pain, and 8-10: severe pain), before the treatment and two and six weeks after the treatment. The Oswestry Disability Index (ODI) was also measured in the treatment groups, and the patients were examined with 10 disability items. The scores of each item vary between 0-5; the greater the score, the higher the patient's disability (27). During follow-ups, no other treatments were performed to improve the pain, and in the case of a VAS of >4, nonsteroidal anti-inflammatory medicine would be advised. The patients' satisfaction with pain relief was measured and scored by directly asking the patient (0: bad, 1: moderate, 2: good, 3: excellent). In the case of complications, it was recorded. The above items were measured by trained nursing staff.

The duration of follow-up was 6 weeks and was carried out by calling, interviewing, and revisiting the patients. To avoid excluding the study subjects, their records were completed, and they were continuously followed for their visits to the clinic for assessing the improvement of their pain.

Data were analyzed using the SPSS software, version 19.

After testing for normal distribution using the Smirnov-Kolmogorov test, quantitative variables were compared using a T-test, Mann-Whitney test, repeated measurement ANOVA, paired T-test, and one-way ANOVA between two groups. Qualitative variables were also compared using the Chi-square test between the two groups. The level of significance was $P<0.05$.

Results

Overall, 58 people (46.8%) were non-obese and 66 people (53.2%) were obese. Among them, 58 people (46.8%) had a BMI between 20-25 kg/m^2, 38 people (30.6%) had a BMI between 25-30 kg/m^2, and 28 people (22.6%) had a BMI >30 kg/m^2.

Figure 1 depicts the changes in pain scores at different time periods-before and two weeks and six weeks after ESI in the two obese and non-obese groups, which showed no statistically significant difference (P=0.685).

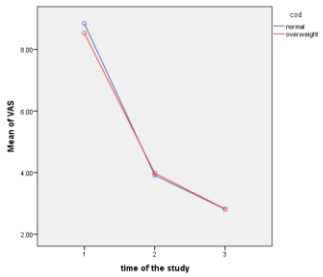

Figure 1. Changes in pain scores at different time periods in the two obese and non-obese groups

Figure 2 depicts changes in ODI scores at different times periods before and two weeks and six weeks after ESI-in the two obese and non-obese groups, which demonstrated no statistically significant difference (P=0.995).

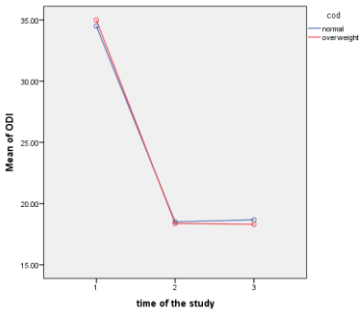

Figure 2. Changes in the ODI scores at different time periods in the two obese and non-obese groups

Figure 3 depicts changes in pain scores at different times periods-before and two weeks and six weeks after ESI-in three groups with different BMIs, which showed no statistically significant difference (P=0.198).

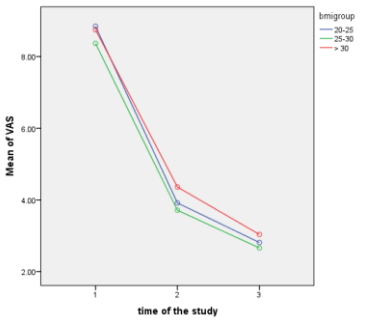

Figure 3. The changes in the pain scores at different time periods in three groups with different BMIs

Figure 4 depicts changes in ODI scores at different times periods-before and two weeks and six weeks after ESI-in three groups with different BMIs, which showed no statistically significant difference (*P*=0.603).

Table 1 compares the demographic data of the two groups.

Table 2 compares the clinical data of the BMI groups and Table 3 compares the clinical data of the three groups divided by the duration of pain, which showed no statistically significant difference (*P*>0.05).

Table 4 shows the changes in pain and ODI scores at different time periods in both obese and non-obese groups.

None of the patients showed complication caused by the ESI procedure.

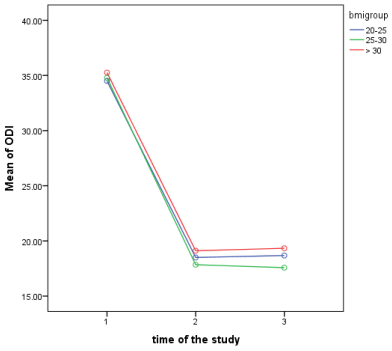

Figure 4. Changes in the ODI scores at different time periods in three groups with different BMIs

Table 1. Demographic data of the two groups.

		Obese group (n=66)	Non- obese group (n=58)	*P*
Age (yr.)		40.4±14.8	30.4±8.8	0.0001
Weight (kg)		78.0±7.8	68.2±10.1	0.0001
Height (cm)		164.8±8.6	170.6±8.9	0.001
BMI (kg/m^2)		29.1±3.5	23.3±1.6	0.0001
Duration of pain (month)		9.3±4.7	8.9±4.5	0.611
Sex	**Male**	39 (59.1%)	46 (79.3%)	0.016
	Female	27 (40.9%)	12 (20.7%)	
Duration of pain (month)	**< 3**	4 (6.1%)	4 (6.9%)	0.968
	3-6	22 (33.3%)	20 (34.5%)	
	>6	40 (60.6%)	34 (58.6%)	
Pain Location:	**L4-L5**	30 (45.5%)	28 (48.3%)	0.753
	L5-S1	36 (54.5%)	30 (51.7%)	
Smoking	**Yes**	27 (40.9%)	23 (39.7%)	0.887
	No	39 (59.1%)	35 (60.3%)	
The duration of motor block (min)		127.3±3.1	123.9±3.6	0.002

Table 2. Compares the clinical data of the BMI groups

		20-25 (n=58)	25-30 (n=38)	>30 (n=28)	*P*
VAS before injection		8.8±1.2	8.4±1.4	8.8±1.2	0.193
VAS 2 weeks after injection		3.9±1.2	3.7±1.0	4.4±1.2	0.079
VAS 6 weeks after injection		2.8±1.1	2.6±1.2	3.0±1.4	0.464
ODI before injection		34.6±6.3	34.8±7.5	35.3±6.9	0.895
ODI 2 weeks after injection		18.6±5.0	17.8±5.2	19.2±4.4	0.526
ODI 6 weeks after injection		18.7±4.2	17.6±4.4	19.3±4.0	0.231
Patient Satisfaction (2 weeks after injection)	**Moderate**	10 (17.2%)	7 (18.4%)	4 (14.3%)	0.254
	Good	40 (69.0%)	25 (65.8%)	24 (85.7%)	
	Excellent	8 (13.8%)	6 (15.8%)	0 (0.0%)	
Patient Satisfaction (6 weeks after injection)	**Moderate**	18 (31.0%)	17 (44.7%)	12 (42.9%)	0.331
	Good	40 (69.0%)	21 (55.3%)	16 (57.1%)	

Table 3. Compares the clinical data of the three groups divided by the duration of pain (month)

		< 3 (n=8)	3-6 (n=42)	>6 (n=74)	*P*
VAS before injection		8.3±1.5	8.7±1.3	8.7±1.2	0.612
VAS 2 weeks after injection		3.8±1.0	4.2±1.1	3.8±1.2	0.334
VAS 6 weeks after injection		2.6±1.2	3.0±1.2	2.7±1.3	0.557
ODI before injection		40.7±8.1	36.4±6.6	33.3±6.3	0.002
ODI 2 weeks after injection		17.5±5.3	19.7±5.0	18.0±4.8	0.171
ODI 6 weeks after injection		19.7±6.2	19.7±4.3	17.6±3.8	0.024
Patient Satisfaction (2 weeks after injection)	**Moderate**	1 (12.5%)	4 (9.5%)	16 (21.6%)	0.288
	Good	7 (87.5%)	31 (73.8%)	51 (68.9%)	
	Excellent	0 (0.0%)	7 (16.7%)	7 (9.5%)	
Patient Satisfaction (6 weeks after injection)	**Moderate**	2 (25.0%)	13 (31.0%)	32 (43.2%)	0.313
	Good	6 (75.0%)	29 (69.0%)	42 (56.8%)	

Table 4. Changes in the pain and ODI scores at different time periods in both obese and non-obese groups

		Obese group (n=66)	Non- obese group (n=58)
VAS	**before injection**	8.5±1.3	8.8±1.2
	2 weeks after injection	4.0±1.1	3.9±1.2
	P	0.0001	0.0001
VAS	**2 weeks after injection**	4.0±1.1	3.9±1.2
	6 weeks after injection	2.8±1.3	2.8±1.1
	P	0.0001	0.0001
ODI	**before injection**	35.0±7.2	34.6±6.3
	2 weeks after injection	18.4±4.9	18.6±5.0
	P	0.0001	0.0001
ODI	**2 weeks after injection**	18.4±4.9	18.6±5.0
	6 weeks after injection	18.3±4.3	18.7±4.2
	P	0.870	0.620

Discussion

In the current study, changes in the pain and ODI scores at different time periods-before and two weeks and six weeks after ESI-between the obese and non-obese groups showed no significant differences. However, after the injection, pain scores in both obese and non-obese groups decreased significantly at different time periods. The ODI scores collected after two weeks showed a significant decrease; however, comparing the scores in the second and sixth weeks showed no significant decrease. The findings of this study were in line with most previously conducted studies (52-56).

According to our study, the changes in pain and ODI scores at different time periods-before and two weeks and six weeks after the ESI-between the three groups with different BMIs (20-25,25-30, and >30 kg/m^2) showed no significant difference. However, after the injection, the pain scores of each of these three BMI groups decreased significantly at different time periods. The ODI scores collected after the second week showed a significant decrease; however, comparing the scores in the second and sixth weeks after the injection showed no significant decrease.

In addition, the pain scores indicated a significant decrease two weeks after the injection among males; however, comparing men and women demonstrated no significant difference at other time periods. ODI scores of the men and women showed no statistically significant difference at these time periods.

Comparing pain scores, based on the duration of the medical condition, obtained at different time periods, indicated no statistically significant difference. The ODI scores obtained six weeks after the injection among patients who suffered from the condition for more than six months showed a significant increase.

So far, the mechanism of the immediate action of lumbar ESI has been unknown. Materials found in the herniated nucleus disc had significant acute inflammatory effects on the epidural tissue, nerve root, and dorsal root ganglion (57-59). Inflammatory mediators such as phospholipase A2, tumor necrosis factor-alpha, interleukin-6, interleukin-8, and prostaglandin E2 were observed in the degenerative material and the herniated disc (59-65). Some previous studies reported increased intradiscal cytokines in patients with discogenic low back

pain (64). The direct impact of nucleus pulposus on epidural space, nerve root, and DRG indicates changes in histology and nerve functions (66-68). Furthermore, some studies have shown the direct impact of the selected inflammatory mediators and cytokines as well (69-71). The acute nerve root compression caused inflammatory changes associated with changes in nerve functions (72,73). With the development of edema, an increase in intraneural pressure, and a decrease in neural blood flow, the perineural and intraneural have been changed and have the ability to penetrate. Moreover, the infiltration of inflammatory cells, edema, and intraneural fibrotic changes co-occur with a chronic increase in pressure (74-76).

In the first few days after the ESI, most of the patients reported pain relief. It was assumed that this pain reduction was due to the known anti-inflammatory effect of medicine. The ESI has multiple probable effects on the **s**ensitized and inflamed tissue including the cell membrane stability (CMS), the reduction in nerve and tissue edema, the direct anti-inflammatory effect, the synthesis/neuropeptide function inhibition, the prostaglandin synthesis inhibition, the neuroinflammatory discharge suppression, the **s**ensitized dorsal horn neurons suppression, and the change in neuronal blood flow (77-86).

Furthermore, the anti-inflammatory effects associated with the local anesthetic injection can strengthen the effects of steroids (87-89). Recently, the interferon-gamma in epidural lavage samples showed that the response to ESI in the lumbar area might be equal to the reduction level of interferon-gamma (90-91).

On the other hand, the immediate response to ESI in the lumbar area may be associated with the direct local anesthetic impact on the active generating of epidural, neural, or perineural pain or their neural branching. When the patient's pain is due to inflammatory factors such as disc or inflammation of epidural structure, a local anesthetic injection with a direct effect on the sensitive site leads to an immediate reduction of pain. The pain relief can be enhanced by diluting or limiting the local washing of active epidural inflammatory mediators (92). When the pain is related to adjacent structures of the epidural space, the applied anesthetic solution can directly result in pain relief through the epidural structure or its neural branching. The immediate response to the ESI in the lumbar area may be indicative of a target area with the potential to predict the therapeutic response to the ESI in the lumbar area.

Inactivity, a lack of regular exercise, and obesity are risk factors for disc herniation. Weight gain puts extra stress on the disc. A disc is a soft pad between vertebrae that bear our weight. Disc herniation creates nerve pressure in the spinal canal (93).

Obesity is one of the factors that lead to pathology in the lumbar area. It plays an important role in the onset of low back pain and response to treatments. Obesity is one of the important causes of decreased response to treatment, especially in high-grade degenerative lumbar vertebral (4).

In a comparative study carried out on two groups of obese and non-obese individuals, transforaminal ESI's resulted in similar success rates in both treatment groups (50). This is in coherence with the current research findings.

In another study, the authors demonstrated that the two groups of obese and non-obese subjects, were similar during the study in terms of pain relief and improvement and that the ESI had similar pain relief impacts on both obese and non-obese patients. Due to the improved function of obese patients after treatment, the weight loss process can also occur more easily; thus, the treatment in these patients is associated with a dual effect (54).

In the event of failure of conservative treatments, considering the increased postoperative complications as a result of a high BMI, the use of non-surgical treatment methods in this group of patients becomes significant (12).

In the treatment of low back pain, first, pharmacotherapy and physical therapy take priority, and then, therapeutic interventions with the least invasion such as ESI, radiofrequency, spinal cord stimulation, and spinal opioids may be selected (94-96). For the lumbar epidural injection, local anesthetic, local steroid, or a combination of local anesthetic and local steroid can be used (21).

Studies have indicated that the use of a combination of local anesthetic and local steroid is preferable (97). The combination of local anesthetic and local steroid was used in the current study. It seems that local anesthetic relieves pain after a short term; however, local and systematic anti-inflammatory steroids take effect after a long term. The systemic effects of corticosteroid injections done for relieving radicular pain caused by disc herniations may remain for several days to weeks (98).

The limitations of this study were low sample size, and changes in patients' perceptions of their health status, which could influence the evaluation of the impact of the therapeutic interventions.

In the present study, injecting 40 mg of steroids was not associated with side effects, which was consistent with other studies (54,99). According to some previous

studies, lower dosages of steroids were associated with fewer side effects; therefore, 40 mg of steroids can also be used for diabetic patients (99).

In the current study, significant improvements in patient's function during the course of the study can be indicative of the absence of other causes of low back pain pathology, so only a discopathy at one level can be considered as the pathological cause of low back pain. Moreover, the mechanical effects of the liquid injection and pharmacological effects of steroids helped the improvement of low back pain.

This method can be considered as an appropriate choice; however, it cannot be regarded as an alternative to open surgery.

Therefore, pain fellowships and neurosurgeons are advised to consider ESI's for these patients according to the protocol of this study. We suggest to carry out this study with a longer follow-up period, different dosages of corticosteroids, and different volumes of epidural injection on patients with herniated discs and different BMI's. Additionally, during the follow-up period, the weight loss process of obese patients should be evaluated.

The ESI is an effective, safe, minimally invasive, and cost-effective method that can result in pain relief and improvements in patient function after a short period of time. Hence, it is suggested that this treatment is considered for all patients with acute/chronic low back pain as well as radiculopathy.

Acknowledgments

The clinical trial study is funded by the Vice-chancellor for research of Shahid Beheshti University of Medical Sciences. Furthermore, we would like to thank the Research Team for their work in making this study possible.

References

1. Shiri R, Karppinen J, Leino-Arjas P, Solovieva S, Viikari-Juntura E. The association between obesity and low back pain: a meta-analysis. Am J Epidemiol 2010;171:135-54.
2. Hu H-Y, Chou Y-J, Chou P, Chen L-K, Huang N. Association between obesity and injury among Taiwanese adults. Int J Obes (Lond) 2009;33:878-84.
3. Tilg H, Moschen AR.Adipocytokines: mediators linking adipose tissue, inflammation and immunity. Nat. Rev Immunol 2006;6:772-83.
4. Samartzis D, Karppinen J, Cheung JP, Lotz J. Disk degeneration and low back pain: are they fat-related conditions? Global Spine J 2013;3:133-144.
5. Garzillo Mand Garzillo T. Does obesity cause low back pain? J Manipulative Physiol Ther 1994;17:601-4.
6. Leboeuf-Yde C. Body weight and low back pain. A systematic literature review of 56 journal articles reporting on 65 epidemiologic studies. Spine 2000;25:226-37 .
7. Leboeuf-Yde C, Kyvik K, Bruun N. Low back pain and lifestyle. Part II – Obesity. Information from a populationbased sample of 29,424 twin subjects. Spine 1999;24:779-83.
8. K¨a¨ari¨a S, Leino-Arjas P, Rahkonen O, Lahti J, Lahelma E, Laaksonen M. Risk factors of sciatic pain: a prospective study among middle-aged employees. Eur J Pain 2011;15:584-90.
9. Heli¨ovaara M. Body height, obesity, and risk of herniated lumbar intervertebral disc. Spine 1987;12: 469-72.
10. Shiri R, Karppinen J, Leino-Arjas P, Solovieva S, Viikari-Juntura E. The association between obesity and low back pain: a meta-analysis. Am J Epidemiol 2010;171:135-54.
11. Urquhart D, Berry P,Wluka A, Strauss B, Wang Y, Proietto J, et al. Increased FatMass is Associated with High Levels of Low Back Pain Intensity and Disability. Spine 2011;36:1320-5.
12. Patel N, Bagan B, Vadera S, Maltenfort M, Deutsch H, Vaccaro A, et al. Obesity and spine surgery: relation to perioperative complications. J Neurosurg Spine 2007;6:291-7.
13. Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015;386:743-800 .
14. Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2163-96.
15. Benditz A, Madl M, Loher M, Grifka J, Boluki D, Linhardt O. Prospective medium-term results of multimodal pain management in patients with lumbar radiculopathy. Sci Rep 2016;6:28187.
16. Katz JN. Lumbar disc disorders and low-back pain: socioeconomic factors and consequences. J Bone Joint Surg Am 2006;88:21-24 .
17. Arnold B, Brinkschmidt T, Casser HR, et al. Multimodale Schmerztherapie Konzepte und Indikation [Multimodal pain therapy: principles and indications]. Schmerz 2009;23:112-20.
18. Anson P. Experts say epidural steroid injections overused. (Accessed May 1, 2016 at http://www.painnewsnetwork.org/stories/2015/8/19/experts-sayepidural- injections-overused).

19. Berkman ND, Lohr KN, Ansari M, et al. Grading the strength of a body of evidence when assessing health care interventions: an EPC update. J Clin Epidemiol 2015;68:1312-24.
20. Kreiner DS, Hwang SW, Easa JE, et al; North American Spine Society. An evidence-based clinical guideline for the diagnosis and treatment of lumbar disc herniation with radiculopathy. Spine J 2014;14:180-191.
21. Manchikanti L, Kaye AD, Manchikanti K, Boswell M, Pampati V, Hirsch J. Efficacy of epidural injections in the treatment of lumbar central spinal stenosis: a systematic review. Anesth Pain Med 2015;5:e23139.
22. Chou R, Hashimoto R, Friedly J, Fu R, Dana T, Sullivan S, et al. Pain Management Injection Therapies for Low Back Pain. Rockville, MD: Agency for Healthcare Research and Quality (US); 2015.
23. Botwin KP, Gruber RD, Bouchlas CG, Torres-Ramos FM, Freeman TL, Slaten WK, et al. Complications of fluoroscopically guided transforaminal lumbar epidural injections. Arch Phys Med Rehabil 2000;81:1045-50.
24. Carette S, Leclaire R, Marcoux S, Morin F, Blaise GA, St-Pierre A, et al. Epidural corticosteroid injections for sciatica due to herniated nucleus pulposus. N Engl J Med 1997;336:1634-40.
25. Falco FJ. Lumbar spine injection procedures in the management of low back pain. Occup Med 1998;13:121-49.
26. Fredman B, Zohar E, Ben Nun M, et al. The effect of repeated epidural sympathetic nerve block on "failed back surgery syndrome" associated chronic low back pain. J Clin Anesth 1999;11:46-51.
27. Morcet N, Guggenbuhl P, Rolland Y, Meadeb J, Bousquet C, Veillard E, et al. Cervical epidural injection technic under computed tomography guidance in the treatment of cervicobrachial neuralgia. J Radiol 1999;80:161–2.
28. Watters WC, Baisden J, Gilbert TJ, Kreiner S, Resnick DK, Bono CM, et al. Degenerative lumbar spinal stenosis: An evidence-based guideline for the diagnosis and treatment of degenerative lumbar spinal stenosis. Spine J 2007;8:305-10.
29. Barre LC, Lutz GE, Southern D, Cooper G. Fluoroscopically guided caudal epidural steroid injections for lumbar spinal stenosis: A retrospective evaluation of long-term efficacy. Pain Physician 2004;2:187-93.
30. Fukusaki M, Kobayashi I, Hara T, Sumikawa K. Symptoms of spinal stenosis do not improve after epidural steroid injection. Clin J Pain 1998;14:148-51.
31. Cuckler JM, Bernini PA, Wiesel SW, et al. The use of epidural steroids in the treatment of lumbar radicular pain. A prospective, randomized, double-blind study. J Bone Joint Surg Am 1985;67:63-6.
32. Atlas SJ, Delitto A. Spinal stenosis: Surgical vs. nonsurgical treatment. Clin Orthop 2006;443:198-207.
33. Kalichman L, Hunter DJ. Diagnosis and conservative management of degenerative spondylolisthesis. Eur Spine J 2007;17:327-35.
34. Boswell MV, Trescot AM, Datta S, et al. Interventional techniques: Evidence-based practice guidelines in the management of chronic spinal pain. Pain Physician 2007;10:7-111.
35. Rosenberg SK, Grabinsky A, Kooser C, Boswell MV. Effectiveness of transforaminal epidural steroid injections in low back pain: A one-year experience. Pain Physician 2002;5:266-70.
36. Ciocon JO, Galindo-Ciocon D, Amaranath L, Galindo D. Caudal epidural blocks for elderly patients with lumbar canal stenosis. J Am Geriatr Soc 1994; 42:5936.
37. Botwin KP, Gruber RD, Bouchlas CG, Torres-Ramos FM, Sanelli JT, Freeman ED, et al. Fluoroscopically guided lumbar transforaminal epidural steroid injection in degenerative lumbar stenosis: An outcome study. Am J Phys Med Rehabil 2002;81:898-905.
38. Botwin KP, Sakalkale DP. Epidural steroid injections in the treatment of symptomatic lumbar spinal stenosis associated with epidural lipomatosis. Am J Phys Med Rehabil 2004;83:926-30.
39. Bahk JH, Kim JH, Lee JS, Lee SC. Computed tomographic study of lumbar (L3–4) epidural depth and its relationship to physical measurements in young adult men. Reg Anesth Pain Med 1998;23:262-5.
40. Chen KP, Poon YY, Wong CH. The depth to the epidural space. Ma Zui Xue Za Zhi 1989;27:353-6.
41. Clinkscales CP, Greenfield ML, Vanarase M, Polley LS. An observational study of the relationship between lumbar epidural space depth and body mass index in Michigan parturients. Int J Obstet Anesth 2007;16:323-7.
42. Segal S, Beach M, Eappen S. A multivariate model to predict the distance from the skin to the epidural space in an obstetric population. Reg Anesth 1996;21:451-5.
43. Watts RW. The influence of obesity on the relationship between body mass index and the distance to the epidural space from the skin. Anaesth Intensive Care 1993;21:309-10.
44. D'Alonzo RC, White WD, Schultz JR, Jaklitsch PM, Habib AS. Ethnicity and the distance to the epidural space in parturients. Reg Anesth Pain Med 2008;33:24-9.
45. Carnie J, Boden J, Gao Smith F. Prediction by computerised tomography of distance from skin to epidural space during thoracic epidural insertion. Anaesthesia 2002;57:701-4.
46. Kao MC, Tsai SK, Chang WK, et al. Prediction of the distance from skin to epidural space for lowthoracic

epidural catheter insertion by computed tomography. Br J Anaesth 2004;92:271-3.
47. Lai HC, Liu TJ, Peng SK, Lee KC, Luk HN, Lee SC. Depth of the thoracic epidural space in paramedian approach. J Clin Anesth 2005;17:339-43.
48. Han KR, Kim C, Park SK, Kim JS. Distance to the adult cervical epidural space. Reg Anesth Pain Med 2003;28:95-7.
49. Lin CH, Lu CH, Ning FS. Distance from the skin to the cervical epidural space. Acta Anaesthesiol Sin 1995;33:161-4.
50. Hamza J, Smida M, Benhamou D, Cohen SE. Parturient's posture during epidural puncture affects the distance from skin to epidural space. J Clin Anesth 1995;7:1-4.
51. World Health Organization. Obesity: Preventing and Managing the Global Epidemic. Geneva: World Health Organization, 2000:1-254.
52. Gökçek E, Tarıkçı Kılıç E, Kaydu A, Fatih Şahin O. The Effects of Body Mass Index on Caudal Epidural Steroid Injection. Ann Med Health Sci Res 2017;7:428-31.
53. McCormick Z, Plastaras Ch. Lumbosacral transforaminal epidural steroid injections are equally effective for treatment of lumbosacral radicular pain in the obese compared to non-obese population: A pilot study. J Back Musculoskelet Rehabil 2013;26:183-8.
54. R1Pinar Baysal A, Baysal O, Erkılınç A, Emre Gürcü M, Emre Gölboyu B, Ekinci M, Orki T, et al. Does Obesity Effect the Treatment of Back Pain? J Clin Anal Med 2016;7:510-4.
55. Schaufele MK, Hatch L, Jones W. Interlaminar versus transforaminal epidural injections for the treatment of symptomatic lumbar intervertebral disc herniations. Pain Physician 2006;9:361-6.
56. Rados I, Sakic K, Fingler M, Kapural L. Efficacy of interlaminar vs transforaminal epidural steroid injection for the treatment of chronic unilateral radicular pain: prospective, randomized study. Pain Med. 2011;12:1316-21.
57. Grönblad M, Virri J, Tolonen J, Seitsalo S, Kääpä E, Kankare J, et al. A controlled immunohistochemical study of inflammatory cells in disc herniation tissue. Spine 1994;19:2744-51.
58. Olmarker K, Blomquist J, Strömberg J, Nannmark U, Thomsen P, Rydevik B. Inflammatogenic properties of nucleus pulposus. Spine 1995;20:665-9.
59. Saal JS. The role of inflammation in lumbar pain. Spine 1995;20:1821-27.
60. Franson RC, Saal JS, Saal JA. Human disc phospholipase A2 is inflammatory. Spine 1992;17:129-32.
61. Takahashi H, Suguro T, Okazima Y, Motegi M, Okada Y, Kakiuchi T. Inflammatory cytokines in the herniated disc of the lumbar spine. Spine 1996;21:218-24.
62. O'Donnell JL, O'Donnell AL. Prostaglandin E2 content in herniated lumbar disc disease. Spine 1996;21:1653-5.
63. Kang JD1, Stefanovic-Racic M, McIntyre LA, Georgescu HI, Evans CH. Toward a biochemical understanding of human intervertebral disc degeneration and herniation. Contributions of nitric oxide, interleukins, prostaglandin E2, and matrix metalloproteinases. Spine 1997;22:1065-73.
64. Burke JG, Watson RW, McCormack D, Dowling FE, Walsh MG, Fitzpatrick JM.. Intervertebral discs which cause low back pain secrete high levels of proinflammatory mediators. J Bone Joint Surg Br 2002;84:196-201.
65. Weiler C, Nerlich AG, Bachmeier BE, Boos N. Expression and distribution of tumor necrosis factor alpha inhumanlumbar intervertebral discs: a study in surgical specimen and autopsy controls. Spine 2005;30:44-53.
66. Olmarker K, Rydevik B, Nordborg C. Autologous nucleus pulposus induces neurophysiologic and histologic changes in porcine cauda equina nerve roots. Spine 1993;18:1425-32.
67. Takebayashi T, Cavanaugh JM, Cüneyt Ozaktay A, Kallakuri S, Chen C. Effect of nucleus pulposus on the neural activity of dorsal root ganglion. Spine 2001;26:940-5.
68. Yabuki S, Igarashi T, Kikuchi S. Application of nucleus pulposus to the nerve root simultaneously reduces blood flow in dorsal root ganglion and corresponding hindpaw in the rat. Spine 2000;25:1471-6.
69. Chen C, Cavanaugh JM, Ozaktay AC, Kallakuri S, King AI. Effects of phospholipase A2 on lumbar nerve root structure and function. Spine 1997;22:1057-64.
70. Olmarker K, Rydevik B. Selective inhibition of tumor necrosis factor- alpha prevents nucleus pulposus-induced thrombus formation, intraneural edema, and reduction of nerve conduction velocity: possible implications for future pharmacologic treatment strategies of sciatica. Spine 2001;26:863-9.
71. Ozaktay AC, Kallakuri S, Takebayashi T, Cavanaugh JM, Asik I, DeLeo JA, et al. Dorsal root sensitivity to interleukin-1 beta, interleukin-6 and tumor necrosis factor in rats. Eur Spine J 2002;11:467-75.
72. Rydevik B, Brown MD, Lundborg G. Pathoanatomy and pathophysiology of nerve root compression. Spine 1984;9:7-15.
73. Garfin SR, Rydevik B, Lind B, Massie J. Spinal nerve root compression. Spine 1995;20:1810-20.
74. Yoshizawa H, Kobayashi S, Morita T. Chronic nerve root compression. Pathophysiologic mechanism of nerve root dysfunction. Spine 1995;20:397-407.
75. Kobayashi S, Yoshizawa H, Yamada S. Pathology of

lumbar nerve root compression. Part 1: intraradicular inflammatory changes induced by mechanical compression. J Orthop Res 2004;22:170-9.
76. Iwamoto H, Kuwahara H, Matsuda H, Noriage A, Yamano Y. Production of chronic compression of the cauda equina in rats for use in studies of lumbar spinal canal stenosis. Spine 1995;20:2750-7.
77. Takahashi N, Yabuki S, Aoki Y, Kikuchi S. Pathomechanisms of nerve root injury caused by disc herniation: an experimental study of mechanical compression and chemical irritation. Spine 2003;28:435-41.
78. Byrod G, Otani K, Brisby H, et al. Methylprednisolone reduces the early vascular permeability increase in spinal nerve roots induced by epidural nucleus pulposus application. J Orthop Res 2000;18:983-7.
79. Devor M, Govrin-Lippmann R, Raber P. Corticosteroids suppress ectopic neural discharge originating in experimental neuromas. Pain 1985;22:127-37.
80. Lee HM, Weinstein JN, Meller ST, Hayashi N, Spratt KF, Gebhart GF. The role of steroids and their effects on phospholipase A2. An animal model of radiculopathy. Spine 1998;23:1191-6.
81. Tachihara H, Sekiguchi M, Kikuchi S, Konno S. Do corticosteroids produce additional benefit in nerve root infiltration for lumbar disc herniation? Spine 2008;33:743-7.
82. Kawakami M, Weinstein JN, Chatani K, Spratt KF, Meller ST, Gebhart GF. Experimental lumbar radiculopathy. Behavioral and histologic changes in a model of radicular pain after spinal nerve root irritation with chromic gut ligatures in the rat. Spine 1994;19:1795-802.
83. Katz WA, Rothenberg R. Section 3: The nature of pain: pathophysiology. J Clin Rheumatol 2005;11: 11-15.
84. Ji RR, Woolf CJ. Neuronal plasticity and signal transduction in nociceptive neurons: implications for the initiation and maintenance of pathological pain. Neurobiol Dis 2001;8:1-10.
85. Melzack R, Coderre TJ, Katz J, Vaccarino AL. Central neuroplasticity and pathological pain. Ann N Y Acad Sci 2001;933:157-74.
86. Bisby MA. Inhibition of axonal transport in nerves chronically treated with local anesthetics. Exp Neurol 1975;47:481-9.
87. Cassuto J, Sinclair R, Bonderovic M. Anti-inflammatory properties of local anesthetics and their present and potential clinical implications. Acta Anaesthesiol Scand 2006;50:265-82.
88. Onda A, Yabuki S, Kikuchi S, Satoh K, Myers RR. Effects of lidocaine on blood flow and endoneurial fluid pressure in a rat model of herniated nucleus pulposus. Spine 2001;26:2186-91.
89. Scuderi GJ, Cuellar JM, Cuellar VG, Yeomans DC, Carragee EJ, Angst MS. Epidural interferon gamma-immunoreactivity: a biomarker for lumbar nerve root irritation. Spine 2009;34:2311-17.
90. Cuellar JM, Golish SR, Reuter MW, Cuellar VG, Angst MS, Carragee EJ, et al. Cytokine evaluation in individuals with low back pain using discographic lavage. Spine J 2010;10:212-8.
91. Vad VB, Bhat AL, Lutz GE, Cammisa F. Transforaminal epidural steroid injections in lumbosacral radiculopathy: a prospective randomized study. Spine 2002;27:11-6.
92. Lean MEJ, Han TS, Seidell JC. Impairment of health and quality of life using new US federal guidelines for the identification of obesity. Arch Intern Med 1999;159:837-843.
93. McCormick Z, Plastaras C. Lumbosacral transforaminal epidural steroid injections are equally effective for treatment of lumbosacral radicular pain in the obese compared to non-obese population: a pilot study. J Back Musculoskelet Rehabil 2013;26:183-8.
94. Karaeminoğulları O, Aydınlı U, Degenerative lomber spinal stenosis. TSOT (Turkish Society of Orthopaedics and Traumatology) Journal, 2004;3:1-10.
95. Buttermann GR, Treatment of lumbar disc herniation: epidural steroid injection compared with discectomy. A prospective, randomized study. J Bone Joint Surg Am 2004;86:670-9.
96. Last AR ,Hulbert K, Chronic low back pain: evaluation and management. Am Fam Physician 2009;79:1067-74.
97. Jinshuai Zhai, Long Zhang, Mengya Li, Yiren Tian, Wang Zheng, Jia Chen, et al. Epidural injection with or without steroid in managing chronic low back and lower extremity pain: ameta-analysis of ten randomized controlled trials. Int J Clin Exp Med 2015;8:8304-8316.
98. Schneider B, Zheng P, Mattie R, Kennedy DJ. Safety of epidural steroid injections. Expert Opin Drug Saf 2016;15:1031-9.
99. Owlia MB, Salimzadeh A, Alishiri G, Haghighi A. Comparison of two doses of corticosteroid in epidural steroid injection for lumbar radicular pain. Singapore Med J 2007;48:241-5.