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ORIGINAL ARTICLE

Comparison of efficacy of particulate and non-particulate steroids in patients with lumbosacral pain, non-operated patients with chronic radicular symptoms

Kronik radiküler semptomlu lumbosakral ağrılı, opere olmayan hastalarda partiküllü ve partikülsüz steroid uygulaması etkinliğinin karşılaştırılması

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Summary

Objectives: In our study, we aimed to retrospectively evaluate patients who were given particulate and non-particulate steroids for transforaminal epidural steroid injection due to non-operated chronic low back pain with radicular symptoms in terms of the change in pain and the change in functional capacity before the procedure.

Methods: This study was carried out by examining the files of 130 patients, underwent an interventional procedure. Records of patients pertaining to age, gender, location of pain, Visual Analog Scale, Patient Global Impression of Change, and Oswestry Disability Index Scale (ODI) before the interventional procedure and at the 1st and 3rd months after the procedure were recorded using the hospital automation system and patient follow-up forms.

Results: The functional capacity of the patients was evaluated, and in the comparison of the ODI score before the procedure, at the 1st month, and at the 3rd month, a statistically significant difference was found in the particulate steroid group compared to the non-particulate group at the 1st and 3rd months. When evaluated using the Generalized Linear Models, a statistically significant difference was found in both groups (p=0.039), and the ODI score was approximately 2,951 units lower in patients who were treated with particulate steroids than those who were treated with non-particulate steroids at each measurement time.

Conclusion: In our study, it has been demonstrated that particulate steroids are superior to non-particulate steroids in improving functional capacity in the early period, and non-particulate steroids are advantageous in the long term.

Keywords: Non-particulate epidural steroids; particulate epidural steroids; radiculopathy; transforaminal block.

Özet

Amaç: Çalışmada, radiküler semptomlu opere olmayan kronik bel ağrısı nedeniyle transforaminal epidural steroid enjeksiyonu için partiküllü ve partikülsüz steroid uygulanan hastaların retrospektif olarak işlem öncesi ve sonrası birinci ay ve üçüncü aydaki ağrı değişimi ile fonksiyonel kapasitedeki değişiminin değerlendirilmesi amaçlandı.

Gereç ve Yöntem: Bu çalışmada, girişimsel işlem uygulanan 130 hastanın dosyası incelendi. Girişimsel işlem öncesi ve sonrası birinci ve üçüncü aylarda hastaların yaş, cinsiyet, ağrı lokalizasyonu, görsel analog skala, hasta global izlenim değişimi ve "Oswestry Disability Scale (ODI)" ile ilgili kayıtları hastane otomasyon sistemi ve hasta takip formları kullanılarak kayıt altına alındı.

Bulgular: Hastaların fonksiyonel kapasitesinin değerlendirildiği; işlem öncesi birinci ve üçüncü aylardaki ODI skoru karşılaştırılmasında birinci ve üçüncü ayda partiküllü steroid uygulanan grupta partikülsüz gruba göre istatistiksel olarak anlamlı fark tespit edildi. Genelleştirilmiş doğrusal modeller kullanılarak bakıldığında ise her iki grupta da istatistiksel olarak anlamlı fark saptandı (p=0,039), partiküllü steroid türü uygulanan hastalarda ODI skoru partikülsüz steroid uygulananlara göre ortalama her ölçüm zamanında yaklaşık 2,951 birim daha az bulundu.

Sonuç: Çalışma ile erken dönemde partiküllü steroidlerin partikülsüz steroidlere göre fonksiyonel kapasiteyi iyileştirmede daha üstün olduğu, uzun dönemde ise partikülsüz steroidlerin avantaj sağladığı ortaya konuldu.

Anahtar sözcükler: Partikülsüz epidural steroidler; partiküllü epidural steroidler; radikülopati; transforaminal blok.

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Introduction

Low back pain is one of the important causes of morbidity, which can lead to serious medical and socioeconomic issues.[1,2] It has been shown that 80% of individuals in industrial societies experience low back pain at least once in their lifetime.[3] Radicular pain is often caused by one or more lumbar intervertebral disc herniation in the distribution of the sciatic nerve. The lifetime incidence of this condition is estimated between 3% and 5%.[4]

Although the majority of patients with low back pain benefit from conservative treatments, such as moderate bed rest, medication, lifestyle changes, physical therapy, and exercise, 5%–8% of low back pain cases become chronic.[3,5] Surgical treatment is reportedly required for 14% of patients with chronic low back pain.[6] Developing imaging techniques and associated minimally invasive interventions are alternatives to open surgical methods, particularly in patients without neurological motor loss and myelomalacia. The primary minimally invasive interventional method is a mixture of a steroid and local anesthetic, i.e., injected into the transforaminal epidural area. Transforaminal epidural steroid injection (TFESI) is effective in reducing pain and improving physical functions in patients.[7,8]

Lumbar epidural transforaminal and interlaminar injections with particulate (triamcinolone) or non-particulate (dexamethasone) corticosteroids as well as local anesthetics are generally preferred for the interventional treatment of patients with radiculopathy symptoms.[8] Steroids reduce inflammation and ectopic pressure around the affected nerve and accelerate the ischemic nerve root blood flow, thus effectively leading to pain palliation and tissue healing.[9] In particular, triamcinolone is a preferred particulate steroid agent because of its strong anti-inflammatory properties, low sodium retention, and long-lasting effect.[10] Agents such as dexamethasone, methylprednisolone, triamcinolone, and betamethasone are preferred for epidural steroid treatment due to their minimal mineralocorticoid activity.

In our study, the primary outcome was to retrospectively compare the treatment-related mean change in Visual Analog Scale (VAS), Oswestry Disability Index (ODI), and patient global impression of change (PGIC) with the use of particulate and non-particulate steroids used in TFESI to treat non-operated patients with lumbosacral pain and chronic radicular symptoms. The exploratory outcome was to compare the percentage of patients having more than 50% pain relief with a minimum follow-up of 3 month.

Material and Methods

After obtaining the approval of ethic committee, 130 patients who were admitted to the outpatient clinic between January 2017 and December 2019 were included. The patients who had TFESI administered due to chronic low back and radicular pain for at least 3 months, were at least 18 years of age, had a VAS of >4, did not undergo spinal surgery, and experienced temporary or no benefits from previous medical treatments were screened using patient's forms that are available in our electronic recording system and clinic. The exclusion criteria are as follows: had VAS <4; had piriformis syndrome and failed back surgery syndrome; age <18 years.

Patient records were accessed through the hospital database used by our hospital's data processing unit, and missing information in the files or the electronic system was obtained by contacting the patients through phone and obtaining their consent for the retrospective study. This study was approved by the Ethics Committee of Ankara University Faculty of Medicine (December 09, 2019/İ6-267-19) and conducted in accordance with the Declaration of Helsinki Ethical Principles.

Age, gender, comorbidity, and pain localizations of the patients were recorded. We included the patients who provided (VAS; 0–10; 0, no pain; 10, worst pain imaginable) rating before and at 1 and 3 months after the procedure; overall observation of change with the PGIC at 1 and 3 months after procedure; and underwent functional capacity evaluation using ODI. At least 50% reduction in pain after the algological procedure was considered as a favorable outcome. All patients were followed up at 1 and 3 months after the procedure. By comparing these values with the pre-procedural values, the efficiency of TFESI was interpreted. Data on complications and used pain medications were also recorded.

Statistical Methods

In this study, SPSS 11.5 program was used for all statistical calculations and analyses of data. For the descriptive statistics, mean±standard deviation and median (minimum-maximum) and the number of patients (percentage) were used for the quantitative and qualitative variables, respectively. Betamethasone and Triamcinolone groups were taken as 1.5±1.2 and 2.3±1.8, respectively, the sample was calculated at a power of 0.80 using the Mann–Whitney U test, at a significance level of 0.05, with 59 individuals per group and a total of 118 individuals. The Sample was found sufficient for the research.

In terms of the qualitative variables, difference between the categories of the qualitative variables with two categories was examined using the Student's t test for normal distribution and Mann-Whitney U test for non-normal distribution. To examine the relationship between two qualitative variables, Chi-squared and Fisher's exact tests were performed. Statistical significance between repeated measurements were examined using the one-way analysis of variance. The difference between two quantitative dependent measurements was examined using the paired-t test for normal distribution and Wilcoxon signed-rank test for non-normal distribution. Generalized linear models were used to observe the effect of the group variable on the quantitative variable with repeated measures, such as the effect of particulate and nonparticulate steroid type groups. A p=0.05 was considered statistically significant.

Results

Retrospective analysis showed that TFESI were administered to 225 patients. Of these, 87 were excluded after the procedure because of lack of information, consent, or accessibility; 5 due to malignant disease; 1 due to cerebrovascular disease; and 2 due to other reasons. The patients included in the study were aged between 18 and 82 years with 43 (33.1%) females and 87 (66.9%) male (Table 1).

Levels of Procedure Performed on the Patients

The most frequently treated level was left L4–L5 (38.5%), followed by left L5–S1 (35.3%), and then by right L4–L5 (24.6%). The most common bilateral TFESI level was L4–L5 (21.5%) (Table 2).

Table 1. Patient demographic data

Age	
Mean±SD	55.52±14.31
Median (Min–Max)	56.50 (20.0–83.00)
Gender, n=130 (%)	
Male	43 (33.1)
Female	87 (66.9)

SD: Standard deviation; Min: Minimum; Max: Maximum.

Table 2. The TFESI procedure levels according to the type of particulate and non-particulate steroids

Levels	Steroid type				p
	Particulate (n=59)		Non-particulate (n=71)		
	n	%	n	%	
L1-L2					1.000[b]
Right	0	0.0	1	1.3	
Left	0	0.0	1	1.3	
L2-L3					0.397[b]
Right	1	2.0	1	1.3	
Left	3	5.9	2	2.5	
Bilateral	1	2.0	0	0.0	
L3-L4					0.137[b]
Right	8	15.7	6	7.6	
Left	2	3.9	10	12.7	
Bilateral	3	5.9	2	2.5	
L4-L5					0.576[a]
Right	12	23.5	20	25.3	
Left	17	33.3	33	41.8	
Bilateral	14	27.5	14	17.7	
L5-S1					0.875[a]
Right	10	19.7	12	15.2	
Left	17	33.3	29	36.7	
Bilateral	7	13.7	9	11.4	

TFESI: Transforaminal epidural steroid injection; L: Lumbar: a: Chi-square test; b: Fisher's exact test.

Particulate steroids were used in 51 (39.2%) of the patients and non-particulate steroids were used in 79 (60.8%) patients. Particulate steroids were mostly used at the left L4–L5 (33.3%) and L5–S1 (33.3%) levels and the nonparticulate steroids were mostly used at the left L4–L5 (41.8%) and L5–S1 (36.7%) (Table 2).

Table 3. Pain variation according to particulate and non-particulate groups

Variables	Steroid type		p
	Particulate Mean±SD	Non-particulate Mean±SD	
Initial VAS	7.45±1.59	7.47±1.52	0.915[b]
1st month follow-up VAS	3.53±1.59	4.04±1.14	0.060[b]
3rd month follow-up VAS	4.49±1.33	4.51±1.01	0.678[b]
Initial ODI	48.31±11.30	49.39±10.19	0.618[b]
1st month follow-up ODI	24. 37±9. 28	28.86±9.66	**0.013**[b]
3rd month follow-up VAS	28.16±9.86	31.44±9.36	**0.034**[b]
1st month follow-up PGIC	5.04±1.41	4.57±1.15	**0.017**[b]
3rd month follow-up PGIC	4.33±1.29	4.01±1.15	0.071[b]

VAS: Visual analog scale; ODI: Oswestry disability index; PGIC: Patient global impression of change; SD: Standard deviation; Min: Minimum; Max: Maximum; b: Mann-Whitney U Test.

Change in Pain after the Procedure

The median VAS before TFESI was 7.46±1.54, and those at 1 and 3 months after the procedure were 3.84±1.35 and 4.50±1.14, respectively. The median ODI score before TFESI was 48.97±10.60, and those at 1 and 3 months after the procedure were 27.10±9.73 and 30.15±9.66, respectively.

Patients who underwent TFESI with particulate and nonparticulate steroids, no statistically significant difference was found between VAS at 1 and 3 months (p=0.060 and p=0.678, respectively). Conversely, when the ODI reference values were compared with the ODI values at 1 and 3 months, were found to be statistically significant in the particulate group than the nonparticulate group (p=0.013 and p=0.034). Furthermore, PGIC values in the particulate group were statistically significant than the nonparticulate group at 1 month (p=0.017) (Table 3).

No significant difference was found between the groups in the trends of repeated measurements of VAS at the baseline, 1, and 3 months using generalized linear models (p=0. 401). A significant difference was found among the first three VAS measurements in both the groups (p<0.001). When the differences were analyzed in groups of two, as in baseline–1 month, baseline–3 month, and 1–3 months, a significant difference was found in both the groups (p<0.001 for all the groups) (Fig. 1a).

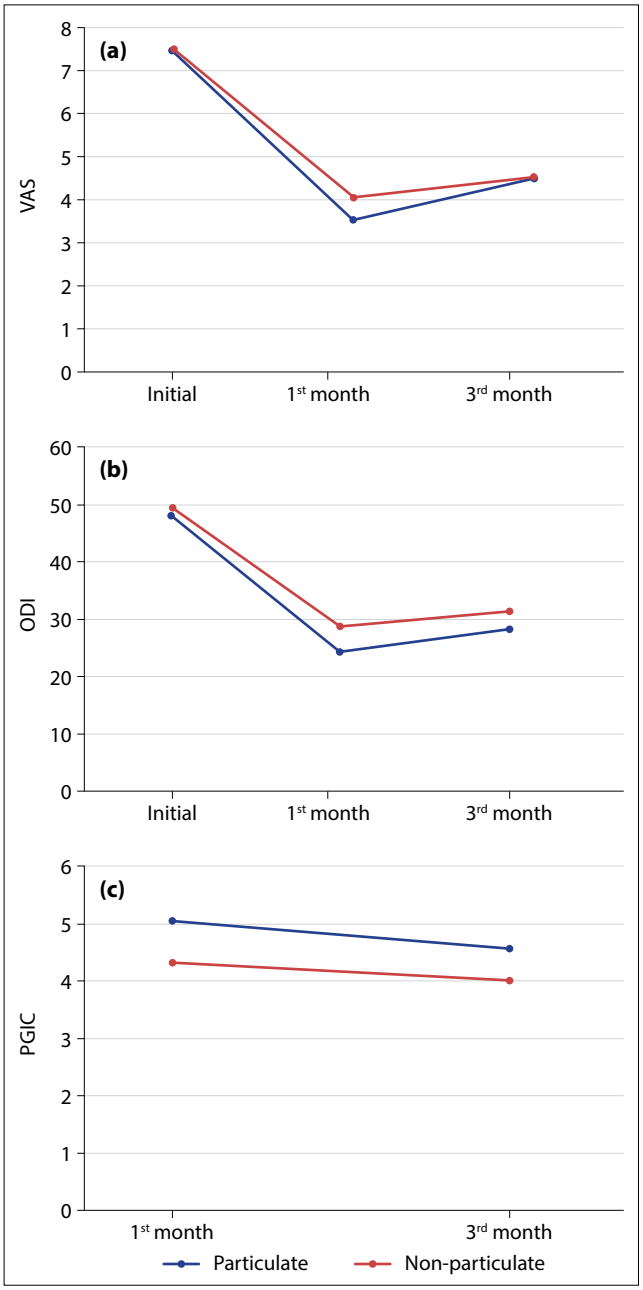

Figure 1. (a) The time-dependent changes between the groups in terms of VAS. **(b)** The time-dependent changes between the groups in terms of ODI. **(c)** The time-dependent changes between the groups in terms of PGIC.

When the difference between the groups in terms of the trend of repeated measurements of ODI at baseline, 1, and 3 months was analyzed using generalized linear models, a significant difference was found (p=0.039). The ODI of the patients in the particulate steroid group was approximately 2.951 units less at each measurement time compared with that of the nonparticulate group. When the significant differences were analyzed in groups of two, as in baseline–1 month, baseline–3 month, and 1–3 months, a significant difference was found in both the groups (p<0.001 for all the groups) (Fig. 1b).

When the difference between the groups in terms of the trend of repeated measurements of PGIC at baseline, 1, and 3 months was analyzed, a significant difference was found (p=0.014). The PGIC score of the particulate steroid group was approximately 0.395 units higher at each measurement time on average compared with that of the nonparticulate steroid group. A statistically significant difference was found between the two PGIC measurements in both groups (p<0.001) (Fig. 1c).

Discussion

The results of this study demonstrate the superiority of particulate corticosteroids over non-particulate corticosteroids in achieving clinically significant "improvement" for patients receiving a transforaminal lumbar epidural injection at 1 month and 3 months' post-injection. For patients receiving particulate corticosteroids, 12% more reported clinically significant improvement at the 1-month time point compared to patients receiving non-particulate steroids, and 9% more patients reported improvement at the 3-month time point with particulate steroids. In addition, the results show a statistically significant difference in ODI change scores at month 1 and month 3, where pain reduction is greater in patients receiving particulate corticosteroids. Considering the limitations and duration of the data we have obtained, it has been determined that particulate steroids are superior in reducing pain compared to non-particulate steroids in terms of short-term effectiveness.

Lower extremity pain due to lumbar and spinal pathology may be related to degenerative disc disease with the development of disc herniation, disc protrusion, and disc extrusion.[11] Intervertebral disc herniation is the most common cause of lumbosacral radiculopathy. The symptoms of 80%–90% of patients with acute low back pain spontaneously regress within 6–8 weeks. In a quarter of these patients, severe pain continued that did not respond to conservative therapies.[12] In recent studies, interventional treatments that can be performed on patients with chronic low back pain and who are resistant to conservative treatments have been increasingly popular.

Epidural steroid injections have been one of the main interventional procedures used since the 1950s.[13] The epidural cavity can be accessed through the caudal, interlaminar, and transforaminal approaches.[14] The development of epidural injections in the treatment of lower extremity pain caused by chronic lumbar and spinal root irritation and obstruction started with caudal epidural injections, followed by interlaminar and transforaminal approaches.[15] Unlike other methods, TFESI allows the application of higher concentrations of steroids and local anesthetics to the target tissue in the anterior epidural area where the pathology is present. Epidural steroid injections have become more frequent and safer with the advances in imaging techniques, such as ultrasonography, particularly CT, and fluoroscopy. In a systematic review by Smith et al.,[16] transforaminal steroid injection was found to be an effective treatment for radicular pain associated with disc herniation. In their study, the rate of patients diagnosed with lumbar disc herniation with ≥50% pain reduction was reported as 63% at 1 month, 74% at 3 months, 64% at 6 months, and 64% at 1 year. Moreover, patients with lumbar spinal stenosis showed a success rate of 49% at 1 month, 48% at 3 months, 43% at 6 months, and 59% at 1 year. Rosenberg et al.[17] conducted a study to evaluate the effectiveness of TFESI and analyzed the patients by dividing 82 patients into four groups. The group with the lowest procedure success included operated patients with post-laminectomy syndrome. Improvements were reported at 2 months, 6 months, and 1 year of follow-up as 23% in the post-laminectomy syndrome group, 59% in the group with discogenic pathologies and hernia, 35% in the group with spinal stenosis, and 67% in patients with no MR diagnosis and all other patients. It is believed that low rates in the post-laminectomy syndrome group are due to the variety of factors that may cause pain in post-laminectomy syndrome, due to previous surgery and postsurgical structural changes. In our study, patients with post-laminectomy syndrome were excluded and the success rates in 130 patients were 51.5% in terms of VAS and 55.3% in terms of ODI at 1 month. VAS and ODI in the 3 months were 38.4% and 33.8%, respectively.

Steroids injected into the epidural cavity provide anti-inflammatory effect, neural membrane stability, and peripheral nociceptor entry regulation. All steroids used in spinal injections are prednisolone derivatives. Particulate corticosteroids tend to be larger in size (0.5–100 µg) and less water soluble, causing aggregation and crystallization in hydrophilic media. These include methylprednisolone acetate, prednisolone acetate, triamcinolone acetonide, and betamethasone acetate. In contrast, nonparticulate corticoste-

roids, such as dexamethasone sodium phosphate, are smaller in size (0.5 µg), and more soluble in water.[18]

A cohort study published in 2015 evaluated 1568 patients and showed the superiority of particulate over nonparticulate steroids at 1 month.[19] In a retrospective study conducted by Bensler et al.,[20] 494 patients were included and 40 mg (1 mL) of triamcinolone and 4 mg (1 mL) of dexamethasone were compared. Clinically significant improvements on using particulate corticosteroids were reported in 16% of the patients after 1 week and 10% patients after 1 month compared with patients using nonparticulate steroids. The results showed a significant difference in the NRS scores at 1 week and 1 month and greater pain reduction using particulate corticosteroids, whereas a difference of >30% was observed in the NRS scores at 1 week and 1 month between the two groups. In our study, post-procedural VAS of patients receiving particulate transforaminal steroid, a 50% therapeutically significant pain reduction was detected in 29 (56.82%) of the 51 patients immediately after the procedure and in 19 (37.25%) of patients at the 3-month follow-up compared with baseline. In terms of the post-procedural ODI of patients in the particulate steroid group, significant pain palliation of >50% was seen in 32 (62.74%) patients at 1st month and in 20 (39.21%) of the patients who underwent TFESI at 3 months (p=0.013 and p=0.034, respectively).

Several studies suggest that transforaminal particulate and non-particulate steroid injections have similar effects on pain palliation. El-Yahchouchi et al.[21] conducted a retrospective study of 2,634 patients and compared the use of 80 mg triamcinolone and 12 mg dexamethasone with 10 mg of betamethasone at equivalent doses for transforaminal injection. After 2 weeks (42.5%) and 2 months (45.1%) of follow-up, no significant difference was found in terms of pain reduction and functional improvement. However, dexamethasone was found to be superior in long-term follow-up. Although there was no significant difference in VAS at 1 and 3 months after particulate corticosteroid injections compared to the baseline, we identified a significant difference in the ODI at the end of 1 and 3 months compared to the baseline in our study. We found that there was no difference between the two groups in 3-month long-term improvement. In addition, we showed a significant difference in PGIC scores at 1 month, and a greater reduction in pain in patients using particulate corticosteroids. A double-blind randomized study with 78 patients by Kennedy et al.[22] revealed that the NRS and ODI at 2 weeks, 3 months, and 6 months after single-level transforaminal steroid injection of 40 mg triamcinolone and 15 mg dexamethasone were not significantly different between the two groups; however, there were significant improvements in terms of pain and function. Although 14.6% of the dexamethasone group and 18.9% of the triamcinolone group needed surgery after the procedure, the percentage of patients needing re-injection was significantly higher in the dexamethasone group than in the triamcinolone group (17.1% and 2.7%, respectively; p=0.0052). Despite the differences in our study in terms of longer follow-up period, there was no need for re-injection or surgical intervention for any of our patients for 3 months.

In a study published in 2011,[23] 42 patients with radicular pain due to lumbar spinal stenosis were divided into two groups, and the complication rates during the procedure with Kambin's triangle or subpedicular approach and the efficacy at 2 and 4 weeks after the procedure were compared. No therapeutically significant difference was found between the two groups. In addition, spinal nerve damage occurred in five cases who underwent the subpedicular approach, whereas no complications were observed in the Kambin's triangle approach (p<0.05). Kambin's triangle approach is as effective as the subpedicular approach for short-term effect and it provides significant advantages. Kambin's triangle approach can be an alternative method for TFESI in cases where access to the anterior epidural cavity is difficult.

In 2014, the Food and Drug Administration (FDA) published a safety announcement stating that the injection of corticosteroids into the epidural cavity of the spine can cause rare but serious complications, including vision loss, stroke, paralysis, and death.[24] In the review published by Manchikanti et al.[25] that analyzed this announcement and the existing literature, it was emphasized that the risks of transforaminal steroid administration should be evaluated differently in the cervical, thoracic, and lumbar regions, and the announcement was criticized because 10 of the 15 cases presented by the FDA were regarding cervical and thoracic epidural injections and that the risk of spinal infarction, paralysis, and death is lower in lumbar transforaminal steroid injection compared to other regions.

No major complications were observed in any of our patients. However, transient headache in three patients, hyperglycemia in two patients and nausea in one patient treated with particulate steroids, pain at the injection site in two patients, and vasovagal reaction in one patient were observed.

Limitations

Our study has several limitations. First, the number of patients included in the study was low. Second, our study design was retrospective. Third, data on the patients' clinical information and oral drug use were scarce. Finally, the 3-month follow-up period is also considered a limitation in terms of comparing the long-term effects.

Conclusions

Low back pain should be considered a separate disease and should be evaluated as a whole with its functional impairment, disease behavior, and psychosocial factors resulting from chronic pain. Low back pain should be treated using a multidisciplinary approach. Although there are many reasons that can cause low back pain, the most common cause of lumbosacral radiculopathy is intervertebral disc herniation, and only a minority of patients have an indication for surgery.

Interlaminar, caudal, and transforaminal methods have been used since years to reach the target area to treat of low back pain. In the transforaminal method, a needle is inserted through the intervertebral foramina at the level of pathology under the guidance of fluoroscopy and a small amount of steroid and local anesthetic mixture is injected into the anterior epidural area. Although supraneural (safe triangle) and infraneural (Kambin's triangle) approaches are used to reach the injection site, the choice of particulate and nonparticulate steroids is selected by clinicians by assessing their advantages and disadvantages in terms of their effect on pain, aggregation, and solubility. Based on the available literature comparing the use of particulate and nonparticulate steroids for lumbar TFESI, the advantages and disadvantages are still controversial. Considering the limitations and follow-up duration of our study, particulate steroids were superior to non-particulate steroids in reducing pain in terms of short-term efficacy; however, in terms of long-term results, nonparticulate steroids were advantageous.

Ethics Committee Approval: The Ankara University Clinical Research Ethics Committee granted approval for this study (date: 09.12.2019, number: İ6-267-19).

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