

Comparison of the Effects of Steroid and Local Anesthetic Combination versus Local Anesthetic alone on Pain in Transforaminal Epidural Injection Applied Simultaneously with Dorsal Root Ganglion Pulse Radiofrequency

Dorsal Kök Ganglion Pulse Radyofrekans ile Eş Zamanlı Uygulanan Transforaminal Epidural Enjeksiyonda Steroid ve Lokal Anestezik Kombinasyonu ile Tek Başına Lokal Anesteziğin Ağrı Üzerine Etkilerinin Karşılaştırılması

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ABSTRACT

Objective: The aim of this study is to compare the effects of steroid and local anesthetic (LA) combination versus LA alone on pain in patients with lumbar radicular pain in transforaminal injection (TFESI) performed before dorsal root ganglion pulsed radiofrequency (DRG-PRF) treatment.

Methods: One hundred twenty-four patients were included in the study. Following routine pre-procedure preparations, Group S (steroid injection group) (n=62) was administered TFESI with 5 mL of a solution containing 8 mg dexamethasone and 0.25% bupivacaine before DRG-PRF. Group NS (no-steroid injection group) (n=62) was administered TFESI with only 5 mL of 0.25% bupivacaine. Then, DRG-PRF was administered at 42°C and 4 minutes for both groups. The Visual Analog Scale (VAS) scores before the procedure and after the procedure at 3rd, 6th week, and 3rd month were recorded.

Results: The pre-procedural VAS scores, demographic data, and procedure level were similar in both groups. While VAS values at the 3rd, 6th weeks, and 3rd months were significantly different from the baseline in Group NS, they were similar to each other (p<0.001, p>0.05). In Group S, the VAS values at the 3rd week and 3rd month were significantly different (p=0.034). When more than 50% reduction in VAS was considered significant pain control in both groups, there was no difference at the 3rd, 6th weeks and 3rd months (p=0.353, p=0.360, and p=0.276, respectively).

Conclusion: Dorsal root ganglion pulsed radiofrequency application is effective in the treatment of lumbar radicular pain. The effect of DRG-PRF lasts longer in the group without steroid administration during TFESI.

Keywords: Chronic pain, radiculopathy, pulsed radiofrequency treatment, steroids, local anesthetics

ÖZ

Amaç: Bu araştırmanın amacı lomber radiküler ağrısı olan hastalarda, dorsal kök ganglionu pulse radyofrekans (DRG-PRF) uygulaması öncesi yapılan transforaminal enjeksiyonda (TFESI) steroid ve lokal anestezik (LA) kombinasyonunun, sadece lokal anesteziğe göre ağrı düzeyine etkilerini karşılaştırmaktır.

Yöntem: Çalışmaya toplam 124 hasta dahil edildi. Rutin işlem öncesi hazırlıkları takiben, Grup S'ye (steroid enjeksiyonu yapılan) (n=62) DRG-PRF öncesi 8 mg deksametazon ve %0,25'lik bupivakain içeren 5 mL solüsyonla TFESI uygulandı. Grup NS'ye (steroid uygulaması yapılmayan) (n=62) ise 5 mL %0,25'lik bupivakain ile TFESI uygulandı. Sonrasında ise her iki gruba da 4'er dakika 42°C, DRG-PRF uygulandı. Hastaların işlem öncesi, işlem sonrası 3.,6. hafta ve 3. ayda Visual Analog Skala (VAS) skorları kaydedildi.

Bulgular: Her iki grupta hastaların işlem öncesi VAS skorları, demografik verileri ve işlem uygulanan seviyeleri benzerdi. Grup NS'de 3., 6. hafta ve 3. ay VAS değerleri bazal değere göre anlamlı olarak farklı iken, kendi aralarında benzerdi (p<0,001, p>0,05). Grup S'de ise 3. hafta ve 3. ay VAS skorları anlamlı olarak farklı idi (p= 0,034). Her iki grupta da VAS'ta %50'den fazla azalma anlamlı ağrı kontrolü olarak kabul edildiğinde, gruplar arasında 3., 6. hafta ve 3. ayda fark yoktu (sırasıyla p=0,353, p=0,360 ve p=0,276).

Sonuç: Lomber radiküler ağrı tedavisinde, DRG-PRF uygulaması etkilidir. Transforaminal enjeksiyonda, steroid uygulanmayan grupta DRG-PRF'nin etkisinin daha uzun sürdüğü gözlenmiştir.

Anahtar sözcükler: Kronik ağrı, radikülopati, pulse radyofrekans tedavisi, steroidler, lokal anestezikler

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INTRODUCTION

The prevalence of lumbar radicular pain (LRP) is 9.9-25% worldwide. The nociceptive afferent fibers of a spinal nerve or its roots are activated ectopically by a disc protrusion, spinal stenosis, facet joint hypertrophy, or fibrosis following lumbar spine surgery, and this causes pain arising in the lower limb and is defined as LRP (1). There is no optimal therapy defined so far. Sixty percent of cases recover with combined therapeutic, pharmacological, and physiotherapeutic management. Resistant cases may require interventional treatments such as epidural corticosteroids, either interlaminar or transforaminal (TFESI), which lead to short-term pain relief. The pulsed radiofrequency (PRF) treatment of the dorsal root ganglia (DRG) can provide an alternative treatment option in such patients for the management of long-term pain relief (2).

The effectiveness of DRG-PRF treatment in LRP has been studied previously. A meta-analysis, including 6 randomized-controlled researches, showed PRF reduced pain scores 12 weeks after the procedure (3). Still, there's no consensus on how to apply the procedure in terms of duration, drug infusion, etc. Some researchers apply corticosteroids while others do not before administering DRG-PRF; therefore, both methods were effective (4-6).

This prospective-observational study aimed to compare the effectiveness of steroid-LA combination versus LA solution before DRG-PRF treatment in LRP.

MATERIAL and METHODS

Selection of patients

The study was conducted between 01.05.2023 and 15.08.2023 after obtaining Bilkent City Hospital Clinical Research Ethics Committee approval (E1-23-3350) in Health Sciences University, Bilkent City Hospital, Pain Clinic. Following obtaining written informed consent from all participants, the study was conducted in accordance with the principles outlined in the 2013 Declaration of Helsinki.

The study included 62 patients in each group according to power analysis. The power analysis was performed using G-power 3.1.9.4. According to the comparison of the frequency of pain relief with DRG-PRF and TFESI at 180 days with 84% vs. 100 % in the study of Arons et al. (5). It was calculated that each group should include at least 50 patients at 91.9% power with an alpha error of 0.05 with Fisher's exact test.

Inclusion / Exclusion criteria

The patients with LRP due to a herniated disc, spinal stenosis, or unsuccessful spine surgery over 18 who have persistent pain for ≥ 3 months following conservative treatment were included.

The exclusion criterias: age less than 18 years, elected for disc herniation surgery, patients with sequestration symptoms, hypersensitivity to radioopaque and corticosteroids, and coagulation deficits.

Procedure

Before the procedure, the eligible patients were prepared with routine laboratory tests and a standard fasting period on the day of application. In the preoperative period, peripheral vascular access was established, and patients were taken to the operating room. Routine anesthesia monitoring was performed. After appropriate positioning by placing a pillow under the abdomen, sedation with 0.02 mg kg⁻¹ intravenous midazolam was applied. An iodine-based solution was used to sterilize the lumbar region, which was then covered with sterile drapes. The procedures were conducted with the guidance of a C-arm fluoroscopy, which is undertaken at an oblique position at approximately 15-20 degrees to optimally observe the foramen intervertebrale for the target level. All the endplates at the application level were in a single-line direction. The C-arm fluoroscope was positioned craniocaudally to correct all the overlaps. Following local infiltration of the skin, a 22-gauge straight radiofrequency cannula (Abbot Medical, Plymouth, USA) was directed to foramen intervertebrale. Final placement of the needle was verified by a lateral image of foramen intervertebrale. The electrode was subsequently placed through the cannula. After receiving convenient responses to sensorial and motor stimulation, Group S received 5 mL of solution, including 8 mg dexamethasone and 0.25% bupivacaine, before DRG-PRF. Group NS received only 5 mL of 0.25% bupivacaine before DRG-PRF. The DRG-PRF treatment was set as follows: temperature of the tip 42°C, pulse width = 20 ms, f = 2 Hz, U = 45 Volt, Z < 500 W, duration of PRF activity 2 X 120 s.

Outcome Evaluation

The demographic variables, medical history including surgeries and medications, presence of neuropathic characteristics of the pain according to Douleur Neuropathique en 4 Questions (DN4), details of the procedure (side, application characteristics), visual analog scale (VAS) scores at the preoperative period and on the 3rd and 6th week and 3rd month follow-up interviews were recorded.

Statistical Analysis

The Statistical Package for Social Sciences (SPSS) version 25.0 software (IBM®, Armonk, NY, USA) was used for statistical analysis. Descriptive statistics were used to summarize the baseline characteristics of the participants. The measurement data were expressed as mean according to the parametric distribution of the variables. The Chi-square test was

used to compare categorical variables between groups. VAS scores in patients with the groups at different time points were analyzed by the Friedman test, and two repeated VAS scores were analyzed with the Mann-Whitney U test within groups. $P < 0.05$ was considered as statistically significant.

RESULTS

The groups are similar in terms of age, sex, and side of treatment ($p > 0.05$). Therefore, the frequency of level of DRG-PRF treatment was similar for L1-2/L2-3, L2-3/L3-4, L3-4/L4-5, and L4-5/L5-S1 levels ($p > 0.05$); but L5-S1/S1 DRG-PRF treatment was more frequent in the group without steroid application. ($p = 0.023$). The frequency of neuropathic pain according to DN4 was similar in the groups ($p = 0.856$) (Table I).

VAS scores of the patients are presented in Table II. VAS scores at different time points - the 3rd and 6th week and 3rd month -

were significantly different in both groups ($p < 0.001$). Baseline scores were higher than VAS-scores of other follow-up times ($p < 0.001$), but VAS scores at the 3rd week, 6th week, and 3rd month did not differ significantly in the group without steroid application ($p > 0.05$). However, there was a meaningful difference in the VAS-3rd week and VAS-3rd month scores in the group with steroid application ($p = 0.034$). The median VAS scores of the groups are demonstrated in Figure 1.

The frequencies of meaningful pain relief, which was accepted as $>50\%$ pain decrease according to baseline VAS scores, are shown in Table III. No significant difference was found in meaningful pain relief rates between the groups at the 3rd week, 6th week, and 3rd month (respectively, $p = 0.353$, $p = 0.360$, and $p = 0.276$). Meaningful pain relief in the groups at follow-up are demonstrated in Figure 2.

Table I: The Demographic and Clinical Characteristics of the Patients

	No-steroid injection group (n=62)	Steroid injection group (n=62)	p	
Age	55.18± 15.24	56.85±11.31	0.488	
Gender	Female	42 (67.7)	33 (53.2)	0.141
	Male	20 (32.3)	29 (46.8)	
Side of treatment	Right	26 (41.9)	18 (29.0)	0.174
	Left	32 (51.6)	42 (67.7)	
	Bilateral	4 (6.5)	2 (3.2)	
Level of DRG-PRFT	L1-2/L2-3	-	1 (1.6)	
	L2-3/L3-4	7 (11.3)	6 (9.7)	>0.05
	L3-4/L4-5	5 (8.1)	7 (11.3)	>0.05
	L4-5/L5-S1	28 (45.2)	38 (61.3)	>0.05
	L5-S1/S1	22 (35.5)	10 (16.1)	0.023
Neuropathic pain frequency	25 (40.3)	27 (43.5)	0.856	

DRG: Dorsal root ganglion, PRFT: Pulsed radiofrequency treatment. Age is expressed as years (mean ± SD) and other variables are expressed as n (%).

Table II: Visual Analog Scale Scores of the Groups

	No-steroid injection group (n=62)	Steroid injection group (n=62)	p
VAS-baseline	7.0 (7.0-8.0)	8.0 (7.0-8.0)	0.010
VAS-3 rd week	2.0 (1.0-4.0)	3.0 (1.0-7.0)	0.010
VAS-6 th week	2.0 (1.0-4.0)	4.0 (1.0-7.0)	<0.01
VAS-3 rd month	2.0 (1.0-4.0)	4.0 (1.0-7.0)	<0.01
P (within groups)			
P (VAS-baseline-3 rd week)	<0.001	<0.001	
P (VAS-3 rd week-6 th week)	0.157	0.102	
P (VAS-6 th week-3 rd month)	0.317	0.157	
P (VAS-3 rd week-3 rd month)	0.083	0.034	

VAS: Visual analog scale. The values are expressed as median (min-max).

Table III: Meaningful Pain Relief of the Groups at Follow-Up

Time of follow-up	No-steroid injection group (n=62)	Steroid injection group (n=62)	p
3 rd week	42 (67.7)	36 (58.1)	0.353
6 th week	40 (64.5)	34 (54.8)	0.360
3 rd month	39 (62.9)	32 (51.6)	0.276

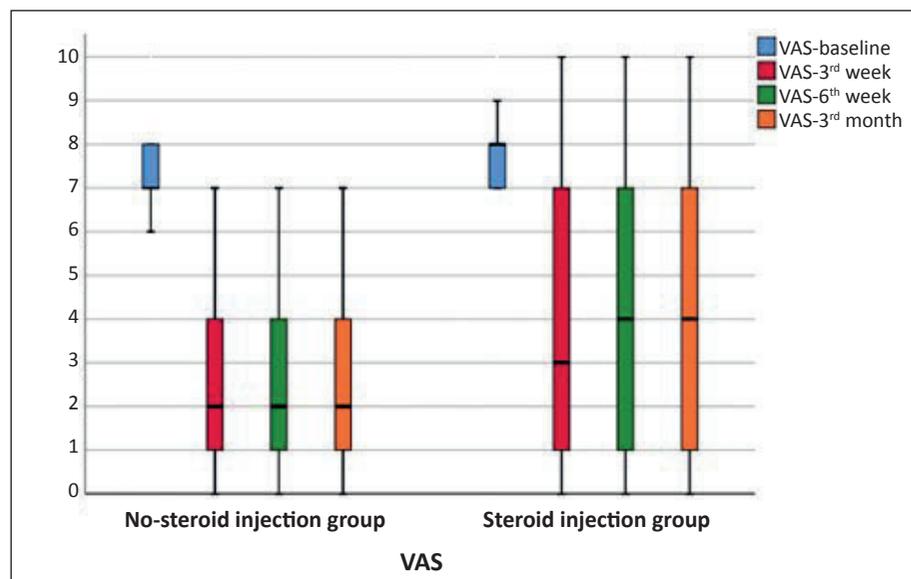


Figure 1: The box-plot graphic of VAS scores at different times in the groups.

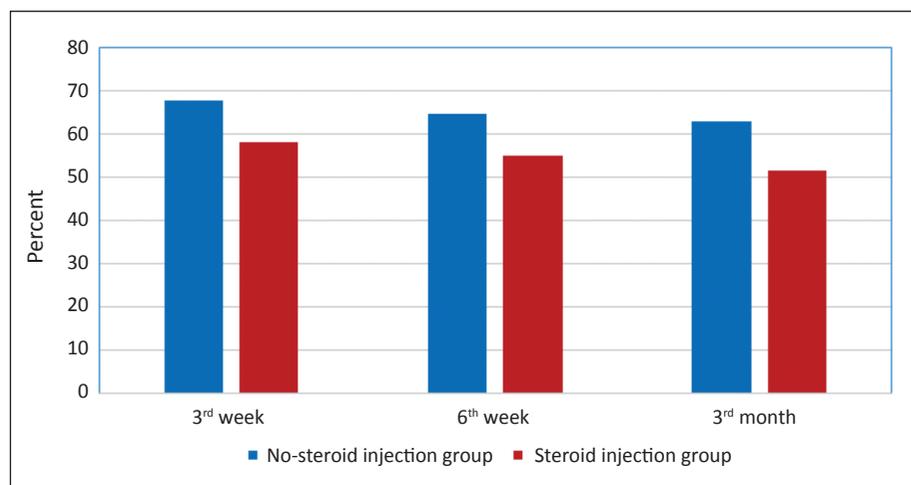


Figure 2: Meaningful pain relief at follow-up for treatment groups.

DISCUSSION

The findings of this study showed that treatment modalities in both groups were effective in the management of LRP. In terms of duration, it was found that the effect of DRG-PRF persisted until the 3rd month in Group NS, which means a longer effect was achieved without steroids. When we evaluate the meaningful effect, pain relief was similar in both groups at all time points.

In PRF stimulation, the current is used to provide heat bursts; the temperature doesn't exceed 42°C, with long resting phases between them. Thus, it prevents irreversible tissue damage but causes microscopic damage to principal sensory nociceptive sensory fibers (C-fibers and A-delta fibers). It rarely damages the larger non-pain-related sensory fibers (A-beta fibers). Also, down-regulation of microglia prevents the release of cytokines and stops pain signals. Finally, PRF stimulation was reported to enhance the noradrenergic and

serotonergic descending pain inhibitory pathways. But still, the exact mechanism involved is not well described (7). Nonetheless, its effects were shown in several studies (8-10). Chang et al. showed that the effect of PRF persisted 3 months after the procedure in their RCT (8). On the contrary, a small RCT with 16/15 patients in each group showed no significant effect of PRF compared to the placebo group, to whom they only applied a needle insertion without any intervention. The PRF group used neither LAs nor steroids (9). Application of PRF with a combination of transforaminal triamcinolone and lidocaine injection after PRF provided pain relief 3 months after PRF (10). Similarly, our study showed that DRG-PRF provided longer pain relief in LRP patients.

Epidural steroid injection has been proven to provide short to moderate-term analgesic effects in LRP. The nerve root compression results in a proinflammatory reaction that activates inflammatory mediators. Recent studies show that TFESI improves outcomes in LRP patients by targeting the medication better at the relevant structure. Although the TFESI with steroids has a better outcome, repeated injection of them may cause bone demineralization, suppression of the hypothalamic-pituitary-adrenal axis, immune suppression, blood glucose derangement, needle trauma, embolization of particulate medication and potential neurotoxicity of medication preservatives (11). Yang et al. showed TFESI with DRG is an effective method for pain control in LRP in their retrospective study, including 34 patients in which they injected 0.2% ropivacaine 5 mL and 2.5 mg betamethasone following two cycles of PRF (12). Two-year follow-up of 230 patients with TFESI and the TFESI-PRF group showed that TFESI combined with PRF in the treatment of LDH could rapidly reduce pain and prolong the analgesic effects (13). On the contrary, some research has showed that interlaminar or transforaminal epidural injections, with or without steroids, have comparable effects on each other (14-16). Machikanti et al. showed no superior effect of steroids in TFESI in a study with 120 patients (17). Also, high-volume TFESI application with or without steroids has comparable effects on reductions and functional improvements among LDH patients 4 weeks after the procedure (14). In this study, we observed that both DRG-PRF and TFESI treatment groups with or without steroids showed an analgesic effect. However, we observed a prolonged analgesic effect for group NS. The exact mechanism of this effect is not known in DRG-PRF. In radiofrequency ablation, it's well known that applying pre-procedural sodium chloride (NaCl) significantly increases lesion size with radiofrequency in a predictable manner, and adding lidocaine to NaCl does not appreciably diminish this effect. Also, the choice of the solution injected before RF procedures is still an area of debate. Substances used in addition to LA, like steroids or NaCl, remain controversial (18).

In conclusion, the results of this study showed that DRG-PRF is effective in addition to TFESI with or without steroids, but TFESI without steroids showed better outcomes in the 3rd month follow-up. We suggest that, related to the adverse effects of steroids in repeated injections, DRG-PRF can be applied without steroids.

AUTHOR CONTRIBUTIONS

Conception or design of the work: US, SD, GB

Data collection: US, GB, SD

Data analysis and interpretation: YCD, SC

Drafting the article: US, SD, GB, EYA

Critical revision of the article: MYA, US, EYA

The author (US, SD, GB, EYA, SS, SC, MYA, YCD) reviewed the results and approved the final version of the manuscript.

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