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Clinical Study

The Effect of Pulsed Radiofrequency Combined with a Transforaminal Epidural Steroid Injection on Chronic Lumbar Radicular Pain: A Randomized Controlled Trial

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Background. Pulsed radiofrequency lesioning (PRFL) of the dorsal root ganglion (DRG) can modulate neural pathways and provide prolonged relief of neuropathic pain, with limited evidence for chronic lumbosacral radicular pain (CLRP). *Objective*. This study compared the effect of PRFL combined with transforaminal epidural steroid injection (TFESI) to TFESI alone on CLRP. *Methods*. Forty adults with chronic radicular pain of at least six-month duration were randomly allocated to undergo either a PRFL of the affected DRG followed by a TFESI (treatment group) or a TFESI alone (control group). Participants and assessors were blinded to the allocation and outcomes were assessed at 1, 2, 3, and 4 months. *Outcomes*. Pain intensity (visual analog score, VAS) was the primary outcome and quality of life (QOL) as measured by the SF-36 was a secondary outcome. *Results*. There was no difference in baseline characteristics between groups. VAS was significantly lower in the treatment group at 2-month and 3-month but not 4-month follow-up. QOL measurements did not differ between groups. *Conclusions*. PRFL of the lumbosacral DRG combined with TFESI showed a modest advantage over TFESI alone in reducing pain intensity; however, this did not persist beyond the 3-month follow-up. There was no effect on QOL.

1. Introduction

Although common, chronic lumbosacral radicular pain (CLRP) can be challenging to treat, as patients often do not respond to conservative pain management strategies such as medication and physiotherapy. Transforaminal epidural steroid injections (TFESIs) have been used to treat both acute and chronic radicular pain [1], providing pain relief that usually lasts less than 3 months [2, 3].

Two types of radiofrequency treatments, continuous and pulsed, have been applied to the dorsal root ganglion (DRG) of the affected nerve root in an effort to provide longer-term relief in CLRP. However, continuous radiofrequency, which is neurodestructive [4], is associated with significant side effects [5]. Moreover, Geurts et al. failed to find a difference between continuous radiofrequency lesioning of the DRG and placebo in a double blind randomized controlled trial [6].

Pulsed radiofrequency lesioning (PRFL) of the DRG is a relatively new technique first described by Sluijter et al. in 1998 [7]. This technique does not raise the temperature of the needle tip to neurodestructive levels and it is therefore considered a neuromodulatory technique [8]. Two retrospective studies examining the efficacy of PRFL for CLRP found a significant benefit, with 92% of patients experiencing pain relief for at least one year [9, 10]. In contrast, a prospective study found a more modest effect with 70% of subjects experiencing 3 months of relief [11]. No complication or side effects have been reported with PRF [7, 12, 13].

We therefore sought to examine the effect of PRFL on CLRP and determine if it could provide an additional therapeutic benefit when added to TFESI.

2. Methods

2.1. Participants. The Institutional Review Board of the Royal Thai Army Medical Ethics Committee approved this study, which was conducted at Phramongkutklao Hospital from July 2013 to February 2014. This study was registered with the Thai Clinical Trials Registry (TCTR 20140303001). All participants provided written and informed consent. Eligible patients were adults aged 18–80 years, with CLRP of at least 6-month duration which was unresponsive to pharmacotherapy or physical therapy, and who had magnetic resonance imaging evidence of nerve root involvement at the targeted levels. Exclusion criteria were patients who were surgical candidates, had associated back pain, significant neurological deficit, coagulopathy, allergy to any of the study medications, psychiatric problems, and language barriers, or were pregnant.

2.2. Procedures. All patient were evaluated by one of the investigators and randomized to one of 2 groups using a computer-generated table. The treatment group (T-group) received PRFL and TFESI, whereas the control group (C-group) received only TFESI. Both patients and assessors were blinded as to the allocation group.

All interventions were performed by one physician (SM) on an outpatient basis using standard monitoring and sedation as required. Patients were placed in the prone position and a C-arm image intensifier (BV Libra, Philips®, Netherlands) was positioned to obtain a 25–30-degree ipsilateral oblique view. After skin infiltration a 22-G, 10 cm long, 5 mm active tip radiofrequency cannula (Diros Technology Inc., Canada) was inserted using a tunnel vision technique and advanced until the needle tip was located in middle of the intervertebral foramen as assessed by a lateral view. Further confirmation was obtained by injecting a contrast solution (Iopamiro 300, Bracco s.p.a.®, Italy) before inserting a probe, which was connected to a generator (Diros OWL URF-3AP, Canada). After insuring that impedance readings were below 500 Ω., sensory stimulation was performed at 50 Hz and needle position adjusted until the patient reported tingling along the sensory dermatome at less than 0.5 V. Subsequently, 2 Hz motor stimulation was performed and a confirmatory motor response sought at a level 1.5 times that of the sensory threshold [14]. All patients underwent sensory and motor stimulation. Those assigned to the C-group underwent a mock PRF treatment (by informing patients that treatment has started) before an injection of triamcinolone 40-mg (L.B.S. Laboratory Ltd., Bangkok, Thailand) and 0.125% bupivacaine in a total volume of 2 mL.

Those in the T-group underwent PRFL at 42°C for 120 seconds (20-ms pulse with a 480-ms interval; using a maximum voltage of 50 V) [13], which was followed by the injection.

2.3. Outcomes. A blinded assessor evaluated all participants before treatment and at 1, 2, 3, and 4 months after the procedure using visual analog scales (VAS; range: 0–100) and the SF-36 questionnaire (Thai version 2) [15]. The primary outcome was the between-group comparison of the VAS. In addition, the number of patients in each group presenting a 20-point reduction in the VAS scores from baseline was compared, as this has been previously used as an indicator of procedural efficacy [9]. Quality of life (QOL) comparison as assessed by the SF-36 questionnaire (Thai version 2) was a secondary outcome.

All patients were followed for a minimum of 4 months after the procedure and monitored for any evidence of infection, hematoma, or nerve root damage.

2.4. Statistical Analyses. The sample size calculation was based on 2 previous studies [3, 11]. Simopoulos et al. [11] compared PRFL to PRFL combined with continuous radiofrequency and found that the proportion of patients with a significant pain reduction in the PRFL group was 0.70. Rosenberg et al. [3] examined the effect of TFESI on a cohort of patients with various spinal pathologies and reported that the lowest proportion of responders was 0.23. Based on these results, 20 patients per group were required to achieve an alpha error of 0.05 and a beta error of 0.2 (Fisher's exact test). An intention-to-treat analysis was planned if any follow-up losses occurred.

Statistical analysis was performed using SPSS version 15 statistical software (IBM Armonk, NY). Categorical data is presented as percentages and continuous data is reported either as means ± SD (when normally distributed) or as medians and ranges (nonnormally distributed).

The number of patients who responded to the procedure was presented as a percentage using the chi-square test or Fisher's exact test for between-group comparisons. Direct comparisons of the VAS and QOL scores throughout the study were tested using repeated-measures ANOVA; p values less than 0.05 were considered significant.

3. Results

Forty patients were enrolled in this study and randomized to one of the two treatment groups (Figure 2). There were no intergroup differences in demographic characteristics, underlying pathology or levels treated (Table 1). Patients' preprocedural pain intensity was 75 ± 14 for the C-group and 72 ± 10 for the T-group. The T-group had lower VAS scores at every follow-up assessment compared with the C-group and these differences were significant at the 2- and 3-month follow-up evaluations (Figure 1). The number of patients with a 20-point or greater decrease in VAS compared to pretreatment levels was detailed in Table 2. There was a trend towards greater efficacy in the T-group for all time periods; however, these differences were only clinically significant at the 3-month follow-up assessment (T-group versus C-group: 13 [65%] versus 4 [20%], resp.; $p = 0.004$). SF-36 scores did not significantly differ with regard to any modality (Table 3) and no significant difference was found in the

Table 1: Patient characteristics at baseline ($n = 40$).

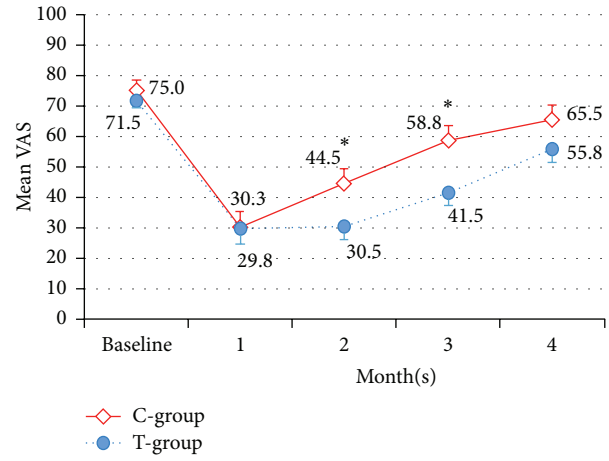
Characteristics	C-group; n (%)	T-group; n (%)	p value
Diagnosis			
Spinal stenosis	7 (35)	7 (35)	1.000
Spondylolisthesis	5 (25)	6 (30)	0.718
Herniated disc	7 (35)	6 (30)	0.740
Previous surgery	1 (5)	1 (5)	1.000
Sex			
Male	10 (50)	10 (50)	1.000
Female	10 (50)	10 (50)	1.000
Age			
Mean ± SD	58 ± 14	57 ± 12	0.855
Pain score	75 ± 14	72 ± 10	0.357
SF-36			
Physical component	48.0 ± 6.6	48.6 ± 6.3	0.754
Mental component	46.4 ± 7.3	47.7 ± 7.6	0.573
Level of intervention			
L5	9 (45)	8 (40)	0.752
S1	9 (45)	10 (50)	0.752
L4 and L5	1 (5)	0 (0)	1.000
L5 and S1	1 (5)	2 (10)	1.000
One-level treatment	18 (90)	18 (90)	1.000
Two-level treatment	2 (10)	2 (10)	1.000

Table 2: The number of patients with a decrease in VAS of 20 points or greater at each follow-up period.

Follow-up period	C-group ($n = 20$)	T-group ($n = 20$)	p value
1 month	16 (80%)	17 (85%)	1.000
2 months	11 (55%)	16 (80%)	0.091
3 months	4 (20%)	13 (65%)	0.004*
4 months	3 (15%)	6 (30%)	0.451

VAS: visual analog score. *Statistically significant.

number of patients whose pain returned to baseline (Table 4). In addition, no procedure related complications occurred in either group during the study period.



VAS: visual analog score, *statistically significant

Figure 1: Visual analog pain score: between-group comparison.

4. Discussion

Our study shows that adding PRFL to TFESI provides an additional therapeutic benefit, with lower pain scores at 2 and 3 months after treatment when compared to TFESI alone. The effect did not extend beyond 3 months, as no intergroup difference was found at 4 months.

Sixty-five percent of patients in the T-group reported a clinically significant level of pain relief for three months. These findings mirror those of a previous retrospective case-series involving 54 patients in which PRFL significantly reduced lumbar radicular pain in 51.7% of patients with disc herniation and 58.9% of patients with spinal stenosis at a 90-day follow-up assessment [14]. In addition, the loss of clinical effect that we found between 2 and 4 months was echoed in a study by Simopoulos et al. [11], who reported a similar pattern in their PRFL group.

Three major analgesic mechanisms have been proposed to explain the effect of PRFL. Firstly, it may change the transmission of pain signals in the dorsal horn by activating C-fos gene expression in the superficial lamina [16] and decreasing glial cell activation [17]. Secondly, it can induce endogenous opioid release by increasing Met-enkephalin levels. Finally, as the effect of PRFL is reversed by serotonin and alpha-adrenergic antagonists, it might work by facilitating descending inhibitory pain pathways. These mechanisms may explain the delayed effect that we note in

Table 3: Physical and mental components of the SF-36; mean (SD).

	Baseline	1 month	2 months	3 months	4 months	p value
Physical component						0.38
C-group	31 (12)	54 (18)	50 (17)	43 (19)	41 (19)	
T-group	33 (10)	52 (17)	51 (11)	47 (12)	41 (11)	
Mental component						0.52
C-group	42 (17)	60 (18)	55 (17)	53 (19)	49 (19)	
T-group	45 (13)	58 (17)	56 (15)	53 (11)	50 (12)	

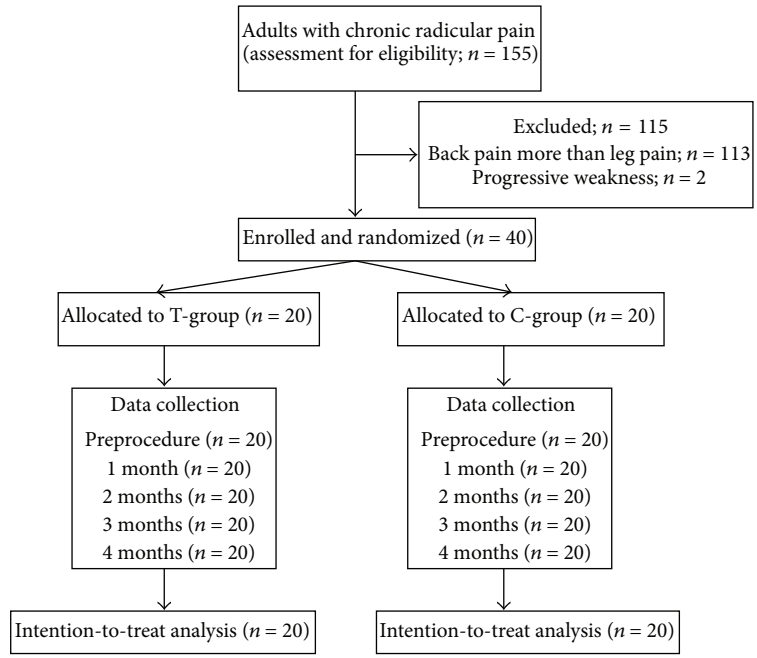


Figure 2: Patient-flow.

Table 4: Number of patients whose pain returned to baseline at each follow-up period.

Month	Number of patients (%)		p value
	C-group (n = 20)	T-group (n = 20)	
1	1 (5)	2 (10)	1.00
2	1 (5)	1 (5)	1.00
3	3 (15)	3 (15)	1.00
4	9 (45)	8 (40)	0.75

our study, with the maximal effect noted at 3 months in the T-group.

Quality of life indicators improved from baseline in both groups; however, no significant intergroup difference was found (Table 4). It is possible that the comparatively greater improvement in pain score observed in the T-group at 2 and 3 months was not sufficient to influence QOL measurements.

In a recent study limited to 3 months of follow-up [18], Koh et al. also found an additional therapeutic benefit in adding PRFL to TFESI for the treatment of chronic radicular pain. However, direct comparison with our study is difficult as the authors used a customized composite score to measure outcome.

Our study presents some limitations. We did not screen patients by performing a preliminary diagnostic TFESI and excluding those who did not respond. This approach has been used in previous studies [11, 18] to eliminate patients who, despite suggestive clinical and imaging findings, have pain unrelated to the target nerve root. However, by excluding subjects who have a long-term decrease in pain after the diagnostic TFESI, this selection process could have biased the results of our study in favor of the PRFL group. The large proportion of patients in both our treatment groups (80–85%) who had a clinically significant pain relief at the one-month follow-up (Table 2) suggested that the possible inclusion of nonresponders had a limited effect on our study. Another potential limitation of our protocol was that adjuvant therapies (physical and pharmacological treatments) were not standardized throughout the follow-up period. However, all medication was prescribed by one doctor to minimize variations (SM) and a single blinded assessor supervised clinical care for all patients during the study period. Additionally, the randomization process ensured that

any effect on outcome was equally distributed between the 2 study groups.

5. Conclusions

Our study found a modest benefit in adding PRFL to TFESI for the treatment of CLRP. The effect on pain scores was greatest at 3 months and had decreased by the 4-month follow-up. No changes in functional measures were seen during the follow-up period. Further research is required to determine if certain subgroups of patients with CLRP could derive greater benefit from this therapy.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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