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Comparing the effectiveness of pulsed radiofrequency treatment to lumbar dorsal root ganglion according to application times in patients with lumbar radicular pain: protocol for a randomised controlled trial

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ABSTRACT

Introduction Lumbar radicular pain (LRP) is a common symptom characterised by a sharp, shooting or lancinating sensation localised to one or more dermatomes of the lumbar spine. Despite its high prevalence and significant impact on quality of life, the most effective conservative treatment for patients with LRP remains uncertain. When conventional treatment methods do not provide satisfactory results, the option of using epidural steroids and/or pulsed radiofrequency (PRF) treatment may be considered as a secondary approach for managing the condition. Ongoing advances in the field have led to a wide range of PRF parameters being investigated and extensively documented. Therefore, this study will aim to evaluate the treatment efficacy, sustainability and adverse effects of PRF application for different durations in patients with LRP.

Methods and analysis This study will be a double-blind, randomised, controlled trial. Eligible patients with LRP who visit the International St. Mary's Hospital pain clinic in Korea will be assigned to three groups (1:1:1 ratio) based on the duration of PRF application: 240, 360 and 480 s. Outcome measures will include an assessment of radicular pain intensity, physical function, global improvement, treatment satisfaction and adverse events. The primary outcome will be a Numeric Rating Scale (NRS) score 3 months after the procedure. The secondary outcomes will be the number of subjects in each group reporting successful treatment defined as a significant decrease of NRS or improved physical function score or high satisfaction at the 3 and 6 months follow-up. X^2 or Fisher's exact test and one-way analysis of variance will be used to compare the outcomes.

Ethics and dissemination This trial was approved by the Ethics Committee of Catholic Kwandong University International St. Mary's Hospital (IS23EISE0018). The findings will be disseminated in peer-reviewed journals and at scientific conferences.

Trial registration number KCT0008612.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study will be the first prospective study to evaluate the effectiveness of different application times of pulsed radiofrequency treatment in patients with lumbar radicular pain.
⇒ This will be a double-blind study where the researcher collecting the data and the operator are blinded.
⇒ The study has a relatively small sample size per arm and a short follow-up period.

INTRODUCTION

Lumbar radicular pain (LRP) is a common manifestation of lower back pain that presents as a sharp, shooting or lancinating sensation localised to one or more dermatomes in the lumbar spine.[1 2] Chronic LRP is often associated with lumbar disc herniation, spinal stenosis or degenerative spondylolisthesis and can persist even after lumbar spine surgery.[2] This condition is often associated with lesions that either directly affect the dorsal root ganglion (DRG) or indirectly affect the spinal nerve and its roots by inducing axonal ischaemia or an inflammatory response.[3]

LRP is highly prevalent and significantly affects quality of life; however, the most effective conservative treatment for patients with LRP remains uncertain.[4 5] If conservative treatments such as medication and physical therapy have not yielded satisfactory results, an epidural steroid injection may be tried. If repeated epidural steroid injections do not work or do not last long, pulsed radiofrequency (PRF) treatment may be considered a secondary approach to managing the condition.[6]

PRF is a relatively new neuromodulation technique that has been effective for many types of pain.[4 5] However, there are conflicting results regarding its effectiveness.[7–9] Although 45 V is a commonly used output voltage for PRF to lumbar DRG, but this varies from study to study, and there is no standard for the most effective output voltage and application time. Therefore, it is necessary to identify the variables that need to be adjusted during PRF to maximise its effectiveness.

Previous studies have shown that longer-duration PRF improves pain relief in trigeminal neuralgia and postherpetic neuralgia.[10 11] The authors of this study aim to evaluate whether the efficacy of PRF in the lumbar DRG of patients with LRP depends on the duration of PRF application. To the best of our knowledge, no study has evaluated the therapeutic effects of PRF according to application time in patients with LRP.

METHODS AND ANALYSIS

Hypothesis

We hypothesised that the longer the duration of standard voltage (45 V) PRF applied to the lumbar DRG, the greater the improvement in pain and the longer the effect would last.

Trial design

We began enrolling subjects on 1 July 2023 with an expected end-of-study date of 30 June 2024. Prior to enrolment, participants will be provided with a written informed consent form as an integral part of the ethical approval process. The study will be a single-centre, double-blind (to both a researcher collecting data and an operator performing RF) randomised controlled trial with three groups in a 1:1:1 allocation ratio. After obtaining informed consent (online supplemental material), the patients will be randomly assigned to one of the three groups using a computer-generated number. The clinical trial and the items to be examined in this study are presented in table 1.

Inclusion criteria

The inclusion criteria for the patients will be as follows:

1. Age ≥20 years old.
2. Chronic LRP lasting≥12 weeks.
3. Mild or moderate lumbar spinal stenosis or disc herniation confirmed by MRI using the Lee grading system[12 13]
4. Failure of conservative management such as physiotherapy, exercise therapy or analgesic medications.
5. Patients who received conventional fluoroscopy-guided diagnostic/therapeutic transforaminal epidural injections of local anaesthetics and steroids.
6. Patients who reported persistent pain (Numeric Rating Scale (NRS) score ≥5) after receiving transforaminal epidural steroid injection (TFESI).

Exclusion criteria

The exclusion criteria for patients are as follows:

1. Patient refusal.
2. Signs of progressive motor weakness or neurological deficits.
3. Severe spinal stenosis in the lumbar spine confirmed by MRI.
4. Allergies to steroids or contrast dyes.
5. Coagulopathy.
6. Epidural steroid injection within the previous 4 weeks.
7. Systemic infection, injection site infection.
8. Malignancy.

Eligible patients for this study will be those who present to our institution and receive two fluoroscopic lumbar epidural steroid injections, 2 weeks apart. Patients who have received two epidural injections will be given a telephone interview 1 week after the second epidural injection.

Table 1 Trial schedule and observation items

Period	Screening (telephone)	Baseline (visit)	During procedure	30 mins after procedure	1 week (telephone)	2 weeks (telephone)	1 month (visit)	3 months (visit)	6 months (visit)
Oral/written consent form	√	√							
Demographic survey		√							
Selection/exclusion criteria	√								
Randomisation		√							
NRS	√	√	√	√	√	√	√	√	√
ODI		√					√	√	√
GPE							√	√	√
Adverse reaction monitoring		√	√	√	√	√	√	√	√

NRS, numeric rating score; ODI, Oswestry Disability Index; GPE, Global Perceived Effect.
GPE, Global Perceived Effect; NRS, Numeric Rating Score; ODI, Oswestry Disability Index.

Patients with no pain relief or only transient pain relief from the two epidural injections (NRS pain intensity of ≥5 points) will be enrolled. Patient recruitment and enrolment will be conducted by a blinded researcher.

Assignment of interventions and blinding

After collecting baseline data, patients will be randomly assigned to one of the three groups based on the duration of radiofrequency application: 240 s (120 s × two cycles), 360 s (120 s × three cycles) and 480 s (120 s × four cycles). At the beginning of the procedure, a nurse will uncover a sequentially numbered opaque envelope containing the group assignments. The generator is operated by the nurse, and the display is hidden from the patient and attending physician. Data on patient demographics, procedural information, and procedural outcomes were collected by a blinded researcher.

Procedure

The patient will be placed in the prone position with a pillow placed under the lower abdomen. After the aseptic preparation of the needle insertion site, the skin will be anaesthetised with 1% lidocaine. A 22-gauge, 4-inch RF cannula with a 10 mm curved active tip (RFK-C101020B; Cosman Medical, Burlington, USA) will then be carefully inserted under fluoroscopic guidance (OEC 9800; General Electric Healthcare, Little Chalfont, Buckinghamshire, UK). The cannula will be directed into the lateral opening of the targeted intervertebral foramen. In the anteroposterior view, the cannula will advance no further medially than the lateral aspect of the pedicle. The final position of the tip of the cannula will be at the 2 o'clock position of the intervertebral foramen in the lateral image. In the anteroposterior view, the tip of the cannula will be at the 6 o'clock position of the pedicle column (figure 1). Further confirmation was obtained by injecting a contrast solution (Bonorex 300; Dai Han Pharm). Once the RF cannula is properly positioned, the stylet will be replaced with the RF probe (CB112-TC; Cosman Medical). Subsequently, the probe will be connected to the PRF generator (Radiofrequency Ablation for Pain Management, G4 RF Generator; Cosman Medical). The final position of the PRF cannula will be determined by whether or not radicular pain occurs in the patient's corresponding nerve segment on sensory stimulation (50 Hz) threshold of 0.3 to 0.5 V. The motor stimulus (2 Hz) will aim to form at a voltage at least 1.5 times higher than the threshold of the sensory stimulus while ensuring that the impedance remains below 400 Ω. After each treatment cycle, the position of the RF cannula was fine-tuned and motor and sensory stimulations were performed to ensure accuracy and confirmation. The three groups will have different PRF application times: 120 s × two times (240 s total), 120 s × three times (360 s total) and 120 s × four times (480 s total). The PRF output voltage will be 45 V for all three groups.

The PRF generator will keep the temperature below 42°C and will be set to a maximum output voltage of 45 V. The pulse width will be set to 20 ms at a frequency of 2 Hz. PRF will be applied for 120 s per cycle. Group 1 will be administered two cycles of PRF and two cycles of sham to blind the patient. In Group 2, three cycles of PRF and one cycle of sham will be applied. Group 3 will be administered four cycles of PRF.

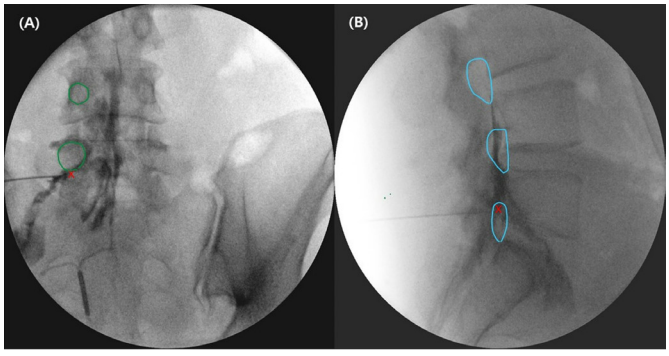

Figure 1 Fluoroscopic images of pulsed radiofrequency to left L5 dorsal root ganglion. Anteroposterior image (A) confirms needle in the mid pedicle line. Lateral image (B) is used to confirm needle depth and to visualise the needle entering the L4-L5 foramen. Contrasts outline the exiting nerve root and epidural space. Green=pedicle, light blue=intervertebral foramen, red X=needle tip position.

Outcome assessment and follow-up

Comprehensive data, including demographic factors, such as age, sex, height, weight and body mass index, will be collected at baseline. Medical history will be assessed for conditions such as diabetes and hypertension. Other baseline information will include the diagnosis, total duration of pain, target level of the affected nerve root and number of previous epidural injections. For intraoperative parameters, we will collect the stimulation voltages used during 50 and 2 Hz electrical stimulation positioning, procedure duration, output voltage, output current, impedance values (before and after the procedure) and electric field intensity ((output voltage)^2/resistance).

Outcome measures will include the following assessments:

1. Assessment of pain intensity at the treatment site, both during and 30 min after the procedure.
2. Assessment of radicular pain intensity at specific time points: 1 and 2 weeks (telephone visit) and 1, 3 and 6 months after the procedure.
3. Assessment of physical function scores before the procedure and at 1, 3, and 6 months after the procedure.
4. Measurement of global improvement and satisfaction with treatment at 1, 3, and 6 months after the procedure.
5. Monitoring and documentation of any adverse events.

Pain intensity at the treatment site and radicular pain intensity will be assessed using an 11-point NRS, ranging from 0 (no pain) to 10 (unbearable pain). The physical function score will be assessed using the 10-item Korean version of the Oswestry Disability Index (ODI)

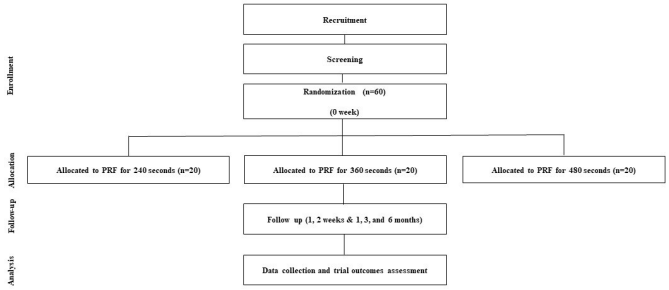

Figure 2 Flowchart of study design. PRF, pulsed radiofrequency treatment.

questionnaire, which ranges from 0 to 100, with 0 indicating no disability. Patient satisfaction and improvement will be measured using the 7-point Likert scale: Global Perceived Effect (GPE). Any adverse events occurring during treatment and follow-up will be documented individually. The flowchart of the study is presented in figure 2.

The primary outcome will be the NRS score at 3 months after the procedure. The secondary outcomes will be the number of responders in each group reporting successful treatment after the 3 and 6 months follow-up period. A successful response will be defined as one or more of the following three outcomes:

1. A reduction in pain intensity was measured using the NRS of at least 50% or a reduction of at least 4 points.
2. Decrease in ODI of at least 10 points.
3. A score of at least 6 on the GPE scale on a 7-point Likert scale.

As the secondary outcomes, NRS scores will be assessed at 1 and 2 weeks postprocedure and at 1 and 6 months postprocedure. ODI scores will be assessed at 1, 3 and 6 months after the procedure. GPE scores will be assessed at 1, 3 and 6 months after the procedure. We will also analyse the degree of reduction in NRS pain and ODI scores at 3 and 6 months postprocedure in relation to preprocedure baseline scores. Any complications that occur during the procedure will be reported accordingly. During the 1, 3 and 6 follow-up visits, close attention will be paid to a comprehensive assessment of adverse events.

Sample size calculation and statistical analysis

Our preliminary study showed that when PRF was applied at 45 V for a total of 240 s, the mean NRS score after 3 months was 3.2 with a SD of 1.3.[14] We considered a difference in NRS scores of 1 or more points to be a clinically significant difference between groups and applied a 5% significance level and 90% power, requiring 18 subjects in each group. Considering a dropout rate of 10%, we will conduct a study with 20 subjects in each group, for a total of 60 subjects.

The intention-to-treat (ITT) analysis will be applied, and the data of every randomised subject will be analysed at each follow-up moment, regardless of lost to follow-up or withdrawal from the study. We will further perform a per-protocol analysis to show if there is a significant difference from the ITT analysis. The categorical variables will be presented as numbers and percentages. The continuous variables will be presented as the mean with SD or median and IQR. To compare data from the three groups, the χ^2 or Fisher's exact test will be used for categorical variables, and one-way analysis of variance (ANOVA) or repeated measures ANOVA will be used for continuous variables. When there is missing data or dropouts, a linear mixed model will be used to analyse the secondary continuous variables. Statistical significance will be set at p value<0.05. All analyses will be performed using SPSS V.26.0 (IBM Corporation, Chicago, Illinois, USA).

ETHICS AND DISSEMINATION

This trial was approved by the Ethics Committee of Catholic Kwandong University International St. Mary's Hospital (IS23EISE0018). This trial is registered with the Clinical Trial Registry of Korea (https://cris.nih.go.kr/cris/index/index.do). The findings will be disseminated in peer-reviewed journals and at scientific conferences.

Contributors CS, J-HP, YS and SukheeP conceived and designed the study. YUK, YS and Soyoon P revised the manuscript. SukheeP will lead to the statistical analysis. JNJ and SoyoonP oversaw the data acquisition. All authors have reviewed and approved the final manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

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