Many patients with chronic idiopathic axonal polyneuropathy (CIAP) suffer from neuropathic pain, which is managed using several oral medications and modalities. However, despite these treatments, pain persists in some patients.

Objective: In the clinical field, clinicians frequently meet patients with neuropathic pain caused by CIAP. The authors investigated the effect of caudal epidural pulsed radiofrequency (PRF) for the management of CIAP-induced refractory neuropathic pain.

Study Design: This is a prospective study.

Methods: Twenty patients with neuropathic pain and a diagnosis of refractory CIAP were recruited. For PRF stimulation, a 22-gauge cannula was inserted into the epidural space through the sacral hiatus under fluoroscopic guidance. PRF stimulation was administered once at 5 Hz with a 5-ms pulse width for 600 seconds at 55 V. The effect of stimulation was evaluated using a numeric rating scale (NRS) at 2 weeks and 1, 2, and 3 months after the procedure. Successful pain relief was defined as a reduction in the NRS score of ≥ 50% as compared with the score prior to treatment. In addition, at 3 months after treatment, patient satisfaction levels were examined; patients that reported “very good” (score = 7) or “good” (score = 6) results were considered to be satisfied with the procedure.

Results: Neuropathic pain was significantly reduced at 2 weeks and at 1, 2, and 3 months follow-up after PRF (P < 0.001, repeated measures one-factor analysis). In addition, at 3 months post-PRF, half of the patients achieved a successful response (≥ 50% pain reduction) and were satisfied with treatment results.

Limitations: A small number of patients were recruited, and we did not perform long-term follow-up.

Conclusion: Caudal epidural PRF may be a good treatment option for managing neuropathic pain induced by CIAP, especially when pain is unresponsive to oral medications.

Key words: Pulsed radiofrequency, chronic idiopathic axonal neuropathy, caudal epidural stimulation, neuropathic pain chronic pain, refractory pain
impairments predominate, and symptoms slowly aggravate (3, 4). Many patients with CIAP suffer from neuropathic pain (5), which is managed using several oral medications (e.g., pregabalin, gabapentin, amitriptyline, and palmitoylethanolamide) and modalities (6,7). However, despite these treatments, pain persists in some patients.

The recently introduced pulsed radiofrequency (PRF) technique is widely used to provide relief from chronic pain (8-15). Although the mechanism of its pain-relieving effect has not been clearly elucidated, the electrical field generated by PRF has been suggested to be responsible for its clinical effect. Its thermal effect is believed to be of minor importance because only a small area around the electrode tip is affected as temperature rapidly diminishes with distance from the electrode. In addition, PRF is applied using brief stimulation and this is followed by a long resting phase, which exposes target nerves and tissues to an electric field without producing sufficient heat to cause significant structural damage (16). Because of this minimal tissue-destructive character, PRF has been rapidly adopted in clinical practice to treat different types of pain, including neuralgia, joint pain, and muscle pain. When PRF stimulation was first introduced, it was usually applied to nerve tissues like dorsal root ganglia and medial branch nerves of the spine (8,9,11,13,14). However, novel stimulation methods have been recently devised, such as intraarticular and interfascial stimulation (10,12). Furthermore, some reports have indicated PRF stimulation administered by placing needle electrodes into the caudal epidural space can be used to control neuropathic pain (17,18).

In the current study, we investigated the effect of caudal epidural PRF stimulation on refractory, neuropathic leg pain following CIAP.

**Methods**

**Patients**

Twenty patients who visited our rehabilitation department with neuropathic pain due to CIAP were included in this study and underwent caudal epidural PRF simulation. The study inclusion criteria were as follows (Table 1): 1) age over 60 years, 2) neuropathic pain (burning, tingling, and numbing in nature) of ≥ 4 on a numeric rating scale (NRS) in both legs, despite oral medications (pregabalin and tramadol/acetaminophen), 3) symmetrical distal sensory or sensorimotor symptoms and signs of the limbs, compatible with polyneuropathy, 4) insidious onset and slow or no progression of the disease over at least 6 months, 5) no identifiable cause after extensive clinical and laboratory investigations, 6) no hereditary polyneuropathy, and 7) electrophysiologic findings compatible with a diagnosis of axonal polyneuropathy. The Institutional Review Board of our hospital approved the study and all patients provided signed informed consent.

**Procedures**

Aseptic techniques were adopted for the caudal epidural PRF procedure. Patients were asked to lie in a prone position for C-arm fluoroscopy (Siemens, Munich, Germany). After local infiltration anesthesia at the injection site, a 22-gauge cannula (SMK pole needle, 150 mm with a 20 mm active tip; Cotop International BV, Amsterdam, Netherlands) was inserted into the epidural space through the sacral hiatus under fluoroscopic guidance (18). The needle-tip was then advanced to the S2-3 intervertebral level (Fig. 1). After confirming correct needle placement in the caudal epidural space using a contrast dye, an electrode was connected to the cannula, and stimulation was conducted (Cosman G4 radiofrequency generator, Cosman Medical, Burlington, MA). PRF was administered at 5 Hz using a 5-ms pulse width for 600 seconds at 55 V so as not to exceed an electrode tip temperature of 42°C. The physician that performed the procedures had 20 years of training and experience and was not involved in the outcome assessment.

**Outcome Measures**

One investigator performed all pretreatment and follow-up assessments and did not participate in any treatment. Pain intensities were assessed using a NRS; allocated scores ranged between 0 and 10, where 0 represented “no pain” and 10 represented “most intense pain imaginable.” NRS scores were determined before treatment and at 2 weeks, 1, 2, and 3 months after treatment. Successful treatment was defined as a > 50% reduction baseline NRS score at 3 months. NRS score reductions percent (ΔNRS%) were quantified by

<table>
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<tr>
<th>Demographic characteristics.</th>
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<tr>
<td>Age (yrs.)</td>
</tr>
<tr>
<td>Male : Female</td>
</tr>
<tr>
<td>Duration of neuropathic pain (mos.)</td>
</tr>
<tr>
<td>NRS score in leg at pretreatment</td>
</tr>
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Values are presented as numbers or means ± standard deviations. Abbreviations: NRS = numeric rating scale
expressing score reductions at 3 months as percentages of baseline scores.

In addition, patient global perceived effect (GPE) was assessed at 3 months post-PRF using a 7-point Likert scale (Table 2) (19,20), and patients that reported very good (NRS score = 7) or good results (score = 6) were considered to be satisfied with the procedure.

Statistical Analysis

Data were analyzed using the Statistical Package for Social Sciences Version 22.0 (IBM Corporation, Armonk, NY). The summary of characteristic variables was performed using descriptive analysis, with the mean ± standard deviation presented for quantitative variables and frequency (percent) for qualitative variables. Changes in NRS scores over time were evaluated using repeated measures one-factor analysis. Multiple comparison results were obtained following a contrast under Bonferroni correction. Statistical significance was accepted for P-values < 0.05.

Results

All 20 patients completed the study protocol. The average NRS score for neuropathic pain declined from 5.4 ± 1.5 at baseline to 3.6 ± 2.1 at 2 weeks, 3.5 ± 1.9 at 1 month, 3.4 ± 1.9 at 2 months, and 3.3 ± 2.0 at 3 months post-PRF. NRS scores changed significantly over time (P < 0.001) (Fig. 2). More specifically, NRS scores at 2 weeks, and 1, 2, and 3 months post-PRF were significantly lower than at baseline (2 weeks, P = 0.001; 1 to 3 months, P < 0.05).

Table 2. Global perceived effects as determined using a Likert scale.

<table>
<thead>
<tr>
<th>Score</th>
<th>% Change</th>
<th>Description</th>
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<tbody>
<tr>
<td>7</td>
<td>≥75 improvement</td>
<td>Very good</td>
</tr>
<tr>
<td>6</td>
<td>50–74 improvement</td>
<td>Good</td>
</tr>
<tr>
<td>5</td>
<td>25–49 improvement</td>
<td>Fairly good</td>
</tr>
<tr>
<td>4</td>
<td>0–24 improvement or worse</td>
<td>Same as before</td>
</tr>
<tr>
<td>3</td>
<td>25–49 worse</td>
<td>Fairly bad</td>
</tr>
<tr>
<td>2</td>
<td>50–74 worse</td>
<td>Bad</td>
</tr>
<tr>
<td>1</td>
<td>≥75 worse</td>
<td>Very bad</td>
</tr>
</tbody>
</table>

Fig. 2. Changes in NRS scores of neuropathic pain during follow-up.

NRS scores reduced significantly from 5.4 ± 1.5 prior to treatment to 3.6 ± 2.1 at 2 weeks, 3.5 ± 1.9 at 1 month, 3.4 ± 1.9 at 2 months, and 3.3 ± 2.0 at 3 months after caudal epidural PRF treatment. *P < 0.05.
Ten of the 20 patients (50%) reported successful pain relief (≥ 50%) at 3 months post-PRF. No adverse effects were observed in any patient after the procedure.

Patient satisfactions with treatment, as determined using the 7-point Likert scale, were as follows; very good (score = 7) in 4 patients (20%), good (score = 6) in 6 patients (30%), and fairly good (score = 5) in 2 patients (10%). No change (score = 4) was reported by 8 patients (40%). No patient returned a satisfaction score of less than 4. Therefore, 10 patients (half of all study participants) were satisfied with their results at 3 months post-PRF.

**Discussion**

In this study, we evaluated the effect of caudal epidural PRF stimulation on CIAP-induced neuropathic leg pain unresponsive to pain medication. Pain severity was significantly reduced at 2 weeks and 1, 2, and 3 months post-PRF. In addition, half of the patients achieved a successful response (≥ 50% pain reduction) and were satisfied with treatment results at 3 months.

In several previous studies on animal models of peripheral neuropathic pain, glial cell (e.g., astrocytes and microglia) activation was observed in the dorsal horn of the lumbar spinal cord (21-25). When activated, glial cells release pro-inflammatory cytokines, such as, interleukin (IL)-1β and tumor necrosis factor-α (TNF-α), which enhance the transmission of pain signals (26-28). Likewise, in the case of CIAP, glial cells may be upregulated following peripheral nerve damage and release cytokines that trigger neuropathic pain.

The effects of epidural caudal PRF stimulation have not been clearly demonstrated. In 2016, Cho et al (29) found microglial activation was significantly reduced, from L3 to S1 in the spinal dorsal horn, after applying epidural PRF in a rat model of lumbar disc herniation and demonstrated that this stimulation reduced the activation of dorsal horn nociceptive neurons at multiple levels of the lumbar spinal cord. Furthermore, these changes prevented the overexpression of pain-related cytokines in the spinal dorsal horn, and thus, inhibited the transmission of pain signals. When applied in the present study, PRF stimulation seemed to act on multi-levels of the spinal dorsal horn in the manner suggested by Cho et al (29) and suppressed neuropathic pain. Additionally, Erdine et al (30) found a disruptive effect of PRF on the sensory nociceptive axons. The lesions occurring after PRF were selectively located in the smaller principal sensory nociceptors (C-fibers and A-delta fibers), but were rarely identified in the larger non-pain-related sensory fibers (A-beta fiber). The electrical field induced by the PRF electrode placed in the soft tissue is rapidly weakened at increasing distances from the electrode. However, in our cases, the PRF electrode was placed into the epidural space, and the current seems to be deflected by the bony surfaces of lumbosacral vertebrae and remain inside the epidural space without weakening (31).

In this study, we were not able to recruit sham control participants for ethical reasons. However, due to the progressive, degenerative nature of CIAP disease (3,4), we believe that the pain reductions observed were due to the administration of caudal epidural PRF and not to natural recovery. Accordingly, we consider our results good evidence for the benefits of caudal epidural PRF in patients with CIAP-induced refractory neuropathic pain.

To the best of our knowledge, only 2 previous studies have addressed the effects of caudal epidural PRF stimulation in humans (17,18). In 2011, Atim et al (17) conducted caudal epidural PRF on 21 patients with coccygodynia and reported about 80% of their patients exhibited positive pain relief. In the other study, which was conducted in 2014, Rohof (18) preformed caudal epidural PRF on 3 patients with post herpetic neuralgia, and found 2 of the 3 experienced a positive long-term effect. The 2 patients that experienced a positive effect had neuralgia in dermatomes L1-4 and T10-11, respectively, and caudal epidural PRF successfully controlled neuralgic pain in these patients. Interestingly, this previous study indicates caudal epidural PRF can effectively manage pain even when the pain source is removed from the active PRF needle-tip in the sacral canal.

**Conclusion**

In conclusion, we found that leg pain due to CIAP refractory to oral medication was significantly reduced at 2 weeks and 1, 2, and 3 months after caudal epidural PRF. However, only one half of our patients achieved meaningful pain relief and was satisfied with treatment at 3 months after PRF. In the clinical setting, if oral medications fail to control CIAP-associated neuropathic pain, clinicians have limited options to manage the pain. Therefore, we believe caudal epidural PRF stimulation is worth considering as a safe modality for managing refractory neuropathic pain following CIAP. However, some limitations of this study should be considered. First, as mentioned above, the present study was conducted without a...
control group. Second, the number of patients recruited was relatively small. Third, we are not able to clearly explain the mechanism underlying how caudal epidural PRF could act on a broad area. Therefore, further studies addressing these limitations are necessary to confirm our findings.

References
