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NEUROMODULATION IN ODONTOGENIC PAIN: A CASE SERIES

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Background: Teeth and other intraoral structures are the most frequent sources of orofacial pain. Pulsed radiofrequency (PRF) is a treatment where an intermittent electrical pulse is applied to a painful nerve.

Case Report: Twelve patients who reported odontogenic were enrolled. After a positive anesthetic block test at the affected nerve, a PRF procedure was performed. After the procedure, patients were asked to report the degree of tolerability of the procedure, and each patient was reevaluated after one and 6 months in terms of overall satisfaction, reduction of pain, and number of attacks.
A total of 18 procedures were performed over 12 patients; 8 patients reported significant clinical improvement .
Maximum and mean self-reported pain ratings decreased significantly at both the one- and 6-month follow-ups.

Conclusion: The use of PRF in treating odontogenic pain appears to show promising results: it is feasible, safe, and associated with little discomfort for the patient.

Key words: Odontogenic pain, neuromodulation, pulsed radiofrequency, interventional pain procedure

BACKGROUND

Odontogenic pain is the leading motivation for seeking dental care (1), and it is linked to the presence of dental pathologies resulting from trauma, abrasions, or infections. In some cases, odontogenic pain is a consequence of complications related to dental procedures or maxillofacial surgery (2).

There is some support for the hypothesis that nerve trauma from an inflammatory environment may underlie the development of chronic orofacial neuropathic pain (3). Such a theory could explain cases of odontogenic pain in which dental care fails to relieve pain (4).

Lesions at the level of the trigeminal nerve and its branches are one of the most important complications of dental procedures (2). The incidence of these lesions varies from 1% (in permanent nerve damage) (5,6) to 13% to 26% (in transient nerve damage) (5,7). The inferior alveolar nerve is the nerve most frequently affected, which often occurs following intervention on the inferior third molar tooth (e.g., local anesthetic injections, tooth removal, implant, or endodontic surgery) (8).

Furthermore, lesions at the nerve level are likely due to anatomical variations in its course (9,10). Other nerve lesions are those affecting the superior alveolar nerve or the nasopalatine nerve (11). Neuropathic pain resulting from these injured nerves causes impairment in normal daily activities, such as talking, eating, drinking, or shaving, and related psychological effects (12).

Pulsed radiofrequency (PRF) has been applied for the treatment of several types of neuropathic pain (13,14).

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The choice of PRF for alleviation of pain was first described in 1996 when it was performed on a dorsal root ganglion (15).

The idea of adopting PRF as a treatment option was motivated by the need to avoid complications from thermal lesions, which occur often in continuous radiofrequency (CRF).

The mechanism by which PRF acts is via a neuromodulatory-type effect (16). Several studies have aimed to clarify histological and biochemical changes in tissues that underwent treatment with PRF. Some mechanisms are described as follows:

- PRF causes endoneurial edema, but this change is transient since studies on dorsal root ganglia show that, after treatment, nerve tissue returns to baseline conditions within 21 days (17);
- dorsal root ganglion stimulation by PRF seems to reduce neuronal excitability with consequent analgesic effect due to its inhibitory action on the generation and propagation of action potentials (18);
- PRF may upregulate "pain genes" (e.g., c-FOS, which appears to be involved in pain-inhibiting processes) (19);
- PRF may also act on the release of proinflammatory cytokines, such as interleukin IL-1b, TNFα, and IL-6, which are downregulated by the electric fields generated by PRF (20);
- PRF may enhance the descending inhibitory noradrenergic and serotoninergic pathways that mediate the modulation of neuropathic pain (21).

The technique of PRF consists of applying an electrical catheter to the target nerves in order to alleviate pain and avoid nerve damage (22).

Our study aims to evaluate pain relief in patients suffering from odontogenic pain who were treated with PRF.

METHODS

The study was conducted following approval by the ethics committee of IRCCS Maugeri Pavia (4 Feb 2020 2395 CE).

All patients who presented to the pain medicine unit for odontogenic pain and who were unresponsive to drug therapy were recruited. Patients were referred to the pain management service by dentists, otolaryngologists, maxillofacial surgeons, and general practitioners.

During the first visit, anatomical irradiation was used to determine the origin of the pain, after which the patients were administered a questionnaire relating to the minimum, maximum, and average pain during a typical day and to the number and intensity of pain episodes.

When possible, optimized medical therapy was arranged. Patients were offered the treatment option of pulsed neuromodulation of the affected nerve or nerves in the event that medical therapy had not shown efficacy. All patients were educated and provided informed consent to undergo any of the procedures.

In cases where no benefit was obtained from the initial therapy at one month and the patient consented to the procedure, an anesthetic block was performed (bupivacaine 0.5% + dexamethasone 2 mg; vol 1-1.5 mL).

After one week, the patient reported the pain relief obtained with the block expressed as percentage from baseline, and in the case of significant transient benefit (i.e., > 50% reduction in pain in the first 12 to 24 hours, with a return to baseline by day 7), the pulsed neuromodulation procedure was performed.

The procedure was performed in the operating room with the patient in a supine position with the head supported.

The anatomical approaches for superior infraorbital block (23), posterior superior alveolar block (24), and inferior alveolar block (25) are described in Table 1. Once the neuromodulation cannula was inserted, a sensory stimulation test (50 Hz) was performed, evoking a sensation of paresthesia in a location consistent with that of the patient's pain for thresholds lower than 0.5 V. In the case of higher thresholds, the needle was adjusted in its orientation and depth until the desired paresthesia was achieved at the lowest possible threshold.

Subsequently, motor stimulation tests (2 Hz) were performed to exclude motor component involvement.

A PRF was delivered for 5 minutes at the maximum voltage tolerated by the patient (beginning at 50 V and increasing or decreasing by steps of 5 V, up to a maximum tolerance (range 35-65 V), maintaining the temperature as a controlled variable at a target of 42°C (the generator automatically varying the duration of the pulse and the off-interval to keep the temperature controlled).

Immediately following the procedure, the patient was asked to qualify their degree of discomfort or pain during the procedure as either mild, moderate, or severe.

At the 1- and 6-month follow-ups, the patient was reevaluated in order to record their current minimum, maximum, and average dental pain as measured by the

Numeric Rating Scale (NRS-11) for pain, which uses an 11 point scale where zero is absence of pain and 10 is the worst pain imaginable.

The degree of general satisfaction was expressed as patient global impression of change (PGIC) using a 7-point Likert scale (ranging from 0 = no change to 7 = big, decisive change).

RESULTS

A total of 21 patients who were referred by dentists or general practitioners were recruited. Of these 21, 12 patients were recommended to undergo PRF, and while the remaining 9 patients showed good response to modified drug therapy, 3 declined to undergo the anesthetic blocking procedure, and one patient who underwent blockade of the alveolar inferior with some benefit opted not to undergo PRF.

The 12 patients received a total of 18 procedures during the study period. Of these 12 patients, 9 were women and 3 were men, with an average age of 50 ± 11 years.

The affected nerves were 2 anterior superior alveolar nerves, 2 posterior superior alveolar nerves, and 8 inferior alveolar nerves in a single bilateral case (after mandible correction surgery).

In addition to their baseline pain, 9 patients reported episodes of acute pain (defined as more intense than baseline pain and with a duration < 30 minutes) during the day. Five patients reported experiencing 3 to 5 such episodes per day, one patient reported experiencing fewer than 3 per day, and 3 patients reported experiencing more than 5 episodes per day.

The median NRS-11 scores before the procedure were as follows: minimum NRS-11 (NRS min) score of 2 (median absolute deviation [MAD], 0.9), average NRS-11 (NRS avg) score of 4 (MAD, 0.6), and maximum NRS-11 (NRS max) score of 9 (MAD, 0.3).

After one month post intervention, the NRS max fell to 5, falling again to 4 at 6 months post intervention. The NRS avg fell from 4 to 1 at the one-month follow-up, whereas the NRS avg was 3 at the 6-month follow-up (Fig. 1).

The statistical analysis of pain relief is summarized in Table 2.

Table 1. Description of the anatomical landmarks.

Anterior and medial superior arch (11-15,21-25)	• Palpate infraorbital foramen with the patient looking straight ahead. • Draw an imaginary line vertically from pupil toward infraorbital ridge's inferior border. • Retracting the cheek, introduce the needle into the mucosa 0.5 cm from buccal surface between premolar and molar apices, posteriorly, superiorly, and medially following the imaginary line.
Inferior arch (31-48)	• Palpate retromolar fossa with thumb • Place the same index finger of the same hand externally over the ramus of the mandible retracting the tissue to visualize the pterygomandibular triangle • Needle parallel to occlusal surface of the teeth and angle between the 1st and 2nd premolar to opposite side insert needle 1 cm above the occlusal surface of the molars
Posterior superior arch (16-18,26-28)	• Retract upper lip laterally and superiorly. • At the root of the upper second molar insert needle at 45° angle posteriorly superiorly and medially. • Advance 1 to 2 cm until contact with bone.

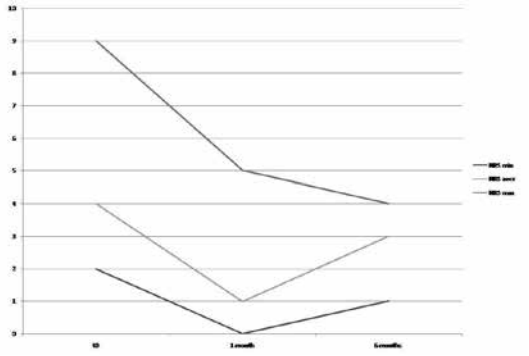

Fig. 1. Pain intensity (minimal, maximum, and average) before procedure and at follow-up.

Table 2. Statistical analysis of facial pain before and after procedure.

	T0-T1	T0-T6
NRS min	NS	NS
NRS avg	$P < .05$*	$P < .05$*
NRS max	$P = .008$	$P = .008$

Abbreviations: NRS, Numeric Rating Scale; NS, not significant
* Sample too small for normal distribution evaluation, W significant, P undeterminable with precision

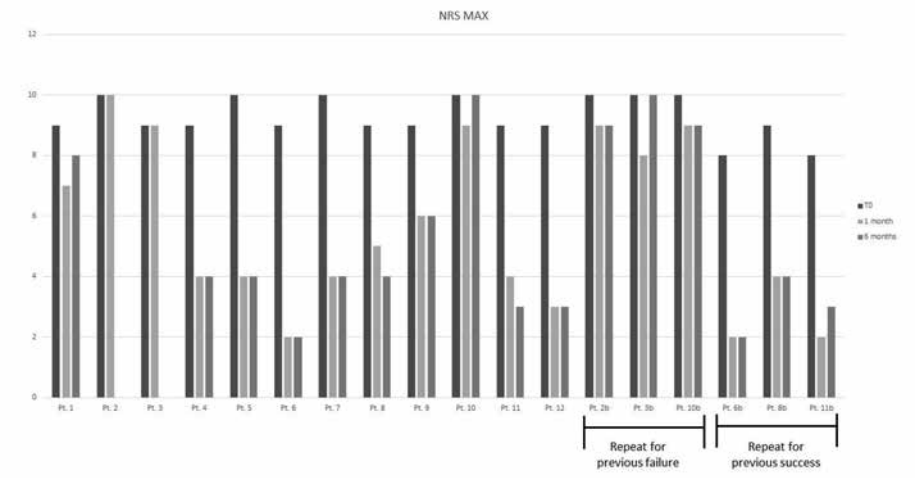

Fig. 2. Reduction in NRS max for each of the procedures .

Recently it has been suggested to evaluate the result of an analgesic procedure not in terms of absolute pain reduction, but in the percentage reduction (26). Following this interpretation, we achieved a reduction of pain of more than 50% in 9 out of 18 procedures (7 of 12 patients). In another patient, we attained a drop of more than 30% of NRS max. This result is similar also after 6 months (Fig. 2).

Improvement in orofacial pain after the first procedure, as indicated by the PGIC, was absent in 4 cases (34%). Of the remaining 8 cases, 5 (42%) reported substantial improvement, 2 (16%) reported completed resolution, and one (8%) reported mild resolution. In no case did patients report a worsening of their pain (Fig. 3).

The procedure was judged by the patients in almost all cases to be mildly or moderately annoying (5 patients and 6 patients, respectively), and only one case (anterior superior alveolar nerve) reported the procedure to be very annoying). The average voltage tolerated by the patient was 40 V.

The procedure was repeated for 2 reasons: (a) the first procedure had not given satisfactory results, or (b) effective pain resolution had subsided. In 3 cases, the first procedure had not given satisfactory results (PGIC = 4) and was repeated after one month in 2 cases. In one case, the procedure was repeated 8 months later due to the patient's decision to follow other treatments first. In all 3 cases, the second procedure did not bring significant clinical improvement (2 cases no improvement and one minimal improvemet). In 3 different cases, the procedure was repeated (after 9 months in 2 patients and after 8 months in one patient) because the effective pain resolution had since subsided. In these 3 cases, an improvement equivalent to that of the initial procedure was reported, and the second procedure was reported to be no less uncomfortable than the initial intervention.

Discomfort from the procedure was reported as mild by 5 patients, moderate by 6 patients, and severe by one patient.

DISCUSSION

This preliminary prospective study represents, to the best of our knowledge, the first attempt to apply PRF in odontogenic pain.

The data presented in our study confirm the characteristics of critical pain severity (in all cases, patients reported a maximum pain of 9 to 10 and an average pain of 4 during a typical day), which is characterized by sudden acute episodes following both stimulation (e.g., eating, drinking, etc.) and spontaneous causes.

In line with the current literature, the greater involvement of the inferior alveolar nerve is confirmed, although the superior buccal arch also appears to be involved.

Odontogenic pain that can be directly observed in pain therapy centers, although accounting for a minimal percentage of cases, has characteristics of high pain intensity and nonresponsiveness to standard medical therapies, necessitating level II treatments. PRF of the target nerves (superior alveolar, inferior, and infraorbital) appears to be a feasible and practical procedure that yields good results; the procedure, even in our limited scope, is shown to be safe, with no worsening of pain seen in any case. These results corroborate what has been described to date on the mechanisms

of action of PRF.

PRF treatments show a statistically significant efficacy—albeit for a few months only—and a notable appreciation by the patient, who is often keen to repeat the treatment. Rather than causing direct damage to the nerve, PRF merely modifies the signals that are sent; it is a safe procedure free from risks such as the development of painful anesthesia or neuropathic damage from the formation of neuromas. The sensory and motor stimulation tests guarantee further safety.

PRF is easy to implement in an outpatient setting, as it does not cause the patient any significant discomfort, rather only mild-to-moderate discomfort.

No significant complications arose in any case; all patients were discharged without incident approximately 2 hours after the procedure.

Another important finding from the literature relating to PRF of other nerve targets is its repeatability. Our study revealed that patients benefitted for a period of approximately 6 to 9 months, and that a second procedure presents the same results in light of the relative consideration of the transient changes that the nerve fibers undergo.

Likewise, even in our limited study, it seems quite understandable that in the case of ineffectiveness of treatment, repetition of the treatment cannot yield better results, and that alternative treatments must necessarily be reviewed.

CONCLUSION

The use of PRF to relieve odontogenic pain appears feasible and practical, in light of its safety and manageability, for all nervous structures that present an ectopic generation of signals from the periphery. The present study, albeit with a limited number of cases, shows how

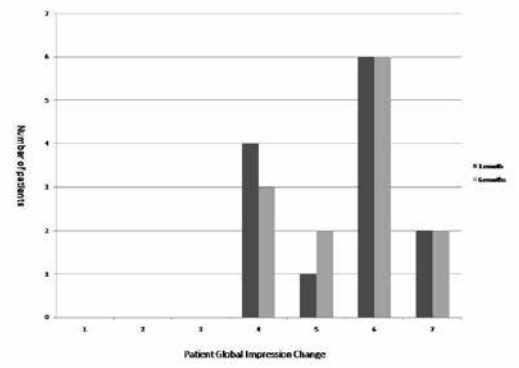

Fig. 3. PGIC after 1 and 6 months.

PRF can be safe and effective even in often-complicated pain profiles like that of odontogenic facial pain. PRF can be attempted on all patients who present odontogenic pain in a well-identified anatomical area corresponding to a nervous area. If successful, the procedure is often destined to be repeated after a few months; however, this therapy is often explicitly requested by the patient due to its benefits, which include the reduction of pharmacological therapy, and the tolerable discomfort evoked by the procedure itself.

Author Contributions

M. Marchesini performed the anesthetic block and the pulsed radiofrequency procedure. C. Rocchetti and M. Marchesini were involved in data collection, data interpretation, data analysis, literature review, manuscript preparation including figures and writing, prepared the first draft of the manuscript and contributed equally to the article. M. Baciarello, L. Demartini, and E.G. Bignami contributed to the revision of the manuscript.

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