REVIEW ARTICLE

Radiofrequency Procedures

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• Abstract: Radiofrequency is a minimally invasive, target-selective technique that has been in clinical use for more than 25 years and has demonstrated success at reducing pain in several chronic pain conditions, including trigeminal neuralgia, chronic low back pain, postherpetic neuralgia, and complex regional pain syndrome. However, the success of radiofrequency in chronic pain has not been adequately reproduced in good-quality, randomized controlled trials, and its use in the management of neuropathic pain is under some debate. In addition, conventional radiofrequency occasionally leads to worsening and even new onset of neuropathic pain. Nevertheless, clinical experience suggests that radiofrequency may be a useful tool in the overall management of refractory neuropathic pain. Pulsed radiofrequency in particular is a minimally destructive procedure that may offer new opportunities and a broader perspective for therapy with radiofrequency .•

Key Words: radiofrequency, neuropathic pain, mode of action, evidence-based review, continuous versus pulsed radiofrequency

Radiofrequency (RF) is a neurolytic technique that uses heat to produce controlled tissue destruction (thermo-coagulation) and thus reduce pain by modulating pain transmission, without causing clinical signs of nerve damage. Pain relief can last for several months before the procedure has to be repeated. RF is classified as a percutaneous minimal invasive procedure for patients whose pain does not respond to appropriate medical and physical therapy.

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During the procedure, an insulated needle is placed in the vicinity of the nerve to be lesioned. The needle position is checked, typically using multiple fluoroscopic X-ray views and by testing motor and sensory nerve stimulation. Once the correct position has been established, a grounded electrode is passed through the insulated needle to the tip. A current is then passed through the electrode, which heats up the surrounding tissue (because of the resistance produced by the body) and causes a lesion around the tip.

There are two types of RF currently in use. Continuous RF uses a constant output of high-frequency electric current to produce temperatures of 45°C or more (the temperature at which permanent nerve damage occurs), resulting in neuroablative thermocoagulation. A more recent technique, pulsed RF (PRF), utilizes brief "pulses" of high-voltage, RF-range (-300 kHz) electric current to produce the same voltage fluctuations in the region of treatment that occur during conventional RF treatment, but without heating to a degree at which tissue coagulates. The heat generated is instead dissipated between pulses. PRF produces a transient inhibition of evoked synaptic activity and continuous RF produces a lasting inhibition. Both continuous RF and PRF treatment induce distance-dependent tissue destruction under the stimulating needle, but the effect is more pronounced with contin uous RF These findings ı suggest that the acute effects of PRF are more reversible and less neurodestructive in nature than the classic continuous RF mode, even in normothermal conditions.

MODE OF ACTION

The mode of action of RF has not yet been elucidated. It was initially attributed to the thermocoagulation of nerve fibers (which denatures the nerves), but contradictory findings-notably that only transient sensory loss in the relevant dermatome is observed, although the pain relief may be of much longer duration-gave rise to the hypothesis that temperature is not the only mechanism responsible for changes in pain transmission.

Thus, it has been suggested that the electric field, rather than temperature, induces changes in the nerve cells and has a neuromodulatory effect on painprocessing mechanisms at the dorsal root ganglion, dorsal horn, and molecular levels by changing gene expression in pain-processing neurons.[2] Exposure of cultured cells to an electric field is associated with upregulation of the nonspecific intermediate-early gene markel; *c-fos* (which codes for the production of Fos protein). *C-fos-based* functional anatomic mapping has been validated as a technique to detect activated neurons. Evidence is accumulating to suggest that changes in early gene expression within the nervous system signal longterm adaptation within particular neural pathways.

Van Zundert et a1. recently compared *c-fos* expression induced by PRF with that induced by continuous RF and sham procedure in the rat.[3] The RF interventions, both pulsed and continuous, produced similar increases in the number of *c-fos* expressing cells. The persistence of expression for seven days after RF treatment, exceeding the length of time for *c-fos* expression caused by the acute effects of surgery, was suggested to be circumstantial evidence for sustained activation of some pain-inhibiting mechanism. Others had previously described sustained depression of synaptic activation by C-fibers in spinal cord recordings for several hours following repetitive stimulation of A-delta fibers.[4] It has been hypothesized, therefore, that PRF might produce prolonged analgesia by inhibiting excitatory C-fibers via long-term depression.

REVIEW OF THE EVIDENCE IN NEUROPATHIC PAIN

In clinical practice, the use of RF may be successful at reducing several chronic pain states such as trigeminal neuralgia (TGN), chronic low back pain, postherpetic neuralgia, and complex regional pain syndrome (CRPS). Although RF procedures have been in clinical use for more than 25 years, evidence regarding its efficacy and safety is still lacking. Many patients seem to have pain relief and there is a vast amount of documentation on outcome. However, these results have not been adequately reproduced in randomized controlled trials (RCTs), and its use in the management of neuropathic pain is under some debate (although PRF has shown more promise in this area). In addition, conventional RF thermal lesioning occasionally leads to worsening and even new onset of neuropathic pain.[3]

The treatment of TGN with selective percutaneous RF thermocoagulation was recently assessed in 1860 patients in whom drug treatment had failed because of lack of efficacy or severe side effects.[6] The therapeutic effectiveness was divided into three grades: excellent, good, and ineffective. Results showed that in the 78.8% of excellent cases, pain disappeared immediately; in the 17.5% of good cases, pain was lessened but not relieved completely; in 3.7% of ineffective cases, the patients remained in pain even after a second round of therapy. An complications affecting this last group (eg, facial hypesthesia and corneal reflex torpidity, difficulty in opening the mouth) resolved within seven days; no severe complications or death occurred. Among the 42 patients treated using X-ray, 3-D CT, or navigational localization, 78.6% were immediately released from their pain. Slight pain was still felt in 19% of patients. A total of 1052 cases were followed up for 8 to 24 months. Pain recurrence was observed in 11.10;" of patients during the first 12 months and 24.8% after 24 months. After a second percutaneous RF thermocoagulation in this group, no recurrence of pain was noted after 2 to 14 months and no long-term complications could be seen.

One of the most recent studies evaluated the clinical results of RF thermogangliocoagulation (RFT) in the treatment of primary TGN.[7] A retrospective study of 152 consecutive cases of primary TGN was undertaken to analyze clinical parameters such as effective rate, ineffective rate, and the rate of complications of patients treated with RFT. Results showed a very high effective rate of 94.1 % and a low ineffective rate of 2.6%. Only 3.3% cases gave up or crossed to other treatment methods (Figure 1). The rate of complications was 15.8%. It was concluded that RFT is an effective method of treating primary TGN, which can partly save the sense of touch. Few severe complications were experienced and the mortality rate was low. Recurrent cases can be retreated with RFT.

While relatively few controlled trials of RF treatments have been performed for neuropathic pain indications, RF trials for pain of spinal origin are more numerous. In 2001, a systematic review of RCTs on RF procedures for spinal pain found six trials that met the inclusion criteria.[8] This small number, along with clinical and technical differences, precluded statistical analysis. However; all studies, whether of high or low quality, reported positive outcomes. It was concluded

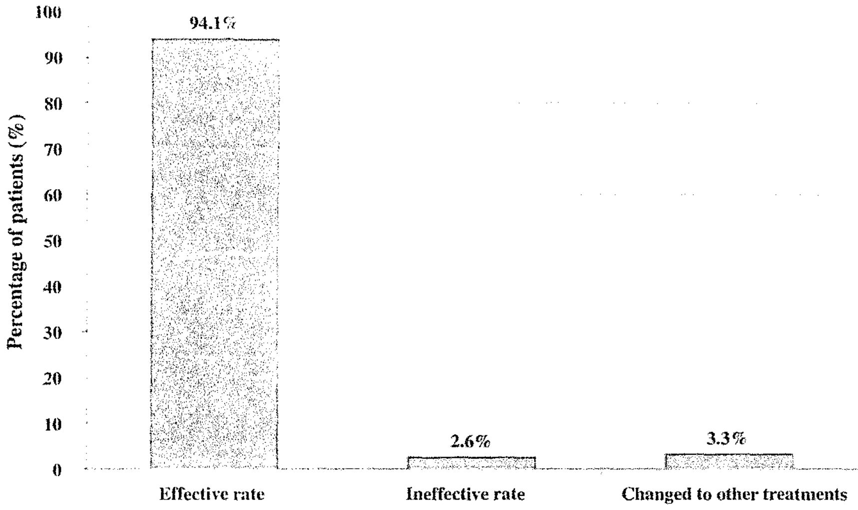

Figure 1. Efficacy of RF thermogangliocoagulation in the treatment of primary TGN.[7] RF, radiofrequency; TGN, trigeminal neuralgia.

that there is moderate evidence that RF lumbar facet denervation is more effective for chronic low back pain than placebo. Limited evidence exists for efficacy of RF neurotomy in chronic cervical zygapophyseal joint pain after Hexion-extension injury. There is limited evidence that RF heating of the dorsal root ganglion is more effective than placebo in chronic cervicobrachialgia. The systematic application of the authors' additional parameter assessments was recommended for future evaluations of RF studies, and should be used in the preparation of future trial protocols of RF procedures for the treatment of chronic pain.

A Cochrane review of RCTs of RF denervation for neck and back pain was undertaken in 2002.[9] Of the seven relevant RCTs identified, six were considered to be high quality. The selected trials included 275 randomized patients, 141 of whom received active treatment. One study examined cervical zygapophyseal joint pain, two cervicobrachial pain, three lumbar zygapophyseal joint pain, and one discogenic low back pain. The study sample sizes were small, follow-up times were short, and there were some deficiencies in patient selection, outcome assessments, and statistical analyses. Analysis confirmed that there was limited evidence that RF denervation offers short-term relief for chronic neck pain of zygapophyseal joint origin and for chronic cervicobrachial pain. There was conflicting evidence on the short-term effect of RF lesioning on pain and disability in chronic low back pain of zygapophyseal joint origin. Limited evidence existed that intradiscal RF thermocoagulation is not effective for chronic discogenic low back pain. The authors concluded that there is a need for further high-quality RCTs with larger patient samples and data on long-term effects, for which current evidence is inconclusive. Furthermore, RCTs are needed in nonspinal indications where RF denervation is currently used without any scientific evidence.

A later study carried out an evidence-based medicine analysis of current literature, assessing the use of interventional treatments options such as RF denervation for the treatment of low back pain.[10] The review determined that the evidence for the use of RF in this indication should be rated "moderate" (level III, according to the guidelines set by the Agency for Health Care Policy and Research). The need for larger, prospective RCTs with uniform inclusion and exclusion criteria, standardized treatment, uniform outcome measures, and an adequate duration of follow-up was emphasized, so that definitive recommendations for the treatment of low back pain can be made.

The procedural limitations of the RCTs of RF neurotomy for low back pain were outlined in a recent review.[11] The literature related to patient selection, diagnostic testing, and the technique of performing lumbar spine RF neurotomy also was critically reviewed and analyzed. Substantial procedural shortcomings were found in all three RCTs identified, and these procedural limitations were not accounted for by the quality assessment of study design, resulting in an inaccurate estimate of clinical effectiveness. Further analysis showed that screening criteria could increase the probability of zygapophyseal joint pain before performing diagnostic blocks. Similar analysis showed that comparative medial branch blocks, rather than single blocks, must be used before RF neurotomy. Anatomical studies demonstrated that the shorter distal compared to the circumferential radius of the RF lesion necessitates placement of the electrode parallel to the course of the nerve along the base of the superior articular process.

Recently, a multicenter, randomized, double-blind, sham treatment-controlled trial was performed to determine the efficacy of RF facet joint denervation in the treatment of chronic low back pain.[12] Primary outcome was determined with a combined outcome measure comprising visual analog scale (VAS), physical activities, and analgesic intake. Secondary outcome measures included global perceived effect and SF-36 Quality of Life questionnaire. A total of 81 patients were randomized to treatment. Results showed no difference between RF facet joint denervation (success 27.5%) and sham (success 29.3%), although the VAS in both groups improved significantly ($P < 0.001$). There also was a significant improvement in the global perceived effect after RF facet joint denervation ($P < 0.05$). It was concluded that in selected patients, RF facet joint denervation appears to be more effective than sham treatment.

RF has been used for neuropathic pain indications to provide prolonged sympathetic interruption. The use of RF lumbar sympatholysis has been evaluated in the long-term management of patients with sympathetically maintained neuropathic pain who had previously responded to sympathectomy or sympathetic blocks.[13] A total of 38 procedures were performed on 20 patients. Results showed that five patients experienced long-term pain relief (5 months to 3 years after the last RF sympatholysis). Fifteen had temporary relief or no relief at all. The procedure was temporarily complicated by an excessively hot, swollen foot and postsympathectomy neuralgia in a few cases. It was determined that a single technique of RF sympatholysis does not appear to be applicable to all patients with CRPS or sympathetically maintained pain (SMP). Despite early successful sympathetic block with RF (as confirmed by a warm foot), long-lasting pain relief was difficult to obtain. It was concluded that individualized patient management is necessary when considering RF sympatholysis in the treatment of patients with SMP.

The role of RF lesions of the stellate ganglion (RFSG) in the management of chronic pain also has been evaluated in a retrospective analysis.[14] SG blockade is used for the treatment of chronic pain in which the sympathetic nervous system is thought to be involved (eg, neuropathic pain syndromes such as CRPS). Results from the authors' pain clinic (mean follow-up 52 weeks) revealed that of the patients who underwent RF-SG blockade, 40.7% noted a greater than 50% reduction of pain, 54.7% reponed no effect on pain, and 4.7% showed worsening of pain. The literature search identified 19 studies that assessed the efficacy of SG blockade; review showed that RF-SG blockade resulted in partial pain relief in 41.3 % of patients, complete pain relief in 37.8%, and no pain relief in 20.9%. It was concluded that the efficacy of RF-SG blockade is in line with that of other SG blockade procedures reported in the literature, and that an RF-SG block is most likely to be beneficial in patients suffering from CRPS type II, ischemic pain, cervicobrachialgia, or post-thoracotomy pain. However, clinical efficacy remains to be proven in a RCT.

Overall, there is a real need for further high-quality RCTs with larger patient samples and data on long-term effects, for which current evidence is inconclusive. To enable future well-designed RCTs, efforts should be made to standardize the diagnostic criteria, the procedure, and documentation of treatment outcome. If and when it is established that particular groups of patients exhibit long-term pain relief from a treatment such as PRF, then demonstrating its mechanisms using basic science neurobiology and persistent pain models will provide important fundamental information to understand and advance the technique.

Further refinement in the design of future prospective RCTs of PRF also might take into consideration additional technical factors. For example, clinical experience and observation indicates that injection of a local anesthetic and steroid prior to lesioning lowers impedance measurements and possibly may improve therapeutic outcome. Moreover, in selecting the equipment for RF, the issue of sharp vs. blunt needle technique favors the use of blunt needles.[11,15] Rare instances of needle tip migration have resulted in the injected material causing arterial clogging and secondary spinal cord infarction. In addition, the length and size of the active, uninsulated needle tip and the number of lesions have led to different outcomes and complications. Such issues need to be resolved to ensure effective therapy with RF.

CONCLUSIONS

The successful results experienced in clinical practice following treatment of chronic pain with RF do not seem to be reflected in the small number of controlled studies that have been carried out to date. RF treatment has been extensively documented, but its reported efficacy varies between studies, a finding that could be attributed to differences in study design, patient selection criteria, and outcome measurements, making meta-analyses difficult. In addition, the set-up of welldesigned RCTs on the efficacy and safety of invasive pain treatment is compromised by several factors: the need for a sham intervention as comparator and the obligation to obtain patient's informed consent (which may result in refusal to participate), and ethical considerations of withholding an active treatment from patients who suffer intractable pain (eg, TGN). These factors may explain the low numbers of RCTs on RF treatment reported until now.

Nevertheless, the application of RF in the management of chronic pain is a useful tool. Its minimally invasive character, target-selective approach, the possibility of outpatient treatment, and the relatively low incidence of side effects and complications-if carried out by a well-trained pain physician in the right setting-justify its use in patients refractory to conservative treatment prior to other more invasive, and often more expensive, treatment possibilities. The development of PRF, the minimally neurodestructive isothermic application of an electric field to the target nerve structures, may open new and broader perspectives for RF trea tInent.

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