Pain Physician 2009; 12:E277-E283 • ISSN 2150-1149

Case Report

Radiofrequency Treatment of the Thoracic Paravertebral Nerve Combined with Glucocorticoid for Refractory Neuropathic Pain Following Breast Cancer Surgery

Ken-ichiro Uchida, MD

From: Department of Anesthesiology, Kurashiki Central Hospital, Japan.

Dr. Uchida is with the Department of Anesthesioogy, Kurashiki Central Hospital, Kurashiki, Okayama, Japan.

Address correspondence:
Ken-ichiro Uchida, MD
Department of Anesthesiology
Kurashiki Central Hospital,
1-1-1 Miwa
Kurashiki, Okayama
7108602
Japan
E-mail: ku7877@kchnet.or.jp

Disclaimer: There was no external funding in the preparation of this manuscript.
Conflict of interest: None.

Manuscript received: 12/01/2008
Revised manuscript received: 01/22/2009
Accepted for publication: 03/17/2009

Free full manuscript: www.painphysicianjournal.com

Background: Neuropathic pain following breast cancer surgery can have a profoundly negative impact on the physical and psychosocial functioning of patients. Radiofrequency treatment has been used as therapy for chronic pain, which also has a problem under debate of its neurodestructive nature. Although the efficacy and safety of using glucocorticoids in nerve block treatment are controversial, they have been used to treat neuropathic pain for many years and have been used to alleviate acute and continued postoperative pain. Neither radiofrequency combined with glucocorticoids nor radiofrequency treatment of the thoracic paravertebral nerve for neuropathic pain following breast cancer surgery has been reported.

Objective: To describe the efficacy of thoracic paravertebral nerve radiofrequency treatment combined with glucocorticoids for refractory neuropathic pain following breast cancer surgery.

Design: A series of 3 patients, who following breast cancer surgery with neuropathic pain that did not respond to conservative treatment, were selected. They received radiofrequency treatment of the thoracic paravertebral nerve combined with betamethasone. If pain remained after this treatment at a dermatome of a different level or at the same level, the same treatment was administered after at least 2 months had passed.

Results: A total of 21 treatments were administered to the 3 patients. After these treatments, all 3 patients experienced pain relief and their quality of life improved as evaluated by the SF-36. Hypoesthesia worsened slightly after treatment. However, anesthesia dolorosa and transient burning pain in the corresponding dermatome, which seemed to be related to neuro-injury after radiofrequency treatment, were not seen.

Conclusion: This case series suggests that it is possible that radiofrequency treatment of the thoracic paravertebral nerve combined with glucocorticoid may help in pain relief and improve the quality of life of patients with refractory neuropathic pain following breast cancer surgery.

Key words: Radiofrequency, neuropathic pain, glucocorticoid, breast cancer surgery, thoracic paravertebral nerve, postmastectomy pain

Pain Physician 2009; 12:E277-E283

As more patients are surviving breast cancer as a result of the progress in treatment, the population at risk for chronic pain after breast cancer surgery can be expected to increase in the coming years (1). Tasmuth et al (2) reported that chronic pain slightly affected the daily lives of about 50% of post-surgical breast cancer patients, and that the effect was moderate or severe in 25% of such women. It has been speculated that many of these patients were undertreated for pain and generally obtained poor pain relief (3). Continuous radiofrequency (RF) lesioning has been reported as

treatment for several chronic pain conditions even though a problem under debate is its neurodestructive nature (4-8). Glucocorticoids have been used to treat neuropathic pain for many years and they alleviate acute and continued postoperative pain by suppressing inflammatory mediators and glial activation and reducing neural activity, sympathetic sprouting and central neuropathic changes such as central sensitization (9).

We hypothesized that the effect of glucocorticoids would be additive to that of RF treatment and that glucocorticoids might avert pain associated with neuroinjury after RF lesioning. There have been no previous published cases on RF treatment of the thoracic paravertebral nerve (TPN) combined with glucocorticoid.

We treated 3 patients with refractory neuropathic pain following breast cancer surgery with RF of the thoracic paravertebral nerve (RF-TPN) at 90°C combined with glucocorticoid.

Methods

Three patients with refractory neuropathic pain following breast cancer surgery were selected to receive RF-TPN combined with glucocorticoid according to the following criteria: 1) presence of irradiating pain in the thoracic region following breast cancer surgery; 2) no response to conservative treatment such as anti-inflammatory drugs, antidepressants, anticonvulsants, opioid analgesics, and topical capsaicin; 3) duration of conservative treatment of more than 6 months; 4) temporary positive response (> 80% pain relief) to intercostal nerve block using local anesthetics and glucocorticoids at each painful dermatome; and 5) pain so severe as to disturb sleep.

In addition, all 3 patients reported continuous aching and burning pain with the worst daily pain described as severe to excruciating and allodynia of the affected area.

After we provided complete information on the RF technique and its possible benefits, risks, and side effects, the patients gave verbal informed consent for the procedure.

Radiofrequency Procedures

The level at which RF treatment was administered was decided by the affected dermatome, the degree of tenderness under the rib using fluoroscopy with a C-arm, and the effect of intercostal nerve block. RF-TPN was performed using real-time fluoroscopy with a C-arm by the laterodorsal approach as described by Waldman (10). Sterile skin preparation and draping were done before each procedure. After 1% lidocaine was injected through a 25-gauge needle at the entry point of the electrode, the electrode (22-gauge 99-mm needle with 4-mm bare tip, TFW 22G×99 mm®) was introduced into the selected nerve using fluoroscopy with a C-arm until paresthesia in the dermatomal distribution of that nerve was obtained. We confirmed that the needle tip was placed in the posterior aspect of the intervertebral foramen on a lateral view (Fig. 1) and that it was no further than half way across the width of the line of the pedicle. After a negative aspiration test, contrast dye (Omnipaque®, Daiichi-Sankyo, Japan) was injected to confirm the location of the nerve that was to be treated and that there was no vascular uptake of contrast (Fig. 2). Once the needle was positioned, the electrode stylet was replaced with a thermocouple electrode. We tested whether the thermocouple electrode was placed in the physiologically correct location by 100-Hz stimulation of the needle tip. We initially set the voltage at 0V and then gradually increased it until the patient felt a tingling sensation. If a tingling sensation in the corresponding dermatome was obtained at a voltage of less than 0.5V, the electrode was assumed to be in the correct position. After verifying that the needle was in the correct position, 1.5 mL of 2% mepivacaine and 2 mg of betamethasone as the glucocorticoid were administered to the TPN. Five minutes later, continuous RF treatment was applied at a temperature of 90°C and duration of 90 seconds with a generator (Neuro Therm JK 3™ system, Croydon, Surrey, UK) that had an automatic temperature control mode to avoid excessive elevation of temperature (11). If the patient still had pain after the treatment at a dermatome of a different level or at the same level, another treatment was administered after at least 2 months had passed. If pain remained on a plural number of intercostal nerve areas, RF-TPN with glucocorticoid was administered to the most painful area.

Evaluation of Pain

Pain was evaluated before and more than 2 months after RF treatment. At each evaluation, the patient was asked to assess pain intensity using a 10-cm visual analogue scale (VAS), in which 0 cm represented no pain and 10 cm the worst imaginable pain and to assess her quality of life (QOL) using the SF-36 (Japanese version) (12). The patient was also asked about side effects of the treatment, such as increase in pain, sensory impairment, pneumothorax, and infection.

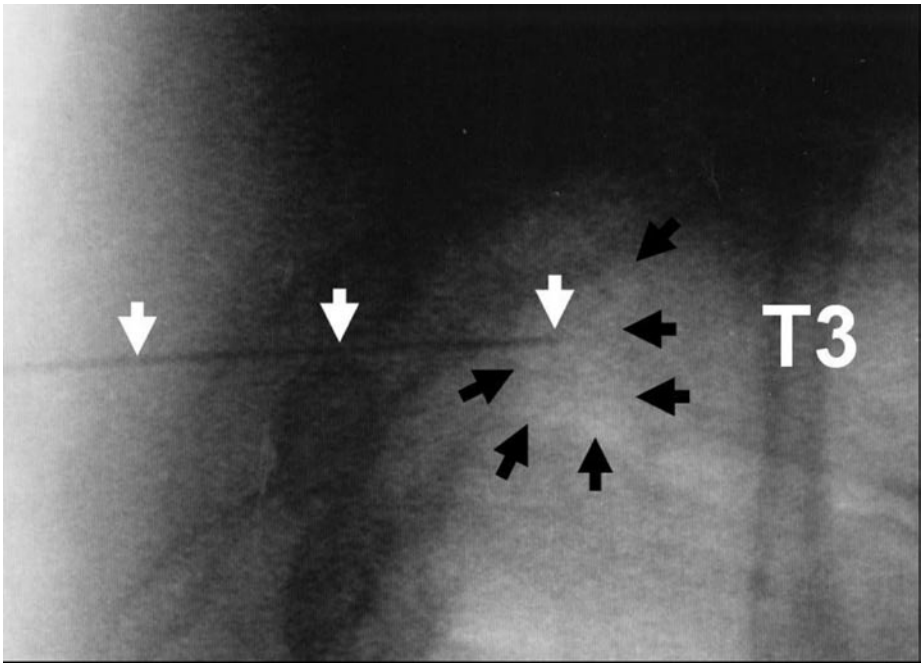

Fig. 1. *Fluoroscopic image of the lateral view before contrast dye was injected, which was obtained during RF-TPN treatment at T3 in Patient 1. The white arrows indicate the electrode. The black arrows indicate the margin of the intervertebral foramen.*

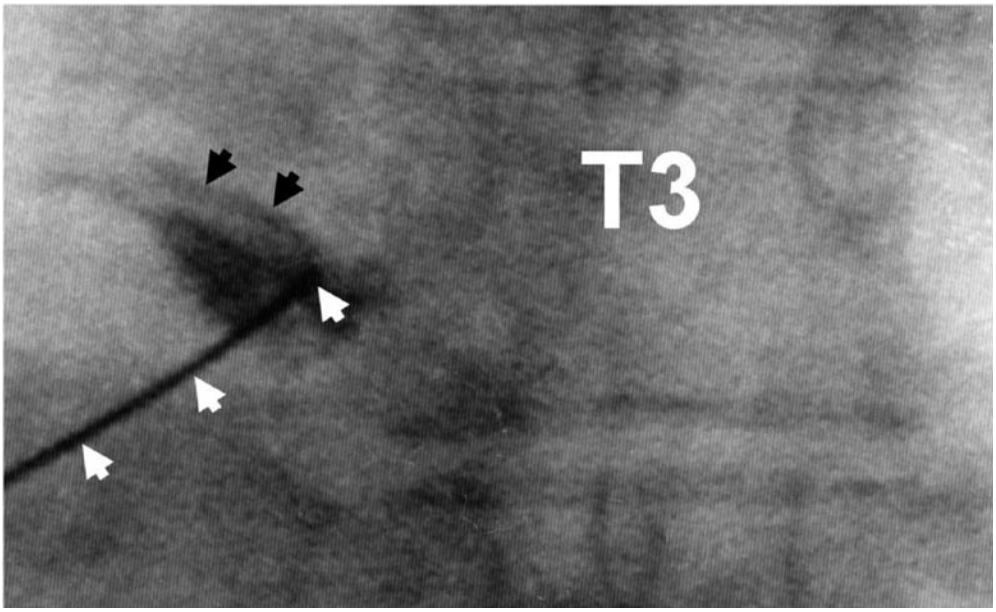

Fig. 2. *Fluoroscopic image of the antero-posterior view after contrast dye was injected, which was obtained during RF-TPN treatment at T3 in Patient 1. The white arrows indicate the electrode. The black arrows indicate the third intercostal nerve.*

Case Reports

Patient 1

The 56-year-old woman underwent a modified radical mastectomy for left breast cancer. Persistent pain intensity was 6.8 cm on the VAS, and was exacerbated by movement. Painful areas included the axilla, medial upper arm, and anterior chest wall. Six months after surgery, left back pain developed. She experienced phantom breast sensation that lasted several weeks after the surgery but it was not accompanied by phantom breast pain. There was hypoesthesia (7-8/10) of the affected area.

Previous interventional treatments, in addition to the pain control measures noted above, consisted of pulsed RF (PRF) treatment (8) of the thoracic paravertebral nerve (PRF-TPN) combined with glucocorticoids at levels T2 and T4. However, the duration of pain relief was only about 2 weeks. Thereafter, we administered RF-TPN at T4 with glucocorticoid as described above. Immediately after the treatment, pain at the intercostal nerve area at T4 disappeared but returned after more than 2 months. RF-TPN treatment with glucocorticoid was administered a total of 8 times at T2 (one time), T3 (4 times), and T4 (3 times), over a period of 4 years.

After RF-TPN treatment was applied at the T3 and T4 levels, pain recurred after the RF treatment, with intervals of recurrence at the identical level ranging from 6 months to 2 years. At follow-up 11 months after the last treatment, pain intensity was reduced (VAS: 2.5 cm). The QOL as evaluated by the SF-36 indicated improvement except for general health and emotional role restriction as shown in Table 1. Hypoesthesia worsened after RF treatment (1–5/10).

Patient 2

The 74-year-old woman underwent a modified radical mastectomy for right breast cancer. Persistent pain intensity was 6.9 cm on the VAS. Movement exacerbated the pain. Painful areas included the axilla, medial upper arm, and anterior chest wall. Three months after surgery, right back pain developed. There was hypoesthesia (1–8/10) of the affected area.

RF-TPN treatment with glucocorticoid was administered as described above a total of 5 times at the T2 (2 times), T3 (2 times), and T4 (one time) levels over a period of 2 years. At the T2 and T3 levels, pain recurred after RF treatment. The interval of recurrence at T2 and T3 was 12 months and 14 months, respectively.

At follow-up 18 months after the last treatment, the persistent pain had changed to intermittent pain and the pain intensity was reduced (VAS: 2.0 cm). The QOL as evaluated by the SF-36 indicated improvement with the exception of vitality (Table 1). Hypoesthesia worsened after RF treatment (1–4/10).

Patient 3

The 54-year-old woman underwent a modified radical mastectomy for right breast cancer. Persistent pain intensity was 5.7 cm on the VAS, and was exacerbated by movement. She experienced phantom breast sensation that lasted for several weeks after the surgery but did not have phantom breast pain. Painful areas included the axilla, medial upper arm, and anterior chest wall. Right back pain began 2 months after surgery. There was hypoesthesia (1–5/10) of the affected area.

RF-TPN treatment with glucocorticoid was carried out as described above a total of 8 times at T2 (2 times), T3 (one time), T4 (one time), T5 (one time), and T6 (3 times) over a period of about 4 years. At the T2 and T6 levels, pain recurred after RF treatment. The interval of recurrence at the identical level ranged from 16 months to 2 years. At follow-up 6 months after the last RF treatment, pain intensity was reduced (VAS: 2.3 cm). The QOL as evaluated by the SF-36 indicated a trend towards improvement except for general health and social functioning as shown in Table 1. Hypoesthesia worsened slightly after RF treatment (1–3/10).

In all cases, the pain at the relevant treated dermatome was always reduced in comparison with previous intensity more than 2 months after each RF treatment.

Therefore, we repeated procedures in order to provide sufficient pain reduction. Anesthesia dolorosa and the other side effects of RF treatment described above were not seen.

Discussion

Neuropathic pain can occur following any surgical procedure on the breast (e.g., lumpectomy, modified radical mastectomy, radical mastectomy) (3). The exact mechanism that produces the pain is unclear, but it is thought to occur through injury during surgery to various types of peripheral nerves (1).

The nerves that may be damaged during breast cancer surgery are mainly supplied through branches of the intercostal nerves (T1-T6) (1).

Table 1. Quality of life as measured by the SF-36 (Japanese version) before and after the RF treatments. RF-TPN with glucocorticoid was administered a total of 8 times in Patient 1, 5 times in Patient 2, and 8 times in Patient 3.

	Patient 1		Patient 2		Patient 3	
	Before	**After**	**Before**	**After**	**Before**	**After**
Physical Functioning	48.1	55.1	12.9	23.4	16.4	23.4
Physical Role Restriction	29.0	52.8	25.6	35.8	15.3	29.0
Bodily Pain	21.6	39.7	30.9	35.3	17.2	35.3
General Health	62.4	62.4	37.0	39.7	34.3	34.3
Vitality	50.2	62.5	44.1	44.1	37.9	44.1
Social Functioning	43.9	57.1	30.8	43.9	24.2	24.2
Emotional Role Restriction	52.3	52.3	35.3	39.6	26.8	31.1
Mental Health	41.1	54.4	38.5	46.5	41.1	49.1

We used RF-TPN treatment to reduce noxious input through the afferent fiber system (13). Stolker et al (14) treated patients with chronic thoracic segmental pain including patients with postmastectomy syndrome by RF of the dorsal root ganglion (RF-DRG) at 67°C for a duration of 90 seconds and reported long-term pain relief. We administered RF-TPN instead of RF-DRG, because we supposed that RF-DRG was a more invasive procedure that requires a Kirschner wire to approach the DRG (14). Cohen et al (15) compared pulsed RF of the intercostal nerves and pulsed RF of the DRG, but did not require a Kirschner wire to approach the thoracic DRG. Approach to the thoracic DRG without a Kirschner wire and even that with a curved-electrode, carry the additional risks of pneumothorax and other visceral, vascular, and neural injuries (16).

Moreover, it has been reported that transforaminal injection has a potential risk of serious neurologic complications such as brain and spinal cord infarction and death (17-20). The leading hypothesis for the mechanism of these complications is unintentional intra-arterial injection of particulate glucocorticoids or contrast medium. In addition, needle-induced vasospasm has been considered (20).

Regarding this point, we thought that there would be a smaller possibility of injury to the radicular artery by RF-TPN than by RF-DRG because of its anatomical distance (20). Moreover, in order to minimize the risk of this complication, we confirmed that the needle was in the correct position by paying close attention with real-time fluoroscopy before injection through the needle as recommended by Lee et al (19).

We used Rinderon® (Shionogi, Japan) as the betamethasone. This drug is water-soluble and does not contain benzyl alcohol, which is neurotoxic and added as a preservative to many corticosteroid preparations (18).

The mode of action of RF treatment has not yet been elucidated. Two hypotheses have been proposed to date (7). One hypothesis is that RF application causes thermocoagulation of nerve fibers that denatures the nerves to interrupt noxious input. The second hypothesis is that the electric field has a neuromodulatory effect on pain-processing mechanisms. It is proposed that conventional RF works primarily by coagulation (though an electric field is generated) and PRF may works via the generation of an electric field (8). As to thermocoagulation, RF treatment for the management of nonmalignant pain is becoming more controversial because of its potential neurodestructive nature that can induce motor deficits, neuritis, and deafferentation pain (4-7,21). However, thermocoagulation by RF treatment is paradoxical in its mode of action. It is believed that the therapeutic effect of RF is achieved by a partial nerve lesion

produced in the nerve (8). On the other hand, while minor nerve injury sometimes produces devastating pain, modest or diffuse deafferentation does not (22). The cause of this effect has not been elucidated. In a clinical study, it was suggested that even long-standing central sensitization can be reversed quickly when the peripheral input is removed (23). RF treatment can reduce the peripheral input and may have the potential to reduce pain.

In our cases, although the hypoesthesia did progress, anesthesia dolorosa was not seen in spite of administration of high temperature and repeated treatments. Regarding motor deficits, RF treatment to thoracic segmental nerves except for T1 which was presented in our paper, has an advantage over that to the cervical or lumbar area, because there is no risk of damaging motor function to the limbs.

As to the second proposed mode of action of RF treatment, Sluijter et al (24) proposed a new technique employing RF, referred to as PRF, which delivers intermittent burst currents of 500 kHz in order to act mainly with the electric field in spite of thermocoagulation. However, there is no available clinical evidence that PRF is more effective than RF in alleviating pain from the thoracic segmental nerves. Before RF treatment, Patient 1 had been given PRF-TPN combined with glucocorticoid at 2 different sites. However, the duration of pain relief was only a few weeks. In contrast, the duration of pain relief was longer with RF treatment. The reason for this difference in response is unclear. This result led us to conjecture that thermocoagulation might be more effective than application of an electric field for alleviating neuropathic pain following breast cancer surgery.

Although the use of glucocorticoids in nerve blocks is controversial, nerve block treatment for neuropathic pain usually consists of a local anesthetic and glucocorticoids (16,25). Pro-inflammatory cytokines secreted at or near the site of a nerve injury are involved in the development and maintenance of central sensitization and neuropathic pain (9). The lesions produced by RF energy are well-demarcated areas of coagulative necrosis surrounded by inflammatory cell infiltrate and hemorrhage. This inflammatory response can lead to increased tenderness, pain, and limitation of movement after RF treatment (26). Glucocorticoids are known to suppress pro-inflammatory cytokines (such as TNFα and IL-1β) and induce expression of anti-inflammatory cytokines (such as IL-10). Moreover, regarding glucocorticoid use in humans, there is already convincing evidence of acute analgesic and antihyperalgesic effects of glucocorticoids after surgery and experimental injuries (9). Therefore, we administered the glucocorticoid with RF-TPN to provide an additive effect to RF treatment. Although the extent of the chemical change in betamethasone by the heat is unclear, we administered betamethasone before RF treatment because we were afraid that diffusion of betamethasone would be disturbed by the thermocoagulated tissue after RF treatment.

In previous reports of thoracic or cervical RF-DRG, transient neuritis and/or burning pain in the treated spinal nerve was noted (14,27,28). However, our 3 patients experienced no transient burning pain after 21 procedures of RF-TPN despite the high temperature and repeated procedures. Dobrogowski et al (26) described that RF treatment with methylprednisolone to the lumbar medial branch tended to reduce the frequency of postoperative pain. Although the site and extent of treatment were different, and the degree of the effect of glucocorticoid remains unclear, these results suggest that it may be possible for glucocorticoids to have the potential to avert the pain related to neuro-injury after RF lesioning.

However, the possibility that RF treatment for neuropathic pain may worsen the pain remains. Therefore, we feel that the practitioners should select patients who are eligible for RF treatment with strict inclusion criteria, and provide adequate explanations and have discussions with the patients before the procedure.

Conclusion

Repeated administration of RF-TPN combined with glucocorticoid reduced pain and improved the quality of life of patients with refractory neuropathic pain following breast cancer surgery in the 3 cases. There were no significant side effects except for worsened hypoesthesia.

We feel that RF-TPN combined with glucocorticoid deserves further study. As after further study, it may represent a viable therapeutic option for patients with refractory neuropathic pain following breast cancer surgery in whom conservative treatments have failed.

References

1. Jung BF, Ahrendt GM, Oaklander AL, Dworkin RH. Neuropathic pain following breast cancer surgery: Proposed classification and research update. *Pain* 2003; 104:1-13.
2. Tasmuth T, von Smitten K, Hietanen P, Kataja M, Kalso E. Pain and other symptoms after different treatment modalities of breast cancer. *Ann Oncol* 1995; 6:453-459.
3. Stevens PE, Dibble SL, Miaskowski C. Prevalence, characteristics, and impact of postmastectomy pain syndrome: An investigation of women's experiences. *Pain* 1995; 61:61-68.
4. Uematsu S, Udvarhelyi GB, Benson DW, Siebens AA. Percutaneous radiofrequency rhizotomy. *Surg Neurol* 1974; 2:319-325.
5. Smith HP, McWhorter JM, Challa VR. Radiofrequency neurolysis in a clinical model: Neuropathological correlation. *J Neurosurg* 1981; 55:246-253.
6. De Louw AJ, Vles HS, Freling G, Herpers MJ, Arends JW, Kleef M. The morphological effects of a radiofrequency lesion adjacent to the dorsal root ganglion (RF-DRG)—An experimental study in the goat. *Eur J Pain* 2001; 5:169-174.
7. Racz GB, Ruiz-Lopez R. Radiofrequency procedures. *Pain Pract* 2006; 6:46-50.
8. Bogduk N. Pulsed radiofrequency. *Pain Med* 2006; 7:396-407.
9. Romundstad L, Stubhaug A. Glucocorticoids for acute and persistent postoperative neuropathic pain: What is the evidence? *Anesthesiology* 2007; 107:371-373.
10. Waldman SD. Thoracic Paravertebral Nerve Block. In: *Atlas of Interventional Pain Management. Second edition*. Saunders, Philadelphia, 2004: pp 227-229.
11. Buijs EJ, van Wijk RM, Geurts JW, Weeseman RR, Stolker RJ, Groen GG. Radiofrequency lumbar facet denervation: A comparative study of the reproducibility of lesion size after 2 current radiofrequency techniques. *Reg Anesth Pain Med* 2004; 29:400-407.
12. Fukuhara S, Bito S, Green J, Hisao A, Kurokawa K. Translation, adaptation, and validation of the SF-36 Health Survey for use in Japan. *Journal of Clinical Epidemiology* 1998; 51:1037-1044.
13. Geurts JW, van Wijk RM, Stolker RJ, Groen GJ. Efficacy of radiofrequency procedures for the treatment of spinal pain: A systematic review of randomized clinical trials. *Reg Anesth Pain Med* 2001; 26:389-393.
14. Stolker RJ, Vervest AC, Groen GJ. The treatment of chronic thoracic segmental pain by radiofrequency percutaneous partial rhizotomy. *J Neurosurg* 1994; 80:986-992.
15. Cohen SP, Sireci A, Wu CL, Larkin TM, Williams KA, Hurley RW. Pulsed radiofrequency of the dorsal root ganglia is superior to pharmacotherapy or pulsed radiofrequency of the intercostal nerves in the treatment of chronic postsurgical thoracic pain. *Pain Physician* 2006; 9:227-235.
16. Waldman SD. *Interventional Pain Management, Second edition*. Saunders, Philadelphia, 2001
17. Rathmell JP, Benzon HT. Transforaminal injection of steroids: Should we continue? *Reg Anesth Pain Med* 2004; 29:397-399.
18. Tiso RL, Cutler T, Catania JA, Whalen K. Adverse central nervous system sequelae after selective transforaminal block: the role of corticosteroids. *Spine J* 2004; 4:468-474.
19. Lee JH, Lee JK, Seo BR, Moon SJ, Kim JH, Kim SH. Spinal cord injury produced by direct damage during cervical transforaminal epidural injection. *Reg Anesth Pain Med* 2008; 33:377-379.
20. Neal JM. Anatomy and pathophysiology of spinal cord injury associated with regional anesthesia and pain medicine. *Reg Anesth Pain Med* 2008; 33:423-434.
21. Sluijter ME. *Radiofrequency, Part I*. Flivopress, Switzerland, 2001.
22. Devor M. Peripheral nerve generators of neuropathic pain. In: J. Campbell, A. Dray, R. Dubner, R. Dworkin, C. Sang (eds). *Emerging Strategies For The Treatment Of Neuropathic Pain*. IASP Press, Seattle, 2006; pp 57-58.
23. Gracely RH, Lynch SA, Bennett GJ. Painful neuropathy: Altered central processing maintained dynamically by peripheral input. *Pain* 1992; 51:175-194.
24. Sluijter M, Cosman E, Rittman W, Van Kleef M. The effects of pulsed radiofrequency fields applied to the dorsal root ganglion – a preliminary report. *Pain Clin* 1998; 11:109-117.
25. Barsley L. Steroid injections: Effect on pain of spinal origin. *Best Pract Res Clin Anaesthesiol* 2002; 16:579-596.
26. Dobrogowski J, Wrzosek A, Wordiczek J. Radiofrequency denervation with or without addition of pentoxifylline or methylprednisolone for chronic lumbar zygapophysial joint pain. *Pharmacol Rep* 2005; 57:475-480.
27. van Kleef M, Barendse GA, Dingemans WA, Wingen C, Lousberg R, de Lange S, Sluijter ME. Effects of producing a radiofrequency lesion adjacent to the dorsal root ganglion in patients with thoracic segmental pain. *Clin J Pain* 1995; 11:325-332.
28. van Boxem K, van Eerd M, Brinkhuize T, Patijn J, van Kleef M, van Zundert J. Radiofrequency and pulsed radiofrequency treatment of chronic pain syndromes: The available evidence. *Pain Pract* 2008; 8:385-393.