



Original Article

A pilot study comparing the efficacy of radiofrequency and microwave diathermy in combination with intra-articular injection of hyaluronic acid in knee osteoarthritis

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Abstract. [Purpose] This study aimed to compare the efficacy of radiofrequency diathermy with that of microwave diathermy in combination with intra-articular injection of hyaluronic acid into the knee of patients with osteoarthritis (OA). [Subjects] A total of 17 patients with knee OA were enrolled. The participants were randomly divided into two groups: a radiofrequency diathermy group (RF group, 9 subjects), and a microwave diathermy group (MW group, 8 subjects). [Methods] Subjects received radiofrequency or microwave thermal therapy 3 times at 1-week intervals. Intra-articular injection of hyaluronic acid was administered 10 min before every thermal therapy session. The outcome was evaluated using the Japan Orthopaedic Association (JOA) and the Lequesne Index (LI) at baseline, at weeks 1 (1 week after the first thermal therapy) and 3 (1 week after the last thermal therapy). [Results] The JOA scale increased significantly after three sessions of thermal therapy in the RF group, while no significant increase was observed in the MW group. LI decreased significantly after 3 weeks in the RF group. In the MW group, there was no significant difference in LI between the two time points. [Conclusion] This study revealed that symptom relief in patients with knee OA was greater with radiofrequency diathermy than with microwave diathermy with concurrent use of hyaluronic acid injection, presumably due to the different heating characteristics of the two methods.

Key words: Osteoarthritis, Knee, Diathermy

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INTRODUCTION

Osteoarthritis (OA) of the knee is the joint disease that is most commonly encountered in clinical practice. Because the articular cartilage is difficult to regenerate, artificial knee replacement is often performed for patients who have end-stage knee OA, and thus have relatively severe symptoms such as pain, instability and limited range of motion. However, to reduce the economic burden on the healthcare system and on patients, it would be desirable to establish conservative therapy that

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can alleviate symptoms and prevent progression to the end-stage disease. Medication, therapeutic exercise, treatments with physical agents or orthosis are conservative therapies for knee OA, and the use of thermal therapy alone as physical therapy or in combination with exercise is recommended in many guidelines for the management of knee OA.

Thermal therapy is categorized into two groups: one has a superficial thermal effect, and it includes hot packs, paraffin baths, or heat generating sheet¹⁾, and the second has deep thermal effects induced by electromagnetic waves or ultrasound²⁾. Superficial thermal therapy, when performed for a short period of time, increases the temperature of only the cutaneous and subcutaneous layers, not inside the joints³⁾. In contrast, the thermal effect of diathermy generated by electromagnetic waves or ultrasound reaches the deep layers, and the penetration depth varies with the heating method, frequency and power output⁴⁾. In our previous study, the knee of patients with OA was contact-heated using a bipolar radiofrequency applicator, which generates electromagnetic waves with frequencies up to tens of megahertz, and observed a marked improvement in the patients' symptoms and function⁵⁾. The purpose of this study was to show the superior clinical effects of radiofrequency diathermy with a bipolar applicator for knee OA over microwave which is widely used in outpatient physical medicine and rehabilitation clinics as a deep thermal modality.

SUBJECTS AND METHODS

Approval for this study was obtained from the Institutional Review Board of Nippon Medical School and subjects provided their written informed consent to participation. The purpose and method, as well as the risk of side effects, such as burns and their countermeasures, and the method of protecting personal information were explained to the subjects, and written informed consent was obtained from them. One of the authors became a subject for temperature measurement inside the joint.

This study was designed as a prospective randomized clinical trial. A total of 17 patients aged 49–88 (mean: 69.1±11.0) years with OA of the medial femorotibial compartment of the knee and no other inflammatory disease, who visited either of two clinics (Hara Orthopaedic Hospital, Minami-Shinjuku Orthopaedic Rehabilitation Clinic) from August 2013 to November 2013, were selected as subjects according to the clinical and radiographic criteria of the American College of Rheumatology as well as standard exclusion criteria⁶⁾. The participants were randomly divided into two groups using computer-generated random numbers: a radiofrequency diathermy group (RF group, 9 subjects) and a microwave diathermy group (MW group, 8 subjects). One of the authors participated as a subject for the measurement of intra-articular temperature. Standard standing anteroposterior radiographs of the knee were obtained of all subjects. Two orthopedic surgeons who had more than 20 years of experience each in analyzing knee radiographs graded the images according to Kellgren-Lawrence (KL) grade⁷⁾.

Knee pain had not improved in any of the subjects, despite the administration of anti-inflammatory drugs or intra-articular injection of hyaluronic acid for 3 months. Thermal therapy using diathermy was started more than 1 month after the last intra-articular injection of hyaluronic acid or corticosteroid. Subjects in the RF group received thermal therapy using a radiofrequency of 8 MHz and 200 W for 20 min 3 times at 1-week intervals. Thermal therapy was performed using Thermotron-RF8 (Yamamoto Vinita, Co, Ltd, Osaka, Japan), which can emit a radiofrequency of 8 MHz. The subject was placed in the lateral position with the knee placed downside, and it was then tightly sandwiched by applicators at the center of the femoral internal and external condyles. The temperature of circulating water in the applicator was maintained at 25 °C so that cooling of the skin was achieved. In the MW group, a Microradar KTM-250 (Ito Co., Ltd., Tokyo, Japan), which can emit microwaves at a frequency of 2.45 GHz was used for thermal therapy. The Microradar probe (circular, 150 mm diameter) was placed approximately 10 cm in front of the patella, and applied (100 W) for 10 min while the subjects sat in a chair with their knees flexed at 90°. Diathermy was performed 3 times at 1-week intervals. After sterilizing the normal left knee of a healthy subject (one of the authors) with iodine, a sterilized thermocouple was inserted from the lateral side, between the patella and femur, to measure the temperature changes inside the knee joint caused by diathermy. Intra-articular injection of hyaluronic acid (Artz, Kaken Pharmaceutical Co., Ltd., Tokyo, Japan) was administered 10 min before every thermal therapy session.

The outcome was evaluated using the Lequesne Index (LI)⁸⁾ and the Japan Orthopaedic Association (JOA) scale⁹⁾. For a comparison of trial periods, the variables of LI and JOA scale were measured at baseline, at weeks 1 (1 week after the first thermal therapy) and 3 (1 week after the last thermal therapy). Repeated measures analysis of variance (ANOVA) was conducted and Tukey's post hoc test was performed when a significant difference between the trial periods was found.

RESULTS

The baseline characteristics of the two treatment groups are shown in Table 1. According to the KL grade, 78% of patients in the RF group and 86% of those in the MW group were KL grade II. At baseline, participants in the two groups did not differ in age or KL grade. Sixteen patients (9 in the RF group, 7 in the MW group) completed the study. One patient in the MW group could not attend all the sessions because of lack of time.

The JOA scale had significantly increased after three sessions of thermal therapy ($p = 0.013$) in the RF group. In the MW group, no significant difference was observed in the JOA scale between any of the time points (Table 2). LI had significantly decreased after 3 weeks ($p = 0.016$) in the RF group. In the MW group, no significant difference was observed in LI among the time points (Table 3).

When irradiated from the front by the microwave applicator that was placed 10 cm away, the temperature inside the

Table 1. Baseline characteristics of the groups

	Radiofrequency group (RF group)	Microwave group (MW group)
Number of patients	9	7
Gender (male/female)	1/8	1/6
Age (years, mean±SD)	71.8±10.7	65.6±11.2
Kellgren-Lawrence grade (KL grade)	I: 1, II: 6, III: 2	I: 1, II: 4, III: 2

Table 2. Temporal change in Japan Orthopaedic Association (JOA) scale scores

	Radiofrequency group* (RF group)	Microwave group (MW group)
Base line	78.3±11.7	75.7±8.38
1 week	81.3±13.9	75.0±7.07
3 week	87.8±9.73	77.9±3.93

Mean JOA scores±SD

Statistical analysis was performed with one-way analysis of variance (ANOVA).

*p<0.05

Table 3. Improvement of the Lequesne index (LI)

	Radiofrequency group* (RF group)	Microwave group (MW group)
Base line	7.00±2.29	7.14±2.12
1 week	5.33±2.23	7.14±1.77
3 week	3.56±2.46	6.86±1.21

Mean LI±SD

Statistical analysis was performed with one-way analysis of variance (ANOVA).

*p<0.05

Table 4. Change in intra-articular temperature of the suprapatellar pouch due to irradiation of radiofrequency and microwave for 10 minutes

	Baseline	3 minute	6 minute	10 minute
RF	34.4	35.2	36.1	37.1
MW-front	33.5	37.2	40.3	42.3
MW-back	33.7	33.7	33.6	33.5

Temperatures are shown in Centigrade.

RF: The Thermotron-RF8 applicator was placed in the middle of the internal and external condyle of the femurs, MW-front: The probe of the Microradar was placed approximately 10 cm in front of the patella, MW-back: The probe was placed approximately 10 cm from popliteal skin surface

suprapatellar pouch increased sharply, and this caused a strong heat sensation in the skin. When irradiated from the backside, however, the temperature inside the suprapatellar pouch did not change. On the other hand the temperature inside the joint was gradually increased by contact-heat of radiofrequency, and there was no heat sensation (Table 4).

DISCUSSION

This study revealed that symptom relief in patients with knee OA was greater with radiofrequency diathermy than with microwave diathermy, presumably due to the different heating characteristics of the two methods. To reveal changes in intra-articular temperature, we previously used the finite element method (FEM) to create simulation models of microwave and radiofrequency diathermy¹⁰. Based on the simulation, the no-contact monopolar applicator used in microwave diathermy increases the temperature of the skin near the applicator to 37.5 °C to a depth of several centimeters from the surface, but the temperature of a large part of the joint cavity is not increased. A previous FEM simulation study also showed that when the

knee is contact-heated by the bipolar radiofrequency applicator, the temperature of the entire joint cavity gradually increases to approximately 38 °C. These simulated results are consistent with our present findings of chronological change in intra-articular temperature after diathermy. The output and application length of the RF and MW groups were different because the larger output and longer irradiation by microwaves causes a strong heat sensation and carries the risk of burn in the skin.

In this study, intra-articular injections of hyaluronic acid were performed just before thermal therapy. Hyaluronic acid was administered because microwave diathermy alone is not effective, causing many patients to drop out of therapy in our preliminary study. In contrast, heat treatment of knee OA with a bipolar radiofrequency applicator alone was effective in a previous study, and no synergistic effect was observed even though hyaluronic acid was injected into the joint in that study⁵).

OA pain is multifactorial. Not only are there multiple potential structures within a joint that are the sources of peripheral nociceptive signals, but there may be central pain sensitization in OA. While there is undoubtedly cartilage damage from the earliest stages of OA, it is unclear why this results in pain, as healthy cartilage is aneural. Although it is not clear how thermal therapy alleviates pain in knee OA, two mechanisms have been proposed: the first mechanism involves heat-induced denervation of nerve terminals in the skin of the knee joint. It has been reported that sensory nerve invasion containing substance P and calcitonin gene-related peptide occurs in tibial osteophytes in human OA patients¹¹). Hypersensitivity of nociceptive nerve terminals to pressure stimulation was seen in the medial femorotibial joint. Percutaneous radiofrequency treatment has been reported to be a beneficial local denervation therapy for knee OA¹²). In the peripheral nerve fibers, the elevation of the superficial skin temperature is accompanied by an increase in the nerve conduction velocity with a concomitant decrease in sensory latency¹³). Although its clinical significance needs to be elucidated, nerve conduction velocity increases by approximately 2 m/s as the temperature increases by 1 °C, and this is thought to be related to nerve denervation or an increase in the pain threshold. In the present study, microwave diathermy hardly provided any pain alleviation because the procedure increased temperature effectively in only the superficial layers near the applicator, but not in the nerve fibers in the vicinity of the medial osteophyte. According to Izumi et al., pain alleviation was rapid and long lasting when magnetic resonance imaging-guided ultrasound was used to heat the medial tibial osteophytes¹⁴).

The second mechanism involves denervation of the peripheral nerve terminals in the subchondral bone. It has been suggested that blood vessels and sensory nerve fibers grow into damaged OA cartilage by crossing the osteochondral junction¹⁵). The subchondral bone in the weight bearing area with cartilage degeneration above cannot be heated by microwave diathermy. On the other hand, based on the knee heating simulation, the bipolar radiofrequency applicator is able to heat a wide area of the subchondral bone, ranging from the femur to tibia¹⁰). It is possible that heating of the nerve terminals, by the bipolar radiofrequency applicator, in the subchondral bone contributes to marked alleviation of pain in knee OA.

We are currently investigating the long-term efficacy of heating in knee OA with an emphasis on basic research into the response of articular cartilage to heating when no mechanical stress is present. Hojo et al. reported that proteoglycan metabolism in cultured chondrocytes was upregulated when heated to 39 °C and 41 °C, but was downregulated at 43 °C¹⁶). Proteoglycan genes are also upregulated at 40 °C in humans, in a process which involves the accumulation of the stress protein, heat shock protein 70 (HSP70), in chondrocytes. In white rabbits, the gene expression of proteoglycan and type II collagen in the articular cartilage was strongly upregulated when the knee joint was heated to approximately 40 °C using a medical 2.45-GHz microwave irradiator¹⁷). Also in rats, the expression of proteoglycan was upregulated when the knee joint was heated to approximately 40 °C by microwave irradiation¹⁸). Furthermore, thermal therapy by ultrasound induces chondrogenesis in rats through the overexpression of HSP70¹⁹). As shown in these studies using small animals, the metabolic process in the cartilage matrix is activated partly through the expression of HSP70 when the knee joint is heated to 40 °C. In addition, the progression of OA was suppressed when the knee joint was heated in the rat¹⁸) and guinea pig (manuscript in preparation) model of OA. These findings strongly suggest that bipolar radiofrequency applicators protect cartilage.

There were three limitations to this study. First, we did not perform long-term follow-up. The second limitation was the small sample number. We plan to perform radiofrequency diathermy for a large number of patients to investigate the long-term and radiological treatment efficacy of heat therapy for knee OA. The third limitation was the size of the radiofrequency apparatus. Development of smaller apparatus convenient for the usual clinical usage is expected.

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