The Effects of a Topical Analgesic and Placebo in Treatment of Chronic Knee Pain

J. William Myrer, J. Brent Feland, and Gilbert W. Fellingham

Chronic knee pain is a prevalent health problem of old and middle age. The authors’ objective was to determine whether a topical analgesic would reduce knee pain and improve the function of a group of 40- to 65-year-old people with chronic knee pain. The experimental design was a double-blind, randomized, placebo-controlled clinical trial. The dependent variables were knee pain, active range of motion, and isometric strength. Forty-six men and women volunteered, of whom 3 dropped out, leaving 23 in the treatment group and 20 in the placebo group. Knee pain was assessed with a visual analogue scale and the knee-pain scale for frequency and severity. Testing took place before treatment and after 21 and 35 days of treatment. The results indicated that although both groups experienced improved pain scores, there were no differences between groups over the treatment period for any of the dependent variables.

Key Words: osteoarthritis, menthol, aging

In the United States, people over the age of 65 are the fastest growing segment of the population (Longino & Murphy, 1995). Census data indicate that, between 1990 and 2010, the number of people older than 45 years will increase by more than 40 million, from 82 million to 124 million (U.S. Bureau of the Census, 1989). Musculoskeletal impairments are among the most prevalent and symptomatic health problems of middle and old age (Buckwalter et al., 1993). As our population grows older, there will likely be a concomitant increase in the volume of disorders associated with aging. Currently, arthritis is classified as the leading cause of activity limitation among Americans and is the most prevalent chronic disease in the United States (Rimmer, Braddock, & Pitetti, 1996). It is estimated that 38 million Americans have the condition, the majority of whom are elderly (Centers for Disease Control, 1994).

Osteoarthritis (OA) is the most prevalent musculoskeletal condition that results in joint pain, and 70% of the U.S. population more than 65 years of age demonstrate radiographic evidence of this disease (Lane & Thompson, 1997). The knee joint is commonly affected. In the United States, OA of the knee has an estimated radiographic prevalence of 3.8 per 100 adults age 25–74 years (Lawrence et al., 1989). Incidence increases progressively after age 40. Before 55 years of age...
it affects more men than women; after 55 the disease is more common in women (Altman, 1990; Towheed & Hochberg, 1997). Pain is recognized as a key symptom in the decision to seek professional medical care, and the pain associated with progressive degenerative diseases such as OA of the knee has been shown to be an important antecedent to disability (Altman; Davis, Ettinger, Neuhaus, Barclay, & Segal, 1992; McAlindon, Cooper, Kirwan, & Dieppe 1992).

Therapy for OA of the knee is directed at decreasing joint pain and increasing function. Both pharmacologic and nonpharmacologic interventions are used. Nonpharmacologic therapy includes patient education, low-impact aerobic exercise, weight loss, and occupational therapy. Pharmacologic therapy usually begins with analgesic medications. The “drug of choice” is acetaminophen, then proceeding to oral non-steroidal anti-inflammatory drugs (NSAIDs) and topical analgesics as needed (Hochberg et al., 1995; Jones & Doherty, 1992; Lane & Thompson, 1997; Towheed & Hochberg, 1997).

A 1987 survey conducted by Simmons Market Research Bureau Inc. in New York determined that 34% of adults in the United States used topical analgesics. The reasons most frequently cited for use were backache, sore muscles, and pain resulting from arthritis or from sports and exercise participation (Barone, 1989). Most topical analgesics can be categorized as counterirritants, agents applied topically that irritate the skin to provide pain relief to underlying tissues such as muscle, ligament, and viscera (Hong & Shellock, 1991). The exact mechanism of counterirritant pain relief is not as yet completely understood. When applied to the skin, counterirritants provide the classic “warmth” or “coolness” of a balm. Some of the most common active ingredients found in topical analgesics are menthol, methyl salicylate, camphor, and capsaicin (Barone). These active ingredients are often used in combination with a variety of other inactive ingredients. Many counterirritants can be derived from natural sources, but most of those used today are synthetically produced (Barone).

A new, “100% natural,” topical analgesic recently came on the market. The product, Joint-Ritis® (Naturopathic Labs Intl., Inc., St. Petersburg, FL) uses the active ingredient of menthol at 16%, combined with oils of eucalyptus, copaiba, citrus, and lavender with moisturizers chondroitin sulfate, glucosamine sulfate, and lanolin. Based on the Food and Drug Administration’s tentative final monograph (Department of Health and Human Services, 1983) for over-the-counter (OTC) drugs, this product claims to give temporary relief of joint pain caused by arthritis. To date no clinical studies have been published substantiating Joint-Ritis’s claim.

Our purpose was to determine whether Joint-Ritis would reduce knee pain and improve function in a group of 40- to 65-year-old men and women who were experiencing chronic knee pain, compared with a placebo that did not contain the active ingredient menthol nor the moisturizers chondroitin sulfate or glucosamine sulfate.

**Methods**

**RESEARCH DESIGN**

This investigation was a double-blind, randomized, placebo controlled clinical trial. Our independent variable was experiment group (treatment and placebo). Our
dependent variables were gender, pain, active range of motion (AROM) of the knee, and isometric strength of the knee flexors and extensors. Our primary variable of interest was knee pain.

PARTICIPANTS

Forty-six men and women between 40 and 65 years of age volunteered and were randomly assigned to either the treatment or placebo group. Two participants in the treatment group and 1 in the placebo group were noncompliant to treatment protocol and were thus not used in our statistical analysis. Inclusion criteria were as follows: age 40–65 years, healthy to the degree that participation in the experiment would not exacerbate any existing symptomatology, having a history of knee pain of at least 3 months, currently experiencing knee pain, and having no known sensitivity to menthol. The treatment group consisted of 9 women (age = 56.8 ± 7.1 years, height = 163.0 ± 5.7 cm, weight = 84.6 ± 22.2 kg) and 14 men (age = 56 ± 5.9 years, height = 178.9 ± 6.3 cm, weight = 90.7 ± 15.8 kg). The placebo group consisted of 7 women (age = 56.4 ± 5.6 years, height = 167.9 ± 4.3 cm, weight = 85.4 ± 23.8 kg) and 13 men (age = 49 ± 5.6 years, height = 183.1 ± 7.8 cm, weight = 96.6 ± 19.6 kg). A university human subject’s institutional review board approved the study, and all participants signed an informed-consent form before participating.

The treatment group (n = 23) had the following diagnoses: 11 OA, 3 meniscus injuries, 1 bone spur, and 8 nonspecific knee pain. The duration of their pain ranged from 3 months to 30 years (8.28 ± 7.72 years). The placebo group (n = 20) had the following diagnoses: 7 OA, 3 meniscus injuries, 1 bone spur, 1 recurrent patellar subluxation, 1 traumatic injury, and 7 non-specific knee pain. The duration of their pain ranged from 6 months to 38 years (11.58 ± 12.53 years).

INSTRUMENTATION

Topical Ointments. The treatment group’s ointment was Joint-Ritis, which contained the active ingredient of menthol, combined with essential oils of eucalyptus, copaiba, citrus, and lavender with moisturizers chondroitin sulfate, glucosamine sulfate, and lanolin. This ointment contained 37.5% essential oils, 16% of which was menthol. The placebo group’s ointment contained all the ingredients found in Joint-Ritis except the active ingredient menthol and moisturizers chondroitin sulfate and glucosamine sulfate. The percentage of essential oils was 36%. An independent laboratory (Celsis Laboratory Group, St. Louis, MO) confirmed that the placebo ointment contained no menthol.

Assessment of Knee Pain. A 10-cm visual analogue scale (VAS) was used to assess the “usual pain” that the participants had experienced during the week before each assessment. Previous research has established this scale to be valid, reliable, and responsive to change (Bellamy, Campbell, & Syrotuik, 1999; Price, McGrath, Rafii, & Buchingham, 1983). The VAS seems to be as responsive as or more responsive than more complex methods. In addition, a single rating by asking patients to estimate their pain “on average” over the week has been found to be an accurate measure of “actual average” pain intensity and more accurate than “current” pain (Bolton, 1999). Scores for the VAS were recorded to the nearest 0.1 cm. The knee-pain scale (KPS) was developed specifically to measure pain related
to behaviors of daily living that are problematic for patients with knee pain (Rejeski, et al., 1995). The KPS measures both the frequency and the severity of pain associated with function. The frequency scale is a graduated five-point scale on which 5 is rated as always and 1 is never. Patients score the following six activities: getting in and out of bed, walking a short distance (one block), getting in and out of a chair, walking up a flight of stairs, getting in and out of a car, and walking down a flight of stairs. The severity scale is a six-point scale with no pain being 1 and excruciating pain being scored a 6. The same six activities used in the frequency scale are used in the severity scale. Possible scores for the frequency and severity portions of the scale range from 6 to 30 and 6 to 36, respectively. The higher the score, the more severe or frequent the pain is. This scale has been found to be a valid and reliable instrument.

Assessment of Active Range of Motion of Knee Flexion and Extension. AROM was measured with a standard universal plastic 10-in. two-arm goniometer. Many investigators have demonstrated that goniometry is both reliable and valid (Gajdosik & Bohannon, 1987; Low, 1976; Riddle, Rothstein, & Lamb, 1987).

Assessment of Isometric Strength of the Knee Flexors And Extensors. Isometric strength of the knee flexors and extensors was measured by a handheld dynamometer (Chatillon CSD 200 Dynamometer, Ametek, Inc., Largo, FL). This method provides a valid and reliable measure of knee strength that is cost-effective and portable for both the research and clinic settings. Bohannon (1986) reported excellent test–retest reliability coefficients of the handheld dynamometer at .97 and .98 for 18 extremity muscle groups.

DATA COLLECTION

Volunteers were screened to ensure that they met the inclusion criteria, and then they signed an approved university institutional review board consent form before they became eligible to participate. On Day 1 of the experiment, before receiving any treatment, each participant’s knees were assessed by a physical therapist (JBF). Participants then filled out a personal information sheet outlining their name, age, sex, height, weight, and medical history relative to their knee pain, including what medications they were currently using for pain relief and how long and in which knees they had been experiencing pain. If participants had pain in both knees we only recorded data on the knee they said on the initial assessment was the worst. We asked participants to maintain their current medication level throughout the duration of the study. Next, each participant filled out a VAS indicating the usual pain they experienced over the preceding week. After this they filled out a KPS. An investigator (JBF) next measured each participant’s AROM of knee flexion as described by Norkin and White (1985). Finally, their isometric knee-extension strength was tested at 90°, 45°, and 20° of knee flexion, and their isometric knee-flexion strength was tested at 90° of knee flexion. For all isometric-strength testing, three trials were performed and the mean of the trials was used for our statistical analysis on each of the 3 testing days. Participants were given a 1-min rest between trials.

Participants sat on a Cybex® Eagle leg-extension machine (Medway, MA) and the testing leg was positioned to the appropriate degree of flexion, 90°, 45°, or 20°, by the investigator (JBF). The dynamometer was then placed on the distal anterior tibia for the extension strength tests and on the distal posterior tibia for the
flexion strength test. Participants were then instructed to gradually increase force against the dynamometer until a maximum contraction was reached and to not lift the thigh off the chair. This lasted for approximately 3 s, after which the peak-force value to the nearest 0.1 kg was recorded. Participants were instructed to push as hard as they could without increasing their pain and to quit pushing if their level of pain increased.

Participants were then randomly divided into one of two groups as follows. Fifty 2-oz bottles (labeled on the bottom from 1 to 50 by the manufacturer) were randomly put in a box. Each participant drew from the box (without looking), and the experimenter recorded the number on the bottom of the bottle and gave two additional bottles with the same number to the participant. Neither the experimenters nor the participants knew who had been given the Joint-Ritis or the placebo ointment. The manufacturer provided the coded bottles of topicals, and the experimenters were not given the codes until the time of data analysis. Each participant was therefore given three 2-oz pump-bottle dispensers containing either Joint-Ritis or the placebo. Again, the placebo contained all the ingredients found in Joint-Ritis except the active ingredient of menthol and the moisturizers chondroitin sulfate and glucosamine sulfate.

Participants were instructed to squirt four pumps (approximately 2 cc) of their ointment on each knee in which they currently had pain and to rub it in for 2 min. They repeated this treatment three times a day, once on arising from bed in the morning, again around midday, and finally before they went to bed. They carried out this treatment for 5 weeks, 7 days a week. Participants were given treatment logs to fill out daily, recording their times of treatment applications. Compliance was calculated in percentages. The total possible number of treatment applications was 105 (three per day for 35 days). The total number of applications on each participant’s treatment log was divided by 105 to obtain his or her compliance percentage. If participants failed to administer their treatments for 3 days in a row, they were dropped from the study. Participants were retested in the same manner as the initial tests on Days 21 and 35 of the experiment.

DATA ANALYSIS

Data were analyzed using SAS PROC MIXED, a data-analysis system designed to appropriately account for both between- and within-participant variability. It is important to model the data-covariance structure appropriately because there are measurements on each participant at multiple time points. Because clinical trials are designed to detect changes in a participant’s response to a treatment over time, it is often desirable to model treatment effects as a line emanating from a starting point. The starting point (or intercept) of the line models the participant as he or she begins a treatment regimen. The participant’s change over time (or slope of the line) models the effectiveness (or lack thereof) of the various treatments. We modeled our data using this paradigm, called the linear-growth curve. (For more background, see Littell, Milliken, Stroup, & Wolfinger, 1996.)

Results

Overall, participants were compliant with the treatment protocol. The range of participant compliance for the treatment group was 55.2–100%, with a mean of
87.1%. The range of participant compliance for the placebo group was 63–100%, with a mean of 87%. Gender was not significant for our primary variable of interest, knee pain as measured by the VAS and the KPS, or for passive ROM. Table 1 presents the means and standard deviations of our pain measurements for both groups for the times tested over the 5-week treatment period. Gender was significant for strength, with the men being stronger than the women for all time periods tested. Table 2 presents the means and standard deviations for the strength and ROM measurements for both groups and both genders for the times tested over our 5-week treatment period.

Table 3 summarizes the results of the changes in our dependent variables within each group and gender over the 5-week treatment period. There were significant decreases in all three pain-scale scores in both the treatment (Joint-Ritis) and placebo group over the treatment period, except for the men in the placebo group. All the knee-strength measurements significantly improved in the men’s Joint-Ritis group but not in the women. In the placebo group the men’s knee-extension strength at 20° and flexion strength at 90° significantly improved, but extension strength at 90° and 45° did not. Like the Joint-Ritis group, the women’s knee strength in the placebo group did not significantly improve over the treatment period. Only the women in the Joint-Ritis group experienced a significant increase in their AROM over the treatment period.

Table 4 summarizes the estimated differences in the slopes (rate of change across time) between the treatment (Joint-Ritis) and placebo groups. It is evident that although both groups received the positive benefits of decreased pain over the 5-week treatment period, there were no differences between the two groups in the degree of these benefits. There were also no differences in the slopes of the knee-strength and passive-ROM variables between groups.

**Discussion**

Pain functions as a debilitator, as well as a motivator, to seek treatment. Chronic-pain sufferers are always on the alert to find something to rid themselves of their
Table 2  Strength and Range of Motion Over the Tested Times, $M \pm SD$

<table>
<thead>
<tr>
<th>Variable</th>
<th>Day 0 (Baseline)</th>
<th>Day 21</th>
<th>Day 35</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
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<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
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<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
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<tr>
<td>Joint-Ritis®</td>
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<tr>
<td>ES 90° (kg)</td>
<td>30.9 ± 10.2</td>
<td>17.6 ± 4.8</td>
<td>35.7 ± 9.6</td>
</tr>
<tr>
<td>ES 45° (kg)</td>
<td>32.6 ± 14.3</td>
<td>15.8 ± 6.5</td>
<td>36.0 ± 15.1</td>
</tr>
<tr>
<td>ES 20° (kg)</td>
<td>25.9 ± 10.4</td>
<td>12.6 ± 6.3</td>
<td>28.6 ± 9.8</td>
</tr>
<tr>
<td>FS 90° (kg)</td>
<td>17.0 ± 6.2</td>
<td>10.1 ± 3.0</td>
<td>17.9 ± 6.7</td>
</tr>
<tr>
<td>ROM (deg)</td>
<td>110.4 ± 13.5</td>
<td>106.8 ± 14.3</td>
<td>111.1 ± 15.3</td>
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<tr>
<td>Placebo</td>
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<tr>
<td>ES 90° (kg)</td>
<td>39.1 ± 11.8</td>
<td>20.3 ± 5.2</td>
<td>41.1 ± 8.2</td>
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<tr>
<td>ES 45° (kg)</td>
<td>34.1 ± 10.0</td>
<td>19.5 ± 5.3</td>
<td>37.1 ± 7.0</td>
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<tr>
<td>ES 20° (kg)</td>
<td>27.8 ± 8.3</td>
<td>15.8 ± 4.4</td>
<td>31.0 ± 7.0</td>
</tr>
<tr>
<td>FS 90° (kg)</td>
<td>16.1 ± 5.1</td>
<td>11.4 ± 3.0</td>
<td>20.3 ± 5.3</td>
</tr>
<tr>
<td>ROM (deg)</td>
<td>120.2 ± 10.8</td>
<td>112.1 ± 13.7</td>
<td>120.6 ± 9.4</td>
</tr>
</tbody>
</table>

Note. ES = isometric knee-extension strength; FS = isometric knee-flexion strength; ROM = active knee range of motion.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Joint-Ritis® Placebo</th>
<th>Placebo</th>
<th>Men</th>
<th>Women</th>
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<th>Women</th>
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<td></td>
<td>t</td>
<td>p</td>
<td>t</td>
<td>p</td>
<td>t</td>
<td>p</td>
</tr>
<tr>
<td>VAS (cm)</td>
<td>t(82) = –2.09</td>
<td>.0396</td>
<td>t</td>
<td>p</td>
<td>t</td>
<td>p</td>
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<tr>
<td></td>
<td>(82) = 0.146</td>
<td>3.29</td>
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<tr>
<td>KPS – F</td>
<td>t(82) = –3.17</td>
<td>.0021</td>
<td>t</td>
<td>p</td>
<td>t</td>
<td>p</td>
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<tr>
<td></td>
<td>(82) = –3.95</td>
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<tr>
<td>KPS – S</td>
<td>t(82) = –3.95</td>
<td>.0021</td>
<td>t</td>
<td>p</td>
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<td></td>
<td>(82) = –3.95</td>
<td>0.88</td>
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<tr>
<td>ES 90° (kg)</td>
<td>t(82) = 3.20</td>
<td>.0020</td>
<td>t</td>
<td>p</td>
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<td></td>
<td>(82) = 3.20</td>
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<tr>
<td>ES 45° (kg)</td>
<td>t(82) = 3.20</td>
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<td>FS 90° (kg)</td>
<td>t(82) = 3.20</td>
<td>.0020</td>
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<td></td>
<td>(82) = 3.20</td>
<td>0.14</td>
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</tr>
<tr>
<td>ROM (deg)</td>
<td>t(82) = 2.17</td>
<td>.0129</td>
<td>t</td>
<td>p</td>
<td>t</td>
<td>p</td>
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<tr>
<td></td>
<td>(82) = 2.17</td>
<td>0.85</td>
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</table>

Note. VAS = visual analogue scale; KPS = knee pain scale; F = frequency; S = severity; ES = isometric knee-extension strength; FS = isometric knee-flexion strength; ROM = active knee range of motion.

Maximum score = 30, minimum score = 6.
burden of pain and dysfunction. The treatment of OA is largely symptomatic, and its first and most consistent symptom is pain (Altman, 1990). Therapy for OA of the knee focuses on decreasing pain and restoring joint function. Pharmacologic therapy begins with analgesic and anti-inflammatory medication. Jones and Doherty (1992) commented, “There is little evidence that the current over reliance on [oral] nonsteroidal anti-inflammatory drugs (NSAIDs) is justified” (p. 357). Toxicity to the gastrointestinal, renal, and pulmonary systems and financial cost are the major drawbacks to using oral NSAIDs as a prolonged treatment for OA of the knee (Altman; Jones & Doherty; Lane & Thompson, 1997; Rosenstein, 1999). This has led many to try topical analgesics as a low-cost and systemically safe alternative to their often expensive and sometimes harmful oral medications.

Topical analgesics can generally be divided into two categories, trolamine salicylate creams and counterirritants, although they can be found in combination. Trolamine salicylate creams are generally odorless, whereas counterirritants characteristically have a pungent odor. In addition, whereas counterirritants such as menthol initially produce a cooling sensation followed by warmth, trolamine salicylate creams do not produce these sensations (Barone, 1989). More important,
the proposed mechanisms of pain relief by counterirritants such as menthol (the active ingredient of Joint-Ritis) and trolamine salicylate creams are quite different. The proposed mechanism of pain relief by trolamine salicylate is through its inhibitory effect on prostaglandin biosynthesis at a local level (Barone; Ciccone, Leggin, & Callamaro, 1991). Topically applied counterirritants cause irritation or mild inflammation of the skin to provide pain relief to underlying tissues (Barone; Department of Health and Human Services, 1983; Hong & Shellock, 1991). The mild inflammation produces increased local circulation and tissue temperature, as well as stimulation of local nociceptors. Stimulation of the skin’s nociceptors inhibits the transmission of the small, unmyelinated C fibers that transmit pain to the higher brain centers while increasing the input from the large A-beta fibers (Melzack & Wall, 1965). This process might additionally stimulate the release of endogenous opiates (Barone; Hong & Shellock). A recent study indicated that menthol (the active ingredient in Joint-Ritis) is endowed with analgesic properties mediated through selective activation of kappa-opioid receptors (Galeotti, Di Cesare, Mazzanti, Bartolini, & Ghelardini, 2002).

Melzack (1999) recently expanded the gate-control theory of pain, with its emphasis on central neural mechanisms, to view pain as a much broader multidimensional experience. This neuromatrix theory proposes that pain is produced by characteristic neurosignature patterns generated by a widely distributed neural network called the body-self neuromatrix. The neuromatrix theory places genetic influences and neural-hormonal mechanisms of stress on a level of importance equal to that of the neural mechanisms of sensory transmission. The product of the neuromatrix is the sensory, affective, and cognitive dimensions of pain (Melzack).

Despite the widespread current use of OTC topical analgesics and their long history, there is a paucity of studies regarding their efficacy. Towheed and Hochberg (1997) systematically reviewed randomized controlled trials of pharmacological therapy of knee OA published between 1966 and August 1994. A total of 80 trials were analyzed; 45 involved oral NSAIDs, and only 2 dealt with topical counterirritants. One of these involved the active ingredient trolamine salicylate, and the other, capsaicin. The second study reported that capsaicin was superior to a placebo in relieving pain in a 4-week trial involving 70 patients. The role of capsaicin was adjunctive, however, because most of the patients continued to receive concomitant arthritis medications (Deal et al., 1991).

Approximately 3 decades ago a series of three experiments examined the immediate effects of a single application of a topical analgesic on pain. In 1970, White and Sage induced delayed-onset muscle soreness to the forearms (wrist extensors) of a group of 40 men and women volunteers. Approximately 48 hr after the soreness was induced, the participants returned to the laboratory. They served as their own controls, with one arm being treated with a topical with the active ingredients of 15% methyl salicylate and 10% menthol and the other with a second ointment having the same base as the first but in which the active ingredients were replaced by isopropyl myristrate and water. The investigators were given coded tubes, and neither they nor the participants knew which contained the topical and which contained the placebo. The application of the ointment and massage was completed in 15 s for each arm. Electromyographic (EMG) electrodes were placed on both forearms over the muscle belly of the extensor carpi radialis longus, and EMG readings were recorded before the induction of muscle soreness, before the
application of the topicals, and immediately after their application. At the conclusion of testing, each participant completed a questionnaire designed to evaluate their perception of pain and any changes in pain level. The results indicated that the topical analgesic significantly decreased the muscle action potential compared with the placebo group (indicating a decrease in muscle spasm) and that there was a significantly greater perception of pain relief immediately after the application of the topical analgesic compared with the placebo.

A year later, White and Sage (1971) did a follow-up study using a similar protocol on 30 patients experiencing joint pain caused by OA (n = 14) or rheumatoid arthritis (n = 16). EMG action potentials were obtained of the participants’ bilateral triceps brachii muscles, as well as pain levels in both shoulders, elbows, wrists, and hands before and immediately after the application of a counterirritant on one limb and a placebo on the other. There was a significant drop in muscle action potentials in the limbs that received the counterirritant. A thymometer was used to obtain subjective pain measurements. The participants used this electronic instrument to match sound frequency (loudness) in decibels to perceived pain levels. Results indicated a significant drop in shoulder, elbow, and wrist pain in the limbs treated with the counterirritant.

White (1973) measured pain, ROM, and digital dexterity in 30 patients with arthritis in the hands before and immediately after application of a topical analgesic on one hand and a placebo on the other. The same formulation of topical analgesic and placebo as previously described was once again used. Both the topical analgesic and the placebo groups experienced increased ROM and digital dexterity. Those treated with the topical analgesic, however, experienced significantly greater results in both areas. Only the topical-analgesic group experienced a significant decrease in pain.

Our double-blind, placebo-controlled study was unique in that its purpose was to determine whether a topical analgesic (Joint-Ritis) would, over a 5-week period, reduce knee pain and improve function in a group of 40- to 65-year-old men and women experiencing chronic knee pain. Assessment was gathered in relation to overall weekly changes rather than immediately after the application of the topical analgesic. This we think gives a much better indication of the efficacy of the treatment. Our results indicated that the topical analgesic produced significant decreases in pain frequency and severity as indicated by the VAS and KPS (Tables 1 and 3). In addition, significant increases in knee-extension and -flexion strength were achieved by the men but not by the women in the topical-analgesic group (Table 3). Significant increases in knee AROM were achieved by the women but not the men in the topical-analgesic group over the 5-week period (Table 3). What was surprising to us, however, was that the placebo group also achieved significant decreases in pain frequency and severity, except for the VAS in the men (Table 3). The men in the placebo group also achieved significant increases in flexion strength at 90° and in extension strength at 20°. When the changes in our dependent variables between experimental groups were analyzed with the slopes, no difference was found between the topical-analgesic group and the placebo group (Table 4).

How might these results be explained? One possible reason for the improvement found in the placebo group is the massage during application of the placebo ointment. Massage can cause increased peripheral circulation and a slight rise in skin temperature. This is thought to inhibit the transmission of pain to the higher
brain centers by the small unmyelinated C fibers while increasing the input from the large A-beta fibers, thus closing the pain gait (Hong & Shellock, 1991; Wakim, 1980). This explanation is unlikely, because previous research found that there was not a significant increase in skin temperature or peripheral blood flow in the arms of participants after a 2-min massage during the application of a placebo (Hong & Shellock).

Another possible explanation is the placebo effect. Shapiro and Shapiro (1997) defined *placebo*, when used as a control in experimental studies, as “a substance or procedure that is without specific activity for the condition being treated” (p. 41). They defined *placebo effect* as “the nonspecific psychological or psychophysiological therapeutic effect produced by a placebo” (p. 1). There have been many attempts to derive overall percentages for patients having a positive placebo reaction, those having nonplacebo reaction, and those having placebo-induced side effects (negative reaction), but because of the differences in participant demographics, diagnoses, symptoms, and psychological groups, “no reliable and valid estimate of placebo reactivity is currently available” (Shapiro & Shapiro, p. 80).

Batterman and Lower (1968) administered analgesic placebo therapy to a group of 173 patients suffering from various musculoskeletal pathologies. In patients suffering from OA, placebo responsiveness was high and its extent was correlated with the amount and success of previous therapy (principally, analgesic therapy). Positive placebo responses from patients with no previous therapy were 34.9%. For patients who had previously received positive results from therapy within the first week, 77.9% had a positive placebo response. When previous therapy had been ineffective, only 29.1% experienced a positive placebo response. The importance of past experience in the perception of pain is part of Melzack’s (1999) neuromatrix theory of pain. The amount of the positive results found in our placebo group that can be attributed to the placebo effect is unknown.

Kienle and Kiene (1996) stated in their critical methodological and conceptual analysis of reports on the magnitude of the placebo effect that in some placebo studies, the so-called placebo group actually got a form of active medication. This presents a very interesting possibility with regard to our placebo. Although we did remove the only active ingredient according to the U.S. Food and Drug Administration (the menthol) and the skin moisturizers chondroitin sulfate and glucosamine sulfate, the essential oils eucalyptus, citrus, copaiba, and lavender were left in the placebo. If a topical analgesic is going to modulate chronic joint pain in a manner other than that which we already discussed, it is likely that one or more of its ingredients would have to be absorbed through the skin and enter into the underlying muscle, tendon, ligament, joint capsule, and synovium of the affected joint. Essential oils such as peppermint and eucalyptus have been used as vehicles to enhance transdermal absorption (Rosenstein, 1999). Eucalyptus is considered an active ingredient in Canada and the United Kingdom and might be responsible for some of the positive effects found in our placebo group. This is purely speculation, because there is an obvious dearth in the literature with regard to transdermal absorption of the essential oils and their clinical efficacy. Clearly this is an area in which more research is necessary.

Our somewhat small sample perhaps leaves some doubt that if we had had had more participants a significant difference between the groups would have emerged.
In answer to that concern we calculated 95% confidence limits, and from those data we calculated the largest possible difference that could have been missed at the end of our 35-day treatment based on our sample size (Table 4). Based on these data, we think that if a difference does indeed exist it is fairly small and probably not of clinical significance.

In summary, our results indicate that although the topical analgesic Joint-Ritis was effective in reducing pain frequency and severity in a group of individuals 40–65 years of age with chronic knee pain, there was not a statistically significant difference between the topical analgesic and the placebo. Possible reasons for this might be the massage involved, the placebo effect, and the positive influence of the essential oils in the placebo. We suggest further research be conducted into the transdermal absorption and medical efficacy of essential oils. With this added knowledge perhaps a “true” placebo could be developed and, with an increased sample size, a new double-blind, placebo-controlled investigation could uncover any differences between the topical analgesic and the placebo if they do in fact exist. This research suggests that there are no such differences.

References


