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Research Note

A Cetylated Fatty Acid Topical Cream With Menthol Reduces Pain and Improves Functional Performance in Individuals With Arthritis

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Abstract. Kraemer, W.J., N.A. Ratamess, C.M. Maresh, J.A. Anderson, J.S. Volek, D.P. Tiberio, M.E. Joyce, B.N. Messinger, D.N. French, M.J. Sharman, M.R. Rubin, A.L. Gómez, R. Silvestre, and R.L. Hesslink Jr. A cetylated fatty acid topical cream with menthol reduces pain and improves functional performance in individuals with arthritis. *J. Strength Cond. Res. 19(2):475–480. 2005.*—This investigation was an extension of a previous study conducted in our laboratory in which we showed that 1 month of treatment with a topical cream (Celadrin®) consisting of cetylated fatty acids was effective for reducing pain and improving functional performance in individuals with osteoarthritis (OA) of the knee (Kraemer et al., *Journal of Rheumatology,* 2004). We wanted to verify that the addition of menthol to the compound would produce a similar percentage of improvement in therapeutic effects. We used a single treatment group with a pre-post experimental design to examine % treatment changes. Individuals diagnosed with OA of the knee ($N = 10$; age, 66.4 ± 11.5 years) and severe pain (e.g., OA, rheumatoid arthritis) of the elbow ($N = 8$; age, 59.1 ± 18.2 years) and wrist ($N = 10$; age, 60.3 ± 16.8 years) were tested for pain and functional performance before and after 1 week of treatment with a topical cream consisting of cetylated fatty acids and menthol applied twice per day. In individuals with knee OA, significant improvements in stair-climbing ability (about 12%), "up-and-go" performance (about 12%), balance and strength (about 16.5%), and range of motion (about 3.5%) were observed, as were reductions in pain. In individuals with severe pain of the elbow and wrist, significant improvements in dynamic (about 22 and 24.5%, respectively) and isometric (about 33 and 42%, respectively) local muscular endurance were observed, as was a reduction in pain. Neither group demonstrated significant changes in maximal grip strength or maximal force production. One week of treatment with a topical cream consisting of cetylated fatty acids and menthol was similarly effective for reducing pain and improving functional performance in individuals with arthritis of the knee, elbow, and wrist. The % changes were consistent with our prior work on the compound without menthol. Further work is needed to determine the impact of menthol in such a cream. Nevertheless, our data support the use of a topical cream consisting of cetylated fatty acids (with or without menthol) for enhancing the potential for exercise training in this population.

Key Words. fatty acids, osteoarthritis, physical performance, quality of life

Introduction

Osteoarthritis (OA) is a progressive, degenerative joint disease estimated to affect more than 21 million individuals in the United States (19). The most common symptoms are pain, stiffness, reduced joint range of motion, and limitations to normal activities that are a part of daily living, such as getting up from a chair, walking, balance, and ascending/descending stairs (8, 9, 11, 12, 24). Because of the debilitating effects of OA, there is a need for alternative treatments that benefit individuals with OA without harmful side effects. Important for strength and conditioning professionals, such treatments would also enhance the ability of individuals to exercise.

One potential treatment that has shown promise is the use of oral and/or a topical blend of cetylated fatty acids (10, 15). Cetylated monounsaturated fatty acids have been shown to provide protection against arthritis in rats (5) and have been shown to increase knee range of motion and reduce pain in individuals with knee OA (10). We recently reported that a topical cream consisting of a proprietary blend of cetylated fatty acids significantly reduced pain and improved physical function in individuals with knee OA (15). In that study, we reported acute improvements in stair-climbing ability, timed "up-and-go" performance, and knee range of motion and a reduction in pain within 30 minutes of the first treatment with this topical cream. Additional improvements were observed after 30 days (i.e., cream was applied twice per day) of treatment. However, we examined only individuals with knee OA, and the topical cream used was only in its developmental stage. Recently, menthol has been added to this topical cream. Menthol has been shown to possess analgesic properties, thereby reducing the sensation of pain (6). Therefore, the present investigation was an extension of our previous research (15). In this study, our purpose was to examine the effects of a topical cream consisting of cetylated fatty acids, along with the addition of menthol, on pain and functional performance in individuals with knee OA for 1 week. In addition, we recruited several individuals with severe pain (e.g., diagnosed with

either OA or rheumatoid arthritis) of the elbow and wrist to examine the potential effects of this treatment on upper-extremity performance (3).

METHODS

Experimental Approach to the Problem

This study was part of a much larger investigation. Using a placebo-controlled, double-blind study, we recently showed the benefits of treatment with a topical cream consisting of a blend of cetylated fatty acids (Celadrin®) (15). Thus, the purpose of the present study was to extend the findings of our previous research and provide further support for the use of cetylated fatty acids (i.e., and the addition of menthol) in the treatment of arthritis. To examine the primary hypothesis of the present investigation, individuals diagnosed with arthritis by a physician were assigned to an experimental group based on the anatomic location of pain (i.e., knee, elbow, or wrist). Each individual applied the cream to the affected area twice per day every day for 1 week and subsequently returned to the laboratory for poststudy functional performance testing. The testing protocols consisted of assessments for pain, stiffness, knee range of motion, postural stability, balance, and ability to rise from a chair, walk, and ascend/descend stairs for individuals with knee OA. For individuals with severe elbow and wrist pain, we measured their grip strength, elbow range of motion, dynamic and isometric muscle strength and endurance, and pain. Because of the significant improvements observed in our previous investigation with the use of a topical cream consisting of a blend of cetylated fatty acids (15) (i.e., as well as the lack of significant changes occurring in a control group using a placebo cream) and the high test-retest reliability (intraclass correlation coefficients of $R = 0.95$–0.99) obtained with our assessments, our study design did not include a control group for this short extension of our previous research, which was performed to determine if improvements had occurred in a magnitude that was similar to that obtained with the topical cream that did not contain the menthol. A pre-post experimental treatment design was used, as the control data had shown no improvements in the measures. Thus, future research will need to directly determine the effects of menthol alone on the associated measures used in this study. It must be clear that the impact of menthol cannot be determined with the current experimental design.

Subjects

All individuals selected for the present study were recruited in conjunction with local physicians. Each participant was informed of the benefits and risks of the investigation and subsequently signed an approved consent form in accordance with the guidelines of the university's Institutional Review Board for use of human subjects. Arthritis was diagnosed by the treating physicians, and 28 individuals (26 women and 2 men) were assigned to 1 of 3 groups: knee ($N = 10$), elbow ($N = 8$), or wrist ($N = 10$) arthritis. Individual demographics were (a) knee: age, 66.4 ± 11.6 years; height, 162.4 ± 6.4 cm; body mass, 83.5 ± 18.4 kg; and years with arthritis, 8.8 ± 7.0; (b) elbow: age, 59.1 ± 18.2 years; height, 158.9 ± 7.6 cm; body mass, 76.8 ± 13.4 kg; and years with arthritis, 5.9 ± 7.0; and (c) wrist: age, 60.3 ± 16.8 years; height, 159.1 ± 6.7 cm; body mass, 74.7 ± 14.4 kg; and years with arthritis, 4.9 ± 5.8.

Functional Mobility Measures

Individuals were assessed for functional performance before and after the 7-day experimental period. For individuals with knee arthritis, the selection of assessments and the sequence performed were (a) the timed "up-and-go" test, (b) the stair-climbing test, (c) the unilateral anterior reach test, and (d) the medial step-down test. For individuals with elbow and wrist arthritis, the selection of assessments and sequence performed were (a) grip strength, (b) peak isometric force of the elbow flexors at 90°, (c) 1 repetition maximum (1RM) of the elbow flexors, (d) isometric local muscular endurance of the elbow flexors at 90°, and (e) number of repetitions performed for the arm curl with a standard resistance. All individuals participated in 2 familiarization sessions prior to initiating the study. All tests were administered by the same investigator to ensure standardization of the procedures and test-retest intraclass correlations producing reliabilities for all of the tests ranging from $R = 0.95$ to 0.99.

Lower-Extremity Assessments. The timed "up-and-go" test was performed by standard procedures (23). The individual sat in a standard armchair. On the verbal signal "Go," each individual ascended from the chair, walked until he/she crossed a tape marker located 3 m away, turned around, walked back toward the chair, and sat down. For the stair-climbing test, each individual ascended and descended a flight of eleven 13.5-cm steps as quickly as possible. The total, ascending, and descending times were recorded. For the unilateral anterior reach test, each individual (with the hands positioned on the hips) extended a leg out as far as possible (while balancing on the opposite leg) over a standard tape measure while keeping the anterior foot close to the floor without touching. Three trials were given per assessment, with the best score recorded for analysis. For the medial step-down test, each individual stepped down medially (from an 11.4-cm step) until the heel of the front foot lightly touched the floor and then returned to starting position (15). One trial was performed per leg, with each individual volitionally performing as many repetitions as possible.

Upper-Extremity Assessments. Maximal grip strength for each hand was assessed with a handgrip dynamometer. The peak isometric force of the elbow flexors was assessed using a linear-movement resistance exercise machine in conjunction with a force plate (Kistler Instrument Corporation, Amherst, NY). The resistance bar was set for each individual to correspond to an elbow angle of 90° (measured with a plastic goniometer) and was loaded such that no movement of the bar was permitted once it had been adjusted to the proper position. Each individual exerted maximal isometric force to the bar, and the subsequent ground reaction force was recorded. Hand and foot positions were standardized and marked for each testing session. Using the same resistance exercise machine, the 1RM arm curl was assessed. Each individual began with the elbows fully extended and proceeded to lift the bar in a full range of motion. Increments of 2.5 kg were added to each set until the individual could no longer complete a full repetition. For the isometric endurance assessment, individuals were positioned in the resistance exercise machine (identical to the peak isometric force assessment) with their hands placed on the bar at

TABLE 1. Pain and performance changes in patients with knee OA during the 1-week experimental period.†

Test	Pre	Post	Adjusted p value
Up and go (s)	9.37 ± 2.9	8.22 ± 2.4	0.004*
Stairs—total time (s)	14.85 ± 6.3	13.05 ± 5.3	0.004*
Stairs—acending (s)	6.86 ± 2.0	5.99 ± 1.8	0.001*
Stairs—descending (s)	7.10 ± 4.4	6.19 ± 3.4	0.029*
Anterior reach—R (cm)	44.65 ± 7.7	50.30 ± 6.0	0.004*
Anterior reach—L (cm)	41.65 ± 9.0	49.90 ± 7.7	0.000*
Step-down—R	13.80 ± 14.0	18.50 ± 18.8	0.109
Step-down—L	12.10 ± 15.2	16.30 ± 14.9	0.058
ROM—SUP ext—R (°)	8.90 ± 5.1	6.90 ± 4.0	0.098
ROM—SUP ext—L (°)	8.10 ± 3.7	5.60 ± 2.9	0.050*
ROM—SUP flex±R (°)	115.10 ± 8.0	120.20 ± 7.6	0.026*
ROM—SUP flex—L (°)	116.50 ± 6.6	120.00 ± 6.8	0.037*
WOMAC—pain	9.35 ± 3.4	5.00 ± 3.8	0.004*
WOMAC—stiffness	3.70 ± 1.8	2.40 ± 2.2	0.090
WOMAC—function	30.55 ± 12.9	16.30 ± 15.0	0.036*

* $p \leq 0.05$.

† OA = osteoarthritic; R = right leg; L = left leg; ext = extended knee and hip position; flex = flexed knee and hip position; ROM = range of motion; SUP = supine; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

an elbow angle of 90°. A standard resistance of 50–60% of individuals' prestudy 1RM was added to the bar, and each individual was instructed to hold the weight at this position for as long as possible. Fatigue and/or failure to maintain the proper elbow and wrist position were criteria for test termination. The total time that the individual was able to maintain this position was recorded. For the dynamic muscular endurance assessment, a standard dumbbell was used (e.g., 5.5 kg for men, 3.6 kg for women) for the unilateral arm curl exercise. Each individual performed as many repetitions as possible with each arm in a full range of motion. All testing was conducted by a certified strength and conditioning specialist who used great care when monitoring individual performance.

Clinical Assessment

Individuals were assessed on the basic clinical range of motion of the knees (i.e., for those with knee OA) and elbow (i.e., for those with elbow arthritis). For knee range of motion, individuals were asked to lie supine with both legs fully extended. They were then asked to flex each knee as far as possible until they felt discomfort. The knee joint angle was measured in both the supine extended and flexed positions using a standard goniometer. Similar procedures were used to measure the fully extended and flexed positions at the elbow joint while the individual was standing. The same investigator performed all measurements, which yielded test-retest reliabilities of 0.99 for both assessments. Pain, stiffness, and physical function of the lower extremities were assessed with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (2, 22). For individuals with elbow and wrist arthritis, a 0 (no pain) to 4 (extreme pain) pain scale was used, similar to that of the WOMAC.

Topical Cream and Application

The topical cream used was a proprietary blend of cetylated fatty acid oil (cetyl myristoleate, cetyl myristate, cetyl palmitoleate, cetyl laureate, cetyl palmitate, and cetyl oleate), PEG-100, stearate, benzyl alcohol, lecithin, carbomer, potassium hydroxide, tocopheryl acetate, menthol, and olive oil (Celadrin®, Imagenetix, Inc., San Diego, CA). Individuals were instructed to apply a standardized amount of cream to the affected area. Daily logs were completed to ensure 100% compliance. In addition, individuals were not taking additional arthritis medications, did not initiate any exercise programs, and were not permitted to practice the performance tests to prevent any training effects during the 1-week experimental period.

Statistical Analyses

Statistical evaluation of all data was accomplished using a paired t-test with α level corrections. Statistical power for the various dependent variables was determined to be 0.80–0.85 for the sample size used at the 0.05 α level (nQuery Advisor software, Statistical Solutions, Saugus, MA). Significance was set at $p \leq 0.05$.

RESULTS

The results of this study are presented in Tables 1–3. For individuals with knee OA, there were significant reductions in the times to complete the up-and-go and stair-climbing tests ($p \leq 0.05$). Unilateral anterior reach performance increased significantly, whereas only a trend for improvement was observed for the medial step-down test. The range of motion of the knee improved significantly in the knee flexion test, as well as in the full extension test for the left leg. WOMAC scales showed significant reductions in pain and improvements in physical function. For individuals with elbow and wrist arthritis, significant improvements were observed only in the local muscular endurance assessments (i.e., isometric endurance test and repetitions of the arm curl). No differences were observed in any strength or range of motion measurements. In addition, the perception of pain was reduced.

DISCUSSION

The findings of the present study support our previous research, indicating that a topical cream consisting of a blend of cetylated fatty acids is effective for (a) improving knee range of motion; (b) improving ability to climb stairs, rise from a chair, and walk; and (b) improving balance, strength, and endurance in patients with knee OA. Unique to the present investigation were the findings that this topical cream also enhances dynamic and isometric local muscular endurance and reduces pain in individuals with severe pain of the elbow and wrist (e.g., OA or rheumatoid arthritis).

TABLE 2. Pain and performance changes in patients with elbow arthritis during the 1-week experimental period.†

Test	Pre	Post	Adjusted p value
ROM—ext. (°)—R	22.50 ± 7.3	21.88 ± 5.3	0.537
ROM—ext. (°)—L	22.88 ± 7.6	22.94 ± 6.7	0.927
ROM—flexion (°)—R	135.75 ± 9.8	139.25 ± 6.1	0.132
ROM—flexion (°)—L	137.88 ± 8.3	139.00 ± 7.3	0.219
Arm curl (repetitions)—R	25.50 ± 18.3	30.30 ± 20.9	0.012*
Arm curl (repetitions)—L	21.63 ± 16.0	27.00 ± 17.7	0.001*
1RM curl (kg)	11.08 ± 6.7	11.65 ± 6.4	0.339
Grip strength (kg)—R	26.38 ± 10.4	26.40 ± 9.1	0.999
Grip strength (kg)—L	24.56 ± 10.2	24.25 ± 8.0	0.744
ISOM endurance (s)	90.45 ± 69.2	120.04 ± 80.3	0.002*
ISOM force (N)	228.88 ± 115.3	238.13 ± 116.8	0.308
Pain (0–4 scale)	2.63 ± 1.1	1.5 ± 0.5	0.015*

* $p \leq 0.05$.
† R = right leg; L = left leg; ext = fully extended elbow position; 1RM = 1 repetition maximum; ISOM = isometric.

TABLE 3. Pain and performance changes in patients with wrist arthritis during the 1-week experimental period.†

Test	Pre	Post	Adjusted p value
Arm curl (repetitions)—R	18.40 ± 10.9	23.00 ± 12.2	0.009*
Arm curl (repetitions)—L	16.80 ± 10.9	20.80 ± 11.2	0.001*
1RM curl (kg)	9.31 ± 5.1	9.77 ± 4.9	0.332
Grip strength (kg)—R	21.35 ± 8.9	21.65 ± 8.5	0.703
Grip strength (kg)—L	19.65 ± 8.3	20.40 ± 7.6	0.304
ISOM endurance (s)	68.87 ± 66.6	97.62 ± 79.5	0.002*
ISOM force (N)	190.70 ± 95.2	203.80 ± 107.8	0.067
Pain (0–4 scale)	2.70 ± 0.8	1.5 ± 0.5	0.003*

* $p \leq 0.05$.
† R = right leg; L = left leg; 1RM = 1 repetition maximum; ISOM = isometric.

The release of pro-inflammatory cytokines (e.g., interleukin-1β and tumor necrosis factor-α) is an important mediator of inflammation. Fatty acids have been proposed to reduce chronic inflammation in individuals with arthritis by reducing the release of leukotriene B4 from stimulated neutrophils and of interleukin-1 from monocytes (4, 17). Other suggested mechanisms for the anti-inflammatory response are reduced expression and activity of proteoglycan degrading enzymes and cytokines, suppression of leukocyte function, changes in adhesion molecule expression and apoptosis triggering, and alterations in signal transduction and membrane fluidity (4, 16, 17). Cetylated monounsaturated fatty acids have been shown to provide protection against arthritis in rats (5), increase knee range of motion, and reduce pain in patients with OA (10). Although the mechanisms remain to be elucidated, our results support the use of topically applied cetylated fatty acids in the treatment of arthritis.

Functional performance is limited in individuals with OA (14). Individuals with knee OA have been shown to walk, ascend, and descend stairs with less velocity than healthy individuals (14). In addition, balance is limited, partially due to strength reductions (8), and the ability to rise from a chair and walk is another functional performance task that is limited in individuals with knee OA (12). Inactivity associated with OA pain results in further loss of muscle strength, power, and endurance in the upper and lower extremities, all of which are detrimental to an individual's quality of life. The results of the present investigation, as well as those obtained in our previous research (15), demonstrate the efficacy of a topical cream consisting of cetylated fatty acids for reducing pain and improving physical function. Improved ability to ascend/descend stairs and to rise from a chair and walk, greater knee range of motion, enhanced balance, and reduced pain were observed after only 1 week of treatment in the present study. Some of these improvements may occur 30 minutes after the first treatment (15). The largest improvements in physical function observed in the present study were in our lower-extremity assessments. These data indicate that OA of the lower extremity may have more detrimental effects to physical performance involving weight-bearing activities.

Few studies that have as their goal improved performance and pain reduction in individuals with arthritis of the elbow or wrist have examined various topical treatments. Most studies have investigated nonsurgical treatments such as analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), glucosamine, and chondroitin sulfate supplementation (21, 26). Although effective, side effects may occur with the chronic use of analgesics and NSAIDs (26). Thus, the development of topical treatments that produce no or minimal side effects is warranted. Recent studies have shown the beneficial effects of herbal supplements and topical creams, including capsaicin, piroxicam gel, articulin-F, willow bark, and phytodolor, for reducing pain in patients with OA (21). Gemmell et al. (7) examined treatment with a topical cream consisting of several herbs in addition to capsaicin and menthol for 42 days and reported a 35–38% reduction in pain and stiffness in patients with OA of the hand and knee. The magnitude of pain reduction in that study was slightly greater than the average pain reductions reported with the use of NSAIDs (i.e., 30%) (25). In the present study, we reported an approximately 43% reduction in pain in individuals with arthritis of the wrist and elbow after only 1

week of treatment with a topical blend of cetylated fatty acids and menthol. Although our methods for the assessment of pain differed from those of previous investigations (i.e., direct comparisons could not be made), the results of the present investigation indicate that favorable reductions in pain are possible with the treatment of a topical cream consisting of a blend of cetylated fatty acids and menthol.

The measurement of handgrip strength has been used as one assessment of physical function in individuals with severe pain in the hand and wrist. Grip strength has been shown to be compromised in individuals with OA of the wrist (3) and hand (13). The reduction in grip strength is mediated, in part, by pain, and this reduction occurs in proportion to the severity of arthritis (13). Topical cream treatments (e.g., herbal formulas, capsaicin) for periods of 1–3 months have had limited effects on grip strength in individuals with arthritis, despite reductions in pain (18, 20). Our findings support these data, as we did not report any changes in grip strength after only 1 week of treatment despite reductions in pain. Thus, it appears that other treatment modalities (i.e., exercise), in addition to treatment with a cetylated fatty acid/menthol topical cream, may be necessary to restore handgrip strength in individuals with arthritis.

A unique aspect of the present investigation was our selection of assessments for local muscular endurance and strength in individuals with severe elbow and wrist pain. No differences were observed in the peak isometric or dynamic strength of the elbow flexors; however, we did report significant improvements in local muscular endurance (e.g., dynamic repetitions completed and isometric time to exhaustion). It was not surprising that maximal muscle strength did not change. The present investigation was only 1 week in duration, and this may have not been long enough to initiate such changes. In addition, no exercise interventions were used. Maximal strength improvements have been shown to be specific to the training stimulus (1) and would therefore be unlikely to change, despite reductions in pain. However, our data demonstrated that submaximal local muscular endurance was responsive to pain reductions. Dynamic muscular endurance improved by about 23%, and isometric local muscular endurance increased by about 36%. Considering that the normal activities that are a part of daily living rely very little on one's maximal lifting ability, our data demonstrate that improvements in functional performance (i.e., improved submaximal endurance) may be obtained with a topical treatment consisting of a blend of cetylated fatty acids and menthol in individuals with arthritis of the elbow or wrist.

PRACTICAL APPLICATIONS

Our data provide further support for the use of a topical cream consisting of a blend of cetylated fatty acids and menthol in the treatment of individuals with arthritis of the knee, elbow, and wrist. In the present investigation, we reported significant improvements in stair-climbing ability, "up-and-go" performance, balance, and range of motion; reductions in pain in individuals with knee OA; significant improvements in dynamic and isometric local muscular endurance; and a reduction in pain in individuals with severe pain in the elbow and wrist. The changes were similar to what we had previously noted. In addition, the use of such topical treatments may allow individuals to better exercise, thereby helping them improve their health and fitness. Strength and conditioning professionals who work with such populations may find that it enhances workout capabilities.

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