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Effects of Treatment With a Cetylated Fatty Acid Topical Cream on Static Postural Stability and Plantar Pressure Distribution in Patients With Knee Osteoarthritis

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[1]Human Performance Laboratory, Department of Kinesiology and Department of Physiology and Neurobiology, Department of Physical Therapy, University of Connecticut, Storrs, Connecticut 06269 and School of Medicine, University of Connecticut Health Center, Farmington, Connecticut 06030; [2]Department of Health and Exercise Science, The College of New Jersey, Ewing, New Jersey 08628; [3]Imagenetix, Inc., San Diego, California 92128.

Abstract. Kraemer, W.J., N.A. Ratamess, C.M. Maresh, J.A. Anderson, D.P. Tiberio, M.E. Joyce, B.N. Messinger, D.N. French, M.J. Sharman, M.R. Rubin, A.L. Gómez, J.S. Volek, R. Salvestre, and R.L. Hesslink Jr. Effects of treatment with a cetylated fatty acid topical cream on static postural stability and plantar pressure distribution in patients with knee osteoarthritis. *J. Strength Cond. Res. 19(1):115–121. 2005.*—The purpose of the present investigation was to examine the effects of 30 days of treatment with a topical cream consisting of cetylated fatty acids on static postural stability and plantar pressures in patients with osteoarthritis (OA) of one or both knees. Forty patients diagnosed with knee OA were randomly assigned to 1 of 2 topical treatment groups: (a) cetylated fatty acid (CFA; N = 20; age = 62.7 ± 11.7 years); or (b) placebo (P; N = 20; age = 64.6 ± 10.5 years). Patients were tested on 2 occasions: (a) baseline (T1), and (b) following a 30-day treatment period consisting of cream application twice per day (T2). Assessments included 20- and 40-second quiet standing protocols on a force plate to measure center of pressure (COP) total excursion length, COP velocity, and rearfoot and forefoot plantar pressure distribution. In the CFA group, a significant reduction in the COP excursion length and velocity were observed at T2, whereas no significant differences were observed in the P group. No significant differences in mean forefoot, rearfoot, or rearfoot-to-forefoot plantar pressure ratios were observed in either group at T2. However, in a subgroup of participants designated to be right- or left-side dominant, improvements in the right-to-left forefoot plantar pressure ratios were observed in both groups. These data indicate that 30 days of treatment with a topical cream consisting of cetylated fatty acids improves static postural stability in patients with knee OA presumably due to pain relief during quiet standing. Such over-the-counter treatment may help improve the exercise trainability of people with OA.

Key Words. postural sway, plantar pressure, center of pressure, standing balance

Introduction

Osteoarthritis (OA) is a degenerative joint disease estimated to affect more than 21 million individuals in the United States (22) and is characterized by enzymatic and mechanical breakdown of the extracellular matrix, leading to degeneration of articular cartilage (27). The most common symptoms are pain and stiffness with accompanying limitations to joint range of motion and performance of normal activities of daily living such as getting up from a chair, walking, static and dynamic balance (e.g., greater postural sway), and ascending/descending stairs (8, 10, 14, 16). In response to pain and stiffness, patients with OA tend to become more sedentary, which further induces muscle atrophy and functional performance limitations. Considering the high incidence of OA in the elderly population, pain-reducing medications such as acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), and cyclooxygenase-2 inhibitors have been common treatments. However, prolonged use of NSAIDs increases the risk of gastrointestinal side effects and renal toxicity, and may inhibit synthesis of cartilage matrix (2, 4, 31). Thus, the need exists for alternative treatments or medications that benefit patients without harmful side effects.

Balance is one skill-related component of fitness that is often limited in patients with knee OA. Control of balance is quite complex but is dependent on vestibular, visual, and somatosensory inputs; central processing; and the appropriate motor response (14). Severe pain, articular damage, and quadriceps muscle weakness associated with OA of the knee contribute to postural instability via loss of motor control and proprioceptive acuity (14, 16), or reduced capacity to maintain equilibrium under static or dynamic conditions. It has been shown that patients with knee arthritis demonstrate more anteroposterior and mediolateral postural sway than age-matched controls (14, 16, 29, 30). In fact, patients with both rheumatoid arthritis and OA of the knee have been shown to have up to 80% reduction in postural stability in the anteroposterior direction (29). One potential reason may be overcompensation during standing via shifting one's weight to the less-symptomatic limb in order to reduce pain associated with skeletal loading. It has been shown that pain reduction in the symptomatic limb (i.e., the limb with the most severe pain for those patients with bilateral knee OA) results in greater loading to that limb during normal gait (17). Thus, a treatment that can relieve knee pain in patients with OA may result in greater weight distribution, which, potentially, could improve static and dynamic postural stability.

A common method used to quantify static standing balance or postural control is the use of a quiet standing protocol on a force plate. Excursion of the center of pressure (COP) and the velocity of COP excursion, as measured by ground reaction forces, are useful indicators of postural control (7, 12, 25). Thus, excessive movement of the COP is a marker of impaired postural stability. Several studies have shown greater COP excursion in patients with knee arthritis using either force plates or other mechanical devices to measure postural sway (9, 10, 14, 29, 30). Considering that excursion of the COP occurs in patients with knee OA, it may be possible that plantar pressures obtained during quiet standing may also change in response postural instability. However, no studies have examined plantar pressures during quiet standing in patients with knee OA undergoing treatment.

We have shown that 30 days of treatment with a topical cream consisting of a blend of cetylated fatty acids significantly reduced pain and stiffness, and improved knee range of motion and functional performance (e.g., stair climbing ability, timed "up-and-go" performance, unilateral anterior reach) in patients with knee OA (19). However, the effect of chronic pain relief on static postural stability in patients with knee OA is less clear. Therefore, the purpose of the present investigation was to extend our previous investigation and examine the effects of 30 days of treatment with a topical cream consisting of a blend of cetylated fatty acids on static postural stability and plantar pressures in patients with knee OA. Hopefully, such over-the-counter treatment will help improve the trainability of patients with OA and enhance their quality of life.

METHODS

Experimental Approach to the Problem

In order to examine the primary hypothesis of the present investigation, patients diagnosed with knee OA by a physician were randomly assigned to 1 of 2 topical treatment groups in a double-blind manner applying either: (a) a cream consisting of a blend of cetylated fatty acids (Celadrin®, Imaginetics, Inc., San Diego, CA); or (b) a placebo cream. Patients were tested before (T1) and following a 30-day treatment period (T2) for static postural stability and plantar pressures during two quiet standing protocols. This study design enabled us to investigate the hypothesis that chronic pain relief would improve postural stability in patients with knee OA.

Subjects

All participants selected for the present study were recruited in conjunction with local physicians from the areas of greater Hartford and Storrs, Connecticut. 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. Knee OA was diagnosed using American College of Rheumatology guidelines (15) by the treating physicians and participants were excluded if they (a) had OA of the hip or ankle, (b) had inflammatory or autoimmune arthritis, (c) were taking steroidal or immune-suppressive agents, and (d) had other serious health problems. Forty-three men and women were originally screened by a physician and began the study. However, 40 participants (N = 20 per group; 34 women and 6 men) completed the study. To ensure no baseline differences between treatment groups occurred, participants were matched for body mass, age, gender, and OA history and randomly assigned to either a cetylated fatty acid topical treatment group (CFA) or a placebo treatment group (P). Participant characteristics are presented in Table 1.

TABLE 1. Subject characteristics.

	CFA (N = 20)	P (N = 20)
Age (y)	62.7 ± 11.7	64.6 ± 10.5
Height (cm)	165.3 ± 7.6	166.0 ± 9.8
Body mass (kg)	85.6 ± 20.6	84.6 ± 21.8
OA (y)	7.9 ± 5.7	8.9 ± 8.7
Knee etiology	8 (1 leg); 12 (both)	6 (1 leg); 14 (both)

Assessment of Postural Stability

Postural stability was assessed using an AMTI force platform (AMTI Corp., Watertown, MA) interfaced with a computer and software program. Three-dimensional ground reaction forces were recorded at 50 Hz. Participants quietly stood on the force plate for 40 seconds barefoot with their arms hanging beside the trunk. During this time, participants were instructed to stand motionless while focusing on an eye-level marker on the wall (i.e., to ensure minimal movement of the head). Foot position was standardized (i.e., normal stance width for each participant) on the force plate and marked with tape; thus, identical foot positions were used during each testing session. Total excursion length of the COP and COP velocity were calculated and used as indicators of the magnitude of postural sway (7, 12, 25).

Plantar Pressure Measurements

Static plantar pressure measurements were obtained using the Mat Scan clinical system (Tekscan, Boston, MA). This computerized system consists of a pressure detection floor mat utilizing 2,288 sensor cells (1.4 sensors·cm^{-2}). Calibration was performed prior to data collection using the participants' body weight. Participants performed a 20-second quiet standing protocol barefoot on the Mat Scan using similar procedures to the postural stability assessment. Foot position was standardized (i.e., using participants' normal stance width) and marked during each testing session. Data were collected at 40 Hz, and peak plantar pressures for each foot were obtained. Peak plantar pressures were averaged over the entire 20-second standing protocol and were expressed per area of the foot. Areas were defined as follows: (a) forefoot—the metatarsal heads and toes, and (b) rearfoot—the heel region (~⅓ of the foot length). The ratios of right-to-left foot and rearfoot-to-forefoot were calculated and used for analysis. In addition, participants were further divided into subgroups depending on which leg bared the majority of weight based on the rearfoot and forefoot plantar pressure right-to-left ratio data (e.g., ratio >1 indicated more weight placed on the right leg; <1 indicated left leg dominance). This enabled examination of whether or not 30 days of treatment resulted in balanced weight distribution (e.g., a ratio closer to 1).

Topical Cream Treatment

The topical cream (Celadrin®, Imaginetics, Inc., San Diego, CA) consisted of a proprietary blend of cetylated fatty

acid oil, the composition of which has been reported previously (13, 19). The placebo cream contained everything but the cetylated fatty acid base material. The topical cream was given to patients in coded tubes so neither the research team involved in testing nor the patients knew which cream was administered. Participants were instructed to apply a standardized amount of cream to both knees. Cream was applied to the anterior, posterior, and lateral aspects of both knees over a 10- to 12-cm area twice per day (at a standardized morning and evening time point) for 30 days. Daily logs were completed to assure that patients strictly adhered to the treatment protocol. Compliance in both CFA and P groups was 100%.

Dietary Standardization

Each participant was instructed to maintain his or her current food and beverage intake throughout the 30-day experimental period. This was to ensure patients did not gain or lose body mass during the study, which could have influenced assessments of postural stability and plantar pressures. Three-day food records were completed prior to initiation of the study and each patient was instructed on how to maintain current dietary practices. As a result, body mass did not change in either group (CFA, pretest = 85.6 ± 20.6 kg, post-test = 85.7 ± 20.5 kg; P, pretest = 84.6 ± 21.8 kg, post-test = 84.5 ± 21.7 kg). In addition, participants were not taking additional arthritis medications during the study but were instructed to maintain their current medication routine (i.e., medications for blood pressure, cholesterol, etc.) throughout the study.

Statistical Analyses

Statistical evaluation of all data was accomplished using a 2×2 analysis of variance with repeated measures. Subsequent pairwise differences were determined using a Tukey post-hoc test when appropriate. Significance was set at $p \leq 0.05$.

RESULTS

The results for COP velocity were as follows: (a) CFA: 3.54 ± 0.7 cm·s^{-1} (T1) to 3.36 ± 0.7 cm·s^{-1} (T2); and (b) P: 3.58 ± 0.8 cm·s^{-1} (T1) to 3.47 ± 0.7 cm·s^{-1} (T2). A significant main effect [$F(1,38) = 14.2$, $p = 0.001$] but no interaction [$F(1,38) = 0.98$, $p = 0.33$] was observed. A significant reduction in COP excursion velocity was observed only in the CFA group ($p = 0.001$). No difference was observed in the P group. The results for total COP excursion length are presented in Figures 1 and 2. A significant reduction in COP length was observed in the CFA group, whereas no difference was observed in the P group. The delta change from T1 to T2 in COP excursion length was significant only in the CFA group.

Plantar pressure data are presented in Tables 2–6. No significant main effects or interactions in mean forefoot, rearfoot, or rearfoot-to-forefoot plantar pressure ratios were observed in either group during quiet standing overall (Table 2). When subgroups of participants were examined based on their right-to-left leg rearfoot ratios (i.e., ratio >1 indicated more weight placed on the right leg, <1 indicated the left leg), still no significant differences were observed (Tables 3 and 4). When subgroups of participants were examined based on their right-to-left leg forefoot ratios, there were some statistically significant differences (Tables 5 and 6). For those participants who placed greater weight on the right leg, significant differences were observed for right forefoot pressure (CFA and P), forefoot right-to-left ratio (CFA and P), and the right rearfoot-to-forefoot ratio (P only). For those participants who placed greater weight on the left leg, a significant difference was observed only for right forefoot pressure (CFA and P). In addition, a trend ($p = 0.10$) was observed for the forefoot right-to-left ratio in CFA only.

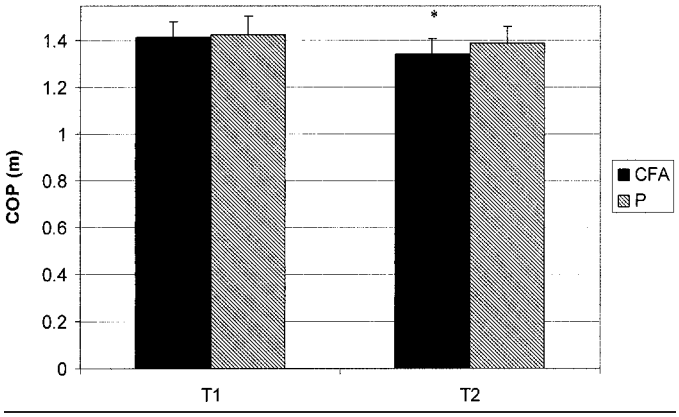

FIGURE 1. Center of pressure (COP) excursion length measurements (m) before and after 30 days of treatment with a topical cream consisting of a blend of cetylated fatty acids (CFA) or placebo (P). *$p < 0.05$ from corresponding time point T1.

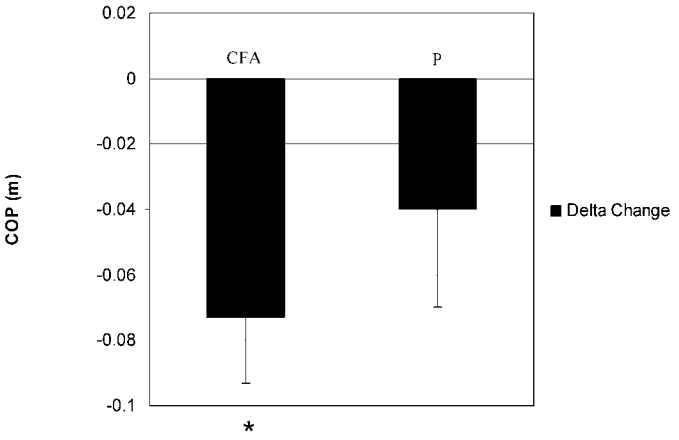

FIGURE 2. Delta change in center of pressure (COP) excursion length measurements (m) before and after 30 days of treatment with a topical cream consisting of a blend of cetylated fatty acids (CFA) or placebo (P). *$p < 0.05$ from corresponding time point T1.

DISCUSSION

The key finding of the present investigation was that 30 days of treatment with a topical cream consisting of cetylated fatty acids significantly improved standing postural stability in patients with knee OA. Specifically, topical fatty acid treatment resulted in reduced COP excursion length and velocity during 40 seconds of quiet standing. The results of this study support our previous research (19) demonstrating the efficacy of treatment with a topical cream consisting of a blend of cetylated acids for reducing pain and improving functional performance in patients with knee OA.

It has been suggested that the major causes of OA-related knee pain are (a) greater mechanical strain (i.e.,

TABLE 2. Total plantar pressure data.

	CFA		Placebo		
Plantar pressure	T1	T2	T1	T2	Probability
Rearfoot pressure (kPa)					
Right	68.8 ± 19.4	69.8 ± 17.7	73.2 ± 22.6	74.9 ± 20.8	0.51
Left	76.8 ± 26.3	79.0 ± 23.0	77.9 ± 21.7	78.2 ± 19.3	0.59
Rearfoot: R:L ratio*	1.01 ± 0.6	0.94 ± 0.3	1.00 ± 0.4	1.01 ± 0.4	0.68
Forefoot pressure (kPa)					
Right	31.9 ± 8.8	32.0 ± 8.3	28.1 ± 7.9	28.2 ± 8.1	0.90
Left	34.3 ± 9.9	34.9 ± 10.7	32.8 ± 8.9	33.1 ± 8.1	0.58
Forefoot: R:L ratio*	0.97 ± 0.3	0.94 ± 0.2	0.87 ± 0.2	0.86 ± 0.2	0.53
Rear/forefoot ratio					
Right	2.39 ± 1.1	2.38 ± 0.9	2.86 ± 1.3	2.93 ± 1.4	0.76
Left	2.45 ± 1.2	2.48 ± 1.1	2.54 ± 1.0	2.51 ± 0.8	0.98

* R = right foot; L = left foot.

TABLE 3. Rearfoot R:L ratio pressure data: right-dominant subgroup.

	CFA (N = 8)		Placebo (N = 7)		
Plantar pressure	T1	T2	T1	T2	Probability
Rearfoot pressure (kPa)					
Right	77.0 ± 16.5	77.3 ± 7.8	93.3 ± 17.6	87.2 ± 21.0	0.44
Left	60.0 ± 12.9	70.2 ± 10.9	69.4 ± 23.5	72.9 ± 27.0	0.13
Rearfoot: R:L ratio*	1.41 ± 0.8	1.11 ± 0.1	1.41 ± 0.3	1.30 ± 0.5	0.28
Forefoot pressure (kPa)					
Right	35.9 ± 6.4	33.6 ± 6.4	28.9 ± 6.8	29.8 ± 9.6	0.51
Left	35.7 ± 8.5	36.5 ± 8.2	35.9 ± 12.5	37.1 ± 10.4	0.56
Forefoot: R:L ratio*	1.04 ± 0.2	0.94 ± 0.2	0.84 ± 0.2	0.81 ± 0.1	0.21
Rear:forefoot ratio					
Right	2.24 ± 0.7	2.39 ± 0.6	3.43 ± 1.3	3.18 ± 1.4	0.67
Left	1.79 ± 0.7	2.02 ± 0.6	2.08 ± 0.8	2.14 ± 0.9	0.26

* R = right foot; L = left foot.

TABLE 4. Rearfoot R:L ratio pressure data: left-dominant subgroup.

	CFA (N = 12)		Placebo (N = 13)		
Plantar pressure	T1	T2	T1	T2	Probability
Rearfoot pressure (kPa)					
Right	63.7 ± 19.9	65.2 ± 20.7	62.4 ± 17.1	68.3 ± 18.1	0.13
Left	87.1 ± 27.5	84.4 ± 27.0	82.5 ± 20.1	81.0 ± 14.3	0.39
Rearfoot: R:L ratio*	0.77 ± 0.2	0.83 ± 0.3	0.77 ± 0.2	0.86 ± 0.2	0.06
Forefoot pressure (kPa)					
Right	29.5 ± 9.5	31.0 ± 9.4	27.7 ± 8.7	27.4 ± 7.5	0.55
Left	33.5 ± 11.0	34.0 ± 12.2	31.1 ± 6.3	31.0 ± 5.8	0.86
Forefoot: R:L ratio*	0.92 ± 0.3	0.94 ± 0.2	0.89 ± 0.2	0.89 ± 0.2	0.72
Rear:forefoot ratio					
Right	2.48 ± 1.3	2.37 ± 1.1	2.56 ± 1.3	2.80 ± 1.4	0.59
Left	2.85 ± 1.3	2.75 ± 1.3	2.79 ± 1.1	2.70 ± 0.7	0.52

* R = right foot; L = left foot.

from localized pressure) on nociceptors in the fibrous capsule, ligaments, tendons, synovium, periosteum, and muscle; (b) inflammation (and subsequent release of chemical mediators); (c) muscle contraction; (d) muscle weakness; and (e) effusion (9). A potential pain-relieving treatment is the reduction of inflammation. The process of arthritic inflammation involves the release of proinflammatory cytokines (e.g., interleukin-1β and tumor necrosis factor-α). Fatty acids have been proposed to reduce chronic inflammation in patients with rheumatoid arthritis by reducing leukotriene B4 from stimulated neutrophils and interleukin-1 from monocytes (5, 21). Other suggested mechanisms for the anti-inflammatory response observed with fatty acid treatment are reduced expression and activity of proteoglycan degrading enzymes and cytokines, suppression of leukocyte function,

TABLE 5. Forefoot R:L ratio pressure data: right-dominant subgroup.

	CFA (N = 12)		Placebo (N = 6)		
Plantar pressure	T1	T2	T1	T2	Probability
Rearfoot pressure (kPa)					
Right	67.8 ± 17.0	71.5 ± 16.5	69.0 ± 18.2	72.7 ± 14.7	0.22
Left	70.6 ± 19.0	71.1 ± 19.1	62.3 ± 8.4	72.0 ± 5.0	0.12
Rearfoot: R:L ratio†	0.98 ± 0.2	1.03 ± 0.2	1.14 ± 0.4	1.01 ± 0.2	0.47
Forefoot pressure (kPa)					
Right	34.6 ± 8.6	33.2 ± 8.0*	32.7 ± 6.8	28.2 ± 7.0*	0.01*
Left	29.6 ± 6.0	31.4 ± 7.2	28.9 ± 5.8	28.0 ± 5.6	0.71
Forefoot: R:L ratio†	1.17 ± 0.1	1.06 ± 0.1*	1.13 ± 0.1	1.00 ± 0.1*	0.002*
Rear:forefoot ratio					
Right	2.20 ± 1.2	2.33 ± 0.9	2.21 ± 0.8	2.73 ± 0.9*	0.03*
Left	2.61 ± 1.4	2.47 ± 1.3	2.19 ± 0.3	2.65 ± 0.5	0.23

* $p < 0.05$ from corresponding point T1.
† R = right foot; L = left foot.

TABLE 6. Forefoot R:L ratio pressure data: left-dominant subgroup.

	CFA (N = 9)		Placebo (N = 13)		
Plantar pressure	T1	T2	T1	T2	Probability
Rearfoot pressure (kPa)					
Right	70.0 ± 23.2	67.6 ± 20.0	75.0 ± 24.7	75.8 ± 23.3	0.80
Left	85.0 ± 33.2	89.5 ± 24.5	84.6 ± 22.3	80.8 ± 22.6	0.91
Rearfoot: R:L ratio‡	1.07 ± 0.9	0.82 ± 0.3	0.94 ± 0.4	1.02 ± 0.5	0.49
Forefoot pressure (kPa)					
Right	28.3 ± 8.2	30.4 ± 8.9*	26.1 ± 7.7	28.3 ± 8.8*	0.02*
Left	40.6 ± 10.8	39.7 ± 13.1	34.5 ± 9.7	35.3 ± 8.1	0.96
Forefoot: R:L ratio‡	0.70 ± 0.2	0.79 ± 0.2†	0.76 ± 0.1	0.80 ± 0.2	0.10
Rear:forefoot ratio					
Right	2.64 ± 1.1	2.44 ± 1.1	3.14 ± 1.4	3.02 ± 1.6	0.16
Left	2.22 ± 1.0	2.49 ± 1.0	2.69 ± 1.2	2.44 ± 0.9	0.97

* $p < 0.05$ from corresponding point T1.
† $p = 0.01$ from corresponding point T1.
‡ R = right foot; L = left foot.

changes in adhesion molecule expression and apoptosis triggering, and alterations in signal transduction and membrane fluidity (11, 20, 21). Our previous research demonstrated pain relief resulting from treatment with cetylated fatty acids (13, 19). Although not measured in the present investigation, it appeared that greater postural stability observed in our sample of patients with OA was a result of pain relief.

Patients with knee OA have been shown to have other functional limitations. Articular damage may result in loss of motor control, motoneuron excitability, and proprioceptive acuity (10, 16). It has been shown that patients with knee OA have reduced quadriceps muscle strength (10, 16, 18), reduced functional performance (e.g., limited ability to ascend/descend stairs, limited ability to rise from a chair and walk, etc.) (16, 19), greater postural sway (10, 14, 16), and altered gait mechanics to accommodate the ensuing pain (8, 24). In our previous study, we showed that 30 days of treatment with a topical cream consisting of a blend of cetylated fatty acids resulted in significant improvements in knee range of motion, stair climbing ability, timed "up-and-go" performance from a chair, local muscular endurance via medial step-down performance, and unilateral anterior reach performance (19). Of interest, we also measured acute performance following 30 minutes of the first topical cream application and reported significant increases in these functional performance tests (19). Thus, it appears that some of the functional limitations observed in patients with knee OA could be minimized with cetylated fatty acid treatment. Along with the data from our previous research (13, 19), the results of the present study support the contention that functional performance may be improved with use of cetylated fatty acids.

Control of postural stability is quite complex but is dependent on vestibular, visual, and somatosensory inputs; central processing; and appropriate motor response to maintain equilibrium (14). Several potential mechanisms may produce postural instability in patients with knee OA. Loss of muscle strength and proprioception in the lower limbs may reduce postural stability (16, 18). Pain has been shown to reflexively inhibit muscle activation around the knee (1) as well as alter the mechanics of standing, normal gait, or both. Knee pain and muscle strength have been shown to be significant predictors of postural sway (10, 14, 18). In addition, Potter et al. (26) have shown greater mediolateral and anteroposterior sway with 15° and 30° of unilateral and bilateral knee-flexion contracture. Unilateral knee-flexion contracture resulted in significant movement of the COP toward the

asymptomatic leg. Based on these findings, nonsurgical treatments designed to improve postural stability in patients with knee OA may include muscle strengthening exercise or pain-relieving treatments or medications. In fact, both aerobic exercise and weight training have been shown to reduce postural sway in patients with knee OA (23). It may be hypothesized that pain reduction can result in patients exerting more effort via reduction in pain-induced reflex inhibitions of the quadriceps (9). Considering that pain reduction in patients with knee OA has resulted in greater loading to the symptomatic leg during normal gait (17), our data provide further support demonstrating that pain relief may reduce static postural instability.

Pain relief has not been shown to enhance postural stability in all studies. Hassan et al. (9) provided short-term pain relief in patients with knee OA through intra-articular injections with 0.5% bupivacaine (a local anesthetic) and 0.9% saline. Both treatments resulted in increased maximal voluntary contraction strength and a greater extent of quadriceps muscle activation. However, pain relief resulted in reduced proprioceptive acuity and no change in postural sway was observed. The reason for the lack of improvement in postural stability with pain reduction and acute muscle strength increase in this study is unclear, but may be related to the assessment for postural sway used. Aside from differences in methodology between this investigation and that of the present study, our data showed that long-term treatment resulting in pain relief did improve postural stability in patients with knee OA.

Unique to the present investigation was the measurement of plantar pressures during quiet standing in patients with knee OA. To our knowledge, this was the first study to examine plantar pressures in patients with knee OA during a treatment intervention. Although plantar pressure measurements have been used to study the extent of neuropathy in patients with diabetes (3, 6), these data remain relatively obscure in patients with knee OA undergoing treatment. Plantar pressures, especially in the forefoot region, have been shown to be important factors for postural control (28). Thus, examination of plantar pressures may provide useful information in addition to COP data for the assessment of postural stability in patients with OA.

Although postural stability improved in the CFA group, no significant differences were observed in plantar pressures during quiet standing when the plantar pressure data were analyzed in total. No changes in mean plantar pressures in the forefoot or rearfoot regions, or with the selected ratios were observed. However, examining the data in total may not reflect potential changes unless further subclassifications are used. For example, some participants may shift weight from the right to the left sides and vice versa when pain relief occurs. These contralateral shifts may balance each other when analyzed in total, thereby leading to no observable differences overall. That is why it was necessary to separate those who favored the right side from those who favored the left side to obtain a more accurate representation. In addition, we used both the rearfoot and forefoot right-to-left ratios for classification (i.e., ratio >1 indicates right dominance; <1 indicates left dominance). For the subgroup of participants that placed a larger magnitude of weight on their right rearfoot ($N = 15$), no significant differences were observed (Table 3). Although the rearfoot right-to-left ratios tended to decrease (more so in the CFA group), these data were not significant, possibly due to the low statistical power observed with an N size of only 15 in this subgroup. For the left-dominant subgroup (Table 4; $N = 25$), no significant differences were observed, although a trend ($p = 0.06$) for increase in the rearfoot right-to-left ratio was observed.

Considering that plantar pressures in the forefoot region demonstrate perhaps greater importance for postural control (28), we also classified participants based on forefoot right-to-left plantar pressure ratios. Unlike the rearfoot and combined data, significant changes were observed in the forefoot region. For right-dominant participants ($N = 18$), reductions in right forefoot plantar pressure and right-to-left ratios were observed in CFA and P. For left-dominant participants ($N = 22$), increases in right forefoot pressures were observed in both groups. In addition, a trend toward an increase in the right-to-left ratio was observed in CFA ($p = 0.10$). Taken together, these data provide some indication that subtle changes occurred in the forefoot region, thereby favoring greater postural stability. However, the majority of changes occurred in both groups, yet no differences in COP measurements were observed in the P group. The reason or reasons for the lack of more substantial improvements in the CFA group are unclear considering the greater magnitude of pain relief and postural stability enhancement. A few factors need to be considered. First, by subclassifying participants into smaller groups, the lower N size reduced statistical power. Thus, some potential changes may have been masked by the low N size. For example, in the left-dominant group, a trend ($p = 0.10$) was observed in the CFA group toward improving the forefoot right-to-left ratio, thereby leading to greater balance. Because the forefoot plantar pressure ratio is critical for postural stability (28) and most of our participants favored the left side (due to greater reported pain in the right knee), significance in this measure may have partially explained the greater improvement in postural stability in the CFA group. Second, we selected different durations of time for our quiet standing protocols (e.g., 40 seconds for the COP measurements vs. only 20 seconds for plantar pressure assessments). It may be speculated that greater fatigue is present with the longer duration of standing; therefore, greater postural sway may have occurred with a longer standing protocol (and perhaps we would have observed more substantial changes if we had selected 40 seconds instead of 20 seconds). Thus, it is possible that 20 seconds may not have been a sufficient duration. Finally, the possibility that other factors associated with pain relief occurred independently of changes in plantar pressures cannot be discarded. Nevertheless, these data indicate that postural stability increased significantly in CFA despite minor changes in plantar pressures.

PRACTICAL APPLICATIONS

In summary, the results of the present investigation indicate that 30 days of treatment with a topical cream consisting of a blend of cetylated fatty acids is effective for improving static postural stability in patients with knee OA. The results this study and our previous investigation support the use of cetylated fatty acids in the treatment of OA. Hopefully, such over-the-counter treatment may enhance the trainability of people with OA in exercise

programs, especially with the importance as it related to successful aging.

REFERENCES

1. ARVIDSSON, I., E. ERIKSSON, E.S.A. KNUTSSON, AND S. ARNER. Reduction of pain inhibition on voluntary muscle activation by epidural analgesia. *Orthopedics* 9:1415–1419. 1986.
2. BRANDT, K. Nonsteroidal anti-inflammatory drugs and articular cartilage. *J. Rheumatol.* 14(Suppl):132–133. 1987.
3. CASELLI, A., H. PHAM, J.M. GIURINI, D.G. ARMSTRONG, AND A. VEVES. The forefoot-to-rearfoot plantar pressure ratio is increased in severe diabetic neuropathy and can predict foot ulceration. *Diabetes Care* 25:1066–1071. 2002.
4. CLIVE, D.M., AND J.S. STOFF. Renal syndromes associated with nonsteroidal anti-inflammatory drugs. *N. Eng. J. Med.* 310: 563–572. 1984.
5. CURTIS, C.L., C.E. HUGHES, C.R. FLANNERY, C.B. LITTLE, J.L. HARWOOD, B. CATERSON. N-3 fatty acids specifically modulate catabolic factors involved with articular cartilage degradation. *J. Biol. Chem.* 275:721–724. 2000.
6. FRYBERT, R.G., L.A. AVERY, H. PHAM, C. HARVEY, L. HARKLESS, AND A. VIVES. Role of neuropathy and high foot pressures in diabetic foot ulceration. *Diabetes Care* 21:1714–1719. 1998.
7. GILLETTE, J.C., N.E. QUICK, AND J.J. ABBAS. Center of pressure measures to assess standing performance. *Biomed. Sci. Instrum.* 38:239–244. 2002.
8. GOK, H., S. ERGIN, AND G. YAVUZER. Kinetic and kinematic characteristics of gait in patients with medial knee arthrosis. *Acta Orthop. Scand.* 73:647–652. 2002.
9. HASSAN, B.S., S.A. DOHERTY, S. MOCKETT, AND M. DOHERTY. Effect of pain reduction on postural sway, proprioception, and quadriceps strength in subjects with knee osteoarthritis. *Ann. Rheum. Dis.* 61:422–428. 2002.
10. HASSAN, B.S., S. MOCKETT, AND M. DOHERTY. Static postural sway, proprioception, and maximal voluntary quadriceps contraction in patients with knee osteoarthritis and normal control subjects. *Ann. Rheum. Dis.* 60:612–618. 2001.
11. HERAUD, F., A. HERAUD, AND M.F. HARMAND. Apoptosis in normal and osteoarthritic human articular cartilage. *Ann. Rheum. Dis.* 59:959–965. 2000.
12. HERTEL J., M.R. GAY, AND C.R. DENEGAR. Differences in postural control during single-leg stance among healthy individuals with different foot types. *J. Athl. Train.* 37:129–132. 2002.
13. HESSLINK, R., D. ARMSTRONG, M.V. NAGENDRAN, S. SREEVATSAN, AND R. BARATHUR. Cetylated fatty acids improve knee function in patients with osteoarthritis. *J. Rheumatol.* 29:1708–1712. 2002.
14. HINMAN, R.S., K.L. BENNELL, B.R. METCALF, AND K.M. CROSSLEY. Balance impairments in individuals with symptomatic knee osteoarthritis: a comparison with matched controls using clinical tests. *Rheumatology (Oxford)* 41:1388–1394. 2002.
15. HOCHBERT, M.C., R.D. ALTMAN, K.D. BRANDT, B.M. CLARK, P.A. DIEPPE, M.R. GRIFFIN, R.W. MOSKOWITZ, T.J. SCHNITZER. Guidelines for the medical treatment of osteoarthritis II: Osteoarthritis of the knee. *Arthritis Rheumatol.* 38:1541–1546. 1995.
16. HURLEY, M.V., D.L. SCOTT, J. REES, AND D.J. NEWHAM. Sensorimotor changes and functional performance in patients with knee osteoarthritis. *Ann. Rheumatol. Dis.* 56:641–648. 1997.
17. HURWITZ, D.E., A.R. RYALS, J.A. BLOCK, L. SHARMA, T.J. SCHNITZER, AND T.P. ANDRIACCHI. Knee pain and joint loading in subjects with osteoarthritis of the knee. *J. Orthop. Res.* 18: 572–579. 2000.
18. JADELIS, K., M.E. MILLER, W.H. EETTINGER, AND S.P. MESSIER. Strength, balance, and the modifying effects of obesity and knee pain: Results from the Observational Arthritis Study in Seniors (oasis). *J. Am. Geriatr. Soc.* 49:884–891. 2001.
19. KRAEMER, W.J., N.A. RATAMESS, J.A. ANDERSON, C.M. MARESH, D.P. TIBERIO, M.E. JOYCE, B.N. MESSINGER, D.N. FRENCH, M.J. SHARMAN, M.R. RUBIN, A.L. GOMEZ, J.S. VOLEK, AND R.L. HESSLINK. Effect of a cetylated fatty acid topical cream on functional mobility and quality of life of patients with osteoarthritis. *J. Rheumatol.* 31:767–774. 2004.
20. KREMER, J.M. Effects of modulation of inflammatory and immune parameters in patients with rheumatic and inflammatory disease receiving dietary supplementation of N-3 and N-6 fatty acids. *Lipids* 31(Suppl):S243–S247. 1996.
21. KREMER, J.M. N-3 fatty acid supplements in rheumatoid arthritis. *Am. J. Clin. Nutr.* 71(Suppl):349S–351S. 2000.
22. LAWRENCE, R.C., C.G. HELMICK, AND F.C. ARNETT. Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. *Arthritis Rheumatol.* 41:778–799. 1998.
23. MESSIER, S.P., T.D. ROYER, T.E. CRAVEN, M.L. O'TOOLE, R. BURNS, AND W.H. ETTINGER. Long-term exercise and its effect on balance in older, osteoarthritic adults: Results from the Fitness, Arthritis, and Seniors Trial (FAST). *J. Am. Geriatr. Soc.* 48:131–138. 2000.
24. OTSUKI, T., K. NAWATA, AND M. OKUNO. Quantitative evaluation of gait pattern in patients with osteoarthrosis of the knee before and after total knee arthroplasty. Gait analysis using a pressure measuring system. *J. Orthop. Sci.* 4:99–105. 1999.
25. PANZER, V.P., S. BANDINELLI, AND M. HALLETT. Biomechanical assessment of quiet standing and changes associated with aging. *Arch. Phys. Med. Rehabil.* 76:151–157. 1995.
26. POTTER, P.J., R.L. KIRBY, AND D.A. MCLEOD. The effects of simulated knee-flexion contractures on standing balance. *Am. J. Phys. Med. Rehabil.* 69:144–147. 1990.
27. SILVER, F.H., G. BRADICA, AND A. TRIA. Relationship among biomechanical, biochemical, and cellular changes associated with osteoarthritis. *Crit. Rev. Biomed. Eng.* 29:373–391. 2001.
28. TANAKA, T., H. TAKEDA, T. IZUMI, S. INO, AND T. IFUKUBE. Age-related changes in postural control associated with location of the center of gravity and foot pressure. *Phys. Occup. Ther. Geriatr.* 15:1–14. 1997.
29. TJON A HEN, S.S.K., A.C.H. GERUTS, P. VAN'T PAD BOSCH, R.F.J.M. LAAN, AND T. MULDER. Postural control in rheumatoid arthritis patients scheduled for total knee arthroplasty. *Arch. Phys. Med. Rehabil.* 81:1489–1493. 2000.
30. WEGENER L., C. KISNER, AND D. NICHOLS. Static and dynamic balance responses in persons with bilateral knee osteoarthritis. *J. Orthop. Sports Phys. Ther.* 25:13–18. 1997.
31. WILCOX, C.M., K.A. SHALEK, AND G. COTSONIS. Striking prevalence of over-the-counter nonsteroidal anti-inflammatory drug use in patients with upper gastrointestinal hemorrhage. *Arch. Intern. Med.* 15:42–45. 1994.

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