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Wireless Versus Wired Iontophoresis for Treating Patellar Tendinopathy: A Randomized Clinical Trial

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Context: The efficacy of the relatively new wireless iontophoresis patch compared with the traditional wired dose controller is unknown.

Objective: To determine the differences among 2 iontophoresis drug-delivery systems (wireless patch versus wired dose controller) and a sham treatment in treating patellar tendinopathy.

Design: Randomized controlled clinical trial.

Setting: Physical therapy clinic.

Patients or Other Participants: Thirty-one participants diagnosed with patellar tendinopathy (men = 22, women = 9, age = 24.5 ± 5.9 years).

Intervention(s): Participants were randomly assigned into 1 of 3 treatment groups: wireless patch, wired dose controller, or sham treatment. Participants in the active treatment groups received six 80 mA/min iontophoresis treatments using 2 mL of 4% dexamethasone sodium phosphate. During each visit, clinical outcome measures were assessed and then the assigned treatment was applied.

Main Outcome Measure(s): Clinical outcome measures were Kujala Anterior Knee Pain Scale, pressure sensitivity, knee-extension force, and sit-to-stand pain assessment using a numeric rating scale. For each clinical outcome measure, we used a repeated-measures analysis of covariance to determine differences among the treatment groups over the treatment period.

Results: Participants reported a clinically important improvement on the Kujala Anterior Knee Pain Scale across all treatment groups, with no differences among groups ($P = .571$). A placebo effect was observed with pressure sensitivity ($P = .0152$); however, the active treatment decreased participants' pain during the sit-to-stand test ($P = .042$).

Conclusions: A placebo effect occurred with the sham treatment group. Generally, improvement was noted in all groups regardless of treatment type, but greater pain reduction during a functional task was evident within the active treatment groups during the sit-to-stand test. The wireless patch and wired dose controller treatments were equivalent across all variables.

Key Words: transdermal drug delivery, therapeutic modalities, tendon injuries

Key Points

- Wireless patch iontophoresis was as effective as a wired dose controller at treating patellar tendinopathy with dexamethasone.
- All groups improved with the 6 iontophoresis treatments, but the active treatments (ie, wireless patch and wired dose controller) were better at reducing participants' pain during a functional task.

Iontophoresis is a transdermal drug-delivery method used to apply anti-inflammatory and anesthetic drugs directly to an area. Iontophoresis uses a mild direct current to repel positive or negative drug ions through the stratum corneum of the epidermis and into the underlying tissues.[1] Iontophoresis has several advantages over other drug-delivery methods; for example, it does not carry the risk of pain or infection of needle injections, nor does it involve the loss of drug potency during first-pass metabolism as in oral ingestion.[2]

Iontophoresis with dexamethasone, an anti-inflammatory corticosteroid drug, has been used to successfully treat tendinopathy conditions such as plantar fasciitis,[3] Achilles tendinitis,[4] and lateral epicondylitis.[5,6] The primary outcome of dexamethasone iontophoresis has been short-term pain relief. Trials with a shorter interval between treatments (≤2 days) had better short-term outcomes than trials with longer durations between consecutive treatments.[5,7] However, Hamann et al[8] in a systematic review concluded that evidence of the effectiveness of iontophoresis for inflammatory musculoskeletal conditions was still limited.

Iontophoresis has traditionally been delivered with 2 leads connecting a dose controller to a drug reservoir electrode and a dispersive electrode. Wireless patches were invented to allow patients to freely perform activities of daily living while receiving treatment. Wireless patches provide similar iontophoresis dosages to wired dose controllers, usually 80 mA/min, but they use smaller current intensities (range, 0.05–3.0 mA) for a longer treatment time (range, 3–14 hours). The first wireless patches were challenging because they provided treatment with a single cell battery until it died. The exact iontophoresis dose was not known, and the current density was unable to overcome the skin's resistance. A newer wireless iontophoresis patch has been developed to

combat the problems of the first generation of patches. The ActivaPatch (ActivaTek Inc, Salt Lake City, UT) contains a microchip that can determine the exact iontophoresis dose provided and adjust the current density according to the patient's skin resistance.

Currently no researchers have tested the effectiveness of wireless iontophoresis patches versus traditional dose controllers in treating tendinopathy conditions. The purpose of our study was to conduct a blinded randomized clinical trial to understand the efficacy of different iontophoresis treatment systems versus a sham group for treating patellar tendinitis. A multicomponent rehabilitation program[9] with eccentric loading[10,11] is often used to treat tendinopathies; however, examining iontophoresis without cointerventions allowed us to determine the difference in effectiveness between the iontophoresis conditions. We hypothesized that the wireless patch would produce similar results to the traditional dose control treatments but both active treatments would result in better patient outcomes compared with a sham group.

METHODS

Participants

Participants with a chief complaint of patellar tendon pain were recruited from 2 orthopaedic physical therapy clinics over a 32-month period (June 2011–January 2014). Participants were screened by 1 of the investigators (J.H.R.), who was blinded to group assignment, before being enrolled in the study. The inclusion criteria were (1) aged 18–45 years, (2) patellar tendon pain lasting longer than 1 month but no longer than 2 years, and (3) clinical diagnosis of midsubstance patellar tendinopathy on physical examination from a physician. The exclusion criteria were (1) contraindications to the use of dexamethasone or iontophoresis, (2) lower extremity surgery within the past 6 months, (3) a confounding diagnosis of the lower extremity, (4) corticosteroid treatment within the past 2 months, (5) current use of prescription or over-the-counter pain medication, or (6) signs of inflammation associated with acute tendinitis. Participants were instructed to resume their normal activity levels; however, they were to refrain from taking pain and anti-inflammatory medications. We used a 7-point Likert scale to confirm that participants were maintaining their normal activity levels throughout the study. Participants reviewed and signed a consent form approved by the human institutional review board (which also approved the study) before enrollment.

Examination Procedures

All participants provided demographic information and completed a series of outcome measures at baseline and throughout the study. Outcome measures were (1) Kujala Anterior Knee Pain Scale, (2) pressure sensitivity measured via an algometer, (3) knee-extension strength measured via a strain-gauge dynamometer, and (4) sit-to-stand test. All outcome measurements were assessed and recorded by a blinded clinician (B.B.M.).

After baseline measurements were obtained, participants were randomly assigned into 1 of 3 groups: (1) wired iontophoresis (n = 11), (2) wireless iontophoresis patch (n = 10), or (3) sham (n = 10). All participants were blinded to their treatment group. Each treatment group was assigned a random letter (A, B, or C). Before enrolling participants, we used a random number generator to match each individual's enrollment number to a group's randomly assigned letter.

Functional Outcome Scale. The Kujala Anterior Knee Pain Scale measures perceived level of disability. The Kujala scale is a 100-point, knee-specific functional scale consisting of 13 self-administered questions; a higher score indicates a greater level of function. The scale evaluates the amount of pain and dysfunction a person experiences during normal daily activities.[12] The scale was reliable (intraclass correlation coefficient [3, 1] = 0.81) and validated in patients with anterior patellofemoral pain, and the minimally clinically important difference (MCID) was an increase of 10 points.[13] Participants completed the Kujala scale at each visit (every 2–3 days) based on their perceived pain and dysfunction since the last visit.

Pressure Sensitivity. Pressure sensitivity was measured with a digital pressure algometer (Accelerated Care Plus Corp, Reno, NV). The device consists of a force gauge that measures the applied pressure in kilograms. Pressure was applied over the central part of the patellar tendon, and the participant was instructed to push a trigger button when he or she first started to feel pain. The device digitally recorded the pressure applied when pain was felt. We took 3 measurements and calculated the average. Pressure-sensitivity measurements were taken at the beginning of each visit, before the treatment was applied.

Muscle Strength. We used a strain-gauge dynamometer to measure quadriceps strength. The dynamometer was attached to the leg of a treatment table. While the participant sat on the end of the treatment table, the knee was placed in 90° of flexion and the distal end of the lower leg was secured to the dynamometer. The participant was instructed to extend the knee as forcefully as he or she could. The force during knee extension was recorded in Newtons. We normalized the participant's force production by body mass (N/kg) for all analyses. Quadriceps muscle strength was measured at the participant's enrollment (pretreatment) and at the end of the last treatment (posttreatment).

Sit-to-Stand Test. Participants were asked to perform 10 repetitions of the sit-to-stand test in a chair. At the end of the repetitions, they marked their pain on a numeric rating scale (NRS). The test was performed at the participant's enrollment (pretreatment), before the third treatment (midtreatment), and at the end of the last treatment (posttreatment). A reduction in 1 point on the NRS has signified an MCID for patients with chronic musculoskeletal pain.[14]

Treatment Procedures

Participants in all 3 groups received 3 treatments each week for 2 weeks, for a total of 6 visits. The clinician who applied all of the treatments was semiblinded to the participants' group assignments. The clinician was supplied with vials labeled A, B, or C that corresponded with the randomly assigned treatment group. Complete blinding of the clinician who provided the treatments was not possible because of the differences in application between the wired and patch iontophoresis. The clinician did not know

Table. Patient Demographics and Examination Measurements at Baseline (Mean ± SD)[a]

Variable	Wireless Patch	Wired Dose Controller	Sham	*P* Value	*F* Value[b]
Demographics					
Age, y	26.5 ± 6.1	21.2 ± 2.2	26.0 ± 7.4	.069	2.946
Height, cm	172.2 ± 7.3	177.2 ± 8.4	176.1 ± 7.2	.313	1.210
Mass, kg	68.9 ± 11.1	80.1 ± 9.5	73.3 ± 5.6	.028	4.073
Activity level, 7-point Likert scale	5.6 ± 1.5	5.2 ± 0.9	5.6 ± 1.3	.811	0.2112
Examination measurements					
Kujala Anterior Knee Pain Scale (range, 0–100)	72.6 ± 14.3	72.5 ± 11.0	69.4 ± 8.0	.812	0.2102[c]
Pressure sensitivity, kg	3.8 ± 2.5	3.5 ± 1.3	7.7 ± 2.3	<.001	12.71
Muscle strength, N/kb	50.0 ± 18.5	48.0 ± 19.9	69.5 ± 24.2	.024	4.303
Sit-to-stand test score (range, 0–20+)	4.4 ± 2.0	3.0 ± 1.6	2.7 ± 1.4	.025	4.248

[a] All baseline values were similar across treatment groups except for mass, pressure sensitivity, muscle strength, and sit-to-stand test scores ($P < .05$).
[b] Except as noted, for all *F* values $df = 2, 28$.
[c] $df = 2, 21$.

participant treatment assignments in the wireless iontophoresis patch and sham groups.

Wired Iontophoresis. We used the Trivarion iontophoresis delivery system with the ActivaDose II Controller (ActivaTek Inc) for each wired iontophoresis treatment. During the treatment, the participant lay on a treatment table. Dexamethasone sodium phosphate, 2 mL at 0.4%, was placed in the drug reservoir, and the drug electrode was positioned directly over the midportion of the patellar tendon (Figure 1A). The dispersive electrode was placed 5 to 6 cm away, on the lateral lower leg over the anterior muscle compartment. The electrodes were connected to their respective leads, negative over the drug electrode and positive over the dispersive electrode. The dose control was set to deliver an 80-mA/min iontophoresis treatment. Intensity was set at 4.0 mA (20-minute treatment time), and the participant was instructed to inform the clinician if the intensity was too strong or painful. If the intensity could not be tolerated at 4.0 mA, it was turned down to a tolerable level, and the treatment time was automatically adjusted to maintain the correct iontophoresis dose.

Wireless Iontophoresis Patch. We used the ActivaPatch (ActivaTek Inc) for each wireless iontophoresis treatment. Dexamethasone sodium phosphate, 2 mL at 0.4%, was placed in the drug reservoir of the iontophoresis patch. The drug reservoir was placed directly over the midportion of the patellar tendon, with the dispersive portion of the patch placed laterally (Figure 1B). The ActivaPatch delivers an 80-mA/min treatment in approximately 2.5 hours at a current intensity of 0.5 mA. We instructed participants to wear the patch for 3 hours and to resume their normal daily activities.

Sham. For each sham treatment, 2 mL of saline was placed in the drug reservoir of the ActivaPatch, which was

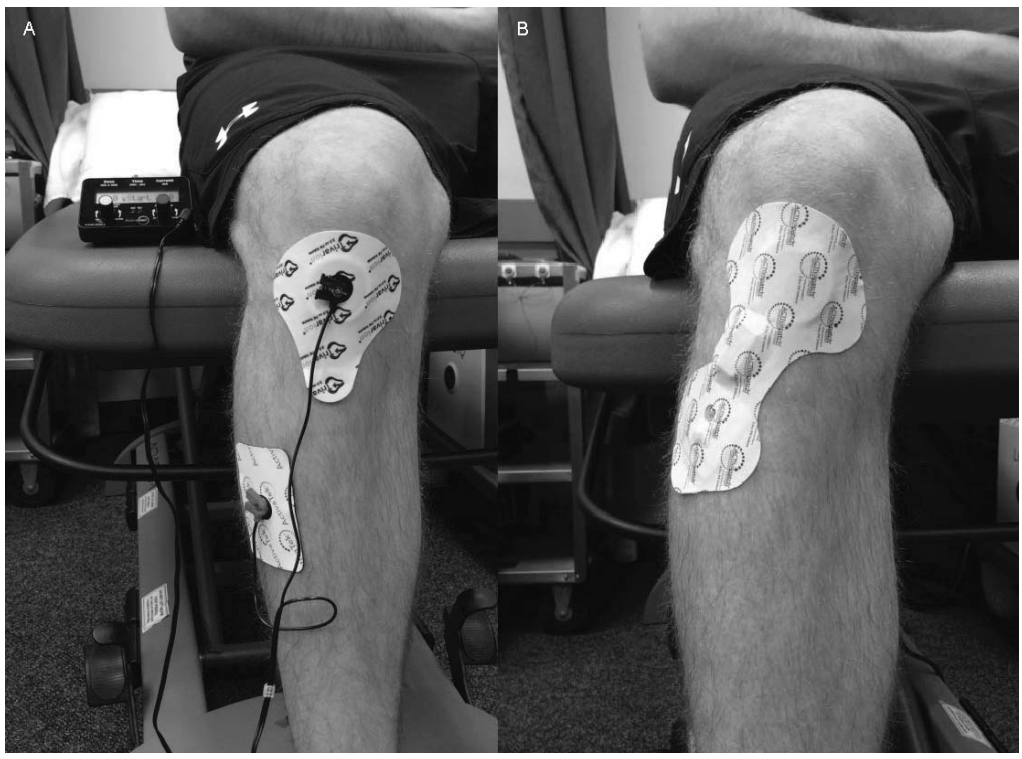

Figure 1. Placement of iontophoresis treatment over patellar tendon for A, wired dose controller, and B, wireless patch.

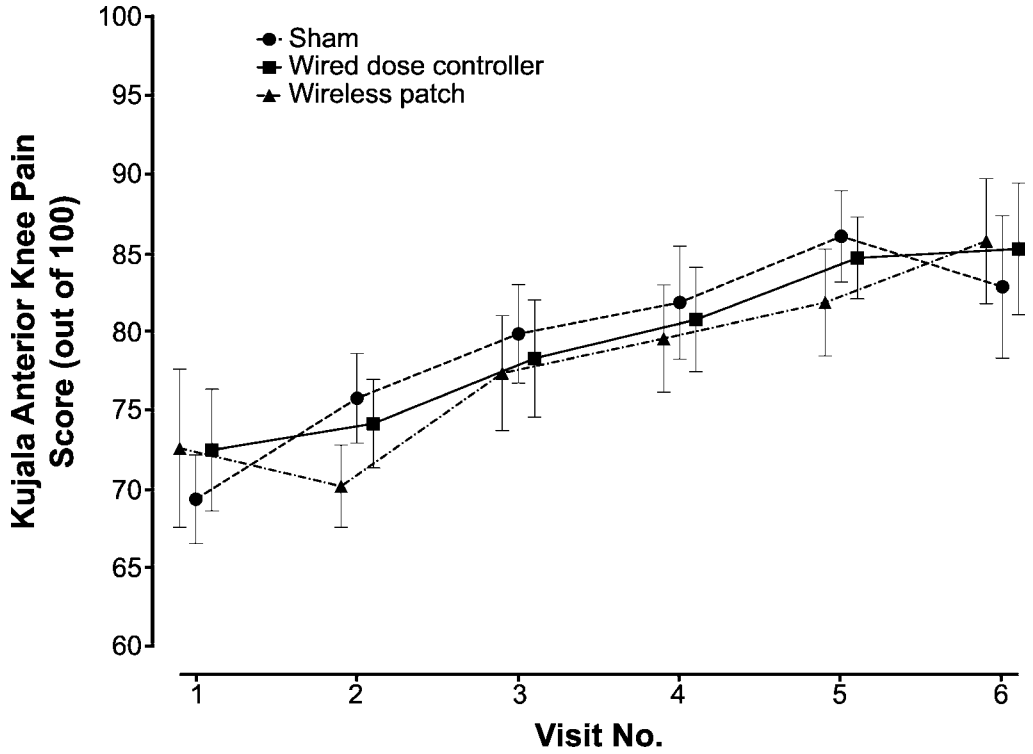

Figure 2. Kujala Anterior Knee Pain Scale. All treatment groups improved from baseline measurements, but the groups did not differ ($P = .571$). Participants' self-reported functional outcome scores were measured at each visit.

placed on the skin in the same fashion as for the wireless iontophoresis patch group. For all sham treatments, the circuit in the ActivaPatch was cut, resulting in no current flow. We instructed the participants to leave the patch on for 3 hours. They were allowed to resume their normal daily activities while they wore the patch.

Data Analysis

Baseline demographic and outcome variable data were compared among treatment groups using 1-way analyses of variance to assess the adequacy of randomization. For each outcome measure, we used a repeated-measures analysis of covariance to determine differences among treatment groups over time (ie, treatment × time interaction). Baseline values served as a covariate to account for individual variations among participants. For each analysis of covariance, the hypothesis of interest was the 2-way interaction of treatment group by time. When appropriate, Tukey-Kramer post hoc analyses were calculated. We used JMP Pro 10 (SAS Inc, Cary, NC) for all statistical analyses and set α at $P < .05$.

We determined Cohen d effect sizes for each outcome measure using the initial visit as the prestudy data and the last visit as the poststudy data.

RESULTS

Participant baseline data are presented in the Table. At baseline, participants were similar in all demographic variables except mass. Differences were evident in 3 of the 4 examination measurements at baseline. The sham group withstood greater pressure at baseline compared with the 2 iontophoresis groups ($F_{2,28} = 12.71$, $P < .0001$). The sham group produced greater force per kilogram of body weight during knee extension at baseline than the other groups ($F_{2,28} = 4.303$, $P = .024$). The wireless iontophoresis patch group experienced more pain during the sit-to-stand test compared with the other treatment groups ($F_{2,28} = 4.248$, $P = .025$).

Participants in all groups self-reported an increase in function on the Kujala Anterior Knee Pain Scale from their first to last visit ($P < .05$), but we observed no differences among treatment groups ($F_{10,122} = 0.862$, $P = .571$; Figure 2). The increase in Kujala Anterior Knee Pain Scale score from baseline to posttreatment reached the MCID threshold (10) in the active treatment groups and was close to the threshold in the sham treatment group. On average, participants reported increases of 11.6 ± 13.8, 12.8 ± 10.5, and 9.4 ± 13.1 points from baseline to posttreatment on the Kujala Anterior Knee Pain Scale after the wired, wireless patch, and sham treatments, respectively.

A placebo effect was associated with pressure sensitivity. Over the course of the 6 treatment visits, the sham group's resistance to pressure sensitivity increased more than that of the wired and wireless patch iontophoresis groups ($F_{10,139} = 113.16$, $P = .0152$; Figure 3). The sham treatment group withstood 4.3 ± 5.4 kg more pressure at the end of the 6 visits compared with baseline measures, whereas the wired and wireless iontophoresis groups increased pressure tolerance by 0.2 ± 2.8 and 2.5 ± 4.5 kg, respectively.

Muscle strength did not change from the first to last visit within or among treatment groups ($F_{2,28} = 2.05$, $P = .148$; Figure 4). However, the active treatment groups showed clinically relevant improvements, with effect sizes of 0.47 (95% confidence interval [CI] = 0.35, 0.61) and 0.27 (95% CI = 0.10, 0.42) for the wired and wireless treatment groups, respectively, compared with the sham treatment

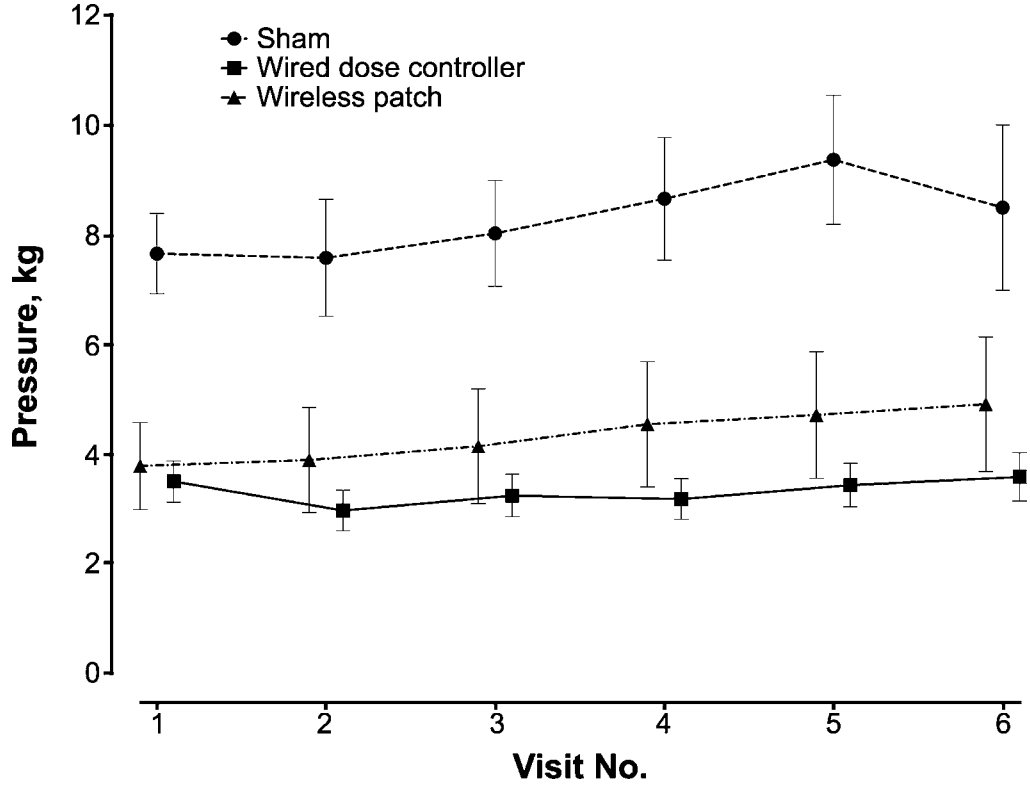

Figure 3. Pressure sensitivity. Compared with the active treatment groups, the sham treatment group withstood greater pressure at baseline ($P < .001$) and displayed an increased pressure threshold over the course of the 6 treatments ($P = .0152$). Pressure sensitivity was measured at each visit using a pressure algometer.

group, which demonstrated a negative effect size of –0.33 (95% CI = –0.57, –0.12). The effect sizes for all outcome variables are reported in Figure 5.

Pain in the wired and wireless patch iontophoresis groups decreased during the sit-to-stand test compared with the sham group ($F_{4,56} = 2.657$, $P = .042$; Figure 6). From baseline to after the sit-to-stand test, the wired and wireless treatment groups' pain scores changed by –1.5 ± 1.5 and –2.0 ± 1.1 points, respectively. The sham treatment decreased participants' scores by –0.1 ± 1.8 points. The wired iontophoresis treatment resulted in a large, clinically meaningful effect size of 1.01 (95% CI = 0.11, 1.88), whereas the wireless patch and sham treatments had CIs that spanned 0, signifying less clinical effectiveness.

DISCUSSION

After 2 weeks of treatment, dexamethasone delivered via iontophoresis reduced pain in patients with musculoskeletal conditions such as knee osteoarthritis,[15] plantar fasciitis,[3,16] and lateral epicondylitis.[5,6] We found similar short-term pain relief using iontophoresis with dexamethasone to treat participants with patellar tendinopathy. Participants in the active treatment groups demonstrated a decrease in pain during the functional sit-to-stand test after 2 weeks or treatment. At baseline, the wireless iontophoresis treatment group had more pain than those receiving the wired or sham treatments. This elevated baseline pain score may have been a factor in the larger effect size we found. The sham group had the lowest pain score at baseline (2.7 ± 1.4), with virtually no difference at the end of the treatment. The wireless patch treatment group had a similar pain score to that of the sham group at baseline (3.0 ± 1.6) but had a clinically meaningful reduction in pain after the 2 weeks of treatment.[14]

With regard to subjective information, a placebo effect occurred with our iontophoresis treatments. All participants, regardless of treatment group, reported a clinically meaningful improvement in functional outcomes, and sham participants withstood more pressure than the active treatment groups. Our results contrast with those of the majority of studies, which demonstrated that iontophoresis with dexamethasone improved participant-reported functional outcomes[4,5,17] and pain[16] compared with the sham treatment groups. It is not entirely clear why we noted larger placebo effects during the sham iontophoresis treatment than other researchers, but our participant population was a possible factor. We recruited much younger participants (mean age = 24.8 years) who were highly active (mean = 5.5 ± 1.2 on a 7-point Likert scale), whereas other investigators studied participants who were considerably older (range of means, 38–54 years). Generally, younger participants have a bigger placebo response than older participants.[18] The differences in mentality and healing response between our participants and those in other studies make comparisons difficult.

Glucocorticoids, such as dexamethasone, have stunted tendon stem cell proliferation,[19] decreased collagen gene expression,[19] increased nontendinous cell formation,[19] and induced cellular senescence[20] (biological aging) at concentrations normally injected. In contrast to the iontophoresis treatment resulting in a placebo effect, we could hypothesize that the delivered dexamethasone inhibited normal healing. However, we still propose that a placebo effect

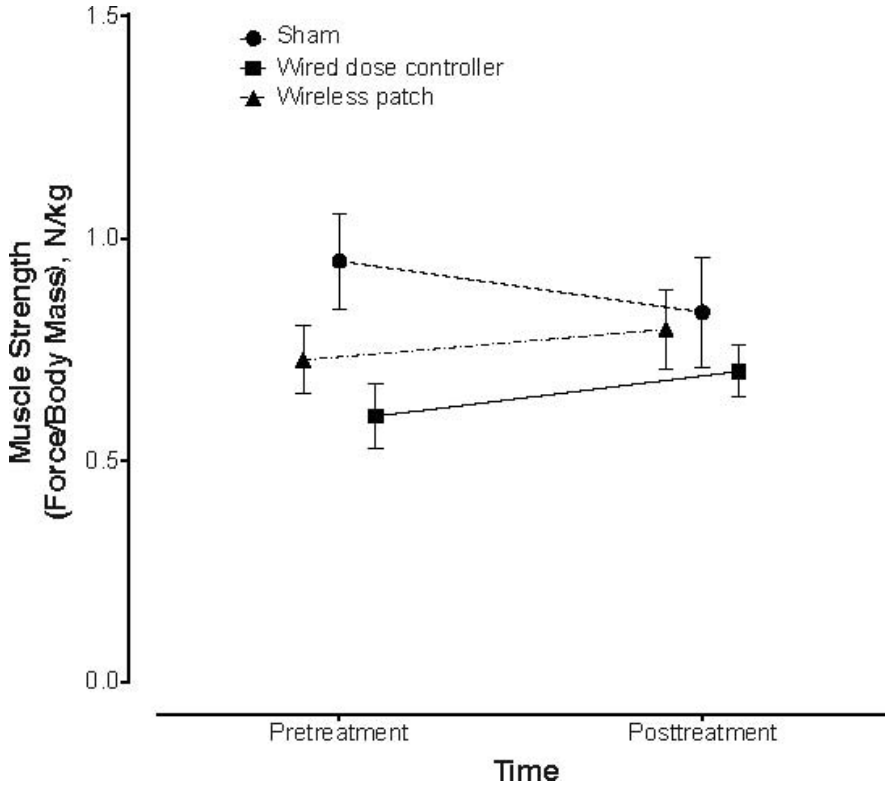

Figure 4. Muscle strength. The force produced by knee extension was measured by a handheld dynamometer at visits 1 and 6 and was normalized by the participant's body mass (N/kg). The sham treatment group produced greater strength per unit of body mass at baseline than the active treatments ($P = .024$). Muscle strength did not increase in the active treatment groups ($P = .148$).

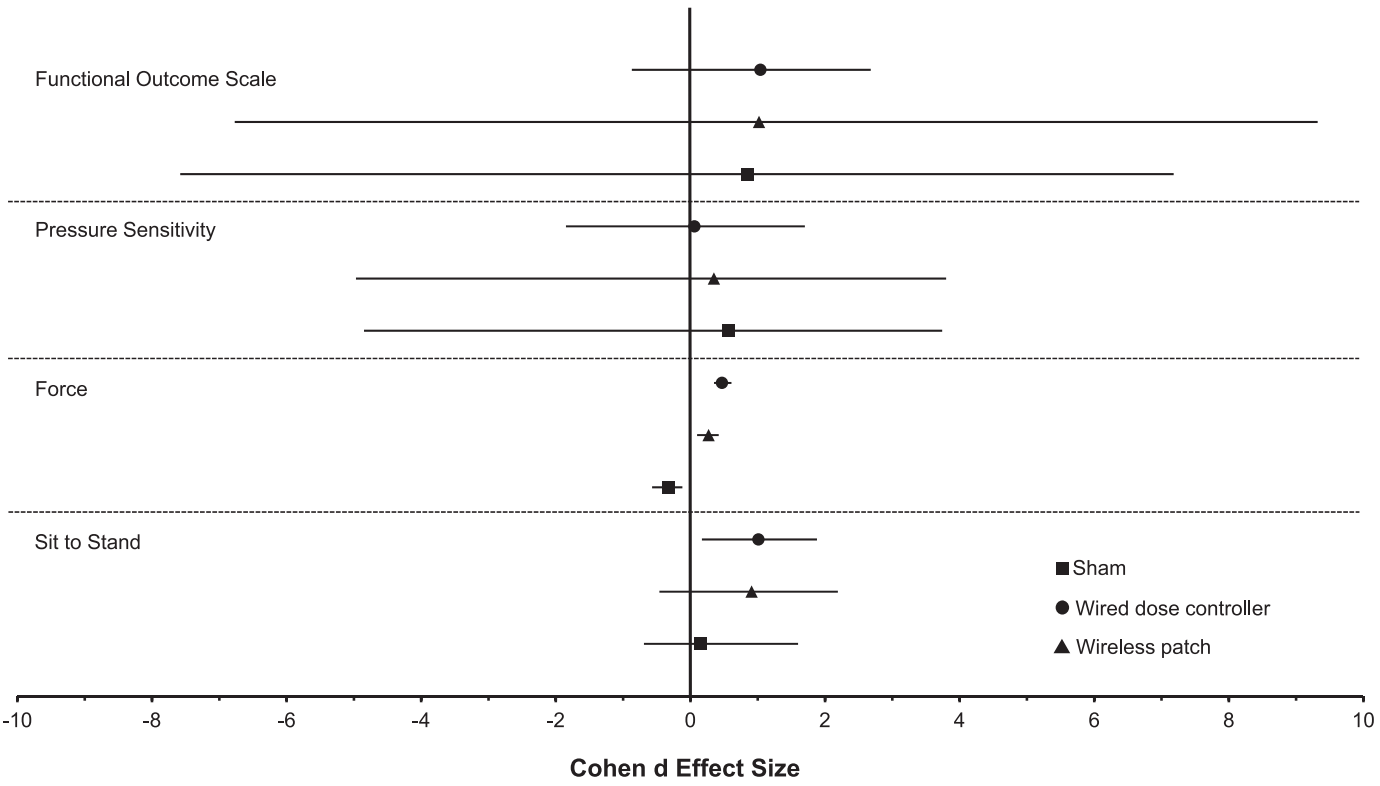

Figure 5. Cohen d effect sizes were calculated using means and standard deviations from visits 1 and 6 data for each outcome measurement. Error bars represent 95% confidence intervals.

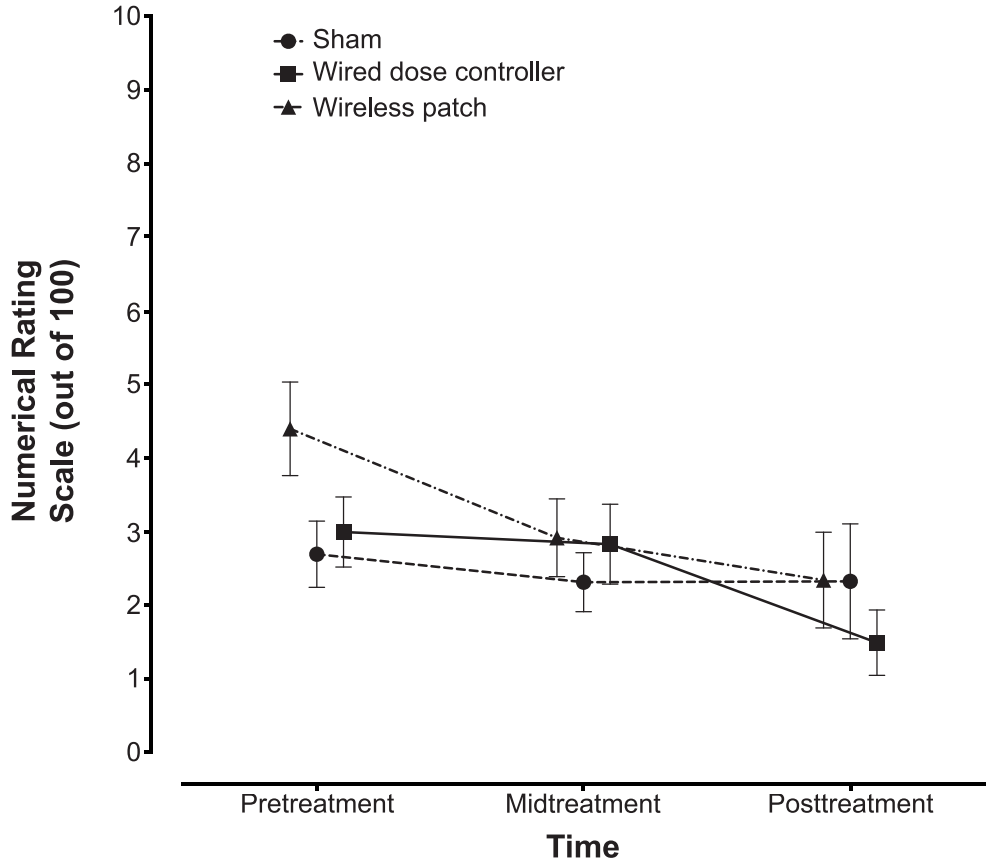

Figure 6. Sit-to-stand test. Both active treatment groups, wired and wireless patch iontophoresis, experienced less pain than the sham treatment group ($P = .042$). The sit-to-stand test was assessed at visits 1, 3, and 6. Participants performed 10 repetitions of sitting and standing and marked their pain on the numeric rating scale.

occurred. Our participants reported improvement in all subjective measurements throughout the 2-week treatments. We would expect a decrease in outcome measures if dexamethasone was, in fact, inhibiting normal healing. Also, dexamethasone delivered transdermally via iontophoresis has resulted in very low tissue concentrations[21,22] (over 100-fold decrease from the injection concentration) and is quickly metabolized to a less potent glucocorticoid.[22] Future research is needed to determine the effect of iontophoresis-delivered concentrations of dexamethasone on tendon healing.

To our knowledge, no other scientists have measured patient-oriented outcomes between the traditional wired dose controller treatment and a wireless patch iontophoresis treatment. We did not find differences between the wired dose controller treatment and wireless patch in any outcome measure, indicating that the 2 delivery methods similarly reduce clinical pain. Clinician and patient preferences should be used to decide which mode of delivery is used.

Authors[23] of a previous study aimed to measure the delivery concentration of dexamethasone after wired dose controller and wireless patch iontophoresis treatments. Anderson et al[23] reported that the wireless patch (Iontopatch; Travanti Medical, St Paul, MN) delivered greater concentrations of dexamethasone into the tissues because of its lower current intensity. They indirectly assessed dexamethasone delivery by measuring skin blanching associated with dexamethasone's ability to vasoconstrict skin. Although greater skin blanching was associated with wireless patch delivery, Rigby et al[22] determined through direct dexamethasone recovery in vivo during iontophoresis treatments that concentration did not differ among varying current intensities if similar iontophoresis doses were used.

With direct in vivo measurements of dexamethasone during and after iontophoresis treatments, we assumed that a greater concentration of dexamethasone would lead to more positive clinical outcomes. However, higher concentrations of dexamethasone may have negative effects on tissue healing, as previously described.[19,20] Currently no researchers have determined the optimal concentration of dexamethasone to be delivered to the target tissues, if a greater concentration of drug within the tissues stimulates greater clinical outcomes, or if a standard minimal concentration is sufficient to bind to the glucocorticoid receptor for the desired anti-inflammatory response. Future study is needed to determine a proper dose-response curve with different iontophoresis dosages and dexamethasone delivery concentrations.

Dexamethasone delivered via iontophoresis did not improve our only objective measure of knee-extension strength. Although the result was not statistically significant, active iontophoresis was associated with moderate effect sizes, leading us to hypothesize that dexamethasone iontophoresis had the clinical benefit of improving objective functional strength. We would assume an increase in patellar tendon healing would lead to greater knee-extension strength.[24] In retrospect, we realize we should have measured knee-extension strength in the contralateral

healthy leg to confirm whether our participants had strength deficits due to their patellar tendinopathy. Patellar tendinopathy has not been shown to create strength deficits of the knee extensors, but patients with a similar condition, Achilles tendinopathy, had limited strength during ankle plantar flexion.[25–27]

Improved objective measures of healing after dexamethasone iontophoresis treatments have been limited.[17,28] Histologic studies of chronic tendon injuries have shown a lack of proinflammation markers such as prostaglandin E_2.[29–31] Possibly, the limited evidence for iontophoresis improving objective measures is because dexamethasone's anti-inflammatory effects are not the primary cause of tendon healing. Instead, dexamethasone may modulate pain, as observed with subjective outcome improvements, or increased blood flow from the direct current may facilitate healing.[22,32] Future investigators should assess the mechanism of healing and pain reduction associated with dexamethasone delivered via iontophoresis.

Iontophoresis with dexamethasone is usually one part of a multiple component rehabilitation program. During our study, participants were instructed to maintain their normal activity levels but to not receive concurrent treatments or medications. By singling out the iontophoresis treatments, we are able to make direct inferences regarding the efficacy of the iontophoresis treatment in treating patellar tendinopathies. With our results indicating that iontophoresis had at least a placebo effect, and other authors[4,5,16,17] reporting decreased symptoms in patients with various tendon injuries, future researchers should determine the extent to which iontophoresis in combination with other treatments may improve the healing and rehabilitation processes. For example, Cleland et al[7] demonstrated positive clinical outcomes from iontophoresis in combination with therapeutic ultrasound, stretching, and intrinsic foot muscle strengthening in patients with plantar heel pain.

Our study inferences are limited by the relatively small sample size in each treatment group and our lack of long-term follow-up. Ideally, a bigger sample size would allow us to make stronger conclusions about each of our experimental measures among the treatment groups. However, performing only a single-site study restricted our ability to collect a significant injured sample within a meaningful time frame. Researchers should follow up by determining the difference in efficacy between the wired dose controller and wireless patch iontophoresis with dexamethasone. We do not know if the 2 iontophoresis delivery methods differed in producing long-term outcomes (>6 weeks). We did not perform a long-term follow-up because of the difficulties we had in retaining participants after the 2-week treatment period. However, authors of many randomized clinical trials with long-term follow-ups have not found differences between iontophoresis and placebo treatments.[3,17,28,33] Tendinopathy conditions have demonstrated self-healing on long-term follow-up no matter what the interventions were.[34]

CONCLUSIONS

Dexamethasone delivered via iontophoresis to treat patellar tendinopathy was primarily successful in reducing participants' pain after a functional sit-to-stand test. We found a placebo effect: a sham treatment group reported similar functional outcome scale improvements to those of the 2 treatment groups. Future researchers should continue to determine the mechanisms of pain reduction and possible tendon healing associated with dexamethasone iontophoresis. Similar outcomes were noted with both the wired dose controller and wireless patch. Therefore, clinician and patient preferences are the biggest factors in treatment mode selection.

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