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ORIGINAL ARTICLE

Effects of Cryotherapy on Arthrogenic Muscle Inhibition Using an Experimental Model of Knee Swelling

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Objective. **Arthrogenic muscle inhibition (AMI) contributes to quadriceps weakness and atrophy in knee arthritis and following joint injury. This laboratory-based study examined the efficacy of cryotherapy in reducing quadriceps AMI caused by intraarticular swelling.**

Methods. **Sixteen subjects without knee pathology participated, and were randomly assigned to a cryotherapy (n = 8) or control (n = 8) group. Surface electromyography (EMG) from vastus medialis and quadriceps torque measurements were recorded during maximum effort isometric contractions. All subjects then received an experimental joint infusion, whereby dextrose saline was injected into the knee to an intraarticular pressure of 50 mm Hg. EMG and torque measurements were repeated. Thereafter, the cryotherapy group had ice applied to the knee for 20 minutes while the control group did not receive an intervention. EMG and torque measurements were again collected. Quadriceps peak torque, muscle fiber conduction velocity (MFCV), and the root mean square (RMS) of EMG signals from vastus medialis were analyzed.**

Results. **Quadriceps peak torque, MFCV, and RMS decreased significantly following joint infusion ($P \leq 0.001$). Cryotherapy led to a significant increase in quadriceps torque and MFCV compared with controls ($P < 0.05$). The difference in RMS did not reach statistical significance ($P = 0.13$).**

Conclusion. **The study demonstrated that cryotherapy is effective in reducing AMI induced by swelling. Cryotherapy may allow earlier and more effective quadriceps strengthening to occur in patients with knee joint pathology.**

INTRODUCTION

Marked weakness and atrophy of the quadriceps muscles are often observed after knee injury, surgery, or in patients with arthritis. This is partly due to ongoing neural inhibition that prevents the quadriceps from being fully activated, a process known as arthrogenic muscle inhibition (AMI) (1–3). AMI is caused by a change in afferent discharge from the damaged joint and has been linked to swelling, inflammation, pain, and structural damage (1–4). The relative importance of these factors is not clearly understood but it is known that swelling alone provokes potent quadriceps AMI as the injection of fluid into uninjured knee joints notably reduces quadriceps torque (4–6), electromyographic (EMG) activity (6–9), and H-reflex amplitude (10–12). It has been reported that as little as 10 ml of fluid may induce inhibition (5,7), and infusions between 20 ml and 60 ml are capable of reducing maximum isokinetic quadriceps torque by 30–40% (4,5). Aspirating or injecting a local anesthetic into the infused joint largely abolishes AMI, confirming the role of articular sensory receptors in this process (5,10).

The ramifications of AMI are of clinical relevance, as this process may hinder rehabilitation by delaying or even preventing effective quadriceps strengthening. In the first few months after injury or surgery, or when joint damage is extensive, AMI is often severe and quadriceps strengthening protocols can be largely ineffective (13–15), an effect attributed to persistent AMI (13). Lasting quadriceps weakness can impair physical function and quality of life, increase the risk of reinjury to the knee joint, and is thought to contribute to the development and progression of osteoarthritis (1,16–19).

Interventions that reduce AMI should enhance rehabilitation by allowing earlier and more effective quadriceps strengthening to take place in patients with knee damage. Recently, some evidence (12) has emerged that suggests that cooling the knee joint may temporarily reduce AMI.

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Table 1. Subject characteristics*

	Control (n = 7)	Cryotherapy (n = 8)
Age, years	36.5 ± 10.6	34.3 ± 11.7
Height, meters	1.71 ± 0.11	1.80 ± 0.04
Mass, kg	70.1 ± 10.2	78.6 ± 12.2

* Values are the mean ± SD.

Icing the knee joint for 30 minutes reversed the decline in quadriceps H-reflex amplitude observed after joint infusion, an effect that lasted for at least 30 minutes after the ice was removed from the knee (12). More recently, Hopkins (9) showed that 30 minutes of cryotherapy may negate the reductions in lower limb peak torque, power, and quadriceps EMG amplitude caused by knee infusion during a semirecumbent stepping task. While these observations are highly promising, they should be interpreted with some caution. First, several methodologic issues limit the validity of the H-reflex as a measure of AMI (20,21). Second, the semirecumbent stepping task in Hopkins' study (9) relied on the activation of many muscles in the lower limb (not just the quadriceps) and was performed at a very low level of muscle activation, making its relevance to quadriceps strengthening questionable. Therefore, the purpose of the present study was to clarify the effects of cryotherapy on AMI by examining changes in quadriceps peak isometric torque, muscle fiber conduction velocity (MFCV), and EMG amplitude (root mean square [RMS]) in response to swelling and cryotherapy.

SUBJECTS AND METHODS

Subjects. Sixteen subjects (10 men and 6 women) volunteered to participate in this study. The mean ± SD age, height, and mass of the subjects are provided in Table 1. Volunteers were excluded from the study if they had a history of pathology in both knee joints, lower limb or spinal surgery, back pain in the last 6 months with associated neurologic signs or symptoms, or any pathology that precluded their participation in maximum strength testing. In the event of a previous knee injury, the contralateral (uninjured) knee joint was used in testing. Subjects attended a familiarization session prior to testing and provided written informed consent for all experimental procedures. Ethical approval for this study was granted by the Northern Regional Ethics Committee.

Quadriceps torque measurements. Subjects were positioned in an isokinetic dynamometer (Biodex Medical Systems, Shirley, NY) for the performance of maximum isometric quadriceps contractions. The lateral epicondyle of the femur was aligned with the dynamometer's axis of rotation. Straps were firmly secured over the distal tibia, the distal third of the thigh, waist, and chest to limit extraneous movement. With the knee positioned in 60° of flexion, submaximal contractions were performed as a warmup prior to data collection. Thereafter, a set of 3 (6-second) maximal isometric quadriceps contractions were performed at each measurement time point. Subjects received a consistent level of verbal encouragement and were blinded to the torque levels they produced. Subjects rested for 2 minutes between each contraction.

Surface EMG. Surface EMG signals were collected from the vastus medialis (VM) during each maximal isometric contraction. This muscle was chosen because previous studies suggest it may be the most sensitive to swelling-induced AMI (10). Prior to the placement of electrodes, the skin was shaved, abraded (Green Prep, Lake Worth, FL), and cleaned with alcohol to reduce signal impedance. A custom-designed double-differentiated active electrode (Delsys, Boston, MA) was placed over the VM, superomedial to the patella. The electrode was positioned perpendicular to a line running from the anterior superior iliac spine to the medial joint line of the knee in accordance with Surface Electromyography for the Non-Invasive Assessment of Muscles guidelines. A ground electrode (Red Dot; 3M, St. Paul, MN) was positioned over the medial malleolus. All EMG signals were amplified (× 1,000), filtered (20–450 Hz) (Bagnoli 2, Delsys), and sampled at 10,000 Hz. For each subject, the measurement of quadriceps torque and VM EMG occurred at 4 intervals: baseline, preinfusion (10 minutes after baseline), postinfusion, and postintervention (cryotherapy).

Joint infusion procedure. All subjects received an experimental knee joint infusion. With the knee resting in slight flexion, a 23-gauge cannula was inserted into the superomedial aspect of the joint. All injections were performed without local anesthesia, under sterile conditions. A pressure transducer (Medex, Dublin, OH) and syringe were attached in parallel with the cannula via a 3-way tap and pressure resistant tubing. Dextrose saline (4% dextrose and 0.19% NaCl) was injected into the joint space in increments of 15 ml or less. Intraarticular pressure (IAP) was monitored for each subject and infusion stopped when IAP reached 50 mm Hg.

Cryotherapy. Subjects were assigned by random number generation to either a cryotherapy group (n = 8) or a control group (n = 8). Following postinfusion measurements, the cryotherapy group had 3 plastic bags of partially crushed ice wrapped around their knee joint for a 20-minute period while remaining seated in the dynamometer. The bags were placed at least 2 cm below the superior border of the patella to prevent alterations in EMG parameters due to cooling at the site of the electrode (12). An infrared thermometer (Fluke, Eindhoven, The Netherlands) was used to monitor surface temperature at the joint line and the VM electrode site, to ensure stability of the recording conditions. The control group did not receive the cryotherapy intervention and remained seated in the dynamometer for 20 minutes before performing postintervention measurements.

Data analysis. The peak quadriceps torque, RMS of the EMG signals, and MFCV were calculated by averaging data

Table 2. Summary of dependent variables recorded at each measurement interval for cryotherapy and control groups*

	Baseline	Preinfusion	Postinfusion	Postintervention†	95% CI‡
PT (nm/kg × 100)					
Control	297 ± 46	292 ± 44	235 ± 44	251 ± 23	232–270
Cryotherapy	296 ± 61	295 ± 65	239 ± 50	277 ± 23	259–295
MFCV (ms^{-1})					
Control	5.26 ± 1.14	5.27 ± 1.01	4.73 ± 0.57	4.52 ± 0.32	4.24–4.81
Cryotherapy	5.57 ± 0.79	5.64 ± 0.90	4.58 ± 0.74	4.97 ± 0.28	4.72–5.19
RMS (% of baseline)					
Control	100 ± 0	100.67 ± 11.80	73.82 ± 26.36	76.48 ± 16.26	63.09–89.88
Cryotherapy	100 ± 0	94.12 ± 8.97	66.58 ± 12.87	90.09 ± 16.24	77.58–102.60

* Values are the mean ± SD unless otherwise indicated. PT = normalized peak torque of the quadriceps; MFCV = muscle fiber conduction velocity of the vastus medialis; RMS = normalized root mean square of electromyography from the vastus medialis.
† Adjusted marginal mean ± SD.
‡ 95% confidence intervals (95% CIs) for postintervention measures.

from the 3 trials at each measurement time point. Peak torque was normalized to a percentage of body mass (kg) for each subject. RMS of EMG activity was calculated from a 1-second period corresponding to the time of maximum activation (visually determined) for each contraction. RMS at each measurement interval was normalized to a percentage of the baseline RMS calculated for each subject. MFCV estimates were obtained based on the time delay in the propagation of EMG signals between 2 electrode pairs with a known interelectrode distance using the formula velocity = distance/time. The time delay was calculated using the peak of a cross-correlation function (for further detail, refer to ref. 22). MFCV data were discarded if cross-correlation coefficients were <0.8.

Statistical analysis. Descriptive statistics were calculated and checked for assumptions related to the normality of the respective distributions. Independent *t*-tests were used to analyze differences in baseline characteristics between the cryotherapy and control groups. A 2-factor (group × time) repeated-measures analysis of variance was performed to identify the stability of the baseline measures and the effects of the infusion of fluid on quadriceps peak torque, RMS, and MFCV. An analysis of covariance was utilized to analyze differences in the postintervention changes seen in the dependent variables across groups. The postinfusion (preintervention) values for each dependent variable were used as a covariate. The alpha level for all statistical procedures was set to 0.05.

RESULTS

Fifteen subjects completed the study. One subject from the control group had a vasovagal reaction during the joint infusion procedure that forced an abandonment of data collection. All other subjects reported minimal discomfort during the experimental procedures. Feelings of "tightness" or "pressure" were commonly used to describe the sensation within the knee joint and many expressed a general "lack of control" over their knee. All subjects reported a full, pain-free range of motion within 48 hours of the experiment, with no visible swelling. There were no significant differences between groups for any of the subject characteristics provided in Table 1 ($P > 0.05$).

Intraarticular pressure. Upon insertion of the catheter into the knee joint, IAP was typically negative or slightly above atmospheric pressure. IAP increased with increasing volumes of infusion for all subjects. The volume required to reach a standardized IAP of 50 mm Hg varied considerably between subjects (median 75 ml, range 17–110 ml).

Quadriceps peak torque. A summary of normalized peak torque values at each measurement interval is presented in Table 2. No significant differences in peak torque were seen between baseline and preinfusion measures for either group ($P = 0.542$) (Figure 1). Peak torque decreased significantly in both groups after joint infusion ($P < 0.001$). Cryotherapy led to a significant increase in peak torque compared with the control group ($P < 0.05$) (Figure 2).

EMG variables. A summary of normalized RMS values at each measurement interval is presented in Table 2. There was no significant change in RMS between baseline and preinfusion measures for either group ($P = 0.22$). RMS decreased significantly in both groups following joint in-

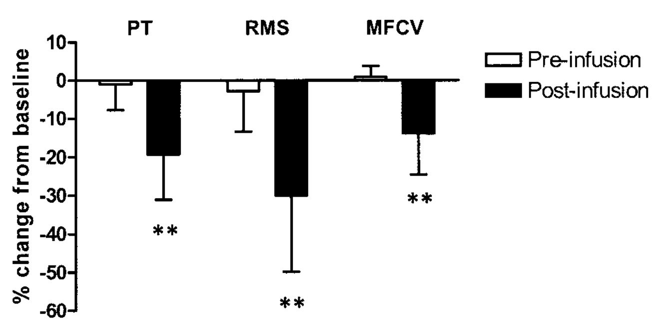

Figure 1. Percentage change in the dependent variables from baseline measures. PT = normalized quadriceps peak torque during maximum voluntary isometric contractions; RMS = root mean square of electromyographic signals recorded from the vastus medialis; MFCV = muscle fiber conduction velocity of the vastus medialis. ** Significant difference from baseline ($P \leq 0.001$). Data are the means and SDs.

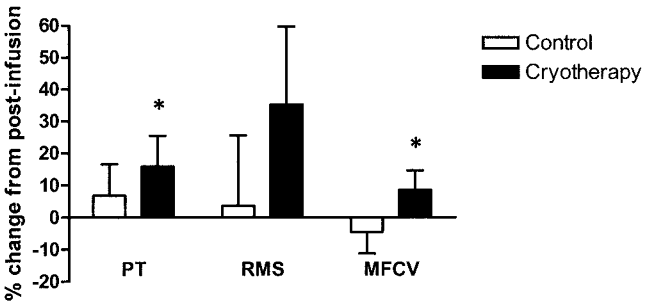

Figure 2. Percentage change in dependent variables from postinfusion measures. PT = normalized quadriceps peak torque during maximum voluntary isometric contractions; RMS = root mean square of electromyographic signals recorded from the vastus medialis; MFCV = muscle fiber conduction velocity of the vastus medialis. * Significant difference between groups ($P < 0.05$). Data are the adjusted marginal means and SDs.

fusion ($P < 0.001$). The increase in RMS observed after cryotherapy did not reach statistical significance ($P = 0.13$) when compared with the control group (Figures 1 and 2).

Acceptable MFCV data (cross-correlation coefficients >0.8) were obtained from 10 subjects (6 experimental, 4 control) and were used in the subsequent analysis. As such, MFCV measures may be described as exploratory. A summary of MFCV values at each measurement interval is presented in Table 2. No significant change in MFCV was observed between baseline and preinfusion measures for either group ($P = 0.542$). MFCV decreased significantly in both groups after joint infusion ($P = 0.001$). Cryotherapy led to a significant increase in MFCV compared with the control group ($P = 0.028$).

Surface temperature. Surface temperatures at the joint line and VM electrode site are displayed in Table 3. These values show that recording conditions at the electrode remained stable during the cryotherapy intervention ($P = 0.636$). However, mean surface temperature over the joint line decreased from 29.7°C to 14.4°C following cryotherapy ($P < 0.001$).

DISCUSSION

The results of this study confirm that icing the knee joint reduces the severity of quadriceps AMI. These muscles are often notably affected by knee joint pathology, with quadriceps strength as an important predictor of functional ability in these patients (17,18,23,24). Normal activation of the quadriceps is essential for shock absorption, regulation of stiffness at the knee, and maintaining dynamic stability of the joint (25–28). The improvements in quadriceps activation observed after cryotherapy are notable in that strength measures returned to within ~6% of baseline values. This represents an effect size of 0.48, a moderate change based upon Cohen's classification of effect sizes (29). These findings have important ramifications for the treatment of patients with arthritic joint disease and following knee injury and surgery. By temporarily reducing AMI, cryotherapy may provide a therapeutic window during which more complete activation of the quadriceps musculature is permitted. Thus, if quadriceps strengthening is performed immediately after icing, earlier and more effective rehabilitation may be allowed, enhancing strength gains and minimizing quadriceps muscle atrophy in patients with knee joint pathology.

The joint infusion technique used in the current study provides a controlled, experimental model of AMI. The advantage of this model is that it permits baseline measures of quadriceps activation in the absence of inhibition. Had the intervention been applied to patients with knee damage and the dependent variables increased, cryotherapy could be said to have a positive therapeutic effect. However, without prior knowledge of the baseline level of inhibition, the degree to which cryotherapy reduces quadriceps activation deficits would be difficult to determine accurately. That is, cryotherapy may have eliminated a small portion of AMI or eradicated it completely. For this reason, the joint infusion model arguably allows a better appreciation of the magnitude and therefore clinical importance of cryotherapy's disinhibitory effect.

The limitation of the joint infusion model is that it does not mimic precisely the changes in articular afferent discharge that may occur when other factors associated with joint pathology (e.g., inflammation, pain, and structural damage) are present. However, there are a number of reasons to suppose that cryotherapy may also be effective in reducing AMI in a patient population. These are outlined below.

First, quadriceps inhibition of a similar magnitude occurs following the infusion of fluid into chronic arthritic knee joints (6,7), suggesting that swelling is still an important cause of AMI when factors such as inflammation, pain, and/or structural damage are present. Second, it is widely accepted that the inhibitory effect of swelling is caused by an increase in the discharge of articular mechanoreceptors innervated by large diameter, group II joint afferents (1,5,30). Similarly, there is strong evidence from

Table 3. Changes in surface temperature at the vastus medialis electrode site and joint line pre- and postintervention*

Group	Electrode temperature (°C) Pre	Electrode temperature (°C) Post	Joint line temperature (°C) Pre	Joint line temperature (°C) Post
Control	31.49 ± 0.99	31.14 ± 0.81	30.34 ± 0.87	30.09 ± 0.97
Cryotherapy	31.25 ± 1.32	31.05 ± 1.25	29.68 ± 1.10	14.4 ± 1.12†

* Values are the mean ± SD.
† Significant difference from preintervention value ($P < 0.001$).

animal studies that (as with swelling) inflammation and pain are associated with an increase in joint afferent discharge due to the peripheral sensitization of articular free nerve endings innervated by smaller diameter group III and IV afferents (31,32). An increase in joint afferent discharge may also occur due to structural damage (e.g., to ligaments) that increases joint laxity and subsequently the discharge of articular receptors involved in signaling the limits of joint motion (2,33). An increase in joint afferent discharge is thought to lead to AMI by enhancing the excitability of spinal interneurons (11,34) that in turn have inhibitory projections to the quadriceps motoneuron pool, preventing full activation of the muscle by descending pathways. Diminishing joint afferent discharge by aspirating or injecting a local anesthetic into the knee joint may dramatically reduce AMI (35,36), in some cases abolishing it almost entirely (5,10).

Cryotherapy may work via a similar mechanism, partially silencing the increased afferent traffic caused by swelling, inflammation, and joint laxity (12). In this regard, icing the knee joint lowers intraarticular temperature (37), and a reduction in temperature has been shown to diminish the sensitivity of sensory receptors in both muscle and cutaneous tissue (38,39). It seems plausible that joint receptors would respond in a similar manner if intraarticular temperature was lowered sufficiently. Additionally, many of the articular nerve branches supplying the knee are superficial at the joint level. Cooling peripheral nerves is known to reduce nerve conduction velocity in a near linear manner (40,41), impeding the propagation of high-frequency impulses (40,42). Thus, it may be that icing the knee joint reduces the discharge of sensory receptors and/or impairs articular nerve conduction, attenuating transmission of the aberrant joint afferent impulses responsible for AMI. Cryotherapy may be as effective when factors such as inflammation, pain, and joint laxity are present as the effects of moderate cooling are virtually identical on large and small diameter sensory fibers (40,41), and it is well established that icing modulates the transmission of nociceptive impulses at the spinal level (43–45) seemingly via segmental and supraspinal mechanisms.

An important aspect of this study is that it is the first to examine changes in MFCV using an acute model of joint injury. A key finding was that AMI may be reflected by a reduction in mean MFCV during maximal effort muscle contractions. MFCV is strongly correlated with motor unit size (46) and muscle fiber diameter (47) as type I muscle fibers making up smaller motor units typically display lower conduction velocities than group II fibers found within large, high-threshold motor units. Thus, the ~15% drop in MFCV we observed after joint infusion provides novel information concerning the type of motor units affected by AMI, suggesting that swelling is likely to inhibit the quadriceps largely by limiting the firing of high-threshold motor units with high MFCVs. A reduction in the firing rate of active motor units may also contribute to the observed effect (48). Conversely, mean MFCV increased significantly postcryotherapy, indicating that icing enhances quadriceps force output by disinhibiting some of the high-threshold motor units affected by AMI and/or enhancing motor unit firing frequency.

In this study, we chose to standardize swelling to IAP rather than infusing a set volume of fluid into the knee joint. Researchers (6,11) have suggested that intraarticular volume provides a relatively poor estimate of capsular tension because both joint afferent discharge (30) and quadriceps inhibition (6) have a stronger correlation with pressure than volume. The relationship between IAP and volume depends on factors that are likely to differ across subjects such as joint size and capsular elastance (49). This is clearly demonstrated in our study, as the volumes needed to reach a standardized IAP of 50 mm Hg ranged from 17 ml to 110 ml. Comparable findings have been reported in both normal (50) and arthritic (6) knee joints.

In conclusion, the findings of this study demonstrate that icing the knee joint for 20 minutes reduces the severity of quadriceps AMI caused by intraarticular swelling. A reduction in AMI may allow earlier and more effective quadriceps strengthening to take place in patients with arthritis or following knee injury or surgery. This has the potential to enhance rehabilitation and improve functional outcomes in patients with knee joint pathology.

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AUTHOR CONTRIBUTIONS

Mr. Rice had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study design. Rice, McNair, Dalbeth.
Acquisition of data. Rice, McNair, Dalbeth.
Analysis and interpretation of data. Rice, McNair, Dalbeth.
Manuscript preparation. Rice, McNair, Dalbeth.
Statistical analysis. Rice, McNair.

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