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Combined Effect of Cryotherapy and Curcumin on the Exercise Induced Delayed Onset of Muscle Soreness (DOMS)

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Abstract
The aim of this study was to determine the effect of local application of cryotherapy and turmeric to alleviate the physical symptoms of DOMS compared to conventional physical therapy programs. The study had 18 healthy, untrained subjects. Subjects were then randomly assigned to 3 groups, 6 participants in each group. Subject of group A (n=6) received physical therapy, group B (n=6) received physical therapy and cryotherapy, and group C (n=6) received physical therapy in combination to cryotherapy and turmeric cream supplementation. Repeated concentric and eccentric contractions were used to induce DOMS in the elbow flexors. A visual analog scale was used to examine perceived muscle soreness, a flexible tape measure was used to measure muscular girth and markers of muscle damage (creatine kinase, CK and lactate dehydrogenase, LDH) were measured. The VAS ratings of elbow flexor soreness was greatly reduced after 72 hours in subjects receiving physical therapy+ cryotherapy and those receiving physical therapy+ cryotherapy+ turmeric supplementation as compared to those receiving only physical therapy. There was significant improvement in the elbow range of motion only after 72 hours post exercise in both subjects receiving cryotherapy and physical therapy and those receiving combination of both cryotherapy and turmeric supplementation and physical therapy. Although there was increase in the biceps brachii girth but it could reach a statistical level. The increase may be due to inflammatory response leading to swelling from unaccustomed eccentric exercise. Plasma CK (but not LDH) activity was significantly improved in subject receiving cryotherapy and physical therapy and subjects receiving combination of cryotherapy, turmeric supplementation and physical therapy. Our result showed that cryotherapy along with local application of turmeric may be beneficial to attenuate exercise induced DOMS. Local application of turmeric along with cryotherapy adds on to the effect of management of DOM.

Keywords: DOMS, cryotherapy, turmeric supplementation, creatine kinase, lactate dehydrogenase

1. Introduction

Delayed onset of muscle soreness (DOMS) is a type of type of soreness that usually results from eccentric muscle contractions in which there is disruption of normal alignment of skeletal muscle resulting in damage to the structure of the sarcomere (Mckune A, 2012; Trombold JR, 2010) [1, 2]. Discomfort at the site of injury, inflammation, oxidative stress, edema, and loss of muscular function and strength etc. could be found with acute muscle damage (Beaton LJ, 2002) [3].

The exact cause of DOMS remains unknown though there are various theories believed to be linked together (Lewis PB, 2012; Soer R, 2009; Cheung K, 2003) [12, 13, 14]. There is a decrease in physical performance that can be attributed to functional impairment as perceived by the individual and decreases in joint kinematics, strength, and neural recruitment patterns which increases risk factors of further injury (Cheung K, 2003) [14]. Although DOMS is not considered a major injury, all of these impairments can lead to an increased risk of injury; therefore, interventions to relieve the signs and symptoms of DOMS have been investigated (Torres R, 2012; Rocha CS, 2012; Hill J, 2014) [15, 16, 17]

Research and technology are becoming more sophisticated, utilizing prior technology supplemented by new ideas. Many efforts have been made to alleviate these symptoms using several treatment measures like pharmacological interventions (Sayers SP, 2001) [4], massage (Gatterer H, 2013) [5], low-intensity exercise (Martin V, 2004) [6], ultrasound application (Kim SK, 2014) [7] and nutritional interventions (Trombold JR, 2010; Beaton LJ, 2002) [2, 3].

There are a broad variety of other interventions to help reduce the symptoms of DOMS; however, the availability of each depends on the resources available to the individual. While athletes on professional teams have wide ranges of modalities available to them, the general public has access to other methods that may be as effective. The collective data generated from these study failed to provide strong evidence for their use and some could not find any reductions in the symptoms of muscle injuries. No single modality has been proven to be the answer to DOMS relative to all the others; as such, each individual discovers the best way to cope with DOMS, often through trial and error.

The purpose of this study was to measure the effects of cryotherapy and turmeric supplementation on the blood markers creatine kinase, CK; lactate dehydrogenase, LDH and DOMS. Cryotherapy is normally used for an initial treatment of any traumatic soft tissue injury. The superficial application of ice results in changes in different tissue levels of skin. A decrease in tissue temperature excites cutaneous receptors to stimulate the sympathetic adrenergic fibers causing the constriction of local arterioles and venules. This process results in a reduction of swelling and a decreased rate of metabolism which, in turn, reduces the inflammatory response, vascular permeability, and the formation of edema (Paddon-Jones DJ, 1997) [18]

Curcumin, the main yellow bioactive component of turmeric has two natural analogues FHM [feruloyl-(4-hydroxycinnamoyl)-methane] and BHM [bis-(4-hydroxycinnamoyl)-methane], which are potent anti-inflammatory agents, results in decrease in swelling and pain. Turmeric is also thought to reduce inflammation by lowering histamine levels and it may also stimulate the adrenal glands to increase production of inflammation reducing hormones.

2. Materials & Methods

Sample Population and Participant Selection

A total of 18 participants aged 18 to 26 years volunteered for this study. Inclusion into the study required that the participants were untrained, meaning that they have not performed strenuous workouts involving heavy weight lifting more than once a week in the six months prior to enrolling in the study. Any physical activity (including aerobic activity) subjects had been performing prior to enrolling in the study was discontinued for the duration of the study. Exclusion criteria included any recent surgeries or existing medical conditions that would prevent them from performing a strength training regimen. Informed consent was obtained from all subjects before beginning the study and subjects were informed that they could withdraw at any time.

Research Design

Participants were randomized into three groups: (1) group A (n=6) received physical therapy (2) group B (n=6) received physical therapy and cryotherapy, and (3) group C (n=6) received physical therapy in combination to cryotherapy and turmeric cream supplementation. The curcumin concentration achieved in the present study was almost 80 ng/ml (0.22 µmoles/L). A visual analog scale was used to examine perceived muscle soreness, a flexible tape measure was used to measure muscular girth, and biochemical blood markers (creatine kinase, CK; lactate dehydrogenase, LDH) were measured

Inducement of Delayed-Onset Muscle Soreness

Repeated concentric and eccentric contractions were used to induce DOMS in the elbow flexors. A dumbbell curl exercises was used to isolate elbow flexors which enables the subject to sit with arms lying on a padded board and placed in front of the body at a 45-degree angle downward from the axilla. Resistance was applied to the elbow flexors allowing the subject to grasp a dumbbell and consecutively extend and flex elbow during a full ROM. A one-repetition maximum (1-RM) of the elbow flexors was determined. The amount of weight the subject could lift concentrically one time before the elbow flexors became fatigued represented 1-RM. Each subject used 70% of their 1RM. The eccentric phase was of 5-6 seconds and each set was separated by a 1-minute rest period. Subjects reported back each day for four days after DOMS was been induced. Each day, girth measurements, pain pressure threshold analysis, and a VAS for muscular soreness were done.

The application of cryotherapy was immediately performed after the end of one of the two sessions of concentric and eccentric contractions. Cryotherapy was applied by massaging the biceps brachii with cold pack (15 ± 1 °C) for 30 min. A thermometer was used to check the temperature, which was regulated by the addition of ice throughout the session.

Muscle Soreness Rating

Measurement of pain was performed before the first workout began as a baseline measure of pain (should be low), and then at the beginning of each subsequent workout before starting the exercise regimen. The intention here was the measure any pain felt within the last 48 hours (between the last workout and that current visit) and to determine overall change in pain. The measurement of pain was performed using validated pain scales- the visual analog scale (VAS). Subjects reported muscle soreness scores corresponding to a visual analog scale with scores from 1, normal, to 10, very, very sore at 12, 24, 48, 60, and 72 hours post exercise. The VAS is effective because it is nondiscrete and therefore has a wider range of metrical characteristics. It is used to elicit a psychometric response that is more helpful in determining pain which cannot be directly measured.

Measurement of Elbow Range of Motion

The effect of DOMS on active elbow ROM was determined using a universal full circle goniometer. The goniometer axis was placed over the lateral epicondyle of the humerus, with the stationary and movable arms aligned along the lateral midline of the humerus and the radius, respectively. Active ROM was measured as the total excursion from full elbow flexion to full elbow extension. The limbs were then marked with a permanent marker to ensure greater accuracy during measurement. Neutral was set at zero or 180 degree (arm straight). The resting elbow angle was recorded pre and post treatment. A standardized testing procedure was established to ensure proper identification of bony landmarks and goniometer alignment. Subjects were given identical instructions prior to each measurement, and a single measurement of total joint excursion was recorded at each session.

Biceps Girth Measurement

Girth of the Biceps muscle was measured with the help of a meter tape, measurement was taken of the muscle belly of biceps muscle, 3 inches above elbow joint.

Biochemical studies

The DOMS was induced in the subjects using repeated concentric and eccentric contractions of the elbow flexors. Venous blood samples were collected from the dominant arm immediately following the arm exercise. Additional blood samples were taken 2, 24, 48, and 72 hours following the exercise. Blood markers (creatine kinase, CK; lactate dehydrogenase, LDH) were measured

Statistical Analysis

Mean and standard deviations for the descriptive characteristics were calculated. An independent t-test was performed to compare pain rating values between different group. ANOVA was used for checking the differences within groups in different times and Repeated Measure and Scheffe Test post hoc were used for checking the differences between groups. P-values at or below 0.05 were considered significant. SPSS Version 20 was used to perform all statistical analysis (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.).

3. Result

Vas Ratings of Elbow Flexor Soreness

There was no consistent or significant difference between all the control and treated group after at baseline (p = NS). After 24 and 48 hours' post exercise, soreness was significantly improved between the subjects receiving only physical therapy and those receiving physical therapy and cryotherapy ($p<0.05$). However, the patient who received physical therapy and combination of both cryotherapy and turmeric supplementation showed the most significant response in muscle soreness ($p<0.001$). The VAS ratings of elbow flexor soreness was greatly reduced after 72 hours in subjects receiving physical therapy+cryotherapy and those receiving physical therapy+ cryotherapy+turmeric supplementation as compared to those receiving only physical therapy (Table 1)

Table 1: Depiction of Pain Scores among the groups

	Baseline	**VAS post exercise 24 Hours**	**VAS post exercise 48 Hours**	**VAS post exercise 72 Hours**
Physical therapy	1.2±3.2	34.3±21.4	41.2±24.78	37.6±29.39
Physical therapy+ cryotherapy	1.3±2.4	20.4±16.7	32.3±21.49	19.6±19.47
Physical therapy+ cryotherapy+ turmeric supplementation	1.2±4.2	17.6±15.8	27.9±19.57	15.4±16.54
P value	0.06^{NS}	0.04*	0.000***	0.00***

Note: $*p<0.05$, $**p<0.01$, $***p<0.001$, NS- Not significant ($p>0.05$)

Elbow Range of Motion Measurement

Results of the goniometric measurement of elbow ROM are shown in Table 2. There was no significant difference in the Elbow ROM between the three group at baseline level (p =0.45), after 24 hours (p = 0.49) and after 48 hours (p = 0.51). After 72 hours the ROM significantly increased in subject receiving cryotherapy and physical therapy as compared to the subject receiving only physical therapy. The elbow range of motion showed further improvement in subject receiving both cryotherapy and turmeric supplementation along with physical therapy.

Table 2: Depiction of Elbow range of motion (ROM) among the groups

	Baseline	**Elbow ROM post exercise24 Hours**	**Elbow ROM post exercise48 Hours**	**Elbow ROM post exercise72 Hours**
Physical therapy	172.29±42.33	168.73±46.47	164.98±39.39	159.36±48.75
Physical therapy+ cryotherapy	173.39±41.48	171.68±43.91	166.79±41.96	165.96±45.92
Physical therapy+ cryotherapy+ turmeric supplementation	175.05±40.84	173.48±41.71	168.86±42.40	169.85±41.86
P value	0.45^{NS}	0.49^{NS}	0.51^{NS}	0.00**

Note: $*p<0.05$, $**p<0.01$, $***p<0.001$, NS- Not significant ($p>0.05$)

Biceps Girth

No Significant differences were noted in the Biceps Girth measurements. All the groups tended to remain as same as possible. No group showed clear improvement as compared to others (Table 3).

Table 3: Depiction of Biceps Girth among the groups

	Baseline	**Girth post exercise 24 Hours**	**Girth post exercise 48 Hours**	**Girth post exercise 72 Hours**
Physical therapy	28.62±12.34	31.97±10.67	34.46±12.23	29.93±9.26
Physical therapy+ cryotherapy	28.81±9.67	29.56±11.56	32.79±11.79	28.96±10.59
Physical therapy+ cryotherapy+ turmeric supplementation	29.05±10.84	30.84±11.61	31.88±12.04	28.58±11.68

Creatine Kinase

The creatinine kinase data showed that there was no significant difference between the 3 groups at baseline and 24 hours post exercise (Table 4). But significant difference were observed at 48 hours, and after 96 hours ($p<0.001$)

Table 4: Creatine Kinase Group comparison at 0, 24, 48, and 72 hours

	Baseline	**CK post exercise 24 Hours**	**CK post exercise 48 Hours**	**CK post exercise 72 Hours**
Physical therapy	129.57	3229.53	1715.67	911.67
Physical therapy+ cryotherapy	136.35	3468.47	1295.68	685.62
Physical therapy+ cryotherapy+ turmeric supplementation	131.48	3123.29	749.33	341.89
P value	0.08^{NS}	0.06^{NS}	0.000***	0.000***

Note: $*p<0.05$, $**p<0.01$, $***p<0.001$, NS- Not significant ($p>0.05$)

Lactate Dehydrogenase
The lactate dehydrogenase data showed that there was no significant difference between the 3 groups at baseline. Table 5 shows that at 24hours, 48 hours and 72 hours the LDH values between the three groups were statistically having significant difference

Table 5: Lactate dehydrogenase Group comparison at 0, 24, 48, and 72 hours

	Baseline	LDH post exercise 24 Hours	LDH post exercise 48 Hours	LDH post exercise 72 Hours
Physical therapy	272.24±44.23	423.65±97.35	547.34±138.69	458.58±114.38
Physical therapy+ cryotherapy	266.35±36.77	311.62±54.56	431.4±112.35	216.12±135.09
Physical therapy+ cryotherapy+ turmeric supplementation	199.57±69.34	250.58±75.49	374.58±112.49	189.46±128.48
P value	0.07^{NS}	0.00**	0.00**	0.000***

Note: *$p<0.05$, **$p<0.01$, ***$p<0.001$, NS- Not significant ($p>0.05$)

4. Discussion
This study has investigated the effects of cryotherapy and turmeric supplementation in combination on markers of muscle damage and soreness caused by DOMS. The results showed that the treatment with ice immediately after the DOMS is able to reduce and minimize DOMS effects caused by muscle damage and that some mechanisms associated with inflammation. Soreness is one of the most effective ways to subjectively document the muscular pain and soreness associated with DOMS. The Visual Analog Scale (VAS) is a unidimensional subjective measurement tool designed to detect the level of perceived soreness and has been a common instrument in assessing DOMS (Cleather DJ, 2007) [10]. Creatine kinase (CK) has long been used as a way of measuring muscle damage (Nelson N, 2013) [11]. A significant increase in CK levels in this study as an inductor of muscle damage was moderated by turmeric supplementation and cryotherapy. Several studies have confirmed that curcumin down-regulates the expression of several pro-inflammatory cytokines involved in proteolysis and muscle inflammation (Singh S, 1995) [21, 29] by suppressing NF—κB signalling (Das L, 2014; Fu Y, 2014) [22, 23]. This mechanism could also be responsible for the reduced inflammatory response to exercise observed in this study.

In the present study it was found that cryotherapy significantly resulted in the improvement of DOMS. By far the most popular and traditional method of alleviating tenderness and pain is cryotherapy, the standard ice bag or bath that is available to anyone. Cold therapy induces vasoconstriction, arresting edema formation by decreasing blood flow, which contributes the fluid that makes its way past the cell membrane, opened by histamine, prostaglandin and bradykinin, which in turn reduces the mechanical pressure on the free nerve endings (Sellwood, Brucker, Williams, Nichol & Hinman, 2007). Slowing down and reducing blood flow also delays the transportation of those chemical mediators that govern cell permeability, decreasing swelling (Sellwood *et al*., 2007). Cryotherapy results in a decrease in the temperature of the body also decreases nerve excitability, a principle maximized by ice immersion as compared to a single ice bag (Hume *et al*., 2004; Kuligowski *et al*., 1998; Bakhtiary *et al*., 2007).

As a constituent of turmeric (Curcuma longa L.), curcumin (diferuloylmethane) has been used for centuries in the traditional medicine of India and the Far East (Corson TW, 2007; Singh S, 2007)[19, 20]. Several studies have investigated the mechanisms by which curcumin exerts its beneficial effect. Early experimental study demonstrated that curcumin suppresses the activation of NF—κB (Jobin C, 1999; Singh S, 1995)[21, 29], an effect of critical relevance in DOMS relief, since NF—κB appears to be involved in the regulation of proteolysis and inflammation in muscle (Alamdari N, 2009)[30]. Therefore, inhibition of NF—κB by curcumin may result in a muscle-protective effect. Consistently, it has been suggested that curcumin may prevent loss of muscle mass during sepsis and endotoxaemia and may stimulate muscle regeneration after traumatic injury (Alamdari N, 2009; Thaloor D, 1999) [30, 24]. Other mechanisms possibly responsible for the anti-inflammatory and anti-oxidant properties of curcumin include induction of heat-shock response (Dunsmore KE, 2001) [25], reduction in the expression of the pro-inflammatory enzyme cyclooxygenase-2 (COX-2) (Chun KS, 2003) and promotion of the antioxidant response by activation of the transcription factor Nrf2 (Shehzad A, 2013) [27].

The greatest limitation in this study is the small sample size. More participants would have increased the likelihood of finding meaningful results. With only 18 participants, the results that are significant or approaching significance should be considered with caution. Additionally, the pain reports were not fully explained and the workout itself was not run as smoothly as it could have been in the beginning of the study. Another limitation is highlighted by the fact that the VAS measurements showed no significant results in terms of important changes in pain perception. Due to the subjectivity of pain report, the results may not have been as accurate as possible.

Given the lack of statistical significance for any of the tested variables, the study indicates that physical therapy, cryotherapy and turmeric supplementation are equally effective at attenuating the symptoms of DOMS and restoring muscular function up to 3 days after muscle damaging exercise.

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