

ORIGINAL ARTICLE

Effects of Whole-Body Cryotherapy in the Management of Adhesive Capsulitis of the Shoulder

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ABSTRACT. Ma S-Y, Je HD, Jeong JH, Kim H-Y, Kim H-D. Effects of whole-body cryotherapy in the management of adhesive capsulitis of the shoulder. Arch Phys Med Rehabil 2012;xx:xxx.

Objective: To compare 2 different treatment approaches, physical therapy modalities, and joint mobilization versus whole-body cryotherapy (WBC) combined with physical therapy modalities and joint mobilization, for symptoms of adhesive capsulitis (AC) of the shoulder.

Design: A randomized trial.

Setting: Hospital.

Participants: Patients with AC of the shoulder (N=30).

Intervention: Patients were randomly assigned to 2 groups. The WBC group received physical therapy modalities, passive joint mobilization of the shoulder, and WBC, whereas the non-WBC group received only physical therapy modalities and passive joint mobilization of the shoulder.

Main Outcome Measures: Visual analog scale (VAS), active range of motion (ROM) of flexion, abduction, internal and external rotation of the shoulder, and the American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form (ASES) were measured before and after the intervention.

Results: A statistically significant difference between groups was found for the VAS, active ROM of flexion, abduction, internal rotation, and external rotation, and the ASES with greater improvements in the WBC group ($P < .01$). Overall, both groups showed a significant improvement in all outcome measures and ROM measures from pre to post at a level of $P < .01$.

Conclusions: There is significant improvement with the addition of WBC to treatment interventions in this sample of patients.

Key Words: Bursitis; Rehabilitation; Shoulder.

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ADHESIVE CAPSULITIS (AC), also termed frozen shoulder, is the one of the most common disorders of the shoulder.¹ Motion restriction and pain can result in a progressive underuse of the affected side and lead to a gross loss of

function.^{2,3} A typical pattern of loss of motion associated with AC is in external rotation, the most significant loss of motion, followed by abduction, flexion, and then internal rotation.⁴

Although an exact cause of AC is not fully understood, a variety of clinical conditions and diseases can contribute to the initiation of AC. These include prolonged immobilization of the shoulder for different reasons including rotator cuff injuries, tendinitis and trauma, postsurgical intervention, acute fractures, missed fractures, dislocations, exacerbation of cervical pain, pain after overuse, and a multitude of different medical conditions.⁵⁻¹¹ AC is more prevalent in women, those in middle age, and in persons with diabetes.¹²⁻¹⁴

A variety of treatment strategies for AC have been developed to alleviate pain and enhance range of motion (ROM) of the shoulder. The mainstay of these is physical therapy, with other options including chiropractic manipulation, corticosteroids either through local injection or systemically, manipulation under general anesthesia, scalene block, surgical intervention (arthroscopic and open arthrolysis), and intraarticular injection of fluid volume.¹⁵⁻²⁰ Although numerous physical therapy interventions, such as heat or ice applications, interferential therapy, transcutaneous electrical nerve stimulation, ultrasound, proprioceptive neuromuscular facilitation techniques, active and/or passive ROM exercises, muscle strengthening exercises, and joint mobilization techniques, are used to treat shoulder AC,^{21,22} mobilization techniques, frequently used by physical therapists and manual therapists, are an important part of the intervention of many physical therapy programs. Several studies^{2,23-25} have found favorable outcomes after mobilization of the shoulder alone or in combination with active exercises or local steroid injections. In those studies, improved ROM of the shoulder, reduction in shoulder pain, and improvement in shoulder function were reported. However, in another study comparing manual mobilization in combination with passive stretching (stretching group) with supportive therapy in addition to exercises within the pain limits (supervised neglect group), the supervised neglect group was found to show better outcomes than the stretching group in regards to shoulder function and the speed of recovery. Although there is growing interest in the use of these techniques for shoulder AC, studies to support the use of these treatments are lacking.

Advances in the delivery of cryotherapy have led to broad application of cold as an anesthetic agent for treatment of orthopedic injuries. Whole-body cryotherapy (WBC) is a tool

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List of Abbreviations

AC	adhesive capsulitis
ADL	activities of daily living
ASES	American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form
ROM	range of motion
VAS	visual analog scale
WBC	whole-body cryotherapy

administered with a brief exposure of very cold air in minimal clothing that is maintained at -110°C to -140°C , generally for 2 to 3 minutes on the surface of the body in a special temperature-controlled chamber to treat symptoms of various diseases.²⁶ Whole-body cryostimulation is usually performed once a day for 10 days, although research regarding frequency is sparse.²⁷

WBC has been found to decrease skin temperature abruptly (-0.38°C decrease in sublingual temperature during a temperature of -100°C WBC in 90s),²⁸ possibly reducing pain and inflammatory symptoms with fibromyalgia, rheumatoid arthritis, chronic low back pain, osteoarthritis, and ankylosing spondylitis.^{29,30} Whatever technique used, the main physiologic responses of the human body to cold temperatures consist of changes in the circulatory system (concentration of blood vessels in the skin followed by their dilation and congestion of the skin),³¹ neuromuscular system (reduction of nerve conduction velocity and muscle tension),³² endocrine system (increase in adrenocorticotropin concentration, β -endorphins, epinephrine, norepinephrine, and testosterone concentration in men),³³⁻³⁶ and immunologic system (increase in cell-mediated and humoral immunity).^{33,37-40} Studies of physiologic changes after human body exposures to WBC have shown changes in antioxidant/prooxidant balance in blood,^{41,42} and an anti-inflammatory⁴³ and analgesic effect.⁴⁴ It is believed that increased β -endorphin concentration combined with decreased nerve conduction in afferent fibers, which are responsible for pain reception, cause analgesic effect.^{34,44} Such complex reactions of WBC on the human body could have a positive effect on the rate of postinjury recovery after conservative AC treatment and reinforce the usefulness of WBC in rehabilitation. Although there has been a growing interest in WBC in rehabilitation, management of AC of the shoulder with WBC has never been investigated. WBC was first introduced toward the end of the 2000s in a few hospitals in South Korea.

Other physical therapy interventions, such as thermal and electrical modalities, are used to relieve pain and increase physical function in patients with AC, and more recently they have been considered as adjuncts to the medical and physical therapy management of the pathologies frequently seen by those specializing in musculoskeletal injury. Thermotherapy, such as a moist heating pad and ultrasound, is the application of heat to the body to relieve pain related to musculoskeletal injuries.⁴⁵ Interferential current therapy is also commonly used by physical therapists to reduce pain.⁴⁶⁻⁴⁸ However, there is insufficient evidence to support or refute the effectiveness of physical agents, such as thermal and electrical modalities, combined with other physical therapy interventions for AC.

The primary aim of this investigation was to determine the most appropriate recovery strategy for shoulder AC. To do so, this study compares 2 different treatment approaches (physical therapy modalities and joint mobilization vs WBC combined with physical therapy modalities and joint mobilization) on symptoms of AC. It is hypothesized that the addition of WBC to physical therapy modalities and joint mobilization for patients with AC is more effective in reducing pain and disability than physical therapy and joint mobilization alone.

METHODS

This study was a single-blinded randomized trial, where the investigator who performed the tests was blinded from group assignments and from the randomization procedures. A total of 30 patients with AC of the shoulder ranging in age from 47 to 66 with an average age \pm SD of 57.2 ± 6.6 years participated in this study, including 24 women (80%) and 6 men (20%). They were treated between August 2009 and January 2010 at the outpatient clinic of the department of physical therapy at the

local hospital. Thirty subjects were randomly assigned to either the WBC group ($n=15$) or the non-WBC group ($n=15$) based on the treatment allocation that was stored in consecutively numbered, opaque sealed envelopes to ensure concealment. The treatment allocation was generated by an administrative assistant. Visual analog scale (VAS) scores, active ROM measures, and the American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form (ASES) scores were obtained at baseline and 4 weeks after randomization by a physical therapist not associated with recruitment and intervention. Subjects were instructed not to discuss any contents of their treatments with the assessor at reassessment in order to maintain assessor blinding.

The WBC group received physical therapy modalities, passive joint mobilization, and WBC, whereas the non-WBC group received only physical therapy modalities and passive joint mobilization. In both groups, the right shoulder was involved in 23 patients (77%) and the left shoulder in 7 (23%). In order to be included in the study, subjects with AC were required to fulfill the following inclusion criteria: (1) aged over 18 years and with an AC diagnosis; (2) have had at least a 3-month history of pain and stiffness of the shoulder; (3) have shown global restriction of active and passive ROM of the shoulder concomitant with at least 25% loss of range in at least 2 motions of the shoulder, as compared with the contralateral side; (4) not have had any previous mobilization, manipulation, or arthroscopy; (5) have demonstrated at least mild pain at the extreme of all motions of the shoulder because of AC, constituting a 3 point on a 10 point VAS^{49,50}; and (6) did not have pathologic radiographic findings. Plain film radiographs of the affected shoulder were obtained in all cases, and the images of the radiographs indicated no abnormality of the affected shoulder in all participants. All subjects reported previous treatments including oral medication and physical therapy interventions, except for manual therapy.

We excluded subjects with a history of type 1 or 2 diabetes mellitus, cancer, rheumatoid arthritis, thyroid disease or cardiovascular disease, a history of any previous disorders of the affected shoulder, a history of trauma to the distal part of the affected limb (eg, elbow, forearm, wrist, or hand), a previous shoulder surgery or recent fracture of the proximal humerus on the same side, any known shoulder problems affecting shoulder ROM (eg, rotator cuff tear or residual tear after repair), shoulder dislocation, and significant glenohumeral arthritis, reflex sympathetic dystrophy, previous stroke with motor deficits, previous distension of the affected shoulder, severe neurologic deficit of the affected limb, extreme muscular size or morbid obesity, and cold hypersensitivity.

We recruited all subjects by referral from an orthopedic surgeon working in the hospital where the current study was performed. All patients were screened by the same orthopedic surgeon and a physical therapist, who had 10 years of clinical experience, prior to inclusion in the study, and to address any questions regarding the study. Prior to the study, all subjects provided written informed consent, and the ethics committee of the local hospital approved the study. Subject characteristics and primary diagnosis are summarized in table 1.

The 2 groups were assessed using a VAS, active ROMs of flexion, abduction, internal and external rotation of the shoulder, and the ASES. The measurements were done prior to the start of intervention and again after 4 weeks. Numerical pain intensity on a typical day secondary to AC was rated using a 10-point VAS with a score of 0 (no shoulder pain during a typical day) to 10 (worst possible shoulder pain during a typical day). The VAS has a test-retest reliability of .60 to .70⁵¹ and a concurrent validity of .76 to .84.⁵¹ Previous studies have re-

Table 1: Study Subject Characteristics

Characteristic	WBC Group (n=15)	Non-WBC Group (n=15)
Sex, no. of female (%)	13 (87)	11 (73)
Age (y)	56.1±6.3	54.9±6.7
Height (cm)	162.2±6.8	164.2±7.2
Weight (kg)	64.5±6.7	61.8±9.6
Affected shoulder side, no. of right side (%)	12 (80)	11 (73)
Duration of symptoms (wk)	4.3±1.2	5.3±1.5

NOTE. Values are mean ± SD or as otherwise indicated.

ported that the responsiveness of the VAS for shoulder pain was moderate to good.^{52,53}

Active ROMs of flexion, abduction, and internal and external rotation of the shoulder were measured with each patient in a supine position using a conventional goniometer at pre- and postintervention, in accordance with the guidelines of the American Academy of Orthopedic Surgeons.⁵⁴ These shoulder measurements using a goniometer have been found to be highly reliable when performed by the same physical therapist.⁵⁵

Reduced ability to manage activities in everyday life secondary to AC was estimated using the 30-point ASES (30 = no limitation of activities of daily living [ADL]; 0 = unable to participate in ADL).⁵⁶ The ASES score was determined by the patient, who rated 10 items, each ranging from 0 (unable to perform the activity) to 3 (no difficulty in performance of the activity). The ASES has a test-retest reliability coefficient of .86⁵⁶ and a convergent validity of .66 to .86.⁵⁶

The interventions were comprised of modalities/joint mobilization combined with WBC or modalities/joint mobilization alone. Hot packs, electrotherapy, and ultrasound were delivered to both groups in order to reduce pain. Both modalities and mobilization took place 3 times per week over a 4-week period (12 sessions in total). The first session of cryostimulation (12 sessions in total and delivered in the morning) was done after modalities/mobilization, and the second session of cryostimulation (12 sessions in total and delivered in the afternoon) was completed after modalities/mobilization/first cryostimulation on days they were done together.

Heat pack therapy was delivered for 15 minutes to provide superficial heating to the patients, followed by 5 minutes of ultrasound treatment (SM-250^a), using a 1MHz, 5-cm² sound head at an intensity of 1.5W/cm² in continuous mode and 15 minutes of interferential current treatment (SM-850P^a) at an intensity of 25mA before administration of mobilization.

Shoulder mobilization was performed for 10 minutes after the heat and stimulation. Mobilization techniques include anteroposterior glide, inferior glide of the glenohumeral joint and anterior, posterior, and inferior capsule stretch of the glenohumeral joint, and distraction of the scapulothoracic joint. To perform the anteroposterior glide of the humerus, the treating clinician's hand was placed over the humerus near the axilla, while the other hand was placed around the humerus above and near the lateral aspect of the elbow. The clinician then glided the humeral head anteriorly and posteriorly, keeping the patient's arm parallel to the body. To perform the inferior glide of the shoulder, the clinician grasped the patient's elbow with 1 hand and palpated with the other hand the distal spine of the scapula posteriorly and below the distal clavicle anteriorly over the humeral head. The clinician then pulled the humeral head inferiorly, while monitoring to see whether the humeral head moved distally in the glenoid cavity. To perform the antero-

posterior glide of the humerus, the clinician abducted the patient's arm to 45° and grasped the humerus with 1 hand near the elbow, stabilizing the lateral aspect of the elbow with the other hand. The clinician then applied forward/backward force while maintaining abduction.

In order to perform the anterior capsule stretch, with the patients' arm abducted the clinician grasped the proximal humerus medially while stabilizing the force arm with the other hand. The clinician then rotated the humerus externally while gliding the humeral head anteriorly. To perform the posterior capsule stretch, with the arm in 90° of flexion and elbow flexion, the clinician grasped the elbow and cradled the forearm while stabilizing the lateral scapular border with the wrist. The clinician then stretched the glenohumeral joint into horizontal adduction. To perform the inferior capsule stretch, with the arm in end-range abduction, the clinician placed the volar wrist of 1 hand over the lateral border of the scapula to stabilize, while grasping the humerus with the other hand above the elbow. The clinician then provided stretch into abduction. For scapular distraction, the treating clinician positioned the participant prone on the treatment table with the forearm behind the back, and then placed the index finger of 1 hand under the medial scapular border while the other hand grasped the superior scapular border. The clinician then distracted the scapula from the thorax.

The above-mentioned mobilization techniques were applied with intensity of grades III and IV according to Maitland's description of the grades of joint movement.⁵⁷ Mobilization was performed by a physical therapist trained in manual therapy, and the subjects were asked to report to the physical therapist about pain during and after treatment.

Prior to the start of WBC, all participants were examined by a physician for any contraindications against cryostimulation. Just before each session of WBC, the participant's systolic and diastolic blood pressure were measured in order to check for the most common contraindication, high blood pressure. Accepted blood pressure ranges for participation for systolic blood pressure was of 120mmHg or less, and for diastolic blood pressure was 80mmHg or less. The WBC group underwent six 4-minute exposures per week (twice a day, 3 times per week) over 4 consecutive weeks (24 visits in total) in a specially designed temperature-controlled unit^b consisting of 2 chambers with different temperatures (-50° and -110°C). Just before entering the cryogenic chamber, the participants thoroughly dried their bodies to eliminate a sensation of cold. During exposures, in order to prevent frostbite, all subjects were instructed to wear cap, earband, triple layer gloves, dry socks, and shoes in the chambers; to slightly move their fingers, arms, and legs by walking; and avoid breath holding. All subjects breathed through a surgical mask to protect the upper airways. The men wore shorts while women wore bathing suits.

Each subject was exposed to the first prechamber (-50°C) for 1-minute before entering the therapy chamber (-110°C). Each subject was exposed to the therapy chamber for 2.5 minutes, and after this each subject was exposed to the prechamber (-50°C) again for 0.5 minutes. Microphones and camera were used to maintain contact with subjects throughout the treatment. After the WBC session, subjects were instructed to walk in a temperate room (24°C) at their normal and comfortable pace for approximately 10 minutes. The temperature in each chamber remained constant during the period of treatment (-50°C and -110°C), and the air in the chambers was dry and clear.

All subjects completed all of the sessions, and no one was seen any less than 12 visits in the modalities/mobilization group and no less than the 24 visits in the WBC group. No

Table 2: Changes in Mean \pm SD Scores of Shoulder Mobility, Differences Within Groups, and Differences Between Groups

Parameter	Group	Before Intervention*	Range	Discharge	Range	P [†]
Flexion	WBC [‡]	116 \pm 6.7	106–128	162 \pm 5.3	153–168	<.01
	Non-WBC [‡]	119 \pm 7.7	103–130	149 \pm 5.9	140–160	
Abduction	WBC [‡]	117 \pm 6.4	105–125	158 \pm 5.3	151–167	<.01
	Non-WBC [‡]	119 \pm 8.0	103–128	145 \pm 5.4	137–156	
Internal rotation	WBC [‡]	34 \pm 2.1	31–37	53 \pm 2.7	48–58	<.01
	Non-WBC [‡]	34 \pm 2.1	30–36	44 \pm 3.3	38–51	
External rotation	WBC [‡]	69 \pm 2.9	64–74	80 \pm 2.6	73–84	<.01
	Non-WBC [‡]	69 \pm 2.8	64–72	75 \pm 2.3	71–78	

NOTES. Units are in degrees. For each group, n=15.

*No significant differences ($P>.05$) between the WBC group and the non-WBC group before intervention for all measurements.

[†]P obtained by analysis of covariance for comparison of postintervention scores of 2 groups under adjustment of baseline scores.

[‡]Significant change ($P<.01$) within the groups (WBC and non-WBC) at discharge compared with before intervention by paired *t* test.

illness or side effects occurred during the experiment. Subjects were allowed to continue taking medications for control of pain if they had started taking them prior to enrollment. All subjects were advised to avoid all other interventions or training or sporting activities associated with the shoulder. Both groups were also instructed to avoid any activities or movements that may have provoked shoulder pain or could have contributed to shoulder symptoms.

Data Analysis

The sample size (15 subjects per group) was determined under the assumption that the analysis had approximately 83% power to detect approximately 1.1 SD difference in mean changes of measured variables between 2 groups at a significance level .05. Analyses were performed on an intention-to-treat principle; thus, all available data from all subjects were included in the analysis. Analysis of covariance using a regression model, which controls for initial differences of the variable examined between the 2 groups based on a pretest measure, was used to compare the changes of outcome measures in pain, ROMs, and the ASES between the 2 groups at discharge. A paired *t* test was used to examine the differences within each treatment group between preintervention and discharge variables. The *P* value of <.05 was considered statistically significant. Dependent variables included VAS, active ROMs of flexion, abduction, internal and external rotation of the shoulder, and the ASES scores. The software package SPSS 14.0 KO^c was used for statistical analyses.

RESULTS

Each group followed its own protocol, and all subjects completed initial and posttreatment active ROMs of the shoulder, VAS, and the ASES assessments. There were no outliers in all scores measured, and data from all subjects were used in the statistical analysis. At baseline, the participants showed ROM

restriction in flexion, abduction, internal rotation, and external rotation of the shoulder and moderate to high pain scores as well as low ASES scores. Moreover, there was no significant difference in the baseline preintervention scores in all measured parameters between the 2 groups (table 2).

After the treatment, all participants reported a clinically meaningful improvement in measured ROMs of the shoulder, pain, and function (tables 2 and 3). A comparison between pre- and postintervention showed a statistically significant improvement for both groups in all measured movement directions, such as flexion, abduction, internal rotation, and external rotation, and VAS scores, as well as the ASES scores ($P_s<.01$).

As the interaction terms between the preintervention scores and experimental groups were not statistically significant in full factorial models for all the outcomes ($P>.05$), main effect models were applied and statistically significant differences were found in all outcome measures between the 2 groups. VAS scores ($F_{1,27}=57.86$, $P<.01$) and all measured ROMs, such as flexion ($F_{1,27}=44.08$, $P<.01$), abduction ($F_{1,27}=55.94$, $P<.01$), internal rotation ($F_{1,27}=51.62$, $P<.01$), and external rotation ($F_{1,27}=33.1$, $P<.01$), as well as the ASES scores ($F_{1,27}=83.88$, $P<.01$) in the WBC group were significantly better than those in the non-WBC group at postmeasurement. For the WBC group, the mean ROM scores \pm SD of flexion, abduction, internal rotation, and external rotation were 162 \pm 5.3, 158 \pm 5.3, 53 \pm 2.7, and 80 \pm 2.6, respectively, at discharge were significantly greater than the non-WBC group (see table 2). Moreover, the mean pain score \pm SD of the WBC group was 2.5 \pm 0.5 of 10 at discharge, which was significantly lower than the non-WBC (see table 3). Finally, the mean ASES score \pm SD was significantly greater for the WBC group (24 \pm 1.4) when compared with the other group (see table 3). More details concerning the outcomes after treatment in both groups for measured dependent variables are provided in tables 2 and 3.

Table 3: Changes in Mean \pm SD Scores on the VAS and ASES for Each Group, Differences Within Groups, and Differences Between Groups

Parameter	Group	Before Intervention*	Range	Discharge	Range	P [†]
VAS	WBC [‡]	6.0 \pm 0.7	5–7	2.5 \pm 0.5	2–3	<.01
	Non-WBC [‡]	6.0 \pm 0.8	5–7	3.7 \pm 0.6	3–5	<.01
ASES	WBC [‡]	12 \pm 1.4	9–14	24 \pm 1.4	22–27	<.01
	Non-WBC [‡]	13 \pm 1.6	9–14	20 \pm 1.2	18–22	<.01

NOTE. For each group, n=15.

*No significant differences ($P>.05$) between the WBC group and the non-WBC group before intervention for all measurements.

[†]P obtained by analysis of covariance for comparison of postintervention scores of 2 groups under adjustment of baseline scores.

[‡]Significant change ($P<.01$) within the group (WBC and non-WBC) at discharge compared with before intervention by paired *t* test.

DISCUSSION

This study compared the effectiveness of 2 different treatment strategies for AC of the shoulder: WBC in combination with modalities and joint mobilization versus modalities and joint mobilization alone. Both treatments improved ROM, pain, and shoulder function after 4 weeks of treatment. The results of this study also confirmed the hypothesis that the addition of WBC to modalities and mobilization is more effective than modalities and mobilization alone. Pain, ROM, and the ASES scores reflected a better outcome for the WBC group than the non-WBC group.

AC of the shoulder has been shown to be a self-limiting disease, which develops over a period of 6 months and may last approximately 24 months, then gradually disappear.⁵⁸⁻⁶⁰ Untreated AC of the shoulder resolves after 12 to 42 months (mean duration of the disease: 30mo).⁶¹ Because subjects from the current study had symptoms for at least 3 months, recovery seen after 1 month of intervention may contribute to modalities/mobilization or a combination of modalities/mobilization and WBC rather than the natural history of the condition. However, because there was no control group in this study, we do not know for certain that the improvement was not because of natural progress of the condition or because of any other factors. For ethical reasons, we did not include a nontreatment group.

Because of a poor understanding of the pathophysiology of AC of the shoulder, management is generally directed at relief of pain and improvement of shoulder function. Nonsurgical treatment is often the first line of management for AC of the shoulder, and the success rate is high.^{62,63} Physical therapy is the foundation of shoulder problem treatment.

As expected, in both groups, the intervention brought major changes to ROM, pain, and function. At discharge of the study, the mean ROM increases were between 9° and 38°, with the flexion showing the largest improvement, whereas the external rotation improved by 9°. The improvement of 4 motions (flexion, abduction, internal rotation, and external rotation) after both treatments seems clinically interesting, with values representing 12% to 43% of the overall improvement. The average improvements in flexion (38°), abduction (34°), internal rotation (15°), and external rotation (9°) are greater than the cited error of measurement ranging from 5° to 7°.^{64,65} The gain in ROM is probably related to the decrease in pain and the treatment effect of joint mobilization. The pain and the ASES also improved by 48% (decreased from 6 to 3.1 in the VAS score) and 76% (increased from 12.5 to 22 in the ASES score), respectively, and these changes were more marked than for the changes in ROM. A previous study⁶⁶ reported that in the shoulder pain and disability index, a change greater than 10% is considered clinically important. Previous studies^{2,67} reported improvement of ROMs and VAS pain scores of the shoulder joint with joint mobilization in patients with AC.

Several possible explanations are suggested for the anatomical, mechanical, and neurophysiologic effects of the joint mobilization technique on AC of the shoulder. Mobilization techniques induce rheologic changes in synovial fluid and increase the exchange between synovial fluid and cartilage matrix, and also enhance synovial fluid turnover. As a result of these changes in the joint, joint mobility is maintained or increased.⁶⁸ In addition, mobilization techniques have also been demonstrated to produce mechanical changes, such as breaking-up of adhesions, realignment of collagen, or enhancement of fiber gliding when stress of specific movements are directed toward specific parts of the capsular tissue.⁶⁹ Further-

more, joint mobilization techniques are assumed to stimulate peripheral mechanoreceptors and inhibit nociceptors.⁶⁹⁻⁷¹

Of particular interest, we were unable to find any reports in the literature of investigations of the effectiveness of a combined treatment of mobilization and modalities with WBC as an intervention for AC of the shoulder. We were also unable to find any article reporting on a comparison of a modalities/mobilization and a combined treatment of a modalities/mobilization and WBC. To our knowledge, this is the first study to investigate the clinical evidence base in support of WBC for treatment of AC of the shoulder. In the present study, after exposure of repeated WBC in addition to modalities/joint mobilization, the WBC group showed greater improvement in pain, ROM of the shoulder, and the ASES scores than the non-WBC group.

WBC conferred added benefit to modalities/joint mobilization in the management of shoulder pain and restriction. The absolute differences in outcome measures between the 2 treatment strategies were 5° to 16° in ROM, 1.2 score in pain, and 4 scores in the ASES. When considering the design of the study and its power calculation, we assumed that 15% to 20% differences in improvement in the variables measured would be clinically significant, and this magnitude of the treatment effect was achieved in the present study. Differences in improvement in all outcome measures between the 2 treatment strategies were 53% in flexion, 58% in abduction, 90% in internal rotation, 83% in external rotation, 32% in the VAS, and 20% in the ASES. We found that the clinical improvement in the WBC group was considerable. Therefore, for patients with AC presenting pain and restriction, the addition of WBC to modalities and joint mobilization could be the preferred treatment strategy.

A number of mechanisms induce the observed changes in patients with AC of the shoulder. One potential candidate could be that the WBC produces local analgesic effects by a lessening of nerve transmission over a large area of the body, combined with an increased endorphine concentration, reducing the perception of pain.^{72,73} Previous studies^{74,75} suggested that in order to produce local analgesia in cryotherapy, skin temperature needs to be below 13.6°C, when nerve conduction and acetylcholine formation become suppressed. This temperature was achieved in the extremities and in the back during the WBC of 2 minutes at -110°C (2.5min of WBC exposure at -110°C in the current study), but not in the hands and feet, which were covered by gloves and socks.⁷⁶ Skin temperature recorded in the calf muscle was 9.04±3.78°C immediately after WBC.⁷⁷ Thus, it is possible that this mechanism may be responsible for alleviating pain further after the addition of WBC to modalities and mobilization.

Another possible explanation for the beneficial pain-alleviating effects of WBC might be cold-induced increase in norepinephrine from both peripheral nerve endings and brain nuclei released by sympathetic stimulation during the exposure of WBC.^{78,79} Previous studies⁸⁰⁻⁸² demonstrated that spinal administration of norepinephrine in experimental animals and epidural injections of an adrenoreceptor agonist in humans, reduced pain. Thus, cold-induced increase in norepinephrine may therefore have a role in pain alleviation in the spinal cord where pain afferents from skin terminate.⁸⁰⁻⁸² Moreover, sustained noradrenaline stimulation caused by accelerated elimination of triiodothyronine and activation of the sympathetic nervous system during long-term cold exposure and repeated WBC could relieve pain and induce an increased sense of well-being.⁸³

Study Limitations

This study has a number of limitations. No control group was included in the study. Without a control group, it was difficult to determine the exact contribution of the treatment to the measured changes. Placebo effect or spontaneous resolution cannot be dissociated from the treatment effect. In addition, the participants in the current study had a much greater external rotation than internal rotation, which is not a typical capsular pattern of the shoulder in which the most limited range occurs in external rotation. This can be explained by the measurement of active ROM of the shoulder instead of passive ROM in the current study. A capsular restriction is always a passive constraint and not just an active constraint, and in most studies, most reliable data for goniometric measurements were done with passive ROM not active ROM. Moreover, the multimodal approach, including physical therapy modalities with joint mobilization and WBC, was used in the current study. Thus, it is unknown whether each component of the intervention is effective. The study sample consisted of a small homogeneous sample of patients with idiopathic AC of the shoulder; thus, our findings cannot be generalized to the whole population with various stages of AC of the shoulder. Finally, no follow-up data were collected. It was not possible to determine the long-term outcomes of the intervention.

CONCLUSIONS

The findings of the present study provide significant evidence in support of the efficacy of a multimodal treatment approach using physical therapy modalities, joint mobilization, and WBC or physical therapy modalities and joint mobilization alone in management of AC of the shoulder. The statistics also suggest that the addition of WBC to modalities and joint manipulation proved to be more effective in improvement of ROM of the shoulder, pain, and the ASES than modalities and mobilization alone. It is our opinion that a well-designed randomized controlled trial using a larger patient population and follow-up is warranted, in order to further enhance these conclusions regarding effectiveness of 2 multimodal treatment approaches for AC of the shoulder.

References

- Tasto JP, Elias DW. Adhesive capsulitis. *Sports Med Arthrosc Rev* 2007;15:216-21.
- Vermeulen HM, Rozing PM, Obermann WR, le Cessie S, Vliet Vlieland TP. Comparison of high-grade and low-grade mobilization techniques in the management of adhesive capsulitis of the shoulder: randomized controlled trial. *Phys Ther* 2006;86:355-68.
- Sandor R. Adhesive capsulitis: optimal treatment of "frozen shoulder." *Phys Sports Med* 2000;28:23-9.
- Hannafin JA, Chiaia TA. Adhesive capsulitis: a treatment approach. *Clin Orthop Relat Res* 2000;(372):95-109.
- Tasto JP, Elias DW. Adhesive capsulitis. *Sports Med Arthrosc Rev* 2007;15:216-21.
- Tuten HR, Young DC, Douoguih WA, Lenhardt KM, Wilkerson JP, Adelaar RS. Adhesive capsulitis of the shoulder in male cardiac surgery patients. *Orthopedics* 2000;23:693-6.
- Bowman CA, Jeffcoate WJ, Patrick M, Doherty M. Bilateral adhesive capsulitis, oligoarthritis and proximal myopathy as presentation of hypothyroidism. *Br J Rheumatol* 1988;27:62-4.
- Mulcahy KA, Baxter AD, Oni OO, Finlay D. The value of shoulder distension arthrography with intraarticular injection of steroid and local anaesthetic: a follow-up study. *Br J Radiol* 1994;67:263-6.
- Neviaser RJ, Neviaser TJ. The frozen shoulder. Diagnosis and management. *Clin Orthop Relat Res* 1987;(223):59-64.
- van der Horst CM, Kenter JA, de Jong MT, Keeman JN. Shoulder function following early mobilization of the shoulder after mastectomy and axillary dissection. *Neth J Surg* 1985;37:105-8.
- Wohlgethan JR. Frozen shoulder in hyperthyroidism. *Arthritis Rheum* 1987;30:936-9.
- Siegel L, Cohen N, Gall E. Adhesive capsulitis: a sticky issue. *Am Fam Physician* 1999;59:1843-50.
- Carette S. Adhesive capsulitis—research advances frozen in time? *J Rheumatol* 2000;27:1329-31.
- Bentley C, Tasto J. Opening the "BlackBox" of shoulder pain. *J Musculoskelet Med* 2001;18:27-40.
- Dodenhoff RM, Levy O, Wilson A, Copeland SA. Manipulation under anesthesia for primary frozen shoulder: effect on early recovery and return to activity. *J Shoulder Elbow Surg* 2000;9:23-6.
- Ekelund AL, Rydell N. Combination treatment for adhesive capsulitis of the shoulder. *Clin Orthop Relat Res* 1992;(282):105-9.
- Gam AN, Schydlowsky P, Rossel I, Remvig L, Jensen EM. Treatment of "frozen shoulder" with distension and glucocorticoid compared with glucocorticoid alone. A randomised controlled trial. *Scand J Rheumatol* 1998;27:425-30.
- Jones DS, Chattopadhyay C. Suprascapular nerve block for the treatment of frozen shoulder in primary care: a randomized trial. *Br J Gen Pract* 1999;49:39-41.
- Omari A, Bunker TD. Open surgical release for frozen shoulder: surgical findings and results of the release. *J Shoulder Elbow Surg* 2001;10:353-7.
- Watson L, Dalziel R, Story I. Frozen shoulder: a 12-month clinical outcome trial. *J Shoulder Elbow Surg* 2000;9:16-22.
- Arslan S, Celiker R. Comparison of the efficacy of local corticosteroid injection and physical therapy for the treatment of adhesive capsulitis. *Rheumatol Int* 2001;21:20-3.
- Carette S, Moffet H, Tardif J, et al. Intraarticular corticosteroids, supervised physiotherapy, or a combination of the two in the treatment of adhesive capsulitis of the shoulder. *Arthritis Rheum* 2003;48:829-38.
- Nicholson GG. The effects of passive joint mobilization on pain and hypomobility associated with adhesive capsulitis of the shoulder. *J Orthop Sports Phys Ther* 1985;6:238-46.
- Dacre JE, Beeney N, Scott DL. Injections and physiotherapy for the painful stiff shoulder. *Ann Rheum Dis* 1989;48:322-5.
- Vermeulen HM, Obermann WR, Burger BJ, Kok GJ, Rozing PM, van Den Ende CH. End-range mobilization techniques in adhesive capsulitis of the shoulder joint: a multiple-subject case report. *Phys Ther* 2000;80:1204-13.
- Westerlund T, Smolander J, Uusitalo-Koskinen A, Mikkelsen M. The blood pressure responses to an acute and long-term whole-body cryotherapy (-110°C) in men and women. *J Therm Biol* 2004;29:285-90.
- Lubkowska A, Szygula Z, Chlubek D, Banfi G. The effect of prolonged whole-body cryostimulation treatment with different amounts of sessions on chosen pro- and anti-inflammatory cytokines levels in healthy men. *Scand J Clin Lab Invest* 2011;71:419-25.
- Taghawinejad M, Birwe G, Fricke R, Hartmann R. Ganzkörperkältetherapie – Beeinflussung von Kreislauf- und Stoffwechselfparametern. *Z Phys Med Baln Med Klim* 1989;18:23-30.
- Metzger D, Zwingmann C, Protz W, Jäckel WH. Whole-body cryotherapy in rehabilitation of patients with rheumatoid diseases—pilot study. *Rehabilitation (Stuttg)* 2000;39:93-100.
- Hirvonen HE, Mikkelsen MK, Kautiainen H, Pohjolainen TH, Leirisalo-Repo M. Effectiveness of different cryotherapies on pain and disease activity in active rheumatoid arthritis. A randomised single blinded controlled trial. *Clin Exp Rheumatol* 2006;24:295-301.
- Jansky P, Jansky L. Sites and cellular mechanisms of human adrenergic thermogenesis: a review. *J Thermal Biol* 2002;27:269-77.

32. Griffin J, Redlin G. Shoulder pain in patients with hemiplegia. A literature review. *Phys Ther* 1981;61:1041-5.
33. Ganta CK, Helwig BG, Blecha F, et al. Hypothermia-enhanced splenic cytokine gene expression is independent of the sympathetic nervous system. *Am J Physiol Regul Integr Comp Physiol* 2006;291:558-65.
34. Leppäluoto J, Westerlund T, Huttunen P, et al. Effects of long-term whole-body cold exposures on plasma concentrations of ACTH, beta-endorphin, cortisol, catecholamines and cytokines in healthy females. *Scand J Clin Lab Invest* 2008;68:145-53.
35. Marino F, Sockler JM, Fry JM. Thermoregulatory, metabolic and sympathoadrenal responses to repeated brief exposure to cold. *Scand J Clin Lab Invest* 1998;58:537-46.
36. Vybíral S, Lesná I, Janský L, Zeman V. Thermoregulation in winter swimmers and physiological significance of human catecholamine thermogenesis. *Exp Physiol* 2000;85:321-6.
37. Banfi G, Melegati G, Barassi A, et al. Effects of whole-body cryotherapy on serum mediators of inflammation and serum muscle enzymes in athletes. *J Thermal Biol* 2009;34:55-9.
38. Jansky L, Pospisilova D, Honzova S, et al. Immune system of cold-exposed and cold-adapted humans. *Eur J Appl Physiol Occup Physiol* 1996;72:445-50.
39. Kozyreva TV, Gonsales EV, Eliseeva LS. β -Adrenoreceptor participation in the formation of the thermoregulatory and immune responses under the effect of rapid deep cooling. *J Thermal Biol* 2004;29:819-24.
40. Rhind SG, Castellani JW, Brenner IK, et al. Intracellular monocyte and serum cytokine expression is modulated by exhausting exercise and cold exposure. *Am J Physiol Regul Integr Comp Physiol* 2001;291:66-75.
41. Lubkowska A, Szygula Z, Klimek AJ, Torii M. Do sessions of cryostimulation have influence on white blood cell count, level of IL6 and total oxidative and antioxidative status in healthy men? *Eur J Appl Physiol* 2010;109:67-72.
42. Miller E, Markiewicz L, Saluk J, Majsterek I. Effect of short-term cryostimulation on antioxidative status and its clinical applications in humans. *Eur J Appl Physiol* 2012;112:1645-52.
43. Kenjo T, Kikuchi S, Konno S. Cooling decreases fos-immunoreactivity in the rat after formalin injection. *Clin Orthop Relat Res* 2002;(394):271-7.
44. Nadler SF, Weingand K, Kruse RJ. The physiologic basis and clinical applications of cryotherapy and thermotherapy for the pain practitioner. *Pain Physician* 2004;7:395-9.
45. Prentice WE. *Arnheim's principles of athletic training: a competency based approach*. New York: McGraw Hill; 2008.
46. De Domenico G. *New dimensions in interferential therapy: a theoretical and clinical guide*. 1st ed. Lindfield: Reid Medical Books; 1987.
47. Kloth L. Interference current. In: Nelson RM, Currier DP, editors. *Clinical electrotherapy*. Norwalk: Appleton and Lange; 1987. p 183-207.
48. De Domenico G. Pain relief with interferential therapy. *Aust J Physiother* 1982;28:14-8.
49. Jensen M, Karoly P, Beaver S. The measurement of clinical pain intensity: a comparison of six methods. *Pain* 1986;27:117-26.
50. Price DD, McGrath PA, Rafii A, Buckingham B. The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. *Pain* 1983;17:45-56.
51. Boonstra AM, Schiphorst Preuper HR, Reneman MF, Posthumus JB, Stewart RE. Reliability and validity of the visual analogue scale for disability in patients with chronic musculoskeletal pain. *Int J Rehabil Res* 2008;31:165-9.
52. Vermeulen HM, Boonman DC, Schüller HM, et al. Translation, adaptation and validation of the Shoulder Rating Questionnaire (SRQ) into the Dutch language. *Clin Rehabil* 2005;19:300-11.
53. O'Connor DA, Chipchase LS, Tomlinson J, Krishnan J. Arthroscopic subacromial decompression: responsiveness of disease-specific and health-related quality of life outcome measures. *Arthroscopy* 1995;15:836-40.
54. American Academy of Orthopaedic Surgeons. *Joint motion: method of measuring and recording*. Chicago: American Academy of Orthopaedic Surgeons; 1965.
55. Riddle DL, Rothstein JM, Lamb RL. Goniometric reliability in a clinical setting: shoulder measurements. *Phys Ther* 1987;67:668-73.
56. Michener LA, McClure PW, Sennett BJ. American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form, patient self-report section: reliability, validity, and responsiveness. *J Shoulder Elbow Surg* 2002;11:587-94.
57. Hengeveld E, Banks K, Maitland's peripheral manipulation. 4th ed. London: Butterworths-Heinemann; 2005.
58. Grey RG. The natural history of "idiopathic" frozen shoulder. *J Bone Joint Surg Am* 1978;60:564.
59. Rowe CR, Leffert RD. Idiopathic chronic adhesive capsulitis ("frozen shoulder"). In: Rowe CR, editor. *The shoulder*. New York: Churchill Livingstone; 1988. p 155-63.
60. Neviasser JS. Arthrography of the shoulder joint: study of the findings in adhesive capsulitis of the shoulder. *J Bone Joint Surg Am* 1962;44:1321-30.
61. Reeves B. The natural history of the frozen shoulder syndrome. *Scand J Rheumatol* 1975;4:193-6.
62. Griggs SM, Ahn A, Green A. Idiopathic adhesive capsulitis. A prospective functional outcome study of nonoperative treatment. *J Bone Joint Surg Am* 2000;82:1398-407.
63. Levine WN, Kashyap CP, Bak SF, Ahmad CS, Blaine TA, Bigliani LU. Nonoperative management of idiopathic adhesive capsulitis. *J Shoulder Elbow Surg* 2007;16:569-73.
64. Boone DC, Azen SP, Lin CM, Spence C, Baron C, Lee L. Reliability of goniometric measurements. *Phys Ther* 1978;58:1355-60.
65. MacDermid JC, Chesworth BM, Patterson S, Roth JH. Intratester and intertester reliability of goniometric measurement of passive lateral shoulder rotation. *J Hand Ther* 1999;12:187-92.
66. Williams JW Jr, Holleman DR Jr, Simel DL. Measuring shoulder function with the Shoulder Pain and Disability Index. *J Rheumatol* 1995;22:727-32.
67. Johnson AJ, Godges JJ, Zimmerman GJ, Ounanian LL. The effect of anterior versus posterior glide joint mobilization on external rotation range of motion in patients with shoulder adhesive capsulitis. *J Orthop Sports Phys Ther* 2007;37:88-99.
68. Noël G, Verbruggen LA, Barbaix E, Duquet W. Adding compression to mobilization in a rehabilitation program after knee surgery: a preliminary clinical observational study. *Man Ther* 2000;5:102-7.
69. Mangus BC, Hoffman LA, Hoffman MA, Altenburger P. Basic principles of extremity joint mobilization using a Kaltenborn approach. *J Sport Rehabil* 2002;11:235-50.
70. Taylor M, Suvinen T, Reade P. The effect of grade IV distraction mobilization on patients with temporomandibular pain-dysfunction disorder. *Physiother Theory Pract* 1994;10:129-36.
71. Donatelli RA. *Physical therapy of the shoulder*. 5th ed. New York: Churchill Livingstone; 2011.
72. Howatson G, van Someren KA. The prevention and treatment of exercise-induced muscle damage. *Sports Med* 2008;38:483-503.
73. Schwane JA, Johnson SR, Vandenakker CB, Armstrong RB. Delayed onset muscular soreness and plasma CPK and LDH activities after downhill running. *Med Sci Sports Exerc* 1983;15:51-6.
74. Bugaj R. The cooling, analgesic, and rewarming effects of ice massage on localized skin. *Phys Ther* 1975;55:11-9.
75. Ekman AC, Vakkuri O, Vuolteenaho O, Leppäluoto J. Delayed pro-opiomelanocortin activation after ethanol intake in man. *Alcohol Clin Exp Res* 1994;18:1226-9.

76. Westerlund T, Oksa J, Smolander J, Mikkelsen T. Thermal responses during and after whole-body cryotherapy. *J Therm Biol* 2003;28:601-8.
77. Savalli L, Olave P, Sendin MIH, Laboute E, Trouve P, Puig PL. Whole-body cryotherapy-110°C. Measure of skin and central temperature to the Sportsman. *Sci Sports* 2006;21:36-8.
78. Pertovaara A, Kauppila T, Jyväsjärvi E, Kalso E. Involvement of supraspinal and segmental alpha-2-adrenergic mechanism in the medetomidine-induced antinociception. *Neuroscience* 1991; 44:705-14.
79. Leppäluoto J, Westerlund T, Huttunen P, et al. Effects of long-term whole-body cold exposures on plasma concentrations of ACTH, beta-endorphin, cortisol, catecholamines and cytokines in healthy females. *Scand J Clin Lab Invest* 2008;68:145-53.
80. Gordh T. Epidural clonidine for treatment of postoperative pain after thoracotomy. A double-blind placebo-controlled study. *Acta Anaesthesiol Scand* 1988;32:702-9.
81. Danzebrink R, Gebhart G. Antinociceptive effects of intrathecal adrenoceptor agonists in a rat model of visceral nociception. *J Pharm Exp Ther* 1990;253:698-705.
82. Pertovaara A, Kalmari J. Comparison of the visceral antinociceptive effects of spinally administered MPV-2426 (fadolmidine) and clonidine in the rat. *Anesthesiology* 2003;92:189-94.
83. Banfi G, Melegati G, Barassid A, et al. Effects of whole-body cryotherapy on serum mediators of inflammation and serum muscle enzymes in athletes. *J Therm Biol* 2009;34:55-9.

Suppliers

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