Treatment of Calcifying Tendinitis of the Shoulder by Acetic Acid Iontophoresis: A Double-Blind Randomized Controlled Trial

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ABSTRACT. Leduc BE, Caya J, Tremblay S, Bureau NJ, Dumont M. Treatment of calcifying tendinitis of the shoulder by acetic acid iontophoresis: a double-blind randomized controlled trial. Arch Phys Med Rehabil 2003;84:1523-7.

Objective: To assess the effects of acetic acid iontophoresis on the treatment of calcifying tendinitis of the shoulder.

Design: Double-blind randomized controlled trial.

Setting: Ambulatory academic hospital in Quebec, Canada.

Participants: Thirty-six subjects with a calcifying tendinitis of the shoulder.

Interventions: Subjects were randomized into 1 of 2 groups: physiotherapy during 6 weeks (10 sessions) plus acetic acid iontophoresis for the treatment group (n=18) and sham acetic acid iontophoresis for the control group (n=18).

Main Outcome Measures: The Shoulder Pain and Disability Index (SPADI), shoulder range of motion (ROM); and radiologic evaluation of shoulder calcifications.

Results: Nine patients dropped out, leaving 27 assessable subjects for analysis. Interim analysis showed that, in both groups, treatment led to improvement, as measured by the SPADI score ($P=.004$), ROM of the shoulder for abduction ($P<.001$), internal rotation ($P=.001$), external rotation ($P<.001$), and the mean number of calcifications per subject ($P=.010$). Although no formal significant intervention effects ($P=.13$) were found for the primary endpoint (SPADI), exploratory analyses suggest a greater improvement in the treatment group ($P=.001$) than in the control group ($P=.33$).

Conclusions: Despite a trend toward greater improvement in the SPADI score in the treatment group, the use of acetic acid iontophoresis and physiotherapy for the treatment of calcifying tendinitis of the shoulder did not result in better clinical and radiologic effects than those observed in subjects treated by physiotherapy alone.

Key Words: Acetic acid; Calcification; Iontophoresis; Rehabilitation; Shoulder; Tendinitis.

CALCIFYING TENDINITIS OF the shoulder is mostly asymptomatic despite a reported incidence of 3%[1] to 20%.[2] This condition, seen most frequently in women,[3] affects mainly 30- to 60-year-old individuals and is bilateral in 25% to 30% of the cases.[4] The etiopathogeny of calcifying tendinitis remains hypothetical. However, it has repeatedly been shown that hydroxyapatite crystals[5] are the main component of the calcifications after the occurrence of fibrocartilage within the tendon.[6] The clinical polymorphism of this condition is common,[7] and, when pain is present along with functional impairment, it is customary to treat these symptoms with anti-inflammatory drugs (orally or injection), analgesics, and, if necessary, various physiotherapy treatments, such as acetic acid iontophoresis[8] and ultrasound therapy.[9] Other treatment alternatives are percutaneous needle aspiration of calcium deposits by using ultrasonography guidance,[10] extracorporeal approach with shockwave therapy,[11] and, more rarely, surgery.[12]

The use of acetic acid iontophoresis in the treatment of calcifying tendinitis of the shoulder was first described in 1955.[8] The physiologic basis for this approach rests on the passage of ionisable substances through the skin—mainly hair follicle and sweat gland canals[13]—through the polar effect of direct (galvanic) current, which thus triggers the migration of the ionized molecules placed under the same polarity electrode toward the opposite polarity electrode.[14] In this way, acetic acid, which is an inorganic anion, is applied under the cathode (negative electrode) and will migrate toward the anode (positive electrode) while submitted to galvanic current. Because the calcification consists mostly of hydroxyapatite crystals, which is insoluble in water but soluble in acidic pH, it is reasonable to expect a regression of the calcification.

In the context of adverse reactions or intolerance to anti-inflammatory agents, acetic acid iontophoresis, because of its noninvasive character, remains a frequently used treatment for calcifying tendinitis of the shoulder[15]; however, a literature search on this treatment performed on the EMBASE (1966–2001) and MEDLINE (1976–2001) databases and recent reviews of the use of iontophoresis in medical use[16,17] failed to identify any clinical study investigating the effectiveness of this therapeutic approach. The only controlled and randomized clinical trial assessing the usefulness of acetic acid iontophoresis and ultrasound for the treatment of calcifying tendinitis of the shoulder[18] has not shown significant clinical or radiologic effects, but that study evaluated the effect of 2 simultaneous treatments and not the effect of acetic acid iontophoresis administered alone.

Given the lack of clinical trials showing the effectiveness of acetic acid iontophoresis in the treatment of calcifying tendinitis of the shoulder, the purpose of our study was to assess the clinical and radiologic effects of acetic acid iontophoresis in the treatment of calcifying tendinitis of the shoulder.

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METHODS

Once the project was approved by the hospital's ethics committee, we recruited patients by posting the project in the 3 pavilions of Centre Hospitalier Universitaire de Montréal Foundation, in Montréal, QC (1998–2001).

Participants

Patients recruited for this project met the following inclusion criteria: were 18 years of age or older, showed symptomatic (painful) tendinitis of the shoulder, and had at least 1 calcification of the shoulder visible on radiography. Excluded were those who were pregnant, had oral or local injection corticotherapy administered during the previous 2 months, had cutaneous contraindication to the application of 5% acetic acid, had adhesive capsulitis of the shoulder, had arthropathy of the shoulder, or had any other medical condition accompanied by pain. After signing a consent form, the participants were divided randomly according to a stratified allocation table: 1 group of patients (treatment group) received acetic acid iontophoresis followed by thermotherapy and range of motion (ROM) exercises of the shoulder, the second group (control group) consisted of subjects who received the same treatment as the first group except that the iontophoresis treatment was a placebo. For the duration of the study, the use of acetaminophen was allowed for all subjects of both groups; a cortisone injection in the shoulder, if given during the treatment, resulted in the subject being removed from the trial.

Methodology

The acetic acid iontophoresis treatment was given to subjects who were seated, their arm resting on a table. An electrotherapy apparatus, Dynapuls 421,[a] was used to administer a galvanic current of 5mA for 15 to 20 minutes The active electrode (cathode) was made of easily malleable lead, had a surface of 5×7.5cm, and was placed on 3 compresses saturated with 20mL of 5% acetic acid applied approximately at the site of calcification of the shoulder. The second electrode (anode), also of malleable lead, had a 4×5-cm surface and was fixed to the anterior side of the distal segment of the ipsilateral arm. The acetic acid iontophoresis material was prepared by physiotherapist A (ST), who used 2 different techniques, as shown in figures 1 and 2; in all control group subjects, a plastic film was used to cover the upper surface of the active electrode, and the compresses that were saturated with acetic acid were placed above the active electrode and not between the skin and the electrode, as technically required to ensure iontophoresis. Once the shoulder and arm of all subjects of both groups had been wrapped with identical elastic bandage, the acetic acid iontophoresis treatment was administered by physiotherapist B (JC). After the treatment was completed, the iontophoretic material was removed by physiotherapist A.

Every subject was given 10 treatments—3 a week for 2 weeks, followed by a weekly session for the remaining 4 weeks. Physiotherapist A prepared and installed the material needed for the acetic acid iontophoresis treatment of all participants in both groups; neither the participants nor physiotherapist B were aware of the true nature of the treatments (acetic acid iontophoresis or placebo) administered to participants; physiotherapist B administered the treatments, followed by thermotherapy and ROM exercises. At all times, only the main investigator and physiotherapist A were aware of the actual allocation of patients.

Measures

The following parameters were assessed before and after the end of treatment.

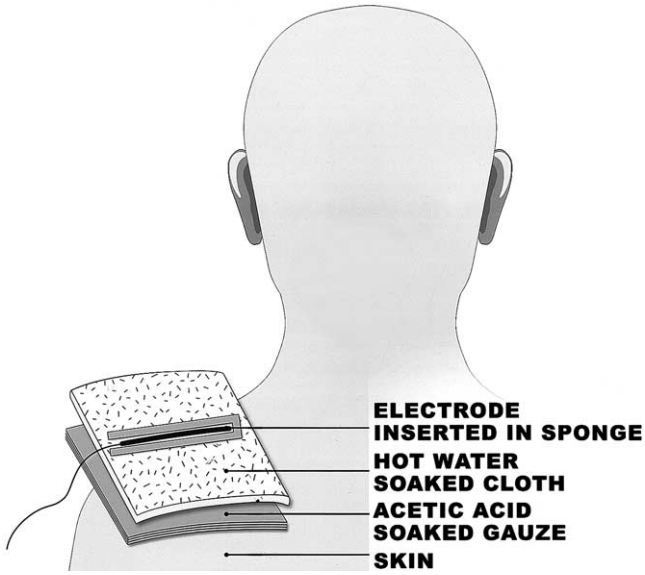

Fig 1. Simplified illustration of the placement of material used in the treatment group.

Pain. Pain and its functional impact on the shoulder were the main parameters of interest (primary endpoint) and were measured by using the Shoulder Pain and Disability Index (SPADI) questionnaire[19] in its French language-validated version (L. Fortin, unpublished observation, 1999). This self-administered questionnaire uses 13 questions, 5 of which deal with the severity of pain on various arm movements involving the shoulder, the pain being assessed by using a visual analog scale (VAS), and 8 questions dealing with functional impairment of the shoulder assessed with a VAS ranging from 0 (no difficulty) to 10 (so difficult that I need help). An overall score plotted on 100 was calculated for the 13 questions as a whole. When compared with other questionnaires measuring shoulder function, the SPADI has proven to be a very satisfactory psychometric tool.[20]

Shoulder ROM. The amplitude of active anterior flexion, abduction, and external and internal rotation of the shoulder was assessed by physiotherapist B by using a manual goniometer (length, 42.5cm), following the same method in all subjects who were evaluated in the dorsal decubitus position, with knees bent at 90°, and feet laying flat; external and internal rotation movements were assessed with the shoulder prepositioned at 90° of abduction or less (maximum abduction according to tolerance). The intraobserver reliability (correlation coefficient) for the assessment values of shoulder movements has been found to be excellent: flexion (r=.98), abduction (r=.90), external rotation (r=.99), and internal rotation (r=.94).[21]

Tendinous calcifications of the shoulder. Radiographs of the shoulder were taken under fluoroscopic control: an anteroposterior view in the neutral position, in internal rotation and external rotation, and a lateral view (supraspinatus outlet view). The calcification sites as well as their number, size (mm^2), and type were documented in the view where they were most easily visible. For our purpose, only the number and the size of the calcifications were considered as endpoints; their measurements before and after treatment were compared. When more than 2 calcifications were present, the size of this cluster (mm^2) was measured and the cluster then counted as a single calcification. Calcifications were classified according to their type[22];

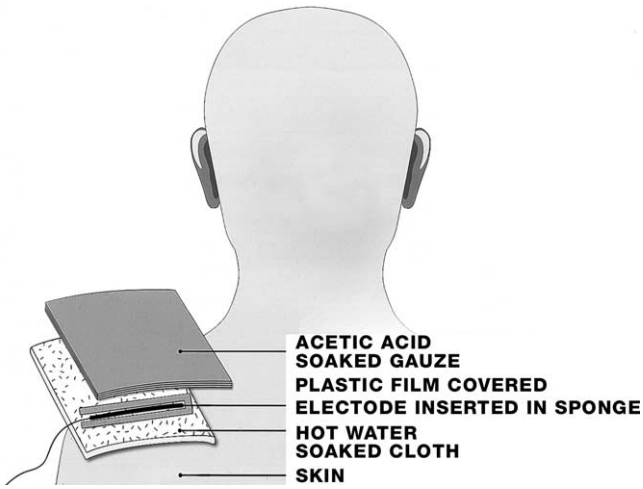

Fig 2. Simplified illustration of the placement of material used in the control group.

Table 1: Characteristics of Assessable Subjects: Pretreatment Values (n=27)

	Treatment Group (n=17)	Control Group (n=10)	*P* Value
Gender, n (%)			
Men	7 (41)	5 (20)	NS
Women	10 (59.8)	8 (80)	NS
Mean age (range) (y)	51.5 (39–71)	47.9 (31–63)	NS
Mean duration of symptoms, n (range) (mo)	27.5 (3–144)	32.4 (3–120)	NS
Right shoulder involved (%)	8 (47)	6 (60)	NS
No. of subjects with calcifications (%)			
n=1	5 (29)	4 (40)	
n>1	12 (71)	6 (60)	

Abbreviation: NS, not significant.

a type 1 calcification shows high density and well-circumscribed borders, a type 3 calcification has blurry borders and looks cloudy, and a type 2 calcification shows a dense or circumscribed appearance. These characteristics were examined because of the varying evolution of calcifications depending on their type—the spontaneous resorption of type 3 calcifications occurs much more frequently than in the type 1 calcifications. All radiographs were interpreted by the same radiologist (NJB), who did not know the group to which the subjects were assigned.

Statistical analyses. Based on a projected "medium" treatment effect size (F=.25), the recruitment of 2 groups of 30 subjects provided an 80% power for group comparisons over time (interaction effect). After verifying the normality and homogeneity of variance postulates, the measures of clinical and radiologic results obtained for both groups before and after treatment were compared by using the 2-way analysis of variance (group, time), with repeated measures on 1 factor. Significant interactions were followed with simple main effects calculations to assess change within each group.

Descriptive profiles of the groups and category data were compared by using Pearson chi-square (without Yates' correction). All data were interpreted at the .05 significance level.

RESULTS

Participants

Thirty-six subjects fitting the inclusion criteria were recruited and randomized in 2 equal groups of 18 participants. The treatment group had 11 women (61%), a mean age of 51.4 years (range, 39–71y), and a mean duration of symptoms of 20.5 months (range, 3–144mo). The control group had 13 women (72%), a mean age of 47.6 years (range, 24–63y), and a mean duration of symptoms of 33 months (range, 3–120mo). The groups showed no significant difference between them. Nine participants were removed from the study, 5 from the control group for superficial second-degree burns under the negative electrode; 2 participants were removed after being treated with cortisone injection in the shoulder, and 2 patients failed to show up for the posttreatment radiography. Therefore, a total of 27 subjects remained in the study, 17 in the treatment group and 10 in the control group (table 1). Four subjects (2 in each group) showed a type III acromion process. No significant pretreatment differences were observed between these 2 groups.

Descriptive Profile of Calcifications

The radiologic characteristics of the calcification (number, site, size, type) of all participants are described in table 2.

Effects of Treatment

Mean SPADI score improved significantly in both groups after treatment ($P=.004$), their evolution (table 3) being similar (interaction effect: $P=.13$).

The mean number of calcifications decreased in a comparable fashion in both groups ($P=.01$), whereas their average size showed no significant variations ($P=.10$). The initial number of 27 calcifications found in the treatment group decreased to 20 after treatment; calcifications in the control group decreased from 14 to 11 (table 4).

Shoulder ROM improved in the 2 groups for abduction ($P<.001$), internal rotation ($P=.001$), and external rotation ($P<.001$), but failed to exhibit a significant difference between the 2 groups (table 5).

Table 2: Site, Type, and Size of Shoulder Calcifications: Pretreatment Values

	Treatment Group (n=27)	Control Group (n=14)	*P* Value
No. of calcifications by site, n (%)			
Supraspinatus	12 (44)	7 (50)	NS
Infraspinatus	14 (52)	3 (21)	.037
Teres minor	1 (4)	1 (8)	NS
Subscapularis	0	3 (21)	
Type, n (%)			
1	7 (26)	6 (40)	NS
2	3 (11)	0	NS
3	17 (63)	8 (60)	NS
Mean size ± SD (mm^2)	133±121	136±167	NS

Abbreviation: SD, standard deviation.

Table 3: SPADI Score Before and After Treatment

	Treatment Group	Control Group	*P* Value	
			Time	G×T*
Before treatment	38±19	45±17		
			.004	.13
After treatment	23±15	40±17		.001†
				.33‡

NOTE. Values are mean ± SD.
*Group by time.
†Within treatment group.
‡Within control group.

DISCUSSION

As mentioned, based on a projected medium treatment effect size, the recruitment of 2 groups of 30 participants was planned. Interim statistical analyses conducted with 2 samples of 17 and 10 subjects indicate that the actual treatment effect obtained for the SPADI scores (the primary endpoint of the study) was similar to this projection. However, it has not been possible to recruit more than 36 subjects despite a long recruitment period (3y) and a very conspicuous posting of this project throughout the 3 pavilions of the Centre Hospitalier Universitaire de Montréal Foundation. Despite the limited sample size available for interim statistical analyses and the lack of a formal significant intervention effect for the group treated with acetic acid iontophoresis, the results of exploratory simple main effects calculations suggest a more pronounced clinical improvement (SPADI) in the treatment group than in the control group (time effect in the treatment group, $P=.001$; in the control group, $P=.33$).

Even if the results obtained from interim analyses could be said to be promising—if the study had been continued—the possibility that acetic acid simply does not cross the skin barrier cannot be completely discarded. Even if investigation into the iontophoretic delivery of drugs[23] had shown the transdermal penetration and passage of anti-inflammatory agents[24] and the probable lack of passage of cortisone in humans,[25] to our knowledge, transdermal penetration of acetic acid has never been shown in humans. Research into the movement of transdermal ionisable molecules with radioactive tracers in animals[26] and humans,[27] using a dye (fluoresceine)[28] or by scanning electrochemical microscopy,[29] has shed light on the different phases of electrophoresis (diffusion, migration, electro-osmosis); however, it does not seem that acetic acid was specifically investigated with regard to its capacity to penetrate transdermally under galvanic current. Finally, given that the penetration of an ionized product depends on a number of variables, including the concentration and diffusing capacity of the product used, the age of the subject (younger skin is more permeable), vascularization, skin hydration (water content of the corneum), condition of the skin, depth of tissue (variable in different articulations), skin pH (which varies according to location), and electric current (the duration of which affects the amount delivered),[30] it becomes obvious that assessing precisely the respective contribution of each variable involved in the iontophoretic process in patients, to most adequately interpret the results, is a complex endeavor.

Table 4: Number and Size of Calcifications Before and After Treatment

	Treatment Group	Control Group	*P* Value	
			Time	G×T
Mean no. of calcifications per subject ± SD				
Before	1.6±.8	1.4±.7		
After	1.18±.7	1.1±.57	.01	.67
Mean size of calcifications ± SD (mm^2)				
Before	133±121	136±167		
After	105±132	80±87	.10	.57

NOTE. Values are mean ± SD.

Table 5: Shoulder ROM Before and After Treatment

	Treatment Group	Control Group	*P* Value	
			Time	G×T
Abduction				
Before	109±29	111±36		
After	133±24	130±30	<.001	.62
Flexion				
Before	143±16	141±24		
After	154±12	143±48	.33	.49
Internal rotation				
Before	52±24	62±27		
After	69±20	71±26	.001	.27
External rotation				
Before	65±12	67±17		
After	75±11	72±16	<.001	.23

NOTE. Values are mean degrees ± SD.

As for the radiologic observations, the 3 resorbed calcifications in the control group were all of type 3, which has the best prognosis of spontaneous resorption. In the treatment group, where 7 calcifications disappeared after treatment, 4 of these were initially of type 3 and 2 of them were of type 2. These results seem to be consistent with the natural evolution of calcifying tendinitis of the shoulder.[7]

Five subjects in the control group had a skin burn of a few square millimeters in surface. Because of the electrolysis of water during iontophoresis, oxidation occurs at the anode and reduction at the cathode. This increases the pH under the cathode, which may induce capillary hyperemia at the skin level (redness), sometimes a sensation of tingling, and, more rarely, an electrochemical burn. Possibly, some of these risks of burning are linked to the preparation of the material for control subjects; this may be so because the lack of compresses (saturated with 5% acetic acid) under the electrode (ie, between the skin and the electrode) and the concentration of electric current on only the lower surface of the cathode (otherwise covered with plastic film on the upper surface) could have promoted a greater density of current at the center of the lower surface of the electrode, resulting in secondary burns. We used the usual recommended technique for the administration of acetic acid iontophoresis and strictly adhered to the recommended safety measures with regard to the duration of treatment[31] and the density of the current used (intensity with regard to the surface of the electrode),[16] which was equivalent to less than $0.5 mA/cm^2$.

In short, the clinical improvement observed in both groups was probably mostly related to the physiotherapy treatments received by all participants. In the context of evidence-based health care, the lack of definite significant results from the use of acetic acid iontophoresis would not firmly support its use in the treatment of calcifying tendinitis of the shoulder. However, the resorption of calcifications obtained in both groups seems

to be related to the natural progress of the disease and not to a particular contribution by acetic acid iontophoresis.

As for the various limitations of this study, one must first mention the sample size; the total number of assessable subjects was below our expectations (difficult recruiting and 9 withdrawals). The lack of significant statistical results must therefore be interpreted with caution, even more so because exploratory analyses support the hypothesis of a positive impact of treatment. At the clinical level, it is furthermore possible that pathologic conditions other than the sole calcifying tendinitis could have contributed to the painful dysfunction of the shoulder, such as rotator cuff disease and/or a phenomenon of subacromial impingement: these conditions were not specifically examined with dynamic ultrasonography and magnetic resonance imaging of the shoulder. Finally, a type III acromion process, found in 4 subjects, has been identified as a risk factor for subacromial impingement syndrome[32]; because this subgroup of the sample was small, we were unable to establish whether these subjects responded differently from other subjects to the treatments.

CONCLUSION

Treatment of calcifying tendinitis of the shoulder with acetic acid iontophoresis and physiotherapy did not result in better clinical or radiologic effects than those observed in subjects treated with physiotherapy alone. It would, however, be advisable to pursue this study with a larger sampling of patients and with better control of the anatomopathologic tendinous conditions associated with calcifying tendinitis to better define the usefulness of acetic acid iontophoresis in the treatment of calcifying tendinitis of the shoulder. Finally, it seems relevant at this point to investigate the transdermal passage of 5% acetic acid administered by iontophoresis.

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