SCIENTIFIC ARTICLE

Steroid Injection and Needle Aponeurotomy for Dupuytren Contracture: A Randomized, Controlled Study

Catherine McMillan, MSc, Paul Binhammer, MD

Purpose To compare flexion deformity at 6 months in patients with Dupuytren contracture who had percutaneous needle aponeurotomy (PNA) combined with a series of triamcinolone acetonide (TA) injections to that of patients who had PNA alone.

Methods Forty-seven patients with Dupuytren disease who were candidates for PNA (at least 1 contracture of at least 20°) participated in the study. Patients were randomized either to receive TA injections immediately following and 6 weeks and 3 months after the procedure or to receive no injections. Injections were administered into cords. The number of injections and the amount of TA per injection was determined based on the number of digits involved and the cord size. All subjects returned for 3 follow-up visits after the procedure, and contractures were measured using a goniometer. Change in total active extension deficit (TAED) was analyzed using a repeated measures analysis of variance to assess for differences between groups, time points, and interaction between group and time point. Descriptive statistics were calculated for all variables of interest. Continuous measures were summarized using means and standard deviations.

Results There was no significant difference in TAED between groups before cord aponeurotomy. Correction at 6 months was 87% of preoperative TAED for the TA group versus 64% for the control group. This difference was statistically significant. The amount of TA administered did not correlate with TAED improvement.

Conclusions The study group who received TA in combination with PNA experienced a significantly greater degree of correction of flexion deformity at 6 months than those who had PNA alone. *(J Hand Surg 2012;37A:1307–1312. Copyright © 2012 by the American Society for Surgery of the Hand. All rights reserved.)*

Type of study/level of evidence Therapeutic II.

Key words Dupuytren disease, randomized controlled trial, percutaneous needle aponeurotomy, triamcinolone acetonide.

Despite being the focus of clinical studies for decades, postsurgical recurrence of Dupuytren disease remains a major challenge.[1–3] Percutaneous needle aponeurotomy (PNA) is associated with a short recovery, low incidence of complication, little pain, and improved hand function.[4–13] Other, more invasive surgical procedures, such as dermofasciectomy, have been associated with lower recurrence rates than PNA[8,9,14–16]; however, many patients are not candidates due to age and/or coexisting conditions,[17,18] or they simply reject the complexity of surgical excision. Although PNA provides these patients with a safe and

From the Division of Plastic and Reconstructive Surgery, Sunnybrook Health Sciences Centre, Toronto, Canada.

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Corresponding author: Paul Binhammer, MD, Division of Plastic and Reconstructive Surgery, Sunnybrook Health Sciences Centre, M1 500 2075 Bayview Avenue, Toronto, Ontario, Canada M4N 3M5; e-mail: p.binhammer@utoronto.ca.

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effective noninvasive surgical option, the rate of recurrence has been reported as 50% or higher in less than 5 years,[5–8] which encourages investigation into potential alternatives.

Injection of the corticosteroid triamcinolone acetonide (TA) into keloids and hypertrophic scars has resulted in a minimum of 50% resolution after 1 or more intralesional injections.[19] Furthermore, a series of TA injections in Dupuytren nodules resulted in modification of disease progression; however, 50% of patients experienced disease reactivation in 1 to 3 years.[20] Because previous evidence suggests that both PNA and TA injections result in at least short-term contracture correction, a study combining these 2 treatment options might yield more favorable outcomes than either option alone. This study prospectively compared the effects of a combined treatment of PNA and TA injections to PNA alone at 6 weeks, 3 months, and 6 months follow-up in patients with Dupuytren disease.

MATERIALS AND METHODS

Consecutive patients diagnosed with true Dupuytren disease presenting with at least 1 joint contracture of at least 20° were invited to participate. Those with diabetes mellitus and those who had previously had hand surgery, including PNA, on the affected hand for any reason were excluded. Study procedures were reviewed by the institutional research ethics board. After informed consent was obtained, subjects were randomized to 1 of 2 groups using an electronic random number generator. The total active extension deficit (TAED) of all contracted joints was measured using the same goniometer before the procedure. The control group had PNA only, and the treatment group (TA group) had PNA and received an injection of TA into the released cord immediately following the procedure. A single surgeon performed the PNA and administered all injections.

Under local anesthesia using 1% lidocaine and alcohol skin preparation, the cord was percutaneously divided, using the bevel of a 16-gauge injection needle. Local anesthesia was restricted to the skin, and a digital nerve block was avoided so that any contact between the releasing needle and the neurovascular bundle could be identified. Multiple points of division were performed along the cord. The procedure was terminated when the finger could be passively straightened to an extended posture, to a TAED of zero. If the digit could not be straightened, further points of release were performed until the digit could be straightened or it was felt that no more points could be released. Supplemental digital block was performed at this point using a long-acting local anesthetic to provide the patient with postoperative anesthesia. A small dressing was applied and usually discontinued within 48 hours. No medications were prescribed. Patients were subsequently fitted with a custom thermoplastic orthosis and were directed to wear it at night for 3 months to maintain digital extension. A daily stretching program was advised for the first 6 weeks to maintain range of motion. Compliance was not measured.

In patients randomized to the TA group, a 25-gauge needle was used to administer injections directly into the cords that caused the contracture immediately following PNA. The preparation used was TA Injectable Suspension USP (40 mg/mL; Sandoz Canada Inc., Boucherville, Quebec). Doses were estimated by the investigator based on previously published guidelines used to treat hypertrophic scars and keloids and Dupuytren nodules.[20,21] A range of 8–48 mg TA was injected per digit, based on the extent of disease, to a maximum of 120 mg per hand to avoid untoward systemic effects. Injections were administered between points of release, with the dose of TA split between points. The TA suspension leaked out at the time of PNA through puncture sites. Follow-up injections at 6 weeks and 3 months in participants randomized to the TA group were administered only to areas of palpable thickness along previously released cords. If no area of palpable thickness was present, no injection was administered. Injections were not administered to newly developed cords. The TA dose, which was estimated based on residual cord size, was split between injection sites. No injections were administered during the 6-month follow-up visit. The TAED was measured in all participants immediately before and after PNA and at 6 weeks, 3 months, and 6 months.

The primary outcome measures were change in TAED and percentage correction from baseline TAED. A repeated measures analysis of variance was performed to assess for differences between the TA and control groups, time points, and interaction between group and time. Two-sample, 2-sided *t*-tests were performed to assess for significant differences between TAED at each follow-up. Baseline characteristics were compared using *t*-tests and the Fisher exact test when appropriate.

A pre-study power calculation indicated that to provide 81% power at alpha = 0.05, a sample size of 18 subjects per group was necessary. When accounting for an anticipated dropout rate of 15%, the total sample size required for enrollment was 44 subjects.

TABLE 1. Baseline Characteristics of Subjects

Variable	TA Group (N = 24)	Control Group (N = 23)	All Subjects (N = 47)	*P* Value (*)
Age, y	61.83 ± 8.3	60.5 ± 9.9	61.2 ± 9.0	.64
Male†	22	19	41	.42
Affected joints†	57	40	97	.12
Affected joints per subject	2.4 ± 1.4	1.7 ± 1.0	2.1 ± 1.2	.11
Affected digits†	38	29	67	.31
Affected digits per subject	1.6 ± 0.8	1.3 ± 0.5	1.4 ± 0.7	.11
Affected middle digits†	5	2	7	.42
Affected ring digits†	14	8	22	.15
Affected small digits†	19	19	38	.99
Affected MCP joints†	32	21	53	.16
Affected MCP joints per subject	1.3 ± 1.0	0.9 ± 0.7	1.1 ± 0.9	.11
Affected PIP joints†	23	19	42	.73
Affected PIP joints per subject	1.0 ± 0.8	0.8 ± 0.6	0.9 ± 0.7	.52

Plus-minus values denote means ± SD.
*t-tests were performed for all comparisons except for variables marked with †), for which the Fisher exact test was performed.

TABLE 2. Contractures of Subjects at Baseline

Baseline Contracture	TA Group (N = 24)	Control Group (N = 23)	All Subjects (N = 47)	*P* Value (*)
All joints				
TAED (°)	103 ± 76	80 ± 45	91 ± 63	.21
MCP joints				
TAED (°)	39 ± 20	47 ± 22	42 ± 21	.21
PIP joints				
TAED (°)	48 ± 24	45 ± 20	46 ± 22	.65

*t-tests were performed for all comparisons.

RESULTS

Fifty-one patients were enrolled in the study. Three subjects discontinued due to geographic location, and 1 subject refused the follow-up injections, resulting in a final sample of 47. Twenty-three subjects were randomized to the control group, and 24 subjects were randomized to the TA group. Only one hand was included in the study for a patient with bilateral disease. Groups did not differ significantly for any baseline characteristic (Table 1) or TAED (Table 2). All patients were completely healed at the 6-week follow-up point.

Mean doses of TA administered per patient immediately following the procedure, at 6 weeks, and at 3 months were 42 mg (range, 16–120 mg), 34 mg (range, 12–100 mg) and 24 mg (range, 0–80 mg), respectively. The total number of cords injected immediately following PNA, at 6 weeks, and at 3 months was 38, 37, and 29, respectively. All participants in the TA group received at least 1 injection at each follow-up visit. Dose of TA and correction of flexion deformity did not correlate significantly. The average number of days from procedure to follow-up visits did not differ significantly between groups for any time period, with the exception of a significantly longer period between the procedure and 3-month follow-up in the control group ($P < .01$). The repeated measures analysis of variance did not detect a significant group by time interaction ($P = .11$), indicating similar trends in each group over time. A time effect was detected ($P < .001$), indicating that TAED decreased significantly over time in both groups.

Mean overall TAED and correction (percentage) for each group at all follow-up points are displayed in Table 3. The mean baseline TAED for the TA group and control group were 103° and 80°, respectively. At 6 weeks, the mean overall TAED for the TA group decreased to 17°, and that of the control group decreased to 19°. At 3 months, mean TAED decreased to 15° for the TA group and to 16° for the control group. At 6 months, the TA group exhibited a mean overall TAED of 15°, indicating maintenance of correction, whereas the control group exhibited an increase in mean overall TAED to 26°. Mean overall TAED values did not differ significantly between groups at any time point. Mean TAED at the metacarpophalangeal (MCP) joint (Table 3) and the proximal interphalangeal (PIP) joint (Table 3) were significantly smaller in the TA group than in the control group at 6 months. No statistical significance was detected between groups for mean TAED at 6 weeks and 3 months at the MCP and PIP joints.

The mean overall correction was significantly greater in the TA group at every time point. At 6 months, no significant difference was detected in correction at the MCP joint; however, mean correction at the PIP joint was significantly greater in the TA group than in the control group. No statistical significance was detected between groups for correction at 6 weeks and 3 months at the MCP and PIP joints.

No subject in either group presented with infection, reported altered sensation within digits after the procedure, or reported any other side effects or complications.

TABLE 3. Mean TAED ± SD and Mean Correction from Baseline (%) at 6 Weeks, 3 Months, and 6 Months

All Joints	TA (N = 24)	Control (N = 23)	*P* Value (*)
6 Weeks			
TAED	17 ± 18	19 ± 14	.68
% Correction	87	74	**.02**
3 Months			
TAED	15 ± 17	16 ± 15	.84
% Correction	88	76	**.05**
6 Months			
TAED	15 ± 18	26 ± 21	.08
% Correction	87	64	**.003**

MCP Joints	TA (N = 32)	Control (N = 21)	*P* Value (*)
6 Weeks			
TAED	2 ± 4	3 ± 6	.28
% Correction	94	93	.93
3 Months			
TAED	1 ± 4	3 ± 6	.18
% Correction	95	94	.8
6 Months			
TAED	1 ± 4	5 ± 7	**.03**
% Correction	95	89	.15

PIP Joints	TA (N = 23)	Control (N = 19)	*P* Value (*)
6 Weeks			
TAED	14 ± 10	19 ± 14	.21
% Correction	66	57	.28
3 Months			
TAED	13 ± 10	16 ± 14	.46
% Correction	66	60	.56
6 Months			
TAED	14 ± 10	25 ± 17	**.01**
% Correction	65	41	**.04**

*Two-sample, 2-tailed *t*-tests were performed for all comparisons, with Welch's correction applied for comparisons in which variance differed significantly. Bolded *P* values denote statistical significance.

DISCUSSION

In this study, combining the molecular effects of the corticosteroid TA with the mechanical effects of PNA resulted in a significantly higher degree of correction than PNA alone, which was maintained throughout the study. These results suggest that complementing PNA with a series of TA injections might play a role in sustaining a level of correction extending beyond that of PNA alone.

Previous studies have reported that long-term correction is better maintained in MCP joints than in PIP joints following PNA.[10,22] Cheng et al[10] observed a mean MCP correction of 70% and a mean PIP correction of 41% at 22 months. A similar trend was exhibited in the present study by both the TA and control groups. The average correction observed at the MCP joint was only slightly larger in the TA group than in control subjects at all time points (Table 3); however, TAED in the TA group was significantly smaller at the MCP joint than that of the control group at 6 months (1° vs 5°).

At the PIP joint, the TA group experienced greater correction than that of the control group at all time points. These differences were significant at 6 months (Table 3). Although long-term comparisons are needed

to clarify the potential of TA to maintain correction, this result is clinically relevant, as the major disadvantage of PNA identified in the literature is that recurrence is more common and severe in the PIP joint.[13,16]

Two patients presented with contractures of the distal interphalangeal joint with a mean preoperative TAED of 52° and a 6-month mean TAED of 10°. Both subjects with affected distal interphalangeal joints were randomized to receive TA injections, preventing a comparison in this study.

Corticosteroid injections have been previously advocated as a treatment for patients with early Dupuytren disease or painful nodules. Injection of a corticosteroid into palmar nodules has shown to result in nodule softening and pain reduction.[20] At the molecular level, steroids function as antifibrotic agents, which reduce cell proliferation and induce apoptosis[10,23–26] by affecting collagen ratios and fibroblast activity.[25,27]

Recently, injectable collagenase has been proposed as a nonsurgical alternative to surgical treatment for Dupuytren disease. The efficacy and safety of collagenase clostridium histolyticum have been established for the correction of MCP and PIP joint contractures in patients with Dupuytren disease.[28,29] A large, short-term, randomized controlled trial by Hurst et al[29] reported significant improvements in 77% of patients with MCP joint disease and 40% of patients with PIP joint disease after a series of collagenase injections over 30 days. A second randomized controlled study[30] supports these findings, indicating that a significantly greater number of cords injected with collagenase than placebo met a primary end point of 0° to 5°. Although collagenase has been advocated as safe and effective,[31] long-term safety has been reported only in a small subset of patients, followed up for 8 years.[32] In addition, data on recurrence are limited, with 1 report of an 8% recurrence rate after 24 months[28] and a second report of recurrence or progression in 4 of 6 patients after 8 years.[32] Additional trials using extensive follow-up periods are essential to establish the long-term effects of repeat collagenase injections and contracture recurrence rates.[13,16,31,33]

Although no significant differences in flexion deformity were detected between groups at baseline, the preoperative flexion deformity of the TA group was 33° larger than that of the control group. The 24 subjects in the TA group had 38 affected digits with 57 affected joints, whereas the 23 subjects in the control group had only 29 affected digits with 40 affected joints. Although attributable to random assignment, it is possible that correction seen in the TA group is a partial result of a greater potential for correction rather than TA injections. Preoperative variance might also explain why, in some comparisons, significant differences were observed in percentage correction, but no significant difference was detected in TAED (Table 3).

Although using a short-term follow-up period is a limitation of this study, 6 months was chosen as an appropriate period to determine whether more extensive investigation is justified. Until long-term follow-up data are obtained, interval steroid injections following PNA on an ongoing, indefinite basis cannot be recommended. An additional consideration is the tendency for participation to decline with longer follow-up. Previous studies assessing contracture recurrence after PNA have used follow-up periods ranging from 22 months[10] to 5 years,[5] indicating that at least 2 years is required to evaluate the effects of TA injections on contracture recurrence.

Sham injections were not administered to control subjects; however, because TAED is an objective physical measure, potential treatment bias is unlikely. In addition, a single surgeon performed PNA, administered all TA injections, and measured all contractures, which prevented this individual from being blinded to study group assignment. Because no injections were administered during the final follow-up visit, the study group was not evident; however, the lack of blinding in this study might present potential bias.

The tendency for TA to leak out through punctured skin resulting from the PNA procedure made it impossible to accurately determine the exact amount of TA retained immediately following PNA. Therefore, definitive conclusions cannot be made regarding the amount of TA that was retained in each cord for this time point. No leakage occurred at 6 weeks or 3 months.

Postoperative splinting and therapy compliance was not assessed, creating potential variance in results, although the benefit of postoperative splinting and therapy have not been established.[33–35] Patient-reported outcomes were not evaluated due to the lack of a validated instrument for specific use in Dupuytren disease patients. Reports of patient satisfaction must play a role in treatment options and should be assessed in all outcome studies.

This study provides short-term evidence that TA injections might play a role in lessening recurrence of joint contracture in patients with Dupuytren disease presenting with contracture angles of 20° or greater. The results observed at 6 months justify subsequent investigations to determine the long-term clinical impact of TA injections combined with PNA.

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