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Sclerosing injections to treat midportion Achilles tendinosis: a randomised controlled study evaluating two different concentrations of Polidocanol

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Abstract Two to three ultrasound (US) and colour Doppler (CD)-guided injections of the sclerosing substance Polidocanol (5 mg/ml) have been demonstrated to give good clinical results in patients with chronic midportion Achilles tendinopathy. This study aimed to investigate if a higher concentration of Polidocanol (10 mg/ml) would lead to a less number of treatments, and lower volumes, needed for good clinical results. Fifty-two consecutive Achilles tendons (48 patients, mean age 49.6 years) with chronic painful midportion Achilles tendinopathy, were randomised to treatment with Polidocanol 5 mg/ml (group A) or 10 mg/ml (group B). The patients and treating physician were blinded to the concentration of Polidocanol injected. All patients had structural tendon changes and neovascularisation in the Achilles midportion. Treatment was US + CD-guided injections targeting the region with neovascularisation (outside ventral tendon). A maximum of three treatments (6–8 weeks in between) were given before evaluation. Patients not satisfied after three treatments were given additional treatment with Polidocanol 10 mg/ml, up to five treatments. For evaluation, the patients recorded the severity of Achilles tendon pain during activity on a visual analogue scale (VAS), before and after treatment. Patient satisfaction with treatment was also assessed. At follow-up (mean 14 months) after three treatments, 18/26 patients in group A and 19/26 patients in group B were satisfied with the treatment and had a significantly reduced level of tendon pain ($P < 0.05$). After completion of the study, additional treatments with Polidocanol 10 mg/ml in the not satisfied patients resulted in 26/26 satisfied patients in both groups A and B. In summary, we found no significant differences in the number of satisfied patients, number of injections or volumes given, between patients treated with 5 or 10 mg/ml Polidocanol.

Keywords Achilles tendon · Chronic pain · Injections · Polidocanol · Randomized · Controlled trial

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Introduction

Grey-scale ultrasound (US) is a reliable method to study tendons [6, 7, 10] and simultaneous use of colour Doppler (CD) adds information about blood flow [7, 8]. Treatment of the chronic painful tendon is known to be difficult, but recent studies using injections of the sclerosing substance Polidocanol have shown promising clinical results [1, 11]. US and CD-guided injections of Polidocanol (5 mg/ml), targeting the region with neovessels/high blood flow on the ventral part of the Achilles tendon (where the vessels enter the tendon), showed good clinical results and return to full tendon loading-activity after a mean of two to three injection treatments [1, 11]. A 2-year follow-up study showed remaining good clinical results, and a sonographically more normal tendon structure than before treatment [5].

Sclerosing therapy is widely used for treating varicose veins as well as teleangiectases [2, 3, 9]. Polidocanol was first developed as a local anaesthetic, and is now widely used as a sclerosing agent with very few side effects [2, 3, 9]. Polidocanol is used in different concentrations, 5, 10 and 30 mg/ml. The active substance is an aliphatic non-ionised nitrogen-free surface anaesthetic.

Polidocanol has a selective effect in the vascular intima causing thrombosis of the vessel [3]. The agent also has an effect if the injection is extra-vascular. This property is important when very small vessels are being targeted. It is plausible that the sclerosing effect of Polidocanol on the vessels might also affect nerves adjacent to the neovessels, either directly (by destruction) or indirectly (by ischaemia).

The aim with this double-blind randomised controlled trial was to evaluate whether there were any differences in the clinical effects between injections of Polidocanol in the two different concentrations, 5 and 10 mg/ml, in patients with chronic painful midportion Achilles tendinopathy/tendinosis. The hypothesis was that the use of higher concentration (Polidocanol 10 mg/ml) would lead to a less number of treatments and lower volumes needed for good clinical results.

Materials and methods

Participants

Forty-eight patients (52 tendons) were included in the study. All were patients referred to the Capio Artro Clinic in Stockholm, Sweden for a chronic painful condition in the Achilles tendon. All patients were diagnosed (clinically and by US and CD examination) with a chronic midportion tendinopathy/tendinosis. All patients had a long duration of pain symptoms during Achilles tendon-loading-activity. No patient had an acute onset of pain. There were no significant differences between the two groups in age, pain or duration of symptoms. In group A (5 mg/ml) there were nine women (11 tendons) and 14 men (15 tendons) with a mean age of 47 years. They had a long duration (mean 26 months, range 6–72 months) of pain symptoms from midportion Achilles tendinopathy. In group B (10 mg/ml) there were six women (6 tendons) and 20 men (20 tendons) with a mean age of 52 years. They had a long duration (mean 28 months, range 2–120 months) of pain symptoms from midportion Achilles tendinopathy. The patient that only had 2 month duration of symptoms had pain symptoms off and on during the last years, but only had continous severe pain symptoms the last 2 months. For more patient characteristics, please see Table 1.

The patients had tried different types of treatment before referral. All patients had tried rest from strenuous Achilles tendon-loading activities (>3 months), 46 patients (22 in group A and 24 in group B) had tried a modified version of eccentric calf-muscle training, and 34 patients (16 in group A and 18 in group B) had tried anti-inflammatory medication (NSAIDs) without any permanent effect on the tendon pain. No patient had received any type of injection treatment.

Twelve patients were on medication for hypertension (four patients in group A and eight patients in group B), one patient in each group was medicated against hypercholesterolemia and one patient (group A) had diabetes type 2. No patient was on any medication known to negatively affect the Achilles tendon function. All patients were physically active (Table 2).

Ultrasound and colour Doppler

All tendons were examined with high-resolution grey scale US and with CD, Acuson Sequoia 512. A linear multifrequency (8–13 MHz) probe was used. The pathological changes in the painful thickened Achilles tendon were recorded. CD was used to diagnose neovascularisation/high blood flow and to locate where the vessels entered the tendon. The contralateral tendon was also examined. The pathological findings detected with US and CD correlated with tenderness in the Achilles midportion.

Interventions

Two different concentrations of Polidocanol were used for the treatment, Polidocanol 5 mg/ml or Polidocanol 10 mg/ml. Polidocanol has a sclerosing effect and a local anaesthetic effect. Participants lay in prone position. Before the treatment, the skin was disinfected with a solution of chlorhexidine and alcohol. The skin was draped with a sterile paper-cover exposing only the middle part of the Achilles tendon. The injection was performed with a 0.7 × 50 mm needle connected to a 2 ml syringe. The same experienced ultrasonographer performed all US and CD examinations. The injection was performed dynamically, with the aid of real-time grey-scale US and CD technique, to inject at the target vessels. The ultrasound probe was held on the dorsal side of the Achilles tendon, parallel with the fibres. The injection was always done from the medial side of the tendon to minimise the risk of contact with the sural nerve. Very small volumes 0.1–0.2 ml (maximum 2 ml) of the substances were injected into the areas of local neovascularisation outside the ventral part of the Achilles tendon, corresponding to the tenderness in the tendon, until the vessels were no longer visible at all. We observed the immediate effect of the injection with both concentrations. Using both US and CD there were no visible qualitative differences in response to the two different concentrations of Polidocanol injected. Both resulted in an immediate closure

Table 1 Basic characteristics of the 52 patients with chronic painful midportion Achilles tendinopathy/tendinosis

Variable	Group A ($n = 26$)	Group B ($n = 26$)	P
Male/female	15/11	20/6	$P > 0.05$
Age	47.4 ± 7.8	51.8 ± 12.4	$P > 0.05$
Body mass index	25.1 ± 3.4	26.8 ± 4.2	$P > 0.05$
Duration of symptoms in months	25.5 ± 17.1	28.0 ± 31.6	$P > 0.05$
VAS during rest at start	21.4 ± 21.1	35.7 ± 28.9	$P > 0.05$
VAS during activity at start	66.3 ± 14.5	66.0 ± 21.7	$P > 0.05$

Table 2 Activity levels of the 52 patients with chronic painful midportion Achilles tendinosis

	Group A	Group B
Football recreational level	1	1
Walking recreational level	6	7
Running recreational level	7	11
Jogging recreational level	5	1
Aerobics recreational level	2	1
Dancing recreational level	1	0
Orienteering elite level	0	1
Floorball recreational level	1	2
Golf recreational level	0	1
Triathlon/multisport elite level	1	1
Basketball recreational level	2	0

Running—occasionally competition

Jogging—never competition

of the vessels. A dressing was applied for 24 h. The patients were allowed careful walking right after the treatment and full Achilles tendon loading-activity was allowed 14 days after treatment. A maximum of three treatments (at least 6–8 weeks in between) were given before evaluation.

Outcome measures

Pain during Achilles tendon-loading-activity. The patients scored their amount of tendon pain during their desired Achilles tendon-loading-activity on a 100 mm long visual analogue scale (VAS). The amount of pain was recorded from 0 to 100 mm, where no pain was recorded as 0 and severe pain as 100. The tendons were examined with grey-scale US and CD technique, before and after each treatment.

Self-reported patient satisfaction with the treatment (satisfied or not satisfied). Satisfied patient—back in previous (before injury) Achilles tendon loading-activity. Not satisfied patient—not back in previous (before injury) Achilles tendon loading-activity.

Numbers of treatments needed for a good clinical result, i.e. satisfied patient—back in previous (before injury) Achilles tendon loading-activity.

Total volume of Polidocanol injected to achieve a good clinical result (satisfied patient).

Sample size/power analysis

The power calculation was based on the findings in the pilot study. Twenty patients in each group were needed to give a power of 80% to find differences between the groups on the amount of pain (VAS), on a 5% significance level.

Randomisation

After receiving oral and written information, the patients selected an envelope (52 opaque envelopes), allocating themselves to either treatment with Polidocanol 5 or 10 mg/ml. The chosen envelope was opened in a separate room by an assistant and the substance was prepared by the assistant for injection. There were no visible differences (colour, density, etc.) between the substances. The equipment (syringe, needle, etc.) was the same for all treatments.

Blinding

The patients, the treating orthopaedic surgeon, the sonographer, who performed all ultrasound and colour Doppler examinations and treatments were blinded to the substance that was injected. The outcome of the treatment was self-assessed by the patients using a VAS and stating if satisfied or not satisfied with the results of the treatment. An assistant collected all VAS results.

Ethics

The investigation was approved by the Ethical Committee at the Medical Faculty of the Ethical Committee of the Karolinska Institute, Stockholm.

Statistical evaluation

The SPSS package (version 11.5, SPSS Inc., Chicago, Illinois, USA) was used for all statistical calculations. Mean and standard deviations were used to describe data. Differences between groups were calculated using a non-parametric test for independent samples (Mann–Whitney *U*

test). When data were categorical, Chi-square test and Fisher's exact test were used to evaluate differences between groups. Differences before and after treatment were calculated with Wilcoxon signed ranks test. A P value of <0.05 was considered statistically significant.

Results

Recruitment. The study period was from November 2004–2007, with a mean follow-up period of 14 months (range 2–35 months).

Baseline data. See Table 1.

Outcomes. In group A (5 mg/ml), the mean VAS after one to three treatments (evaluating the amount of Achilles tendon pain during activity) decreased significantly from 66 ± 14 to 25 ± 28 ($P < 0.05$). Six patients were not satisfied after three treatments. They were offered and accepted treatment with additional injections of Polidocanol (10 mg/ml). After one additional injection there were two patients who were not satisfied. These two patients were satisfied after a fifth injection (Fig. 1).

In group B, that was treated with Polidocanol 10 mg/ml, the mean VAS after one to three treatments (evaluating the amount of Achilles tendon pain during activity) decreased significantly from 66 ± 21 to 24 ± 31 ($P < 0.05$). Seven patients were not satisfied after three treatments. They were offered and accepted treatment with additional injections of Polidocanol (10 mg/ml). After one additional treatment, three patients were not satisfied. These three were satisfied after a fifth injection (see flow chart in Fig. 2).

There were no significant differences between the groups concerning the number of treatments given before a good clinical result—satisfied patient (group A, 2.6 treatments and group B, 2.5 treatments).

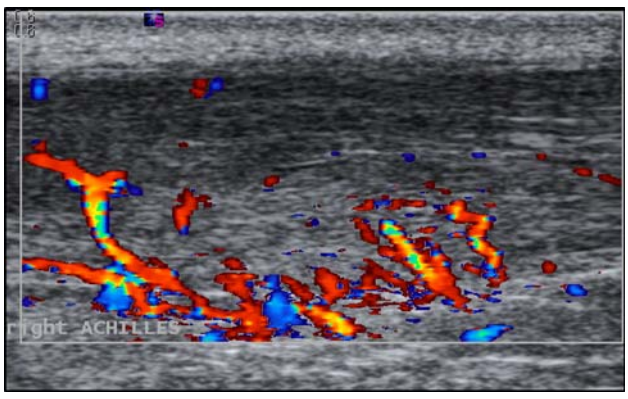

Fig. 1 Ultrasound and colour Doppler findings in a patient with chronic painful midportion Achilles tendinopathy/tendinosis. Longitudinal ultrasound scan showing a widening of the midportion, including structural changes with hypo-echoic regions. Colour Doppler showing neovessels/high blood flow (coloured structures) inside and at the ventral side of the Achilles tendon

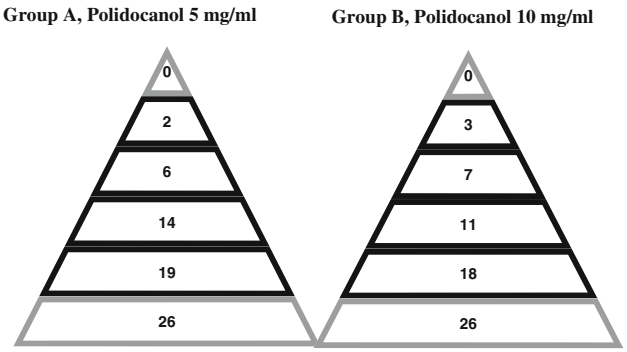

Fig. 2 Randomisation of the 52 included patients, 26 patients in each (5 and 10 mg/ml Polidocanol) group. Each step (result after each injection treatment) shows the number of remaining (not satisfied) patients

There were no significant differences concerning the total volume injected in the two groups before a good clinical result was achieved—satisfied patient (group A, mean 3.2 ± 1.6 ml and group B mean 3.1 ± 1.3 ml).

Before and after treatment there was no significant difference between the two groups in VAS during activity ($P < 0.001$).

Adverse events. There were no adverse events or side-effects in any participant.

Additional outcome after a maximum of five injection treatments.

All patients (group A and group B) reported satisfaction with the result of the treatment.

Discussion

The results of this randomised double-blind trial on patients with chronic painful midportion Achilles tendinopathy/tendinosis showed that there were no significant differences in the clinical results, the number of injection treatments or the total volume injected, between patients treated with the Polidocanol concentrations 5 or 10 mg/ml. Overall, treatment with US and Doppler-guided Polidocanol injections of the sclerosing substance Polidocanol was associated with satisfied patients having a significantly reduced tendon pain during Achilles tendon loading-activity. The patients included in this study were consecutive middle-aged individuals referred to the Capio Artro Clinic after having had a long duration of pain from the Achilles tendon midportion. The majority had walking or running as their recreational Achilles tendon loading-activity, but there were also athletes on elite or recreational level. It is our opinion that this group of patients is representative for the majority of the middle-aged individuals

with the diagnosis chronic midportion Achilles tendinopathy we see at our clinic.

The participants in the study, the ultrasonographer and the orthopaedic surgeon, who performed the treatments were blinded to the two different concentrations of Polidocanol injected. There were no visible differences between the immediate effects (seen with US + CD) of the two different concentrations. The immediate effect of the injection, to stop vascular flow, was the same for both concentrations. Consequently, we do not think that the treatment procedure in itself have biased the results.

To limit bias in the evaluation, the evaluation of the result of the treatment was done by the patient alone. The patients recorded the amount of Achilles tendon pain during their desired type of Achilles tendon-loading-activity on a VAS. The VAS was then collected by an independent assistant. The patients also recorded their satisfaction with the result of the treatment regarding pain and level of activity compared with prior to participating in the study.

We decided to evaluate the results after a maximum of three treatments. This was due to the results in previous studies, showing a mean number of two to three treatments required for good clinical results [1, 11]. Evaluation after three treatments showed that 18 patients in the group that were treated with injections of Polidocanol 5 mg/ml and 19 patients in the group that were treated with injections of Polidocanol 10 mg/ml were satisfied with the result of the treatment. At this endpoint there was a significant reduction on the VAS evaluating pain during Achilles tendon loading-activity in both groups. Furthermore, there were no significant differences between the groups considering the reduction of pain on the VAS, the number of treatments or the volume of Polidocanol injected.

The results indicate that the effects caused by injecting Polidocanol in the area with neovessels/high blood flow outside the ventral Achilles tendon midportion aiming the entrance of the vessels into the tendon, are not related to the concentration of the substance. At least not above the concentration of 5 mg/ml. It could be speculated if the needling procedure in itself was of significant importance for the results. However, from a previous randomized controlled study, we know that Polidocanol injections were associated with good clinical results, while injections of lidocain + adrenalin showed poor results [1]. This demonstrates that the substance in itself, and not only the needling procedure, is of importance for the clinical results. Altogether, it seems that small volumes of a low concentration of Polidocanol (5 mg/ml), injected under US + CD guidance-targeting the region with neovessels/high blood flow outside the ventral tendon, are enough to cure the tendon pain in a high proportion of patients with midportion Achilles tendinopathy. It is of clinical importance to know that only small volumes (<2 ml/treatment, mean 3.1 ml in total) were needed for good clinical results. It has come to our knowledge that high volumes (5–10 ml per treatment) sometimes are being used. Complications, such as thrombosis, have been reported (non published data) after using high volumes. It is important to be aware of that the substance Polidocanol can spread in the soft tissue and communicant veins in the lower leg might be at risk. Also, when using this treatment for patellar tendinosis, high volumes might lead to intra-articular deposition, causing synovitis and fibrosis.

After having completed the randomised controlled trial, patients with a poor result of the treatment were offered additional treatment with Polidocanol (10 mg/ml) injections. All patients accepted, and the results showed that the previous nonsatisfied patients, 6/6 patients in group A and 7/7 patients in group B, were satisfied with the treatment and there was a significant decrease on the VAS. But interestingly, there were still no significant differences between the two groups concerning pain on a VAS, satisfaction with the result of the treatment, volume or number of injections given.

There were no adverse effects in this study. This is in accordance with the experiences from the previous studies [1, 11], where there were no complications in the short and longer term perspectives.

In summary, we found no differences in the clinical results, number of treatments or volume injected, between using 5 or 10 mg/ml of Polidocanol when treating chronic painful midportion Achilles tendinopathy with sclerosing Polidocanol injections. For clinical use, we cannot recommend the use of Polidocanol 10 mg/ml instead of Polidocanol 5 mg/ml with the purpose to achieve better and faster clinical effects. Furthermore, it appears that small volumes of Polidocanol could be used for a good clinical result.

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