

No effect of piroxicam on achilles tendinopathy

A randomized study of 70 patients

Mats Åström and Nils Westlin

70 consecutive adult, nonrheumatic patients with a painful achilles tendinopathy were randomized to treatment with either a nonsteroid antiinflammatory drug (piroxicam) or placebo. Both groups received adjunct treatment with a period of rest combined with stretching and strengthening exercises. 52/70 cases were engaged in various sports, notably running. All subjects were evaluated on days 3, 7, 14, and 28 with

respect to pain, tenderness, swelling, ankle joint movement and muscle strength. Results were judged from residual symptoms and an overall assessment of the efficacy. No differences were seen between the groups at any time during the study. The overall result was identical with a rate of success slightly better than 50 percent which corresponds to the placebo response reported in other studies.

The Section of Sports Trauma, Department of Orthopedics, Malmö General Hospital, Lund University, S-214 01 Malmö, Sweden. Tel +46-40 33 10 00. Fax -33 62 00
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Achilles tendinopathy remains a taxing clinical problem and treatment is often unrewarding (Williams 1986). Since inflammation is considered to be an important cause of symptoms (Puddu et al. 1976, Smart et al. 1980, Renström and Johnson 1985, Williams 1986), nonsteroid antiinflammatory drugs (NSAID) have been widely used in the conservative management of this entity (Smart et al. 1980, Renström and Johnson 1985).

Our study is a placebo-controlled, double-blind randomized clinical trial investigating the supplementary effect of NSAID (piroxicam) in the management of painful achilles tendinopathy.

Patients and methods

70 consecutive patients, 50 men and 20 women, age 35 (18-58) years, with a unilateral, painful lesion of the achilles tendon or the distal insertion were enrolled. Contraindications to the use of NSAIDs (allergy; renal, hepatic or hematological disease; pregnancy or lactation; gastric ulcers) were not seen and none of the subjects had signs of rheumatic disease. We excluded subjects with bilateral symptoms, previous surgery on the affected side, symptoms of more than 6 months duration, signs of a total or gross partial rupture and subjects treated with NSAIDs during the previous 6 months or steroid injections around the affected tendon at any time. All patients had pain on exertion (64 cases) and/or morning stiffness (45

cases). The mean duration of symptoms was 70 (1-180) days. Half of the patients had suffered less than two months. 18 patients reported previous occasional symptoms in the same tendon and 3 on the opposite side. Only 2 described an initial trauma but in 17 cases the onset was sudden. Physical findings included distinct tenderness around a limited segment of the tendon (62 cases) or at the calcaneal insertion (8 cases), local swelling (46 cases) and a limping gait (4 cases). A total of 52 patients were engaged in various sports, more than half of them on a competitive level. Running, often combined with other forms of training, was the most common athletic activity (40 patients, mean weekly mileage 30 km). 5 patients were sick-listed at the time of entry. 12 patients were training at a reduced level and 26 patients had been forced to stop all athletic activities.

The study was double-blind and the subjects were randomly divided into two groups (35 patients each) which did not deviate with regard to age, sex, physical activity or clinical variables (Table 1). One group received a nonsteroidal antiinflammatory agent, piroxicam, given in a daily dose of 40 mg for two days and 20 mg thereafter, the other group placebo in identical tablets. The medication was continued for a maximum of 28 days. The first two weeks were mandatory and the last two optional (if symptoms so required). No other analgesic or antiinflammatory drugs were permitted. Both groups also received adjunct treatment with a program of stretching and strengthening exercises. Patients were encouraged to discontinue athletic training for the first 14 days and then gradually resume normal activities.

Table 1. Clinical data

	Piroxicam n 34	Placebo n 33
Age (mean)	35	35
range	18-58	20-57
Men	23	25
Athletics	29	23
Duration (mean days)	79	61
SD	56	49
Pain/swelling		
Tendon	31	28
Insertion	3	5

All subjects were evaluated at the time of entry and on days 3, 7, 14, and 28. At each visit, symptoms, physical signs, and side-effects were recorded. The patient was asked to indicate current pain on a 100 mm visual analogue scale without comparing with previous results. Tenderness was classified by the examiner according to a five-point scale (0 none, 1 slight, 2 moderate, 3 wincing, 4 wincing with withdrawal). Swelling was measured with a caliper at the point of maximum tenderness and expressed as the difference in millimeters between the symptomatic and nonsymptomatic sides. Ankle joint motion was recorded in the weight-bearing position with a goniometer especially designed for this purpose. On the first and last visits muscle strength was determined from the maximum number of toe raises (elevating the heel 5 cm) which the subject was able to do. The right side was always tested first, regardless of the side on which symptoms were located. At the final evaluation (day 28) residual symptoms were graded on a 4-point scale (0 none, 1 slight, 2 improved, 3 unaltered or worse). The patient and examiner independently made an overall assessment of the efficacy, classifying the result as excellent, good, acceptable or poor. The examiner scored *excellent* as slight or no symptoms, returned to normal activities; *good* as slight or no symptoms, not yet returned to normal activities for reasons unrelated to the achilles lesion; *acceptable* as improved but unable to return to normal activities and *poor* as unaltered or worse, regardless of the present level of activities.

Statistics

The groups were compared at each clinical assessment to detect any differences attributable to the drug treatment. Discrete variables (tenderness, residual symptoms and overall assessment) were analyzed by the Chi²-test and continuous variables (pain, swelling, range of motion and muscle strength) by the Student's *t*-test. If a continuous variable showed a skewed fre-

Table 2. Results

	Piroxicam n 34		Placebo n 33	
Day	0	28	0	28
Swelling (mean)	1.9	1.4	2.5	1.4
SD	2.3	1.8	3.0	2.3
Muscle strength				
Sympt. tendon (mean)	29	41	28	36
SD	16	18	18	20
Nonsympt. tendon (mean)	39	43	37	39
SD	23	20	17	20
Residual symptoms				
None		12		8
Slight		7		10
Improved		6		6
Unaltered/worse		9		9
Overall assessment (patient/examiner)				
Excellent	10	12	7	7
Good	10	7	14	11
Acceptable	7	5	5	5
Poor	7	10	7	10

quency distribution the Mann-Whitney rank sum test was also applied. Symptoms and signs noted at the first visit (day 0) were compared with those found at the final evaluation (day 28) in order to demonstrate progress made by the patients during the study.

3 patients were omitted in the final analysis. 1 had had symptoms for more than 6 months, 1 had an old subtotal rupture of the nonsymptomatic tendon and 1 was lost to follow-up. This leaves 34 patients in the piroxicam group and 33 in the placebo group.

Results

There were no differences at any time between the groups with regard to pain (Figure 1), swelling (Table 2), muscle strength (Table 2) or ankle joint movement (Figure 2). In Figure 2 the range of motion is represented by ankle extension on the symptomatic side since this is the best indicator of achilles pain. Tenderness was also rated equal in the two groups. At the first visit 28/34 patients in the piroxicam and 26/33 in the placebo group had slight or moderate tenderness while the rest had more severe symptoms. On day 28 11 patients in the piroxicam and 8 in the placebo group had no tenderness and 21 patients in each group only slight or moderate tenderness. Although the drug treatment offered no advantage over placebo, patients in both groups did improve during the study. A decrease in pain ($P < 0.001$) and tenderness ($P < 0.001$) was

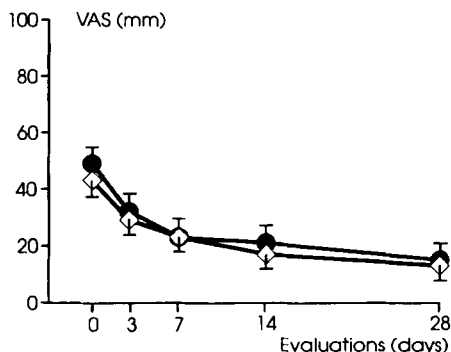


Figure 1. Pain assessed by a 100-mm visual analogue scale (mean $\pm$ SEM). ● Piroxicam; ◇ Placebo.

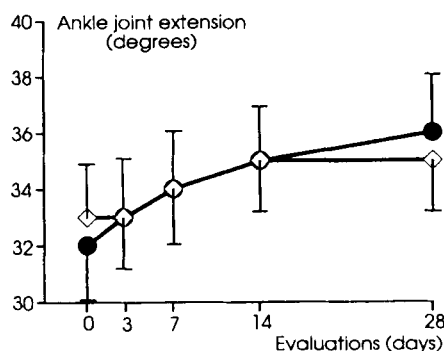


Figure 2. Ankle joint extension on the symptomatic side (mean $\pm$ SEM). ● Piroxicam; ◇ Placebo.

noted. Swelling was difficult to record accurately. Although a decreasing trend was found, values were highly variable and the total improvement subtle ($P > 0.05$). Increase in ankle joint motion was modest but significant on the symptomatic side ($P < 0.05$). Muscle strength increased by 30 percent as pain in the tendon subsided but remained unchanged on the non-symptomatic side ($P < 0.05$ and $P > 0.05$, respectively). There were no differences between the groups regarding sick-listing, medication, or side-effects. Only 5 patients, 2 in the piroxicam and 3 in the placebo group, were sick-listed for an average of 5 days. Patients generally continued medication slightly more than 3 weeks. In each group 3 patients had slight dyspeptic symptoms and one a minor change of bowel habits. No one stopped treatment because of side-effects.

Symptoms at final evaluation (Table 2) and overall assessment of efficacy (Table 2) were similar in the two groups ($P > 0.05$). Slightly more than 50 percent of the patients had few, if any, symptoms and were graded as a good or excellent result.

11 patients, 5 in the piroxicam and 6 in the placebo group, had symptoms less than 14 days. This subgroup was of special interest since acute cases are known to respond favorably to drug therapy. The number of patients is too small for statistical analysis but in the final evaluation they achieved an almost identical result.

Discussion

Piroxicam is well established as a nonsteroid antiinflammatory drug. Overall efficacy and tolerability compares favorably with other members of this group

(Brogden et al. 1984). NSAIDs are frequently prescribed for the treatment of soft tissue pain of unspecified origin (Lopez 1982) and injuries caused by over-use or trauma (Abbott et al. 1980, Lacey et al. 1984, Lereim and Gabor 1984). Superior results have been observed in acute cases (Abbott et al. 1980, Sundqvist et al. 1987) and in patients with severe initial symptoms (Lacey et al. 1984, Dupont et al. 1987).

Most studies are based on mixed patient populations and some are non-randomized or do not include a placebo. In two randomized placebo-controlled studies dealing with a single diagnosis (sprained ankle) NSAID proved to be no better than placebo (Andersson et al. 1983, Dupont et al. 1987).

NSAIDs have been used frequently in the conservative management of achilles pain but the efficacy of this treatment is not very well documented. Sundqvist et al. (1987) presented a double-blind randomized study of achilles paratenonitis comparing the effect of a standard antiinflammatory drug (indomethacin) to that of glucosaminoglycan polysulfate which is chemically related to heparin. Acute and subacute cases did fairly well, whereas chronic cases responded poorly to indomethacin, indicating that inflammation may be of minor importance in patients with longstanding or recurrent symptoms. However, the benefit of indomethacin in the former group cannot be distinguished from the natural course of events, since no placebo group was included.

Our study is one of the very few addressing the problem of painful achilles tendinopathy and the only one including a placebo group. Patients with painful achilles lesions are commonly diagnosed as paratenonitis, central degeneration of the tendon, tendinitis, minor partial ruptures and retro-calcaneal bursitis. In reality they constitute a uniform group with very similar signs and symptoms. In our experience an exact

diagnosis requires surgical exploration and a symptomatic diagnosis such as "painful achilles tendinopathy" is therefore preferred in nonsurgical cases. Our results demonstrate that piroxicam does not promote symptomatic relief in patients with achilles pain. The rate of success was slightly better than 50 percent which corresponds to the placebo response observed in other studies (Lacey et al. 1984). Rest and physical rehabilitation were primarily used as adjunct treatment for psychological reasons and were not assessed individually. The relative importance of rest, exercises and the placebo response therefore cannot be ascertained in our study. A significant increase in muscle strength and range of motion occurred only on the symptomatic side. This could be a sign of decreasing pain rather than an effect of the exercise. Our patients represent a mixture of acute and chronic conditions typical for routine clinical work. In a study limited to acute cases piroxicam might have proved more effective (Sundqvist et al. 1987). However, our data do not support this assumption.

We conclude that a non-steroid antiinflammatory agent (piroxicam) does not afford symptomatic relief in achilles pain; a limited rate of success was noted, presumably due to the combined effect of rest, exercises and the placebo response; the design of our study did not enable us to determine the importance of the placebo response versus the adjunct treatment.

Acknowledgements

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