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SCIENCE DIRECT
Physical Therapy in Sport 5 (2004) 194–199
Physical Therapy in sport
www.elsevier.com/locate/yptsp

Original research

The effect of essential fatty acids and antioxidants combined with physiotherapy treatment in recreational athletes with chronic tendon disorders
A randomised, double-blind, placebo-controlled study

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Received 6 June 2003; revised 4 June 2004; accepted 4 June 2004

Abstract

Study design: Randomised, double-blind, placebo-controlled study.

Background: Chronic tendon disorder is a major problem for many athletes and conservative treatment varies substantially. A treatment method with essential fatty acids and antioxidants combined with physiotherapy has attracted some attention and is evaluated in this study.

Methods and measures: In a randomised, double-blind, placebo-controlled trial 40 volunteers active in recreational sports with chronic tendon disorders were assigned to the study. The subjects were divided in two groups, one consuming a daily dosage of essential fatty acids and antioxidants and one consuming similar placebo. Furthermore, the subjects received 16 sessions of ultrasound treatment over 32 days. Evaluation was pain scores, rated on a visual analogue scale and quantification of normal sports activity during treatment.

Results: In the treatment group there was a significant reduction of pain compared with the placebo group ($P < 0.001$) after 32 days. There was a mean decrease in pain score of 99% in the treatment group compared with a mean decrease of 31% in the placebo group. Sport-specific activity increased by 53% in the treatment group and increased by 11% in the placebo group.

Conclusions: The results suggest beneficial effect of essential fatty acids and antioxidants in combination with physiotherapy treating chronic tendon disorders.

Keywords: Essential fatty acid; Antioxidants; Chronic tendon disorders; Repetitive strain injury (RSI); Physiotherapy treatment; Double-blind; Placebo-controlled

1. Introduction

Pain is the primary symptom in most patients with chronic tendon disorder (CTD), followed by decreased function. In many patients, painful restriction of range of movement limits the ability to perform sport or even daily activities. Until recently relatively little has been known about the aetiology of these common problems and the underlying patology. Lately, however, several investigators have shown that the pathology underlying these conditions is collagen degeneration or tendinosis (Ledbetter, 1992). A short description of CTD is given in Table 1.

It is believed that the cause of many injuries is repetitive strain injury (overuse) followed by an inflammatory response. Typical findings in the later, chronic stage are; absence of inflammatory cells, loss of collagen continuity and an increase in ground substance vascularity and cellularity leading to the tendinosis cycle as described by Ledbetter (1992).

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doi:10.1016/j.ptsp.2004.06.002

Table 1
Overuse tendon conditions

Diagnosis	Macroscopic pathology	Histologic findings
Tendinosis	Intratendinous degeneration, microtrauma or vascular compromise	Collagen disorientation. Fibre separation. Increased mucoid ground substance. Increased prominence of cells and vascular spaces. Focal necrosis or calcification
Tendinitis	Degeneration of the tendon and vascular disruption. Inflammatory repair response	As above with evidence of tear. Fibroblastic and myofibroblastic proliferation, haemorrhage, and organizing granulation tissue
Para-tenonitis	Inflammation of the outer layer of the tendon (paratenon) alone	Mucoid degeneration in the areolar tissue. Scattered mononuclear infiltrate possibly with focal fibrin deposition and fibrinous exudat
Para-tenonitis with tendinosis	Paratenonitis with intratendinous degeneration	As in tendinosis with mucoid degeneration possibly with fibrosis and scattered inflammatory cells in the paratenon alveolar tissue

Management of this broad diagnosis includes advice, analgesics, non-steroidal anti-inflammatory drugs (NSAID), steroid injections, and physiotherapy (thermical treatment, soft tissue treatment, stretching). Some or all may give pain relief, but there is no convincing evidence that they alter the natural history (Kannus, Natri, Paakkala, & Jarvinen, 1999). Current methods therefore cannot be considered effectively proven (Almekinders, 1998), and the safety of some of these have even been questioned (Schiøttz-Christensen and Helin, 1997).

A relatively unknown treatment claiming success clinically over the past four years is the combined use of essential fatty acids (EFA), antioxidants, (AO) and physiotherapy (therapeutic ultrasound) in athletes with CTD by Scandinavian doctors and physiotherapists (Steenberg, 1999).

The background for the treatment with essential fatty acids in this context can be found in the role of the essential fatty acids as precursors for the cellular production of eicosanoids, controlling inflammation locally (Gadek, DeMichele, Karlstad, & Pacht, 1999). The main rationale for including a tablet with minerals and vitamins is their antioxidative protection against peroxidative damage to the fairly large amount of unsaturated fats in the treatment. Vitamin C, E and selenium are antioxidants, while zinc and also selenium are constituents of endogenously produced antioxidant proteins (Gutteridge, 1993). In addition, zinc, vitamin B6 and C are necessary for the activity of enzymes or otherwise important in the conversion of fatty acids to active eicosanoid substances (Horrobin, 1982).

The inflammation itself may be initiated by too hard training, a poorly healed old injury or by monotonous repeated movements during training. A lingering inflammatory injury is to some extent controlled by the proportions of different essential fatty acids in the diet, determining the inflammatory responce via eikosanoid production (Gadek et al., 1999) (see Section 5). If large amounts of certain $n-6$ fatty acids are consumed at the expense of $n-3$ fatty acids (FA), the inflammation will be much more potent and more painful (Belch and Wood, 2000). A substitution of the $n-6$ FA's common in the diet with $n-3$ and an alternative $n-6$ FA, that does not support the arachidonic acid pathway, should in theory modulate the inflammatory response. This treatment has been used as a substitute for anti-inflammatory medications without the adverse effects of NSAID agents in open tests and uncontrolled cases (Steenberg, 1999). The treatment has been claimed to give patients pain relief, and at the same time enabling the athlete to perform moderate training activity during treatment (Sindberg, 1999).

Although there has been a small number of studies suggesting that EFA is an effective treatment method for rheumatoid arthritis (RA) (Rothman, DeLuca, & Zurier, 1995; Tate, Mandell, Laposata, & Ohliger, 1989; Zurier, Rossetti, Jacobson, & DeMarco, 1996) and other inflammatory conditions, it has not yet been properly tested as a treatment for any condition.

Reviewing the current literature (Medline Express database) no research has been found evaluating the effect of EFA, AO and physiotherapy on athletes, or other patients, with CTD. In view of the large number of patients with CTD and the lack of studies, it was decided to examine the effects of the above in a randomised, clinical, double-blind, placebo-controlled study.

2. Methods

2.1. Subjects

Forty voluntary subjects active in recreational sports with CTD were assigned to the study. The inclusion criteria were as follows: The athletes were required to be active, recreational sportsmen/women with a CTD, pain lasting for more than three months; 18 years or older; and providing written, informed consent. Subjects were excluded if they had bilateral symptoms, if they had a systemic disease of the musculoskeletal system, or if they had been treated with physiotherapy, NSAID's or steroid injections within the last 3 months. They were also excluded if they had used analgesic or anti-inflammatory drugs or other medication, which could have influenced the injury during the last month. Subjects who met the (selection) criteria were referred to the research centre by their general practitioner. The ethical committee of Bodø Fysikalske Institutt, Bodø, Norway, approved the protocol.

On enrolment all patients underwent a physical examination. In order to limit variation between researchers, several sessions practising physical examination and diagnostic interpretation (8–10; until practically similar results were obtained based on the judgement of an experienced monitor) were carried out before the start of the study. The diagnosis of CTD was established using diagnostic guidelines for such pathology described by Cyriax (Ombregt et al., 1995). After enrolment baseline values of outcome measures were assessed.

2.2. Interventions

The two groups were instructed to take a daily dosage of eight capsules. The active treatment capsules contained 376 mg eicosapentaenoic acid (EPA), 264 mg docosahexaenoic acid (DHA) and 672 mg gamma-linolenic acid (GLA). Besides the capsules participants also took 1 antioxidant-complex tablet (100 μg selenium, 15 mg zinc, 1 mg vitamin A, 2.2 mg vitamin B_6, 90 mg vitamin C and 15 mg vitamin E). The placebo treatment consisted of eight capsules with soy-oil and a placebo tablet. The placebo capsules and tablets were of the same appearance, size and colour as the active treatment. To some extent, the taste of the capsules would be different, due to the characteristic fish oil taste in the verum-capsules, however, the participants were instructed to swallow both tablets and capsules intact in connection with a meal. Pharma Nord ApS, Denmark provided active ingredients (Bio-Sport®) and placebo. The subjects received dosages sufficient for 32 days, and were instructed to take the supplements orally after a chosen meal (e.g. breakfast) and record the date and time in their diaries.

A randomised code list of numbers generated by a random number generator computer programme was used to assign the participants to either the active treatment or placebo. The test preparations were packed in identical boxes at Pharma Nord's production facility in Denmark and numbered according to the code list before being forwarded to the research clinic. The code list was sealed and was not broken until all data from the trial were available.

Physiotherapy consisted of therapeutic ultrasound (US). All subjects were given 16 sessions of US (Sonicator Mettler 730) at 1 MHz, 2.0 W/cm^2, pulsed mode, 5 min per session, applied to the area of injury. The reason for using ultrasound is to facilitate the healing in the tissue affected, enabling the supplements to modulate this process. The chosen dose of ultrasound has been shown to increase blood supply to injured areas (Enwemeka, Rodriguez, & Mendosa, 1990; Jackson, Schwane, & Starcher, 1991), and increase the permeability of the cell membrane (Dyson, Low, & Reed, 1990; Dyson, Preston, Woledge, & Kitchen, 1999).

The subjects were instructed to carry out the sports activity they were used to before the injury during treatment, starting at the level they reported when they entered the study (baseline). All subjects were instructed to specify this activity in a training diary.

2.3. Outcome assessment

The primary outcome measure for each subject was complaints related to pain during sporting activity. The subjects were asked to record their pain score at baseline, and after 8, 16, 24 and 32 days (end of treatment) by means of a visual analogue scale (VAS), on which the patient could indicate their assessment along a distance of a 10 cm scale, ranging from 0 ('painfree') to 10 ('the worst pain I have ever experienced'). The subjects also indicated their pain score on VAS after an isometric test (Borg, 1998) administered by the researchers at baseline, 8, 16, 24 and 32 days, to see how this would influence the experience of pain. The test was performed with a non-specific resistance applied to the joint nearest to the injured area. The isometric evaluation was used to assess whether the experience of pain would be different during a standardised influence.

Secondary outcome measure was quantification of sports-activity at baseline, during, and at the end of treatment. Sports-activity was recorded as the time spent and activity performed and recorded in the diary each day by the subject, compared with an estimated 100% training effort (the level before the injury), and was controlled by the researchers.

The subjects were asked to document their training activity and consumption of test medication in a dairy. Failure to comply excluded the subject from the study.

Pharma Nord Research, Denmark, using a computer generated random number program, randomized all dosages of EFA and AO and placebo preparations. The treatment code was sealed and not available to the researchers. After the end of the clinical trial the code was broken and results controlled and marked by an independent observer. This procedure allowed blinding of both the patients and the researchers.

Statistical data was analysed using Analyse It for Microsoft Excel, and a Mann-Whitney *U*-Wilcoxon Rank Sum W Test was carried out using SPSS for MS Windows Release 6.0. Subjects who had not been treated according to protocol during the intervention period were excluded. These were cases of non-compliance with treatment and violation of protocols.

3. Results

A total of 40 subjects were allocated to the study, 20 receiving EFA, AO and US, and 20 receiving placebo and US. During the intervention period nine subjects were excluded from the study due to non-compliance with treatment and/or violation of research protocol. Therefore, 31 subjects concluded the study, 17 in the EFA, AO and US group and 14 in the placebo and US group. Based on the small sample size an intention-to treat analysis was not performed. The following analysis is based on treatment received.

Table 2
Demographic data and baseline characteristics of patients who completed study

	Treatment groups	
	EFA, AO and US ($n=17$)	Placebo and US ($n=14$)
Mean age	31	32
Male	13	12
Female	4	2
Mean debut of pain experience (months)	5.8	7.1
Mean time used in sport-specific training activity (h/w)	6.5	7.6
Specific sport activity		
Weight training	10	9
Ballgames	3	2
Marshal arts	2	2
Racket sports	2	
Mountain climbing		1
Diagnosis (overuse tendinopathies)		
Supraspinatus tendinopathy	5	5
Biceps (long tendon) tendinopathy	4	5
Flexor tendinopathy (medial epicondyle)		1
Extensor tendinopathy (lateral epicondyle)	4	1
Patella tendinopathy	2	2
Infraspinatus tendinopathy	2	

Demographic data of the subjects concluding the study is shown in Table 2.

3.1. Outcome

The mean improvement of the primary outcome measure, subjective pain score, at each point of the follow up is shown in Fig. 1.

The difference in improvement was in the same direction at all follow ups with 12 out of 17 (71%) subjects in the EFA, AO and US group recording no pain at day 32 at the end of treatment. Both groups had a reduction in subjective pain score. The reduction in the EFA, AO and US group was statistically significant ($P<0.001$) compared with placebo with a mean decrease in pain score at 99%. The placebo group had a mean decrease in pain score of 31% at the end of treatment.

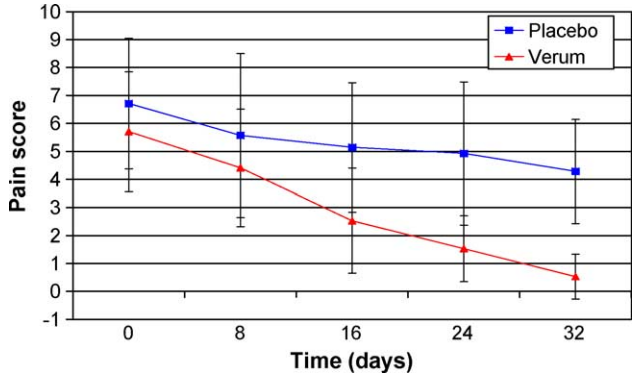

Fig. 1. The mean change of subjective pain score (±SD).

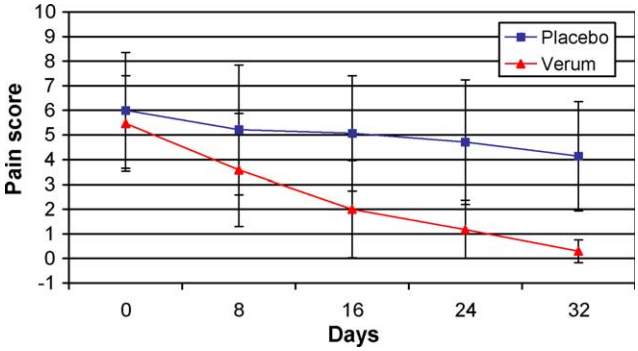

Fig. 2. The mean change of subjective pain score after isometric test (±SD).

The mean improvements of subjective pain score after an isometric test, at each follow up during treatment, are shown in Fig. 2. At the 32nd day, 11 out of 17 (65%) in the EFA, AO and US group scored no pain, and the mean decrease in pain score in the group was 99% and significant ($P<0.001$) compared with placebo. The placebo group had a mean decrease in subjective pain score after the isometric test of 37% at the end of treatment.

The secondary outcome measure, sports activity at baseline, 16 and 32 days, is shown in Figs. 3 and 4. In the EFA, AO and US group (Fig. 3) there was a mean increase of 53% in sports activity from baseline to the end of trial. In the placebo and US group the sports activity increased 11% from baseline until the end of trial (Fig. 4).

3.2. Adverse reactions

There were no adverse reactions reported after consuming the EFA, AO or placebo during or at the end of trial, nor

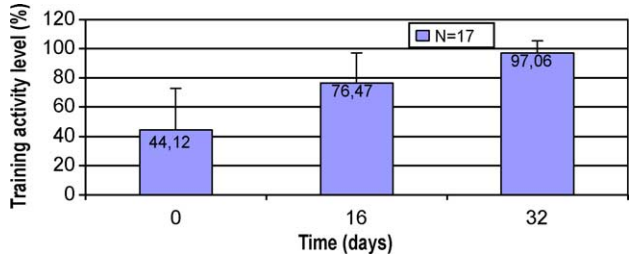

Fig. 3. Estimated level of sports activity compared with the level before injury in the EFA, AO and US group (±SD).

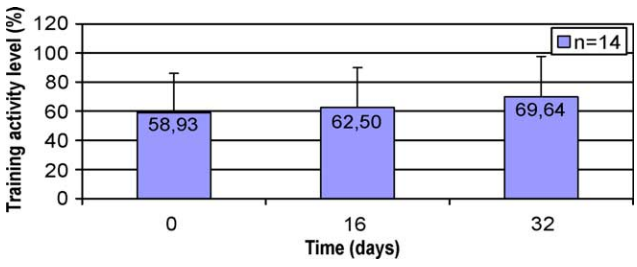

Fig. 4. Estimated level of sports activity compared with level before injury in the placebo and US group (±SD).

were any negative reactions reported after ultrasound treatment. All subjects included in the final analysis confirmed to have consumed the EFA + AO/placebo every day and all subjects fulfilled the criteria of filling in the training diary.

4. Discussion of results

The major baseline characteristics were evenly distributed among the two groups (Table 2). At baseline the primary outcome parameter, pain score, was also comparable in the two groups (Figs. 1 and 2).

Pain score decreased in both groups but significantly more so in subjects receiving essential fatty acids and antioxidants ($P < 0.001$). There was not a large difference in pain score with or without performance of the isometric test. The training activity also improved more in the treatment group, even though this activity was somewhat higher in the placebo group at baseline.

This indicates that the treatment with essential fatty acids and antioxidants significantly improved recovery from these specific injuries, and that it facilitated the amount of training in the treatment period.

It cannot be excluded that the physiotherapy treatment given to all patients supported the effect of the nutritional treatment.

The results of this trial correlates with previous experience from more than 200 uncontrolled cases, showing an effect within 2–3 weeks from the start of the treatment (Steenberg, 1999). More severe cases seem to require a longer period of treatment, typically up to 2 months, according to these open experiences.

5. General discussion

An increasing number of people have become aware of the health benefits of regular exercise. This awareness has resulted in an increasing number of persons doing strenuous exercise at irregular intervals, and as a result, sports injuries have been an increasing problem in the more exercise conscious public (Perry, 1992).

The role of overuse in the pathogenesis of chronic tendon injuries and disorders is not completely understood. It has been speculated that when a tendon is overused, it becomes exhausted and loses its basal reperative ability (Jarvinen et al., 1997), the repetitive microtraumatic processes thus overwhelming the ability of the tendon cells to repair the fibre damage. The intensive, repetitive activity, which often is eccentric by nature, may lead to cumulative microtrauma which further weakens the collagen cross-linking, non collagenous matrix, and vascular elements of the tendon (Kannus, 1997). Overuse has also been speculated to cause chronic tendon problems, by disturbing the micro- and macrovasculature resulting in insufficiency in the local blood circulation (Jozsa & Kannus, 1997). Decreased blood flow simultaneously with an increased activity may result in local tissue hypoxia, impaired nutrition and energy metabolism, and together these factors are likely to play an important role in the sequence of events leading to tendon degeneration (Jozsa & Kannus, 1997).

Ultrasound has satisfactorily been shown to increase blood supply and increase collagen synthesis to injured areas (Enwemeka et al., 1990; Jackson et al., 1991) thus suggesting a more rapid healing process and possible enhancement of the effects of the diet supplements given in this trial. Ultrasound facilitates increased production of blood vessels and fibroblasts and increases the permeability of the cell membrane (Dyson et al., 1990, 1999). It is also speculated that ultrasound has a way of restarting the healing process by initiating a local acute inflammatory response (Dyson et al., 1990, 1999). Dyson et al. (1990, 1999) have found that ultrasound does not dampen inflammation, rather it speeds up the inflammatory process.

The inflammation and pain associated with RSI can be thought to be the result—among other things—of an imbalanced fat intake. Traditional western intakes of large amounts of $n-6$ animal or plant fat (compared with $n-3$ fat from plants or marine oils) may result in a change in the transformation of fatty acids to eicosanoids in the body (Fan & Chapkin, 2000). The precursor fatty acids available for the eicosanoid production are highly determinant for several important processes in the body, among these the regulation of the inflammation in case of an injury (Gadek et al., 1999).

$n-6$ animal fatty acids, as precursors for eicosanoids controlling an inflammation, predominantly gives rise to class 2 eicosanoids. The $n-6$ fatty acid GLA and the $n-3$ fatty acids used in this study, on the other hand, are transformed into class 1 and 3 eicosanoids, respectively, which have a less potent inflammatory signal (Deluca, Rothman, & Zurier, 1995). Thus, the treatment with fatty acids in this study has the potential to dampen inflammation and pain without inhibiting the healing process, as with the traditional NSAID treatment. This could explain the greater training activity observed in the treatment group at the end of the supplementation period.

A traditional western diet with a high intake of saturated fats, trans fatty acids, a high blood glucose level and alcohol consumption could also reduce the enzymatic production of class 1 and 3 eicosanoids by delta-6-desaturase (Horrobin, 1982), contributing to the inflammation in RSI. Supplementation with $n-3$ fatty acids bypasses this enzymatic pathway. In addition, an adequate availability of some of the vitamins and minerals (zinc, vitamin B6 and vitamin C) used in the treatment group is essential for the conversion of fatty acids to eicosanoids (Horrobin, 1982), giving a further rationale for treatment with a combination of fatty acids and vitamins/minerals.

6. Conclusion

The study indicates that EFA and AO in combination with physiotherapy significantly improves the condition chronic tendon disorders in recreational athletes. This confirms previous uncontrolled experiences and strengthens the biochemical rationale for the use of essential fatty acids in inflammatory disorders. Further studies confirming this on a larger scale are encouraged.

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