Rheumatology 2008;47:390–391
Advance Access publication 15 February 2008
doi:10.1093/rheumatology/ken011

Editorial

Conservative management for tendinopathy: is there enough scientific evidence?

Tendinopathies account for a substantial proportion of overuse injuries in sports, and are prevalent in the workplace. The essence of tendinopathy is a failed healing response, with haphazard proliferation of tenocytes, some evidence of degeneration in tendon cells and disruption of collagen fibres and subsequent increase in non-collagenous matrix [1, 2]. Over the past few years, various new therapeutic options have been proposed for the management of tendinopathy. Despite the morbidity associated with tendinopathy in athletes, management is far from scientifically based, and many of the therapeutic options described and in common use lack hard scientific background.

Physical therapy, rest, training modification, splintage, taping, cryotherapy, electrotherapy, shock wave therapy, hyperthermia, pharmaceutical agents, such as NSAIDs and various peritendinous injections, have all been proposed most essentially to follow the same principles. Managements that have been investigated with randomized controlled trials include non-steroidal anti-inflammatory medication, eccentric exercise, glyceryl trinitrate patches, electrotherapy (microcurrent and microwave), sclerosing injections and shock wave treatment. Surgery should be reserved to patients in whom conservative management has proved ineffective for at least 6 months.

Despite this abundance of therapeutic options, very few randomized prospective, placebo-controlled trials exist to assist in choosing the best evidence-based management. There are no randomized studies that compare different conservative and surgical management regimens.

Pharmacological management strategies are essentially based on empirical evidence. Even though tendon biopsies show an absence of inflammatory cell infiltration [1, 2], anti-inflammatory agents (NSAIDs and corticosteroids) are commonly used. What may appear clinically as an 'acute tendinopathy' is actually a well-advanced chronic failure of healing response, in which there is neither histological nor biochemical evidence of inflammation. Evidence for the effectiveness of any available drug management regimen is at best controversial when tested in randomized controlled trials [3]. The available literature suggests that, in the absence of an overt inflammatory process, there is no rational basis for the use of NSAIDs in chronic tendinopathy [4].

Scandinavian authors have shown that, in their hands, a programme of eccentric exercise is effective in the non-operative management of tendinopathy [5, 6] to counteract the failed healing response which underlies tendinopathy, by promoting collagen fibre cross-linkage formation within the tendon, thereby facilitating tendon remodelling [7]. Although evidence of actual histological adaptations following an adapted programme of eccentric exercise is lacking, and the mechanisms by which a programme of eccentric exercise may help to resolve the pain of tendinopathy remain unclear, clinical results following such an exercise programme appear promising [5, 6]. Though effective in Scandinavian population [5, 6], the results of eccentric exercises observed from other study groups [7, 8] are less convincing, with only up to 60% of good and excellent outcome after a regimen of eccentric training both in athletic and sedentary patients. In general, the overall trend suggested a positive effect of an exercise programme, with no study reporting adverse effects.

Nitric oxide is a small free radical generated by a family of enzymes, the nitric oxide synthases. In a series of experiments performed over the last 15 yrs, nitric oxide played a crucial beneficial role in restoring tendon function [9]. Recently, three randomized, double-blind clinical trials evaluated the efficacy of nitric oxide administration via an adhesive patch in the management of a variety of tendinopathies [10–12]. All three clinical trials showed a significant positive beneficial effect of nitric oxide donation to the clinical symptoms and function of patients with Achilles tendinopathy [11], tennis elbow [10] and supraspinatus tendinopathy [12]. These results seem to be stable with time, at least in the Achilles tendon.

Sonographically guided intratendinous injection of hyperosmolar dextrose yielded a good clinical response in patients with chronic tendinopathy of the Achilles tendon in a pilot study [13]. Sclerosing injections with polidocanol resulted in a significant improvement in knee function and reduced pain in patients with patellar tendinopathy in a randomized controlled trial [14].

The role of physical modalities in the management of tendinopathies remains unclear, and it is not possible to draw firm, evidence-based conclusions on their effectiveness.

Low-energy shock wave therapy (SWT) to address the failed healing response of a tendon is not widely known among the medical community. A shock wave is defined as an acoustic wave at the front of which pressure rises from the ambient value to its maximum within a few nanoseconds [7]. Typical characteristics are high peak-pressure amplitudes (500 bar) with rise times of <10 ns, a short lifecycle (10 ms) and a frequency spectrum (16 Hz–20 MHz) ranging from the audible to the far ultrasonic level [15]. This rapid rise is followed by periods of pressure dissipation and negative pressure before gradually returning to the ambient pressure. The shock wave entering the tissue may be reflected or dissipated, depending on the properties of the tissue. The energy of the shock wave may act through mechanical forces generated directly or indirectly via cavitation [16]. The rationale for its clinical use being stimulation of soft tissue healing and inhibition of pain receptors, and hence, SWT has been thoroughly investigated experimentally during the past decade.

There is no consensus on the use of repetitive low-energy SWT, which does not require local anaesthesia, and on the use of high-energy SWT, which requires local or regional anaesthesia [16].

Low energy SWT has been used in patients with chronic tendinopathy. The randomized controlled trials on this subject are statistically and clinically heterogeneous, thus making conclusions from pooled meta-analyses difficult to interpret. We have tested low-energy SWT for chronic Achilles tendinopathy using a randomized controlled trial design [7]. Low-energy SWT and eccentric training produced comparable results, and both management modalities showed outcomes superior to the wait-and-see policy. The likelihood of recovery after 4 months was comparable after both eccentric loading and SWT, but success rates were 50–60%.

Hyperthermia induced by microwave diathermy raises the temperature of deep tissues to 41–45°C using electromagnetic power [17]. Microwave diathermy has been used in physical medicine and sports traumatology in Central and Southern Europe. Hyperthermia induced into tissue by microwave diathermy can stimulate repair processes, increase drug activity, allow more efficient relief from pain, help removal toxic wastes, increase tendon extensibility and reduce muscle and joint stiffness [17]. The biological mechanisms that regulate the relationship between the thermal dose and the healing process of soft tissues with low or high water content or with low or high blood perfusion are unknown. A recent randomized controlled trial in athletes showed that hyperthermia is effective in the short-term management of supraspinatus tendinopathy [18]. This modality warrants further studies with a greater number of patients and a longer term follow-up to confirm its therapeutic effectiveness. Nevertheless, adequately designed prospective controlled clinical studies need to be completed to confirm the therapeutic effectiveness of hyperthermia with large number of patients, longer-term follow-up and mixed populations. It is possible that it only exerts a relatively short lived, but nevertheless useful, analgesic effect.

Ultrasound therapy is a widely available and frequently used electrophysical agent in sports medicine. However, systematic reviews and meta-analyses have repeatedly concluded that there is insufficient evidence to support a beneficial effect of ultrasound at dosages currently being introduced clinically. A new direction for ultrasound therapy in sports medicine has been proposed by research demonstrating that ultrasound can have clinically significant beneficial effects on injured tissue when low-intensity pulsed ultrasound (LIPUS) is used [19]. LIPUS refers to pulsed-wave ultrasound with a spatial-averaged, temporal-averaged intensity $\leq 100\,\mathrm{mW/cm^2}$. This intensity is categorized as low relative to the range that is commonly used in physical therapy ($0.5\text{–}2\,\mathrm{W/cm^2}$) [19].

LIPUS is beneficial in accelerating fracture healing in clinical studies and to stimulate union in 86% of fractures displaying non-union [19]. Although established in the intervention of bone injuries, recent efforts have been directed towards the effect of LIPUS on injuries to other connective tissues [19].

LIPUS therapy has been tested in a randomized, double-blind, placebo, controlled trial in patients with chronic lateral epicondylitis [20]. It was no more effective for a large treatment effect than placebo for recalcitrant lateral epicondylitis.

The current issue of *Rheumatology* contains an extremely well-executed randomized controlled trial on the use of LIPUS in the management of patellar tendinopathy [21]. Warden *et al.* randomized 37 patients between active or inactive LIPUS [21]. Using both intention-to-treat and per protocol analysis, they concluded that LIPUS does not provide any additional benefit over and above placebo in the management of symptoms associated with PT.

As pointed out from the authors, one explanation for the absence of a beneficial LIPUS effect in their investigation is the relatively short intervention period (12 weeks) [21]. It is possible that a longer treatment period may have evidenced an effect of LIPUS. However, for practical reasons, the clinical utility of an intervention that requires longer than 12 weeks to generate a treatment effect is questionable, and we suspect that few patients would have agreed to a longer period of treatment in the absence of an effect. Likely, the intervention period was of sufficient duration to allow a LIPUS effect to be detected, if one had existed.

A genetic component has been implicated in tendinopathies, but investigations into the genetic factors involved in the aetiology of tendinopathy are still in their infancy [22]. In the equine model, good results have been achieved with mesenchimal cell therapy, but these are preliminary results [23], and tissue engineering, though stimulating, is still far from clinical application [24]. An enhanced understanding of these factors holds the promise of new approaches to the prevention and management of these common conditions.

All musculo-skeletal physicians attempt to give their patients the best available management at their disposal. Recently, the concept of 'evidence-based medicine' has come to the forefront attempting to recognize and define the best scientific observation that might influence practice. Further randomized controlled trials are necessary to better clarify the best therapeutic options for the management of tendinopathy.

Disclosure statement: The authors have declared no conflicts of interest.

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Accepted 4 January 2008
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