

# Effective for Inflammation Associated with Back Pain

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## Abstract

Among physicians today it is still common not to distinguish between the acute and chronic stage of tendon pain, either in terms of diagnosis or treatment. Thus treatment is often aimed at reducing acute, prostaglandin mediated inflammation in both acute and chronic stages of tendon pain. This was confirmed. In the chronic stage anti-inflammatory treatment will at best have symptomatic effects. The effects will not be curative and a number of studies now support that it actually has negative effects. Adverse events in the cardiac, gastrointestinal and renal systems accompanying treatment with NSAID are well documented. Injection of corticosteroids only provides temporary relief from pain.

**Keywords:** Chronic stage; NSAID; Tendon rupture; Decision making; Medical rationale; Tendinosis

## Introduction

Anabolic processes are negatively affected, which inhibits maturation and remodelling of tendon tissue and increases the risk of tendon rupture. PTs are alert and quick to pick up new treatments in clinical use, sometimes even before there is substantial evidence to either support or refute their use. This was also confirmed regarding the use of graded eccentric exercise for chronic tennis elbow. In addition to medical rationale, cultural factors may be part of clinical decision making. These factors include traditions in the education and training of staff, health care organization, availability of equipment and other resources, and patients' expectations. Indeed, cultural factors seem important explanations of why medical staff selects certain treatments, and why treatment guidelines may differ considerably between countries [1]. Differences in cultural factors may also explain some of the differences between GPs and PTs observed. Enhanced communication between these professional groups, who often work alongside each other, often with the same patients, could harmonize treatment practice to the benefit of both patients and health care staff. GPs could gain insight into new treatment options from PTs, who are often quick to pick up new trends in treatment. PTs, on the other hand, could benefit from discussing the evidence base of treatments with GPs, who often have a more conservative treatment approach. In the last decade there has been growing interest in exercise as a treatment for tendinosis, and in spite of some methodological weaknesses a number of studies now support the effects of this treatment. A more straightforward exercise versus wait list trial than used in previous studies and supports the idea that exercise is more effective than expectation in chronic tennis elbow. The additional cost of active physiotherapy measures as compared with expectation has been questioned, and a simplified exercise protocol for tennis elbow has been requested. The suggested exercise protocol used in Papers II and III is of a simple, low-cost kind that can be performed at home with a plastic container and an armchair. It does not require costly measures such as assistance from health care staff or specific exercise machines [2].

## Discussion

Whether eccentric is more effective than concentric graded exercise has been a matter of debate. A previous small-scale study of short duration found no significant differences between eccentric and concentric exercise in chronic tennis elbow. Eccentric exercise reduced pain faster than concentric exercise in chronic tennis elbow. This

supports previous studies on Achilles tendinosis showing eccentric exercise to be superior to concentric exercise. Exercise induces reorganization of the CNS and may thus affect central sensitization. It is possible that some of the difference seen is attributable to better and more effective reorganization in the CNS in response to eccentric than to concentric exercise. But the difference may also be attributed to effects on peripheral tissue. Exercise has anabolic effects on muscle and tendon cross-sectional area [3]. It is well known that eccentric exercise has superior anabolic effects on muscle synthesis as compared with concentric exercise. The fibroblast activity in tendons, however, responds to loading in an either/or fashion. This makes it somewhat of a surprise that one mode of exercise would be better than another for chronic tendon pain. Tendons and muscles work as functional units. The extra-cellular matrix of tendons and muscles share a similar structure of collagen scaffolding governed by fibroblasts [4]. It may be that the pain in TE is not solely related to the tendon but also to the muscles, where eccentric exercise has greater anabolic effects. Alternatively, since eccentric exercise induces greater and faster quantitative changes in muscles, it may also be that in the long run this puts more stress on the tendon, encouraging greater stimulation for collagen synthesis and matrix reorganization [5]. The implications of these findings are that a chronic soft tissue pain condition such as chronic tennis elbow should not be treated with rest but with graded exercise. This is in line with other studies and with findings of pain psychologists, who point out the negative effects of inactivity and associated fear-avoidance behaviour and suggest graded activity or graded exposure as a means of overcoming this problem. In addition to these psychological effects and the exercise-induced reorganization in the CNS, graded exercise, directed specifically towards the painful tissue, will have direct effects on that tissue. These anabolic effects will positively affect matrix turnover and may directly or indirectly affect pain associated processes related to halted matrix turnover and to

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chronic, neurogenic inflammation. During PET scan with the NK1 specific radioligand GR205171, both the voxel volume and the signal intensity of this volume were significantly higher in the affected than the unaffected arm in subjects with unilateral chronic tennis elbow [6]. Increased expression of NK1 receptors is known to occur as part of acute inflammation. To my knowledge, however, this is the first time increased expression of NK1 receptors in peripheral tissue has been visualized in a chronic pain condition. The true nature of such a condition is still uncertain. Central sensitization is well documented and probably part of the cause. Based on the findings in Paper IV as well as in other studies, it seems likely that peripheral sensitization also takes place. This sensitization may be at least partly explained by chronic neurogenic inflammation consisting of tripartite interaction among the immune cells, tissue cells and nerves. It is different from acute inflammation, which is dominated by inflammatory cells, local oedema and increased blood flow, but shares the feature of pain [7]. The endogenous production and release of substance P and other neurotransmitters from peripheral nociceptive neurons creates the prerequisites for a vicious circle, which may at least partly explain the longevity of the condition. Neurogenic inflammation does not, however, exclude other simultaneous mechanisms or up-regulation of other receptor systems in the peripheral painful tissue. Despite promising results in rodents, systemic blockade of NK1 receptors in human beings has not shown any convincing analgesic effect. Transient presentation of the NK1 receptor has been suggested as one possible explanation, supported by evidence that the NK1 receptor can be internalized. Overlapping pathways for signal transduction in the nerve system of human beings may be another explanation of why blockade of only one path does not have any significant effect [8]. In human beings there are several overlapping systems for pain signalling, which seem to be part of the phylogenetic evolution of a robust sensory system. This may in part explain the better effect in rodents. There will always be a balance between blockade of a mediator so central in action that there is a risk of hazardous side effects, e.g. blockade of TNF- $\alpha$ , and blockade of mediators so peripheral in action that no effect is obtained. If the NK1 receptor is a key receptor in neurogenic inflammation, systemic blockade may affect chronic inflammatory conditions. Clinical studies of NK1 receptor blockers that failed to deliver analgesic effects in human beings were mostly done on models of acute pain, not on inflammatory pain. If overlapping signalling pathways dilute the analgesic effect of systemic treatment, local treatment remains to be investigated. Combination therapy aimed at NK1 receptors and other receptor systems, e.g. opioid receptors, also remains to be studied [9]. Treatments affecting the substance P – NK1 system may, in other words, not completely have played out their role. PET scan has potential as research tool for physiological processes associated with pain, not only in the CNS but also in peripheral tissue. The NK1 specific radioligand GR205171 can be used to study the substance P NK1 system, but other tracers may be developed to study other receptor systems such as glutamate–NMDA/AMPA, NGF–TrkA or CGRP–CGRP- receptor. The combination of PET and functional magnetic resonance tomography provides a tool for detailed anatomical mapping along with the study of physiological processes. A large number of treatment methods for chronic tennis elbow were used by GPs and PTs in Uppsala county [10]. None of the methods used was properly evidence-based at the time of the survey and some

were even known to be ineffective. GPs used passive measures such as sick leave and anti-inflammatory medication to a large extent. GPs and PTs used ergonomic advice and stretching to similar extents, but differed regarding the use of exercise, which was used by many PTs but only by one GP. Enhanced communication between these professional groups could improve treatment for patients as well as professional satisfaction and scientific evolution.

## Conclusion

A musculoskeletal pain condition such as chronic TE responds favourably to graded dynamic exercise aimed at the painful tissue, even if it is performed according to a simple, standardized, low-cost, home exercise protocol. The exercise should be specifically designed to put load on the affected tissue, be performed regularly with gradually increasing load, have a minimum of two months duration, and should stress the eccentric work phase. The substance P–NK1 receptor system seems to play a part in the peripheral, painful tissue of a chronic, soft tissue pain condition such as chronic tennis elbow. The increased NK1 receptor availability may represent neurogenic inflammation and may be part of tripartite interaction among the peripheral nerve endings, the immune system and the tissue.

## Acknowledgement

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## Conflict of Interest

None

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