

Anti-Inflammatory Treatment of Muscular Injuries in Sport

An Update of Recent Studies

Louis C. Almekinders

Department of Orthopaedic Surgery, Sports Medicine Section, University of North Carolina, Chapel Hill, North Carolina, USA

Abstract

Stretch-induced muscle injuries or strains, muscle contusions and delayed-onset muscle soreness (DOMS) are common muscle problems in athletes. Anti-inflammatory treatment is often used for the pain and disability associated with these injuries. The most recent studies on nonsteroidal anti-inflammatory drugs (NSAIDs) in strains and contusions suggest that the use of NSAIDs can result in a modest inhibition of the initial inflammatory response and its symptoms. However, this may be associated with some small negative effects later in the healing phase. Corticosteroids have generally been shown to adversely affect the healing of these acute injuries. Animal studies have suggested that anabolic steroids may actually aid in the healing process, but clinical studies are not yet available and the exact role of these drugs has yet to be determined. Studies on anti-inflammatory treatment of DOMS have yielded conflicting results. However, the effect of NSAIDs on DOMS appears small at best. Future research may have to focus on different aspects of these injuries as the emphasis on anti-inflammatory treatment has yielded somewhat disappointing results.

Muscle injuries continue to make up the majority of all sports-related injuries in most epidemiological studies.^[1,2] Although they are generally considered minor injuries, they can account for significant disability because of their frequency as well as their symptoms. There are several causes of muscle injuries. An acute stretch of a muscle can cause a partial or even complete tear of the muscle-tendon unit. These injuries are usually designated as stretch-induced injuries or muscle strains. A direct, non-penetrating hit to the muscle belly is another com-

mon mechanism for muscle injuries. Such muscle contusions can also cause significant damage to the structure and function of the muscle. Finally, repeated eccentric muscle contractions can result in pain, stiffness and decreased function often peaking at 2 days following the eccentric exercise. This delayed-onset muscle soreness (DOMS) may not be a true injury, but more a physiological adaptation to unusual exercise. Nevertheless, it is a cause for disability in athletes and therefore will be included in this review.

For several decades, sports medicine clinicians and researchers have been looking for ways to minimise the disability that follows a muscle injury. Moderate to severe muscle injuries often result in inability to train or compete for at least several weeks. Even after return to practice or competition, weakness, inflexibility and recurrences are problems that can extend the disability from a muscle injury. Anti-inflammatory measures have traditionally been the focal point of our treatment approach. This is usually attempted through drug treatment, but is also the goal of some of the physical modalities used in muscle injuries. This article will review the most current data on the effects of anti-inflammatory treatment on muscle injuries including strains, contusions and DOMS.

1. Pathophysiology of Muscle Injuries

In order to make a sound judgement regarding the appropriateness of certain treatment forms, it is important to have a basic understanding of the pathophysiology of muscle injuries. This section will briefly review the current knowledge on the response of muscle to injury.

The pathophysiological response to muscle injury has been studied extensively in animal models. Both strains^[3] and contusions^[4-6] as well as DOMS^[7] have been studied in this manner. The initial pathology has shown many similarities in strains and contusions. Immediately following the injury there is disruption of the architecture because of ruptured muscle fibres, as well as injury to the connective tissue framework. Haematoma formation and muscle cell death are generally obvious at the site of injury. Within 2 to 3 days an intense inflammatory response develops. Inflammatory cells replace the initial haematoma and macrophages start clearing away necrotic muscle fibres. Whenever basement membranes of the muscle fibres and connective tissue framework of the muscle are still intact, they persist even in this inflammatory phase. Biomechanically the muscle is most impaired at that point. The muscle is weakest both in terms of the ability to withstand passive stretch as well as generate active contractions. Within the first week in animal

models, evidence of muscle regeneration can be found. Regenerating muscle cells or myotubes are seen in the injured area. The preservation of basement membranes and connective tissue framework appears to be crucial for the functional regeneration of these myotubes.^[8] In addition to the regenerative response, fibroblasts mount a scar response. The combined regenerative and scar response results in a healed muscle that has fewer and smaller muscle fibres in the injured area as well as an increased amount of collagenous tissue between the fibres. In animal models the muscle is largely healed after approximately 2 weeks. It is not known whether the healing in human muscle is substantially different. It is possible that the healing process in human muscles takes significantly longer, as suggested by the clinical symptoms that often last for several weeks. In addition, it is possible that the regenerative response is even less likely to occur with a stronger fibrotic response instead.

In DOMS, the essential pathophysiological response is more controversial.^[7] Localised damage to sarcomere subunits within individual muscle fibres has been seen using electronmicroscopy. Overt, complete muscle fibre necrosis is generally not present. A limited inflammatory response is seen after several days with the appearance of inflammatory cells in the muscle. However, the inflammatory changes do not correlate well with the clinical symptoms and therefore may not be the key element of DOMS. Other evidence of structural damage to the muscle can be found, such as the elevation of plasma creatine kinase. A regenerative response appears capable of fully restoring the muscle's architecture. Fibroblast activation does not seem to occur in DOMS as it is seen in strains and contusions.

2. Stretch-Induced Muscle Injuries

Stretch-induced muscle injuries or strains are most common in muscles that span 2 joints. Common examples are the gastrocnemius muscle spanning the knee and ankle, and the hamstring muscles spanning the hip and knee. It is possible that a combination of fatigue, relative high percentage of fast twitch muscle fibres and the dual action required

for both joints can lead to excessive tension within the muscles, resulting in a tear. Experimental work has shown that these tears have a marked tendency to occur at the muscle-tendon junction.^[3] As described in section 1, an intense inflammatory response follows. It remains controversial whether inhibiting this inflammatory response is a uniformly important advantage. Pain and disability following the injury are at least in part due to the inflammatory response. Decreasing the inflammation decreases the symptoms and may allow earlier rehabilitation. On the other hand, inflammatory cells are responsible for clearing away cell debris and necrotic muscle fibres. Without this phagocytic function healing, in particular regeneration, may not be able to begin. Traditional anti-inflammatory treatment has included nonsteroidal anti-inflammatory drugs (NSAIDs) and sometimes physical modalities.

2.1 Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

It is well known that NSAIDs are capable of inhibiting the enzyme cyclo-oxygenase and thereby decreasing the production of prostaglandins which are capable of mediating the inflammatory response following injury. Earlier studies indicated that prostaglandin levels and oedema can be decreased in animal models by NSAIDs.^[9] In addition, there appeared to be a delayed and possibly diminished inflammatory response. More recent studies seem to have confirmed these earlier findings. Obremsky et al.^[10] found increased contractile force in the NSAID-treated muscles early following the injury, but this was associated with delayed degradation of damaged tissue later on. Similarly, muscle regeneration appeared to be slowed by the NSAID treatment. They were unable to detect a significant difference in the outcome with regards to passive and active strength of the muscle. It remains unclear from this study whether the differences found are important in the clinical situation. In the only available clinical study, Reynolds et al.^[11] studied the effects of NSAIDs in a double-blind, placebo-controlled, randomised investigation on hamstring strains. They found significantly increased, persistent pain

in the severe strains at day 7 compared to the placebo group. Swelling and isokinetic muscle strength was not significantly different between groups.

When looking at the animal and scant human data, it appears that there is not a compelling case for the aggressive use of NSAIDs in stretch-induced muscle injuries. Although no major problems have been noted, it is also important to consider the cost, potential adverse effects, the few negative effects that have been reported and the fact that there are no major advantages found. If NSAIDs are used, the studies suggest that they be used early in the post-injury period and discontinued once the acute inflammatory response has peaked.

2.2 Corticosteroids

To date, there are no reported human or animal studies on the use of corticosteroids in acute muscle strain injuries. Most studies on the use of corticosteroids in acute soft tissue trauma have shown negative effects on the healing of these injuries.^[12] Studies using a muscle contusion model, as will be discussed in section 3, have confirmed these effects. Currently, there appears to be no good argument in favour of the use of corticosteroids in acute muscle strain injuries.

2.3 Physical Modalities

Treatment of strain injuries by physical means remains popular. Early treatment with rest, ice, compression and elevation has become a standard approach to most acute soft tissue injuries in spite of the relative lack of scientific foundation for these treatments. Later during the healing phase, stretching and strengthening exercises are often added. Thorsson et al.^[13] reported on the clinical use of external compression immediately following an acute muscle injury including strain injuries. No significant difference in the size of the haematoma to the time to recovery was found compared to control patients. Although no significant harmful effects are seen from rest, cooling, compression and elevation, it remains unclear whether they are effective in acute muscle injuries.

3. Muscle Contusion

Most of the recent studies on muscle injuries have used an animal, muscle contusion model. In this model the injury can be controlled very well, which is difficult to do in clinical studies. Clinical studies on this topic remain extremely scarce.

3.1 Nonsteroidal Anti-Inflammatory Drugs

Jarvinen et al.^[14] studied the effects of NSAIDs in a muscle contusion model. In rat gastrocnemius muscle, they found a slight delay in the inflammatory response in the early post-injury period. Later, they noticed a decrease in tensile properties in the NSAID-treated group. These results seem consistent with the animal studies on the use of NSAIDs in strain injuries as discussed in section 2.1. There appear to be some anti-inflammatory effects within the muscle early on, which may be associated with some early clinical improvement such as less pain. However, later during the recovery phase some small negative effects are found.

3.2 Corticosteroids

The effects of anti-inflammatory steroids are in essence similar to those found with NSAIDs, with the exception that the effects appear more exaggerated. Beiner et al.,^[15] using methylprednisolone in their animal contusion model, saw an early positive, muscle-sparing effect with improved muscle function directly following the injury. However, later in the post-injury period there was a marked disruption of the healing process with poor muscle function. They concluded from their animal study that corticosteroids are likely to be detrimental if used during the healing period. Jarvinen et al.^[14] reported similar results with the use of hydrocortisone given orally after a gastrocnemius contusion injury in rats. Delayed resolution of the haematoma, retarded muscle regeneration and decreased tensile properties were associated with the corticosteroid treatment. Neither study used direct injection of corticosteroids in the affected area as originally reported by Molloy and McGuirk^[16] for the prevention of myositis ossificans. Future research may be

able to determine a more optimal route, timing and dosage regimen of corticosteroids that allows the use of this drug with its initial muscle sparing effect and avoids the detrimental effects noted thus far.

Until this research has been done, corticosteroids do not appear to have a place in the treatment of acute muscle contusions.

3.3 Anabolic Steroids

Although they are not considered to have anti-inflammatory properties, anabolic steroids have received some renewed attention as a drug for the treatment of muscle injuries. In an early study,^[17] it was found that a testosterone derivative was able to increase the number of muscle progenitor cells in injured muscle. More recently, Beiner et al.^[15] confirmed this finding and found more rapid healing and restoration of force generating capacity with nandrolone decanoate in a contusion model. Interestingly, both studies found this was associated with an initial increase in inflammatory cells. This suggests that the initial inflammatory response is indeed a crucial part of the entire healing response and future studies should not automatically assume that inflammation needs to be decreased at all stages of the healing process.

3.4 Physical Modalities and Hyperbaric Oxygen

Relatively little work has been done to investigate the effects of non-drug therapies on muscle contusion. In a study on the clinical effects of external compression of the injured muscle,^[13] no significant beneficial effects were found in muscle contusions. In an experimental animal study,^[18] hyperbaric oxygenation did not facilitate healing of a surgically-induced muscle crush injury. Although stretching and strengthening exercises have not specifically been studied, it appears logical to continue using them as the mainstay for non-drug therapy. Weakening because of post-injury disuse and inflexibility due to scar formation are clearly negative sequelae of a muscle injury.

4. Delayed-Onset Muscle Soreness

The pain that follows intense, eccentric muscle activity has been the focus of numerous investigations. It is clear that DOMS is associated with predictable discomfort and decreased muscle performance that peaks at about 24 to 48 hours following the eccentric exercise. Some of the studies have focused on the inflammatory aspects of this phenomenon in an attempt to decrease the symptoms by treatment with anti-inflammatory drugs and modalities.

4.1 Nonsteroidal Anti-Inflammatory Drugs

There are several investigations that have studied the effects of NSAIDs on DOMS in human, placebo-controlled studies. The results of these studies have been somewhat conflicting. However, it appears that the majority of the studies have not found a significant, beneficial effect from the NSAIDs. Subjective pain scores were only slightly improved in some studies,^[19,20] and essentially not affected in others.^[21,22] Most studies did not find an improvement in the level of creatine kinase (CK) levels as a result of NSAID use. CK is often used as a objective serological marker for DOMS. Some studies actually found a negative effect on some of the indices of muscle damage.^[22,23] Similarly, muscle performance during DOMS does not appear to improve significantly with NSAID use. Most investigators have concluded that the inflammatory component of DOMS is not an essential part of this phenomenon and therefore anti-inflammatory treatment is unlikely to yield dramatic results. The theory that mechanical damage is largely responsible for the symptoms of DOMS appears to be favoured at this point.^[24]

4.2 Corticosteroids

Hasson et al.^[25] studied the effect of dexamethasone iontophoresis on the symptoms of DOMS. No significant effects were noted on muscle function in this study. There was a slight improvement in muscle soreness perception in the treated patients. No other studies have been reported that

confirm this finding. The use of oral corticosteroids in the treatment of DOMS has not been studied.

4.3 Massage Therapy and Other Modalities

Other treatment forms to ameliorate the symptoms of DOMS continue to be the subject of recent investigations. They have generally resulted in conflicting findings. It has been theorised that physical therapy techniques could improve the healing response following eccentric exercise-induced muscle damage by diminishing stiffness and improving local circulation. Mild, positive effects from massage have been reported.^[26,27] However, other investigators^[28,29] were unable to find improvement as a result of massage therapy. In addition, modalities like microcurrent electrical stimulation,^[29] therapeutic ultrasound,^[30] transcutaneous electrical stimulation^[31] and intermittent pneumatic compression^[32] have not been shown to produce significant clinical improvement in DOMS.

5. Conclusions

In spite of numerous efforts with experimental and clinical studies, the effect of anti-inflammatory treatment on muscle injuries remains somewhat disappointing. It appears that there is a coupling of the inflammatory phase and the subsequent regenerative phase in muscle injuries. Inhibiting the initial phase may be associated with negative effects in the subsequent phase. It is still possible that this phenomenon is explained by the continued use of the anti-inflammatory agent during the regenerative phase. Therefore, it seems advisable to study these drugs in a regimen where they are only administered during the initial post-injury period and discontinued thereafter.

In addition, it seems reasonable to shift our research efforts to other forms of treatment, as anti-inflammatory treatment appears marginally effective at best. Anabolic steroids have shown some promise in animal studies, although this may raise ethical concerns when used in athletes. Growth factors or even gene therapy may hold promise as a treatment for muscle injuries as they potentially can have a direct effect on muscle regeneration.

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Correspondence and reprints: Dr *Louis C. Almekinders*, CB# 7055, University of North Carolina, Chapel Hill, NC 27599-7055, USA.