The Use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) in Treating Delayed Onset Muscle Soreness (DOMS)

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Background Information

Introduction

Non- steroidal anti-inflammatory drugs (NSAIDs) are the most commonly used of all medications in developed countries with a worldwide market of over US$6 billion every year (Krenz, 2008; Lanier, 2004). The widespread availability of over-the-counter NSAIDs such as ibuprofen, aspirin and sodium naproxen has allowed tens of millions of individuals to minimize the pain, swelling and inflammation linked with mild to moderate athletic injuries (McAtee, 2008). The anti-inflammatory effect of these drugs makes them highly sought after by athletes experiencing muscular discomfort or pain from delayed-onset muscle soreness (DOMS). NSAIDs are used by athletes of all ages and at all levels of competition to treat muscle injuries and soreness resulting from participation in sport (Lanier, 2004).

Delayed Onset Muscle Soreness

Muscle injuries make up most of all sports-related injuries and although they are often considered minor, they may account for significant disability because of their frequency and symptoms. Pain, stiffness, and decreased muscle function resulting from repeated eccentric muscle contractions contribute to DOMS (Almekinders, 1999). Although the pathology associated with DOMS is generally sub-clinical, the sensations experienced with this injury can range from slight stiffness that eventually subsides during daily activities to tremendous, debilitating pain making it difficult to move (Hume, 2004). Treatment for DOMS is of particular importance to athletes because athletic

performance and preparation are impaired when an athlete is sore or injured. Any treatment that limits the extent of damage or quickens recovery would be of interest and practical value to athletes, trainers, coaches and therapists (Connolly, 2003).

Non-Steroidal Anti-Inflammatory Drugs

For several decades, sports medicine clinicians and researchers have been investigating ways to reduce the debilitating effects that follow a muscle injury. DOMS, a moderate muscle injury, often results in inability to train or compete for several weeks. Upon returning to practice or competition, the athlete is often weak and inflexible and often re-injures the same muscle, which will further extend the disability. Anti-inflammatory measures have traditionally been the focal point of the treatment approach for DOMS (Almekinders, 1999). One of the many treatment modalities advocated to facilitate recovery of muscle function and alleviate the symptoms of DOMS are NSAIDs (Connolly, 2003). Many athletes use these medications prophylactically (to prevent injury) and therapeutically (to treat injury) during the on and off-season (Lanier, 2004). NSAIDs inhibit the synthesis of prostaglandins that are mediators of inflammation. The inflammatory process is thought to be involved in the development of DOMS and is the rationale for the widespread use of NSAIDs in the treatment of sports injuries (Lanier, 2004).

Initiation of DOMS

Type of Exercise Causing DOMS

Eccentric exercise receives attention as a beneficial means of exercise, but it has also been shown to contribute to muscle damage in early stages of exposure to eccentric exercise, also known as DOMS (Connolly, 2003). Eccentric movement causing forceful

lengthening of muscle fibers produces greater damage than contractile movement causing shortening of muscle fibers. Muscle tissue is made to contract forcefully, thus it is much easier for muscles to forcefully contract rather than forcefully lengthen. Micro-tears occur when an athlete performs exercises that require the muscle tissues to greatly lengthen such as in running downhill, descending stairs, or lowering weights back to a starting position. Activities only requiring muscle fiber contraction do not generally cause damage and produce much less muscle soreness. An abnormally lengthened fiber undergoes much more tension than the same fiber in a relaxed or contracted state because it has to endure a higher load-to-fiber cross-sectional ratio, thus is more susceptible to damage. A contracted muscle is better at handling the same amount of load because there is a greater amount of tissue to move the resistance (Nessel, 2010). Evidence has shown that fast-twitch muscle fibers are more susceptible to eccentric contraction-induced damage than slow-twitch fibers. This is most likely due to the weakness in fast twitch fibers or selective recruitment of fast-twitch motor units for eccentric exercise (Connolly, 2003). Vigorous eccentric muscle contraction followed by soreness and pain and resulting in structural damage to the contracting muscle fibers and their surrounding tissues marks the onset of DOMS (Nessel, 2010)

The Symptoms Associated With DOMS

The injury itself is a mechanical disruption to sarcomeres that proliferates secondary to an inflammatory response causing swelling and localized pain. Typical symptoms associated with DOMS are loss of strength, pain, muscle tenderness, stiffness and swelling (Connolly, 2003). Enzyme leakage into the blood is a marker for tissue damage and signals for inflammation around the traumatized area. Increased swelling

produces increased pressure against nerves at the site of injury which signals the brain to discomfort, then to pain, and then to weakness and reduced range of motion. The body attempts to protect the injury from worsening by making movement painful and difficult (Nessel, 2010). Discomfort is experienced in a localized area because connective tissues surrounding muscle is densely packed with pain receptors and when the tissues are damaged, signals are sent to the many receptors in order for the body to begin the inflammatory and healing process. Generally, discomfort increases within the first 24 hours following physical activity, peaks somewhere between 24 and 72 hours, then decreases and eventually diminishes between 5 and 7 days after cessation of exercise (Hume, 2004).

Mechanism of NSAIDs for DOMS

The Inflammatory Response

High- tensile forces during eccentric exercise that damage muscle and connective tissues result in an acute inflammatory response, consisting of oedema formation and inflammatory cell infiltration (Hume, 2004). The inflammatory response is associated with muscle protein degradation and prostaglandin synthesis (Lanier, 2004). Prostaglandins are produced in every tissue of the body excluding erythrocytes, and take part in many different physiological processes (Stone, 2004). Prostaglandin synthesis aids the inflammatory process by increasing vascular permeability, sensitizing pain neurons to mechanical, thermal and chemical stimulation, and intensifying the protein degradation process. Degradation of muscle tissues at the injury site attracts neutrophils, lymphocytes and monocytes that are converted to macrophages and increases vascular permeability (Lanier, 2004). The accumulation of histamine, potassium and kinins from

phagocytosis and cellular necrosis, in addition to elevated pressure from swelling and increased local temperature activates nociceptors within the muscle tissues leading to sensations associated with DOMS (Hume, 2004). Swelling results from the movement of cells and fluid from the bloodstream into the interstitial spaces and can contribute to the sensation of pain (Connolly, 2003). Excess movement may heighten soreness by increasing intramuscular pressure, which causes a stimulus for pain receptors already sensitized by prostaglandins. Knowledge regarding the mechanisms of DOMS has led to treatment strategies aimed at alleviating its symptoms, restoring maximal muscle function in a timely manner, and reducing the severity of the initial injury. The use of NSAIDs such as aspirin, diclofenac, ibuprofen, naproxen sodium and ketoprofen has become a highly researched and popular method of treating DOMS (Hume, 2004).

Effects of NSAIDs on Inflammation

NSAIDs work to reduce inflammation by inhibiting the cyclooxygenase COX enzyme which is necessary for prostaglandin synthesis; when inflammatory prostaglandins cannot be made vascular permeability is not increased, swelling is limited and less soreness is experienced at the site of muscle injury. Most NSAIDs, including ibuprofen, inhibit the COX enzyme via allosteric regulation and the NSAID will occupy the enzyme's active site, preventing the substrate arachidonic acid from binding to COX and thus preventing the conversion of arachidonic acid to prostaglandin. Two forms of COX (COX-1 and COX-2) start the reaction that converts arachidonic acid to prostaglandin. COX-1 is an enzyme found in tissues throughout the body and helps to regulate cellular activities such as renal function and maintenance of gastric mucosa. COX-2 is more important and active in the inflammatory response linked to DOMS, thus

is more often inhibited by NSAIDs. Aspirin has a different mechanism, and inhibits prostaglandin synthesis via irreversible acetylation of the COX enzyme. Different from the commonly used aspirin and ibuprofen, various other NSAIDs prevent inflammation by blocking the lipoxygenase (LIPOX) enzyme pathway, which is the pathway responsible for production of leukotrienes, the fatty molecules of the immune system that contribute to inflammation and oedema. The more common COX inhibitors work efficiently to reduce inflammation, but can lead to the development of commonly reported side effects if used chronically (Lanier, 2004).

Adverse Effects of NSAIDs

The easy accessibility to NSAIDs over-the-counter and their reported ability to relieve pain has led to widespread use among athletes. Routine use of NSAIDs has been related to certain side effects including gastrointestinal (GI) complications, kidney damage and liver damage (Hume, 2004). Most of the problems associated with using NSAIDs are associated with decreased prostaglandin synthesis in the GI and kidney. Side effects to these organs may include haemorrhage, stomach ulcers, bowel obstruction and vasodilation of renal vessels. Less common adverse effects include increased risk for hepatotoxicity and congestive heart failure for those at risk (Stone, 2004).

Gastrointestinal (GI) Complications

Gastrointestinal bleeding related to the use of NSAIDs is the 15th leading cause of death in the United States (Lanier, 2004). Since they interfere with blood circulation and tissue repair throughout the body, it is important that they be taken along with food in order to protect the stomach walls. New tissues are constantly being added to the stomach lining so the stomach has the ability to tolerate constant exposure to strong acid

and digestive enzymes (Nessell, 2010). Due to the fact that NSAIDs effect blood circulation, they are not recommended for people with bleeding abnormalities because they inhibit platelet aggregation, which increases bleeding time. Risk factors associated with GI complications also include age, history with ulcers, smoking, alcohol abuse, chronic use of NSAIDs, consumption of large doses of NSAIDs and the use of two or more NSAIDs taken at the same time. Athletes often fall into the risk factor category associated with consumption of large doses of NSAIDs, which generally refers to consumption of 1500-1800 mg/day. Athletes tend to take larger doses than the general population because higher amounts are required to produce anti-inflammatory effects as compared to the amount needed to relieve pain. Normally, athletes consume NSAIDs specifically to reduce inflammation caused by muscular injuries, while the general population more commonly takes NSAIDs specifically to relieve pain (Lanier, 2004). Athletes, and anyone else consuming large amounts of NSAIDs over a long period of time should be sure to always consume NSAIDs with food, and to pay close attention to stomach issues because they may be a direct result of NSAID consumption.

Renal Complications

More recently, it has been realized that the number one cause of kidney failure in the United States came from the overuse of NSAID medication because they can diminish blood circulation to the kidneys over time (Nessel, 2010). Renal complications due to NSAID overuse are more common in endurance athletes because of the large amounts of fluids that are lost during prolonged, exhaustive training. Endurance athletes can easily become dehydrated which results in decreased blood flow to the kidneys. As discussed earlier, NSAIDs inhibit prostaglandins, which are important to renal function

because they increase glomerular filtration rate. Dehydration due to excessive fluid loss during prolonged exercise, coupled with NSAID consumption to prevent muscle pain and inflammation may result in acute renal failure. Endurance athletes, like distance runners and cyclists, should consider the risk factors associated with NSAID use and be especially sure to consume enough fluids if they choose to use NSAIDs during training or competition (Lanier, 2004).

Cardiovascular Complications

It is not recommended that individuals with a history of heart disease use NSAIDs because there is evidence suggesting that chronic NSAID use increases the risk of congestive heart failure for these people. NSAIDs are proposed to increase the cardiovascular system's resistance to blood flow making it more difficult for blood to efficiently oxygenate tissues. Lack of oxygen to heart can lead to the death of cardiac tissues. NSAIDs can interfere with drugs used to treat heart conditions such as diuretics and angiotensin-converting enzyme (ACE) inhibitors and can counteract aspirin's cardio protective effects if taken synergistically. There is no evidence that NSAIDs cause cardiovascular complications in individuals with pre-existing heart disease, but they can exacerbate issues in individuals with history of cardiovascular illness (Lanier, 2004).

Respiratory Complications

NSAIDs have been shown to cause adverse effects on the respiratory system, especially if taken by individuals with asthma. Exercise induced asthma is becoming more common among individuals who regularly engage in highly intensive physical activity. NSAIDs inhibit the COX enzyme and thus prevent synthesis of respiratory prostaglandins that are important for relaxing bronchial muscle, thus bronchoconstriction

can result from NSAIDs. Athletes with asthma may experience even greater respiratory dysfunction as result of NSAID consumption (Lanier, 2004).

Alternative Treatment Methods for DOMS

Sports Creams

Currently, the most common form of NSAID administration is oral but the proposed side effects and risk factors of oral NSAID treatment have initiated the development of topical anti-inflammatory remedies (Hyldahl, 2010). Sports creams have both anti-inflammatory and counterirritant properties, but in order for the cream to actually reduce inflammation, enough time must be given for the cream to absorb through the skin and fascia and into the muscle. Sports creams are applied to the skin over-lying the painful injured muscle where they penetrate the epithelial layer of the skin, stimulate sensory neurons and can evoke a range of sensations. Effectiveness of sports creams in treating DOMS depends on the type used, amount of time it is used, frequency use and severity of muscular injury. Creams generally ease pain, which assists in decreasing discomfort, but their effects on the recovery process and muscle dysfunction are still unknown (Hill, 2002).

Compression and Cryotherapy

The initial treatment recommended for DOMS is R.I.C.E (rest, ice, compression, and elevation). Various modes of applying ice and pressure are used routinely in clinical settings to assist with pain relief, and to reduce inflammation and swelling (Connolly, 2003). The superficial application of ice reduces the temperature of the skin, muscle and tissues, which reduces swelling and oedema. Compression has the ability to reduce severity of muscle soreness by limiting oedema and thus relieving symptoms associated

with oedma such as decreased range of motion, pain and swelling (Hume, 2004). Techniques such as cold-water immersion, intermittent pneumatic compression and compression sleeves have shown evidence of being effective in reducing symptoms of DOMS. In one study, a treatment of cold-water immersion for 15 minutes immediately after eccentric elbow flexor exercise and every 12 hours for a total of 7 treatments was effective in reducing stiffness and lowering creatine kinase levels (Connolly, 2003). In another study, fifteen healthy non-strength-trained men used a compression-sleeve after performing arm curls; the subjects found that the compression-sleeve decreased their perception of soreness, reduced swelling and promoted recovery of force production (Hume, 2004). Although research is limited, there is evidence that compression and cryotherapy can help to reduce symptoms associated with DOMS.

Stretching and Massage

Arguably, the most commonly practiced treatments for DOMS is passive stretching and massage which is contradictory to the fact that there is little scientific evidence to support the effectiveness of this treatment. The combination of pre-exercise warm-up with stretching and post exercise massage is to be more beneficial than treatments practiced individually (Connolly, 2003). Massage includes several different techniques, which are used to reduce pain, increase muscle blood flow and increase muscle temperature. An increased blood flow during vigorous massage may reduce prostaglandin production, reducing further damage associated with the inflammatory process while increased muscle temperature is proposed to increase muscle compliance and reduce muscle stiffness. Static stretching post-exercise is proposed to disperse the accumulation of fluid following tissue damage. A study examining the use of warm-up,

stretching and massage in combination reported that warm-up and stretching before eccentric exercise with the forearm flexors for 30 minutes, and massage after exercise, was effective in reducing the severity of muscle damage. Although there is little evidence to support the efficacy for using stretching and massage separately to treat DOMS, practicing the techniques in combination may prove beneficial (Hume, 2004).

Nutritional Supplements and Homeopathy

Nutritional supplements have become a popular means of treating muscular injuries, including DOMS (Connolly, 2003). Homeopathy, the form of therapy based on the "treat like with like" principal, uses mineral, plant and animal products to treat injury. Substances including fish oil, ethanol, herbs, pollen extract, and various vitamins and minerals have been investigated for their use to prevent the symptoms of muscle damage. Fish oil is thought to decrease the inflammatory process through alteration of the eicosanoid pathway, while isoflavones are thought to reduce the inflammatory pathway through their role as a tyrosine kinase inhibitor. Ethanol is thought to reduce a leakage of muscle proteins after eccentric exercise while pollen extract is a free radical-scavenging preparation, which is thought to attenuate or eliminate tissue destruction (Hume, 2004). Antioxidants such as vitamin C and E taken before exercise are believed to reduce muscle damage, also because of their ability to destroy free radicals (Connoly, 2003). One of the most popular homeopathic medicines of choice is Arnica due to its analgesic, antibiotic and anti-inflammatory properties (Hume, 2004). Although, many homeopathic and nutritional supplements have proposed benefits for DOMS, there are inconsistencies in the research. Whether or not these types of supplements work often depends on factors including: muscle group damaged, mode of exercise used, dosage, and duration of

supplement use, all of which factors should be considered if an individual plans to start taking something new (Connolly, 2003).

Conclusion

NSAID use among athletes ranging in age, competition level and sport has skyrocketed in recent years due to the plethora of over-the-counter products that can be found. The anti-inflammatory properties of NSAIDs makes them highly sought after to treat DOMS, the muscular injury resulting from an inflammatory response to connective tissue or muscle damage, often experienced by athletes. A variety of NSAIDs have been evaluated for their effectiveness in treating the symptoms of DOMS, and although they have been found to reduce symptoms and shorten injury time, they have also been associated with harmful side effects. Long-term, chronic NSAID use has been associated with increased risk for GI, renal, respiratory, and cardiovascular complications. Knowledge of the potential risks of chronic NSAID use has increased popularity of alternate treatment approaches such as topical creams, compression and cyrotherapy, stretching and massage, and homeopathy. Studies using NSAIDs and other treatment modalities have shown varying results based on a variety of factors including: dosage, time of administration, duration of use, frequency of use, severity of injury, and type of exercise that caused injury. When deciding on a treatment method for DOMS, the severity of damage and the individual response should be considered and the treatment should be balanced with the natural time course for recovery. All in all, prevention is the most efficient way to "cure" DOMS; most treatments reduce the severity of the muscle damage, but don't necessarily correct the injury. Treatment for DOMS is an individual choice, and before resorting to NSAIDs the person should be aware of potential side

effects and consider various other therapies and products that can be used to assist them in their recovery.

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