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Amit M. Deokar  
*University of Kentucky*

Shawn J. Smith  
*University of Kentucky*

Hatim A. Omar  
*University of Kentucky, hatim.omar@uky.edu*

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Chapter 23

ACUTE MUSCULOSKELETAL SPORTS INJURY AND TOPICAL NSAID

Amit M. Deokar*, Shawn J. Smith and Hatim A. Omar
Department of Pediatrics, Division of Adolescent Medicine, University of Kentucky, Lexington, Kentucky, United States.

ABSTRACT

The objective of this chapter is to summarize the current standards of pain management in minor sports related musculoskeletal injuries. We also address the topical form of non-steroidal anti-inflammatory drug as an effective pain management option in an out-patient setting. Design: Quantitative systematic review of randomized controlled trials. Methods: The data was obtained through literature review of articles published in the last 10 years. In addition, FDA information on non-steroidal anti-inflammatory medications was also reviewed. The patient population studied in the articles included children and adults. Conclusion: Current standards of managing pain resulting from sports injuries involve a number of analgesic drugs including non-steroidal anti-inflammatory drugs. The topical form of this class of drugs is an effective method for pain management of minor musculoskeletal sports-related injuries.

INTRODUCTION

When compared to the 1970’s, there has been increased participation in sports activities. Despite an increased awareness of safety measures, the participants are still at an increased risk from sports-related injuries [1]. Various agencies are involved in the surveillance and epidemiologic data on sports-related injuries. National Health Interview Survey is one such agency that collects data for the National Center for Health Statistics (NCHS) [2]. Musculoskeletal injuries are one of the primary reasons that patients seek medical attention in
the out-patient family practice setting [3]. Throughout the United States, a large portion of emergency department (ED) visits is following acute sports-related injuries [4]. Approximately 3.7 million sports-related injuries occur in people of all ages and each year about 2.5 million ED visits resulting from sports injuries occur in the pediatric population [4].

The use of nonsteroidal anti-inflammatory drugs (NSAIDs) for pain from musculoskeletal injuries is well known and extensive [3]. Musculoskeletal injuries include injuries to muscle, ligaments, tendons, and non-fracture injuries. Treatment of such injuries is generally geared toward reducing the swelling and pain by using methods such as cold compression and an anti-inflammatory agent [5]. Typically, the use of NSAIDs is due to their anti-inflammatory, analgesic, and anti-pyretic properties. The basis of the pharmacological action of NSAIDs is their ability to inhibit cyclooxygenase (COX) enzymes thereby blocking the formation of certain prostaglandins (PGs). Besides reducing the inflammation, this inhibition of PG synthesis may potentially result in serious side effects such as gastrointestinal disturbance and altered renal function [3,6]. Cyclooxygenase-2 (COX-2) inhibitors such as Rofecoxib (Vioxx™) were popular analgesics especially in the last decade. This was because they do not inhibit the beneficial effects of PG’s, and thus have fewer side effects on the gastric mucosal lining. They also do not affect bleeding time and platelet function [6]. Because of serious cardiovascular side effects reported with the use of COX-2 inhibitors, some of these products were withdrawn from the US markets in 2004 [7].

Due to non-availability of topical form of analgesics in the US market, and because of the negative side effects from a systemic non-steroidal anti-inflammatory drug, an alternative delivery method such as topical can be utilized. A topical route of NSAIDs has the benefit of superior local drug delivery. At the same time the systemic side effects that may arise from oral NSAIDs are reduced by using the topical route [5]. A sufficiently high concentration of the drug is necessary to penetrate the skin, muscles, and synovial fluid and this is seen when an NSAID is topically administered. In addition to this benefit, the topical form also allows a constant and slow release of the drug [5].

We conducted a literature search using PubMed and included terms such as “topical NSAIDs”, “oral NSAIDs”, “sports injuries”, “musculoskeletal injuries”, and “pain management.”

Through the synopsis of articles below, this review attempts to emphasize the effectiveness of NSAIDs on pain from acute musculoskeletal sports injuries. It also addresses the use of a topical route as an effective and safe method for NSAID delivery.

**DISCUSSION**

Sports-related injuries that involve the ligaments, muscle, tendons, and bones are fairly common in sports activities. Some studies indicated that there has been a considerable increase in such injuries due to an increased involvement in sports activities [1,4].

Non-steroidal anti-inflammatory drugs are used frequently in pain management of musculoskeletal sports injuries [5]. In a randomized controlled trial (RCT) done in an ED setting on patients 6-17 years, who had sustained a musculoskeletal sports injury, an oral non-steroidal, Ibuprofen, was compared with Acetaminophen and Codeine [8]. Patients in the Ibuprofen group showed significant improvement compared to the other two groups, as
demonstrated on the Visual Analog Scale (VAS). There was twice as much decrease in pain (24 mm versus 12 mm or 11 mm) on this scale (p<0.001). The effectiveness of NSAIDs is due to their mechanism of action that causes inhibition of prostaglandins at the injury site. Oral NSAIDs, when administered in such a situation achieve a relatively higher drug level systemically [3,6]. Although this may result in relief of pain symptoms, it may potentially lead to serious side effects such those on gastro protection and renal function. They may also interfere with coagulation mechanisms [9].

There are various routes by which NSAIDs can be delivered. One option is to use the topical route. Topical NSAID’s when applied to an inflamed area results in local drug delivery and fewer systemic side effects from high plasma drug levels. One multicenter controlled clinical trial published in the year 2000 compared the effectiveness of the topical Diclofenac Sodium patch to a placebo in patients who had sustained a sports-related injury. Out of the two weeks of treatment, the daily pain relief on days 3, 7, and 14 was superior in the Diclofenac group (p=0.044). Another double blinded RCT conducted in Europe compared the Diclofenac patch to a placebo patch, reported significant (p<0.0001) pain relief in adult patients who sustained an acute impact sports injury and those who received the active drug [5]. This study also reaffirmed the safety and reduced systemic side effects from use of a topical form of an NSAID. Local side effects such as rash or itch occurred similarly in both active as well as inactive patch [5]. Another study (randomized double blinded, placebo-controlled) conducted in Europe concluded the efficacy of topical Ketoprofen compared to a placebo in patients who had a benign ankle sprain. This topical NSAID was also tolerated well, with only local side effects [10]. Recently, a prospective, randomized, open study compared two topical agents, Ketoprofen and Diclofenac gel in patients who sustained an acute, benign, sports-related injury. The efficacy of transdermal (TDS) Ketoprofen in relieving pain was comparable to the Diclofenac gel. The TDS Ketoprofen was found to be superior to the Diclofenac gel (64% versus 46%, p=0.004) leading to a high cure rate on day 7 of the treatment [11].

Despite growing evidence that supports the effectiveness of topical NSAID’s in pain relief and minimizing the systemic adverse events, several limitations exist for the type of studies conducted thus far in this area. For example, the randomized controlled clinical trials have compared a placebo over a topical form of NSAID to examine the effectiveness and safety profile. While placebo controlled studies are usually preferred to compare the effectiveness of a new drug, it may affect the standard of care for some of the patients. In addition, not many studies have been done exclusively in the pediatric population. Data from the studies done in adults may help researchers conduct clinical trials in children.

Topical Diclofenac Sodium formulation is available for use in Europe and other countries [5]. In the United States, Diclofenac is available as an oral as well as a topical form. The topical application is a 3% gel that was FDA-approved for Actinic Keratosis in 2002. As of October 2007, the topical Diclofenac Sodium patch was in its Phase 1 clinical study, which is being conducted by Cerimon Pharmaceuticals [12]. Numerous clinical trials in the United States are currently undergoing that are looking at the use of topical NSAID for breast pain and osteoarthritis [13]. The efficacy of topical non-steroidal anti-inflammatory drugs over a placebo has been noted in various trials involving acute sprain injury as well as chronic conditions such as rheumatoid arthritis [14]. Once approved, the topical form of anti-inflammatory drugs is likely to revolutionize the standard of care in pain management of acute benign sports-related musculoskeletal injuries. The use of topical non-steroidal drugs
for chronic pain will also be of particular advantage in the elderly population due to their safety profile (14).

REFERENCES


