

## Background

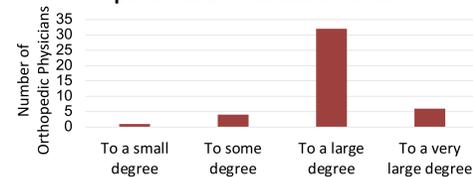
- Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used for pain relief and inflammation.
- NSAIDs are often administered after injury to minimize the athlete's pain level or soreness and shorten the time they are left out of competition.
- Additionally, NSAID use has increased over time (Table 1), and many healthcare professionals (HCPs) state that the efficacy of NSAIDs encourages their prescribing of these medications (Figure 1).
- However, many HCPs do not consider how NSAID therapy may negatively affect the body's long-term healing processes. Others have recently started questioning if NSAIDs may affect the body's natural healing processes.

**Table 1: Change in NSAID Use in the USA Over Time**

	All NSAIDs		Prescription NSAIDs	
	NHANES III (1988-1994) N=16,533 % (SE)	NHANES (1999-2004) N=13,744 % (SE)	NHANES III (1988-1994) N=16,533 % (SE)	NHANES (1999-2004) N=13,744 % (SE)
NSAID User	16.6 (0.6)	26.1 (0.8)	15.9 (0.7)	9.5 (0.4)
NSAID Non-user	83.4 (0.6)	73.9 (0.8)	84.1 (0.7)	90.5 (0.4)

**Table 1:** The table above describes changes in NSAID use over time in the USA, as assessed by the National Health and Nutrition Examination Survey (NHANES).

**Figure 1: Rating of the Importance of Factors for Prescribing NSAIDs Among Orthopedic Physicians (N=45): Importance of Medication Effect**



**Figure 1:** This bar chart describes orthopedic physician ranking for factors of importance in prescribing NSAIDs. Of 45 physicians, 32 said NSAID efficacy has a "large effect" on their prescribing trends, and six said it has a "very large" effect.

## Objective

The objective of this poster is to review current standards of treatment following athletic injuries based on published guidelines, and to gather data through electronic databases in order to analyze qualitative and quantitative research on NSAID use following injuries related to physical exercise and recovery.

## Methods

- A literature search was performed utilizing PubMed and Medline (OVID). Additionally, the references mentioned in each article were reviewed to identify additional sources.
- The search was limited to publications in English and Human Populations.
- Search terms included "Anti-inflammatory Agents, Non-steroidal/ae, tu," "Exercise/," "Muscle, Skeletal/de, in," and "Athletic Injuries/".
- Results from the literature search were investigated for effects of various NSAIDs on recovery from exercise-related injuries.

## Results

**Table 2: Summary of Protocols and Results from Literature Search**

Drug	Protocol	Results
Diclofenac	Subjects were assigned to take oral diclofenac, suprofen, or placebo, three times daily over a period of one week.	Diclofenac was determined to be more effective than suprofen and placebo in all endpoints including motility, swelling, and pain.
	The subjects were randomly allocated to one of three treatment regimens and were dosed for seven days. All subjects had suffered a mild to severe unilateral ankle sprain on the same day or within the previous 24 hours.	Diclofenac was shown to be statistically significant at lowering pain at rest compared with placebo group after day two and three. Diclofenac's ability to decrease pain experienced while walking after one and two hours, and after day two and day three was also supported. Diclofenac showed no change in treatment for the volume of the injured foot when compared with placebo.
Naproxen	Subjects completed ten sets of seven to ten eccentric actions with each quadriceps femoris with a load equal to 85% of the eccentric one repetition maximum followed by ten days of naproxen sodium or placebo.	The results suggest naproxen improved recovery after eccentrically biased exercise.
	Men and women consumed naproxen sodium or placebo after performing 64 unilateral eccentric (ECC) knee extensions using 75% of each ECC 1-repetition maximum.	The results showed concentric strength loss was greater in the placebo group than NSAID, isometric strength declined less for NSAID, and thigh soreness was greater for placebo. The study concludes that naproxen decreased muscle injury, strength loss, and soreness following ECC exercise.
Indomethacin	14 healthy male endurance athletes ran 36 km and were divided into two groups to receive either 100 mg indomethacin per day or placebo. The muscle biopsies were collected before the run and on days one, three, and eight.	There was no increase in the number of satellite cells for individuals who consumed NSAIDs, meanwhile, the placebo group showed a significant difference at day eight. This suggests that NSAIDs have a negative regulatory effect on the various stages of myogenesis and regeneration.
	Male distance runners completed two one-hour treadmill runs where one trial was preceded by 48 hours of oral indomethacin dosing or no treatment.	The dosing of oral indomethacin for 48 hours did not affect natural cell-mediated cytotoxicity (NMC) before or after one hour of high-intensity running exercise. The drug also did not affect NMC as determined by whole blood or isolated PBMC assay methods.
Ibuprofen	19 subjects performed the eccentric leg curl exercise. Subjects in the ibuprofen group (N=9) were administered 400 mg of oral ibuprofen every eight hours within a 48-hour period. Placebo was administered to ten subjects.	The ibuprofen group showed a significantly lower value of muscle soreness after 24 hours as well as a lower value of creatine kinase level after 48 hours. This study demonstrates that intake of ibuprofen cannot assist in restoring muscle function but can decrease muscle soreness.
	12 males and 6 females (average age 24 years) were assigned to train each side of the biceps on alternate days. The subjects received 400 mg of ibuprofen immediately after training on one arm and placebo on the alternate arm.	It was determined that there was no effect on muscle hypertrophy and strength. There was no difference between placebo and ibuprofen in terms of muscle soreness following the first week.

**Table 2:** This table elaborates some main research findings from the comprehensive literature search. Listed within the table are studies that discuss the effects of diclofenac, naproxen, indomethacin, and ibuprofen on various clinical endpoints. These studies offered mixed conclusions about the results of NSAIDs following an athletic injury.

## Results (Cont.)

Diclofenac was determined to help with pain, swelling, and motility, but did not affect the volume of the injured foot in one study. Naproxen was suggested to have effects on recovery after exercise and decreased overall muscle soreness.

Satellite cells are crucial for skeletal muscle adaptation to exercise by contributing to hypertrophy and repairing myofibers. Additionally, NCMC cells are thought to be repressed by long bouts of exercise. The studies concluded that indomethacin did not affect NCMC but did decrease the number of satellite cells, suggesting negative effects on regeneration with administration.

Conclusions from the ibuprofen studies were mixed, with one study concluding ibuprofen lowered muscle soreness following exercise, while the other stated there was no difference following one week.

## Limitations

- Randomized, controlled trials featured very small patient populations.
- Limited data and lack of recent studies, especially for indomethacin, which may lead to questioning of the prescribing of NSAIDs for athletic injuries.

## Conclusions

Results demonstrated a common trend in the decreased perception of muscle soreness following NSAID use. These effects, however, may only be relevant for the first few days of treatment. The results of NSAIDs on muscle regeneration and the anti-inflammatory pathway across studies are varied. Still, data suggests that the COX pathway does play a role in normal satellite cell activity, which affects muscle regeneration. Overall, prescribers should consider short-term NSAID use in patients to relieve muscle soreness, but the role of long-term use may need to be reassessed. Given the small number of participants in these studies, it may be beneficial to increase the number of subjects in future studies.

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