Effect of Ibuprofen Use on Delayed Onset Muscle Soreness of the Elbow Flexors

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Abstract:
This study evaluated the effectiveness of ibuprofen in treating delayed onset muscle soreness (DOMS) of the elbow flexors when taken prior to and following exercise. Twenty subjects receive either 2,400 mg/day ibuprofen or a placebo four times per day. Subjects performed intense eccentric exercise of the elbow flexors to elicit DOMS. Concentric and eccentric peak torque production against an isokinetic resistance of 0.52 rad/s, range of motion at the elbow, and subjective soreness of the elbow flexors were measured. ANOVA indicated no significant group-by-time interaction for concentric peak torque, eccentric peak torque, or pain. A significant interaction was revealed for range of motion. There was a significant difference within each group's ROM but no interaction between groups. It was concluded that the use of 2,400 mg/day ibuprofen prior to and following intense eccentric exercise was no more effective than a placebo in treating DOMS of the elbow flexors.

Article:
Nonsteroidal anti-inflammatory drugs (NSAIDs) are increasingly being utilized as a therapeutic modality to treat athletic injuries. The most common athletic injuries, that is, sprains, strains, and contusions, are frequently characterized by inflammation and pain, and NSAIDs are often used to minimize these characteristics. Because NSAIDs act primarily through the inhibition of an enzyme-mediated pathway of prostaglandin production, they are used to alter the inflammatory response underlying prostaglandin synthesis (18).

The NSAID ibuprofen, in addition to altering prostaglandin production, also exhibits analgesic effects (13, 18, 19) and is used for mild pain relief. While not as potent as some of the NSAIDs in the same class, such as naproxen (Naprosyn), ibuprofen is an effective anti-inflammatory agent because it inhibits cyclo-oxygenase activity (1, 3, 14, 18, 20). Cyclo-oxygenase is the primary mediator in the metabolism of arachidonic acid, a phospholipid present in cell membranes that is released during cell membrane disruption. This metabolic process yields prostaglandins as a product (4, 18). Prostaglandins, along with another cyclo-oxygenase product, prostacyclin, play the primary roles in inflammation as both are potent vasodilators and pain-producing agents (18).

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With respect to inflammatory-characterized pathologies, Smith et al. (20) reported that arthritic patients treated with ibuprofen had reduced joint swelling, pain, and duration of morning stiffness as well as increased strength and time to onset of fatigue. In a study of athletic injuries, Muckle (19) showed that professional soccer players suffering from comparable soft tissue injuries were able to return to competition an average of 3 days earlier when taking 2,400 mg/day ibuprofen than when taking 3,600 mg/day aspirin. Bourne (2) showed that of 55 athletes suffering from similar grades of acute athletic injuries, 14 of 28 subjects receiving ibuprofen were able to resume activity within 2 days following injury and only 5 of 27 subjects receiving an analgesic (paracetamol) were able to return within 2 days of injury.

A combination of clinical symptoms that often occur subsequent to muscle injury and that are often treated with nonprescription NSAIDs is termed delayed onset muscle soreness (DOMS). Although temporary, DOMS is often a very debilitating condition that can adversely affect performance or discourage activity altogether. The response of muscle tissue to exercise, especially eccentric action of high intensity or prolonged exercise, is initially catabolic (8, 9, 21). Theoretically, the immediate breakdown of the tissue structure could be treated using NSAID therapy in an effort to reduce the inflammatory response that follows muscle tissue damage at the cellular level. The extent of exercise-induced damage and the subsequent inflammatory response depends upon the type, intensity, and duration of exercise. Eccentric contraction of a muscle against resistance produces more damage to the muscle fiber than does concentric exercise (21). Eccentric contraction is also cited as the primary cause of exercise-induced muscle soreness and DOMS (6, 9, 21).

Physiological characteristics of muscle damage, such as soreness, swelling, decreased range of motion, and decreased strength, have traditionally been treated therapeutically with various modalities (e.g., cryotherapy, heat, exercise, massage, etc.). It is also common for the clinician to recommend NSAIDs to decrease the magnitude of these characteristics. Investigation into the effects of ibuprofen on the symptoms associated with muscle damage has been minimal. Hasson et al. (15) found that independent groups taking either 400 mg ibuprofen three times per day beginning 4 hr prior to exercise or a group taking 400 mg ibuprofen three times per day beginning 24 hr after exercise experienced significantly less pain 48 hr postexercise and a significantly smaller decline in muscular strength 48 hr postexercise compared to a control group and a placebo group. In contrast to these findings, Donnelly et al. (6) found that ibuprofen did not differ from a placebo in the treatment of pain and decreased muscular strength and endurance associated with DOMS in the quadriceps through 72 hr postexercise.

The purpose of this study was to determine if a 2,400 mg/day dosage of ibuprofen prior to and following exercise would alter the subjective pain, decreased range of motion, and decreased muscle strength associated with delayed onset muscle soreness.

METHODOLOGY

Subjects
Ten male and 10 female healthy subjects (22.1 ± 6.9 years, 172.5 ± 10.3 cm, 66.8 ± 19.5 kg) were recruited to participate in this study. None of the subjects had a known allergy to aspirin or ibuprofen, had performed upper body weight training within the previous 6 months, or were experiencing pain in the arms. The DOMS-inducing exercise protocol was thoroughly explained
to all subjects and they read and signed an informed consent form approved by the University of Virginia Human Investigation Committee. The subjects were asked to refrain from using any medications or other therapeutic modalities for the duration of the study.

Subjects were assigned on a double-blind basis into two groups of 10 subjects. Randomization resulted in one group (control) consisting of 8 males and 2 females, the other (experimental) of 8 females and 2 males. The experimental group received 2,400 mg/day ibuprofen (600 mg four times per day) for 5 days; the control group received an identical-appearing placebo that was taken four times per day for 5 days. Ingestion of ibuprofen or the placebo began at 0 hr and was followed 24 hr later by a pretest to determine concentric and eccentric elbow flexor peak torque, elbow range of motion (active elbow extension), and subjective soreness felt in the elbow flexor muscles. Immediately following the pretest, each subject completed an intense eccentric exercise session that induced DOMS.

**Testing Protocol**

**Peak Torque.** Concentric and eccentric peak torques (PT) were measured on a Kin Com isokinetic dynamometer (Chattex Corporation, Hixon, TN) against a set velocity of 0.52 rad/s (30°/s). Each subject was seated with the nondominant arm positioned at approximately 70° shoulder flexion and 45° elbow flexion. After a familiarization protocol and a 2-min rest period, subjects were asked to maximally contract the elbow flexors concentrically through a 45° to 120° arc of active elbow flexion. Subjects were given a brief rest and were instructed to maximally contract eccentrically against the resistance arm's movement back to the 45° starting position. This two-contraction sequence was performed three times. The three concentric and the three eccentric curves were then independently averaged to produce individual average torque curves for concentric and eccentric contractions. The highest value of each curve was used as the PT value for data analysis. Because of the mixed-gender subject pool and the unequal distribution of males and females in the two groups, peak torque was expressed as Newton-meters per kilogram of body weight to minimize the effect of absolute strength differences that are normally present between genders.

**Range of Motion.** Elbow range of motion (ROM) was measured goniometrically by the same researcher throughout the duration of the study. Subjects were seated with the shoulder at approximately 90° flexion and were instructed to actively move the elbow into full extension, either to physiological limitation or to pain tolerance. The measurement of elbow extension on a 360° goniometric scale was then recorded. This procedure was repeated and the two measures were averaged to produce a mean measurement of elbow extension that was used for data analysis.

**Pain.** Subjective soreness was measured at the same time ROM was evaluated. Upon reaching full elbow extension, the subject indicated the degree of pain experienced on a visual pain scale (5). The pain scale was a 10-cm horizontal line that represented a pain continuum. The left end of the line represented no pain and the right end represented *unbearable pain*. No other descriptive labels were placed on the line. Each subject marked the pain scale to indicate how much pain was felt relative to the two descriptive terms. A new visual pain scale was used for each test period. Each subject's mark was then measured from the left end to the nearest 1/2 cm, with this measurement being used for data analysis.
Exercise Protocol
The exercise protocol that was used to induce DOMS consisted of eccentric resistive exercise to relative exhaustion. Each subject stood with arms to the sides while a researcher placed a 11.34-kg dumbbell in the nondominant hand. The researcher then raised the dumbbell to the fully flexed elbow position. The researcher released the dumbbell and instructed the subject to lower the weight in a controlled manner over 3 s to full elbow extension. The researcher then raised the weight to the flexed-elbow position and the eccentric contraction was repeated. This process continued until the weight could not be controlled for 3 s, at which time the weight was reduced by 2.27 kg. The 9.07-kg dumbbell was used until it could not be controlled over 3 s and was then replaced with a 6.80-kg dumbbell, and so on. This continued until either the subject could not control a 2.27-kg dumbbell over the 3-s time period or the subject completed 30 repetitions with the 2.27-kg dumbbell.

Statistical Analysis
Concentric PT, eccentric PT, ROM, and pain were measured at the 24 hr pretest, 48 hr following the exercise protocol (time = 72 hr from beginning of ingestion), and 96 hr after the exercise protocol (time = 120 hr). Four repeated-measures ANOVAs were used to analyze the data with Tukey post hoc tests used to test differences between means. Alpha levels were set at .05 for all statistical tests.

RESULTS
Repeated-measures ANOVA showed no significant group-by-time interaction for concentric PT, eccentric PT, or subjective soreness (p < .05). There was, however, a significant main effect across time for concentric PT (p < .001), eccentric PT (p < .001), and subjective soreness (p < .001). A significant group-by-time interaction was found for range of motion (p = .007). A Tukey post hoc test revealed a within-group effect (p < .05) from the 0 hr to 48 hr time period for both the treatment group and the placebo group but did not reveal a difference between groups (Table 1).

Concentric PT deficiencies at 48 and 96 hr for the placebo group were 36.1% and 23.1% of the pretest value, respectively, and treatment group deficiencies were 49.2% and 36.2%, respectively (Figure 1). Eccentric PT deficiencies at 48 and 96 hr were 40.0% and 21.8% of pretest values, respectively, for the placebo group and 50.0% and 37.7% of pretest values, respectively, for the ibuprofen group (Figure 2). Subjective soreness experienced at 48 and 96 hr for the placebo group was 4.4 and 1.45 (on a 0 to 10 scale), respectively, and for the treatment group was 5.70 and 3.65, respectively (Figure 3). Decrements in elbow ROM (from active full extension) at 48 and 96 hr for the placebo group were 22.6 and 10.6°, respectively, and for the ibuprofen group 15.7 and 23.4°, respectively (Figure 4).

| Table 1 Analysis of Variance Statistical Summary |
|-------------------------------|-----|-----|-----|-----|-----|
| Source of variation          | SS  | DF  | MS  | F   | P   |
| Concentric peak torque       |     |     |     |     |     |
| Group                        | .12 | 1   | .12 | 4.40| .050|
| Error                        | .50 | 18  | .03 |     |     |
Within groups
Time
Group-by-time
Error
Eccentric peak torque
Between groups
Group
Error
Within groups
Time
Group-by-time
Error
Subjective soreness
Between groups
Group
Error
Within groups
Time
Group-by-time
Error
Range of motion
Between groups
Group
Error
Within groups
Time
Group-by-time
Error
DISCUSSION
The major finding of this study was that a comparison between ibuprofen and a placebo revealed no significant group-by-time interactions for concentric PT, eccentric PT, or pain. This indicates that there was no statistically significant difference between the ibuprofen group and the placebo group for any of these three testing parameters at either of the two posttests (48 and 96 hr postexercise). The significant main effect across time for these three parameters indicates that the total subject pool had different PT values at 0, 48, and 96 hr and perceived differing degrees of pain at 0, 48, and 96 hr.

The decrease in strength and increase in perception of pain for all subjects were expected as part of the DOMS model used in this study. Subjects were expected to experience more pain 2 to 4 days after exercise than they did before exercise. Based on previous studies (6, 15, 21), we expected peak torque to be less at 48 and 96 hr after exercise than before exercise.

Concentric PT decreased in both groups, but neither the ibuprofen nor the placebo group decreased significantly more than the other. Evaluating the concentric PT of the entire test population, we found a mean deficiency of 42.7% at 48 hr and 29.7% at 96 hr. Eccentric PT exhibited similar results of decreased PT at 48 hr (45.0%) and 96 hr (29.8%). The deficiencies of concentric and eccentric PTs illustrate the main effect across time. There was a significant decline in PT at 48 hr and 96 hr relative to the pretest for the entire population, but one group did not show a greater deficiency. These results differ from the
findings of Hasson et al. (15), where concentric PT and eccentric PT deficiencies were significantly less in a group receiving prophylactic ibuprofen (n = 5) and a group receiving therapeutic ibuprofen (n = 5). Hasson et al. used both males and females, creating unequal distribution of each gender into each group; when the researchers evaluated quadriceps strength, they measured absolute isometric force production, thus ignoring the absolute strength difference between men and women. Although randomization resulted in an unequal distribution of males...
and females into our test groups, we measured muscular strength relative to body weight (Newton-meters per kilogram body weight); thus, any differences should have been minimized. Hasson et al. monitored test parameters only up to 48 hr postexercise and did not report limitations on activities of daily living.

Donnelly et al. (6) tested isometric quadriceps strength in 32 subjects receiving 2,400 mg/day ibuprofen or a placebo. Through 72 hr after a DOMS-inducing exercise program, isometric quadriceps strength never decreased more than 10%. The authors found no significant difference between the ibuprofen or placebo group and reported that strength returned to normal levels by 72 hr postexercise. The quadriceps muscle group was used in Donnelly et al.’s study and no activity limitations were reported. Like Hasson et al., Donnelly et al. evaluated muscular strength by measuring voluntary contraction of the quadriceps. Perhaps the greatest factor underlying the characteristic strength deficiency is muscular soreness. This soreness will intensify when the affected muscle fibers must change length during contraction, stretching, or a combination of both. Because of this, we believed that muscular strength evaluation through a dynamic ROM would show greater strength deficiencies than isometric strength testing.

Our results are similar to Donnelly et al.’s in that no difference was found, but our subject population still showed a significant strength deficiency 96 hr postexercise, which may be due to a limitation on use of the affected arm and/or our evaluation of muscular PT through a 75° ROM.

To our knowledge, the long-term effects of ibuprofen use in the treatment of soft tissue injury have not been investigated in the athletic population. By isolating a target muscle group and inducing an inflammatory response subsequent to injury, it is possible to investigate the effects of an NSAID on recovery time following injury. To maintain maximal control over the study, the muscle group should not undergo any other treatment and, if possible, should be immobilized.
By using the nondominant arm and by isolating the elbow flexors, we maintained control over the postexercise recovery period in hope of minimizing use of the affected muscle.

ROM was actually a function of subjective soreness in this study. Subjects were asked to actively extend the elbow to physiological limitation or to pain tolerance. Because no subject recovered full extension (relative to pretest values) by 96 hr, pain undoubtedly played a role in ROM limitation. Joint stiffness and decreased mobility are common following muscle injury, and movement may be discouraged more by the stiffness than by pain, but the subjects were extending the elbow to the point that any further extension would be too painful; thus, ROM was a function of how much pain subjects were experiencing. If ibuprofen did function as an analgesic agent in this study, it would be expected that ROM would have increased in the ibuprofen group. As an analgesic, ibuprofen can decrease the magnitude of pain felt but probably cannot elicit total relief. Thus,

![Graph](image)

Figure 4 — Mean range of motion in degrees of elbow extension and standard deviations. *Mean for ibuprofen group at 0 hr > mean at 48 hr (p < .05). †Mean for placebo group at 0 hr > mean at 48 hr (p < .05).

there would still be a point of pain toleration, or a point at which the stimuli would elicit pain. Under the influence of an analgesic, this toleration point would likely be found at a greater magnitude of painful stimuli (i.e., increased stretch of the affected muscles). The two groups were expected to report similar amounts of pain because they were asked to extend the elbow to pain tolerance, and if ibuprofen was effective in reducing pain, the experimental group’s ROM at absolute pain tolerance should have been greater than that of the placebo group. The ibuprofen probably did provide mild pain relief in the subjects, but we were assessing subjective soreness during a dynamic activity. We did not measure subjective soreness at a resting position, which may have shown a decrease in perceived pain. We viewed movement of the arm as a form of therapy following injury and thus tried to minimize use of the arm. Repeated movement, either active or passive, especially to the end range of motion likely would influence the tolerable range of motion while testing. Unlike the researchers investigating subjective soreness of the anterior thigh (quadriceps) in which walking or stair climbing would utilize active contraction and stretch
of the muscles, we attempted to isolate a target muscle group that did not have to be used often during activities of daily living.

There was no difference, however, between the two groups. Like the PT results, there was a significant deficiency in ROM at 48 hr (19.3°) and 96 hr (17.00), which illustrates the expected main effect across time. We expected ROM to decline up to approximately 48 hr and then approach pretest values. There was negligible improvement of ROM from 48 hr to 96 hr for the entire population (Figure 4).

Further investigation into the long-term effects of ibuprofen on tissue healing and recovery is needed. None of the values recorded at 96 hr equaled pretest values for any of the four test parameters. Thus, physiological processes were still occurring as recovery continued. Investigation needs to be conducted well past the 96 hr time period, because the inflammatory response following exercise can last more than 3 weeks (9).

Additionally, research needs to be directed at the effects of ibuprofen and NSAIDs on the effects of healing. NSAIDs are known to interfere with chemotaxis of monocytes as well as inhibit neutrophil aggregation (14). Monocytes produce cytokines, which are responsible for most of the physiological responses accompanying injury, and neutrophils produce elastase and collagenase, which increase vascular permeability via degradation of the vasculature and healthy tissue near the injury site (9). It is possible that the use of NSAIDs may impair and lengthen the healing process. More research should also be directed at dose-specific effects. It is likely that the potential impact of NSAIDs on healing time is dose dependent and that the small dose in this study would have a minimal impact on healing.

Decreased muscular strength, decreased joint ROM, and pain have all been linked to DOMS (6-8, 10-12, 16, 17, 21), and this study supports the evidence that each results from intense eccentric exercise. As found in most studies involving induced DOMS, peak values occurred at approximately 48 hr postexercise and, except for ROM in the ibuprofen group, approached pretest values thereafter. The design of this study was strengthened by the fact that relative immobilization of the injured muscle was achieved by using the nondominant arm, thus minimizing the effects of daily living activities. It is advised that future investigations include a control group. A placebo, although used to represent a "nondrug" or control group, can also elicit altered posttest performance values. Therefore, a control receiving no treatment should be used to determine if any placebo effects occur.

The dosage of ibuprofen used should be carefully determined to minimize side effects and to attempt to standardize the dosage that is active at the site of injury. We used 2,400 mg/day ibuprofen because this is generally considered the highest recommended dosage to be administered without a physician's prescription. The FDA recommends a daily dosage of ibuprofen of 30-40 mg/kg body weight/day (18). This may be more applicable to a mixed gender study, as a subject of low body weight will probably receive much different effects from a fixed 2,400 mg/day dosage than a subject of high body weight.

In conclusion, we found that a 2,400 mg/day dose of ibuprofen taken before and following exercise had no significant effects compared to a placebo in the treatment of DOMS of the elbow.
flexor muscles. There is a need for further research investigating the long-term effects of NSAIDs on soft tissue healing.

REFERENCE