Retrospective Review

Does nabumetone enhance recovery times in the setting of work-related musculoskeletal injury?

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Date of submission: 12 January 2016 , Date of Publication: 23 March 2016

Abstract:

Background: NSAIDs are a key component in the management of work related musculoskeletal injuries in occupational medicine practice. Nabumetone has been reported to be a more potent NSAID in the occupational setting in comparison to ibuprofen. We undertook this study to determine whether nabumetone may improve recovery times in patients suffering from work related musculoskeletal injuries.

Objective: To determine whether early treatment with nabumetone shortens recovery times in patients suffering from work related musculoskeletal sprains and strains in comparison to ibuprofen.

Methodology: 67 patients suffering from work related musculoskeletal sprains and strainsthat were treated in the occupational medicine practiceover a predetermined date interval were randomly selected. Retrospective chart review determined the average recovery time in days for those patients treated with nabumetoneand the average recovery time for those patients treated with ibuprofen.

Results: For patients treated with nabumetone or ibuprofen, the mean recovery time from initial worker's compensation claim to discharge was 46 days and 68 days, respectively. The findings suggest that nabumetone may provide a 32% enhancementin recovery time compared to ibuprofen.

Limitation: This was not a prospective study, rather a retrospective chart review. The study is limited by small sample size, a lack of uniformity among patients,andlack of attention to the side-effect profiles of the medications.

Conclusion: There was a significant enhancement in the recovery times of patients treated with nabumetone. This suggests that there may be a role of nabumetone in the early and aggressive treatment of musculoskeletal injuries in the occupational setting.

Key words: nabumetone, musculoskeletal, occupational, work-related, ibuprofen

Introduction:

The use of non-steroidal anti-inflammatory medications is a key component of the treatment of work-related musculoskeletal strains and sprains. Choosing which non-steroidal anti-inflammatory medication to use in the proper clinical setting can be challenging. The purpose of this project was to determine whether early and aggressive treatment with nabumetone can enhance recovery times for work-related sprains and strains in comparison to early treatment with ibuprofen. Anecdotal clinical experience at some occupational clinics suggests that nabumetone may have more potency in comparison to ibuprofen. However, there have been

no systematic studies done to support this claim. The belief that nabumetone may have greater potency stems from its slightly different chemical structure and mechanism of action, as well as anecdotal reports of affirmative clinical experience. For example, it is the practice pattern of some occupational medicine physicians in the United States to treat patients unresponsive to ibuprofen with a trial ofnabumetone.

Methodology:

67 patients suffering from work related musculoskeletal sprains and strains that were treated in the occupational medicine practice over a predetermined date interval were randomly selected. A retrospective chart review was approved by the institutional review board of the Loma Linda University Medical Center. Using a retrospective chart review, we determined 1) the average recovery time in days for those patients treated with nabumetone at a dose of 500 mg by mouth twice daily within the first week of their presentation and 2) the average recovery time for those patients treated with ibuprofen at a minimum dose of 600 mg by mouth twice daily in the first week of presentation. No attention was paid to past surgical history or ethnic background. The patients included in the study were between the ages of 25 and 67 with an approximately equal distribution of males and females. Patients who were treated with both nabumetone and ibuprofen during the same claim were excluded from the study. Patients who had reached maximum medical improvement or who failed to achieve remission of pain prior to discharge were also excluded. The results were then analyzed for statistical significance.

Those patients who met the inclusion criteria of taking nabumetone at a miminum dose of 500 mg by mouth twice daily within the first week of their workers compensation claim or ibuprofen at a minimum dose of 600 mg by mouth twice daily within the first week of their workers compensation claim were identified and recorded. The date of initial consultation and date of discharge were then ascertained via retrospective chart review. These dates were recorded, allowing us to develop a quantitative measurement of approximate recovery time based on the data of onset of injury to date of pain remission and discharge.

Statistical analysis:

The 2-tailed p value was calculated at 0.03. Despite the small sample size of the data, the 2-tailed p value suggests that the data is statistically significant. The data suggests a 32% enhancement in recovery time for patients treated with nabumetone in preference to ibuprofen for work-related musculoskeletal sprains and strains (95% CI=2.28-41.72).

Results:

24 patients treated with nabumetone within the first week of presentation were identified within the predetermined project date interval. The mean recovery time for these patients from initial worker's compensation claim to discharge was 46 days (range 6-120 days). 43 patients treated with ibuprofen within the first week of presentation were identified within the predetermined project date interval. The mean recovery time for these patients from the initial worker's compensation claim to discharge was 68 days (range 5-153 days). The findings suggest that nabumetone may enhance recovery times in the occupational setting for sprains and strains.Stated differently, the data suggest an overall 32% enhancement in recovery time when the patient is treated early and aggressively with nabumetone in preference to ibuprofen (2-tailed p value = 0.03; 95% confidence interval 2.28-41.72).

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Discussion:

The vast preponderance of musculoskeletal work-related injuries can be divided into certain major categories. These include sprains, strains, and contusions. Historically, the early and aggressive use of NSAID medications has been an important component in the treatment of sprain and strain injuries in order to hasten recovery and the patient's return to work. In addition to short-term recovery benefits, NSAIDs have been shown to have anti-inflammatory properties that impair osteoarthritic changes and joint degeneration in animal models. It has been theorized that the short-term analgesic and anti-inflammatory properties coupled with the long-term anti-arthritic properties of non-steroidal anti-inflammatory medications result in faster recovery times and diminished long-term disability. This has potential benefits for both patients and employers in the occupational setting (4-9. 13).

There has been some concern about several unwanted side effects of non-steroidal anti-inflammatory medications. These include the relatively common side effect of gastric inflammation, as well as the well-known contraindication of non-steroidal anti-inflammatory therapy in the setting of congestive heart failure and chronic renal failure. A lesser known theoretical side effect of non-steroidal anti-inflammatory therapy is the possible impairment of long-term healing and muscle regeneration after an acute musculoskeletal injury. This theoretical danger stems from the fact that non-steroidal anti-inflammatory medications are known to reduce the inflammatory response in the acute setting, thus possibly causing a delay in long-term healing. An additional danger of non-steroidal anti-inflammatory treatment in the setting of acute injuries is the potential for increased bleeding due to anti-platelet effects. The risks and benefits must be weighed for each patient in deciding whether non-steroidal anti-inflammatory medications are indicated in the occupational setting for the treatment of musculoskeletal injury (14, 15-17, 21).

Although non-steroidal anti-inflammatory medications are generally considered high caliber recommendations in the United States for the early treatment of musculoskeletal injuries in the occupational setting, choosing which non-steroidal agent to administer is often unclear. Nabumetone has possible therapeutic advantages. Clinical experience suggests that nabumetone has greater potency for patients suffering from work-related musculoskeletal injuries, especially in the acute setting, in addition to a possible diminished incidence of gastrointestinal upset (23, 27-31, 33).

Several studies have shown a lesser side effect profile of nabumetone in comparison to other non-steroidal anti-inflammatory drugs. As an example, nabumetone has been shown to have a lower incidence of gastrointestinal upset than other non-steroidal anti-inflammatory drugs. The reason for this is that nabumetone is a non-acidic prodrug which is then metabolized in the liver to an acidic active metabolite, 6MNA (6-methoxy-2-naphthylacetic acid), which has anti-inflammatory properties. In addition, nabumetone has a lower potential to cause mucosal irritation and has less of an effect on prostaglandin synthesis than other non-selective non-steroidal anti-inflammatory medications. Even more importantly, nabumetone is safer to use in patients with heart failure than other non-steroidal anti-inflammatory medications. Nabumetone also has less interaction with blood pressure medications, making it a safer choice in

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patients with hypertension and polypharmacy (34-37, 39).

Conclusion:

There are several possible reasons why nabumetone may enhance recovery times for muscuskeletal sprains and strains in preference to ibuprofen. The reduced incidence of gastrointestinal upset of nabumetone in comparison to ibuprofen might result in better patient compliance with the treatment regimen, thus improving response to the medication. Conversely, nabumetone may in fact provide more potent anti-inflammatory effects than ibuprofen, another mechanism that could account for our observed difference in recovery times. This implies a use for nabumetone in the early and aggressive treatment of musculoskeletal strains and sprains in the occupational setting. Consideringnabumetone's mechanism of action and side effect profile, it is not surprising that patients on this drug recovered faster. The data suggest an overall 32% enhancement in recovery time when the patient is treated early and aggressively with nabumetone in preference to ibuprofen.

Despite the very small sample size of only 67 patients, the p value demonstrated statistical significance. We believe, in light of our clinical experience, the results of this retrospective review, and nabumetone's favorable side effect profile, that nabumetone should be considered early in the management of patients suffering from work-related musculoskeletal sprains and strains. Starting patients on a regimen of nabumetone at a dose of 500 mg twice daily within the first week of their presentation to the worker's compensation clinicmight produce faster recovery times and a diminished side effect profile.

Study limitation:

This was not a prospective study, rather a retrospective chart review. The study is also limited by a small sample size and a lack of uniformity between the duration of treatment and severity of the initial injury. Another limitation includes a lack of attention to the side-effect profiles of ibuprofen in comparison to nabumetone, information which might impact a given patient's treatment plan. An additional limitation of the study is the lack of differentiation between sites of musculoskeletal injury and treatment response. It is possible that these factors might confound the study results.

References:

1) Samad TA, Sapirstein A, Woolf CJ. Prostanoids and pain: unraveling mechanisms and revealing therapeutic targets. *Trends Mol Med.* 2002;8:390-396.
2) Mehallo CJ, Drezner JA, Bytomski JR. Practical management: nonsteroidalantiinflammatory drug (NSAID) use in athletic injuries. *Clin J Sport Med.* 2006;16:170-174.
3) Lazzaroni M, Porro GB. Management of NSAID-induced gastrointestinal toxicity: focus on proton pump inhibitors. *Drugs.* 2009;69:51-69.
4) Radi ZA, Khan NK. Effects of cyclooxygenase inhibition on bone, tendon, and ligament healing. *Inflamm Res.* 2005;54:358-366.
5) Kawaguchi H, Pilbeam CC, Harrison JR, Raisz LG. The role of prostaglandins in the regulation of bone metabolism. *ClinOrthopRelat Res.* 1995;313:36-46.

6) O'Connor JP, Capo JT, Tan V, et al. A comparison of the effects of ibuprofen and rofecoxib on rabbit fibula osteotomy healing.*ActaOrtho*p. 2009;80:597-605.
7) Bergenstock M, Min W, Simon AM, et al. A comparison between the effects of acetaminophen and celecoxib on bone fracture healing in rats. *J Orthop Traum*a. 2005;19:717-723.
8) Utvåg SE, Fuskevåg OM, Shegarfi H, Reikerås O. Short-term treatment with COX-2 inhibitors does not impair fracture healing. *J Invest Surg*. 2010;23:257-261.
9) Giannoudis PV, MacDonald DA, Matthews SJ, et al. Nonunion of femoral diaphysis: the influence of reaming and non-steroidal anti-inflammatory drugs. *J Bone Joint Surg*. 2000;82B:655-658.
10) Dodwell ER, Latorre JG, Parisini E, et al. NSAID exposure and risk of nonunion: a meta-analysis of case-control and cohort studies. *Calcif Tissue Int.* 2010;87:193-202.
11) Burd TA, Hughes MS, Anglen JO. Heterotopic ossification prophylaxis with indomethacin increases the risk of long-bone nonunion. *J Bone Joint Surg*. 2003;85B:700-705.
12) Sharma P, Maffulli N. Tendon injury and tendinopathy: healing and repair. *J Bone Joint Sur*g. 2005;87A:187-202.
13) Elder CL, Dahners LE, Weinhold PS. A cyclooxygenase-2 inhibitor impairs ligament healing in the rat. *Am J Sports Med.* 2001;29:801-805.
14) Aström M, Westlin N. No effect of piroxicam on achillestendinopathy: a randomized study of 70 patients. *ActaOrthop Scand.* 1992;63:631-634.
15) Dahners LE, Gilbert JA, Lester GE, et al. The effect of nonsteroidalantiinflammatory drug on the healing of ligaments. *Am J Sports Med.* 1988;16:641-646.
16) Ekman EF, Fiechtner JJ, Levy S, Fort JG. Efficacy of celecoxib versus ibuprofen in the treatment of acute pain: a multicenter, double-blind, randomized controlled trial in acute ankle sprain. *Am J Orthop (Belle Mead NJ).* 2002;31:445-451.
17) Slatyer MA, Hensley MJ, Lopert R. A randomized controlled trial of piroxicam in the management of acute ankle sprain in Australian Regular Army recruits. The Kapooka Ankle Sprain Study. *Am J Sports Med.* 1997;25:544-553.
18) Petrella R, Ekman EF, Schuller R, Fort JG. Efficacy of celecoxib, a COX-2-specific inhibitor, and naproxen in the management of acute ankle sprain: results of a double-blind, randomized controlled trial.*Clin J Sport Med.* 2004;14:225-231.
19) Järvinen M, Lehto M, Sorvari T. Effect of some anti-inflammatory agents on the healing of ruptured muscle: an experimental study in rats. *J Sport TraumatolRel Re*s. 1992;14:19-28.
20) Mishra DK, Fridén J, Schmitz MC, Lieber RL. Anti-inflammatory medication after muscle injury: a treatment resulting in short-term improvement but subsequent loss of muscle function. *J Bone Joint Surg*. 1995;77A:1510-1519.
21) Shen W, Li Y, Tang Y, et al. NS-398, a cyclooxygenase-2-specific inhibitor, delays skeletal muscle healing by decreasing regeneration and promoting fibrosis. *Am J Pathol*. 2005;167:1105-1117.

22) Lanier AB, Simpson KJ, Gregory C, et al. Exercise-induced muscle injury and influence of NSAID therapy on kinematics of downhill walking in older adults.*JEPonline*. 2009;12:11-21.
23) Feucht CL, Patel DR. Analgesics and anti-inflammatory medications in sports: use and abuse. *PediatrClin North Am*. 2010;57:751-774.
24) Braund R, Abbott JH. Analgesic choice when treating musculoskeletal sprains and strains. *N Z J Physiother*. 2007;35:54-60.
25) Liu SH, Nguyen TM. Ankle sprains and other soft tissue injuries. Current Opinions in Rheumatology 1999;11:132–7.
26) McGriff-Lee N. Management of acute soft tissue injuries. Journal of Pharmacy Practice 2003;16:51–58.
27) Stovitz S, Johnson R. NSAIDs and musculoskeletal treatment. Physicians and Sports Medicine 2003;31:35–41.
28) Gotzsche PC. Non-steroidal anti-inflammatory drugs. BMJ 2000;320:1058–61.
29) Jarvinen TA, Jarvinen TL, Kaariainen M, Kalimo H, Jarvinen M. Muscle injuries: biology and treatment. American Journal of SportsMedicine 2005;33:745–64.
30) Harvey R. Musculoskeletal disorders: managing sprains and strains. Pharmaceutical Journal 1997;259:292–5.
31) Hertal J. The role of NSAIDs in the treatment of acute soft tissue injuries. Journal of Athletic Training 1997;32:350–8.
32) Tidball JG. Inflammatory processes in muscle injury and repair. American Journal of Physiology. Regulatory, Integrative andComparative Physiology 2005;288(Suppl):R345–53.
33) Peterson GM. Selecting nonprescription analgesics. American Journal of Therapeutics 2005;12:67–79.
34) Wilcox CM, Cryer B, Triadafilopoulos G. Patterns of use and public perception of over-the-counter pain relievers: focus onnonsteroidalantiinflammatory drugs. Journal of Rheumatology 2005;32:2218–24.
35) Mautner K. Nonsteroidal anti-inflammatory drugs and sports injuries: Helpful or harmful? Athletic Therapy Today 2004;9:48–49.
36) McCormack K, Brune K. Dissociation between the antinociceptive and anti-inflammatory effects of the nonsteroidal anti-inflammatory drugs. A survey of their analgesic efficacy. Drugs 1991;41:533–47.
37) Buckwalter JA. Pharmacological treatment of soft-tissue injuries. Journal of Bone and Joint Surgery. American Volume1995;77:1902–14.
38) Orchard J, Best TM. The management of muscle strain injuries: an early return versus the risk of recurrence. Clinical Journal OfSport Medicine 2002;12:3–5.
39) Rahusen FT, Weinhold PS, Almekinders LC. Nonsteroidal anti-inflammatory drugs and acetaminophen in the treatment of an acutemuscle injury. American Journal of Sports Medicine 2004;32:1856–9.
40) Paoloni JA, Orchard JW. The use of therapeutic medications for soft-tissue injuries in sports medicine. Medical Journal of Australia2005;183:384–8.

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