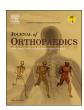
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# Are non-steroidal anti-inflammatory drug injections an alternative to steroid injections for musculoskeletal pain?: A systematic review



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#### ABSTRACT

*Background:* Given the potential side effect profile of steroids, the need for an alternative injectable anti-inflammatory is needed. The purpose of this systematic review was to compare corticosteroid injections with non-steroidal anti-inflammatory drug (NSAID) injections for musculoskeletal pain.

*Methods:* Reviewers with methodological and content expertise searched three databases: PUBMED, Medline and EMBASE. Two blinded reviewers searched, screened, and evaluated the data quality. Data was abstracted in duplicate. Agreement and descriptive statistics are presented.

Results: Four studies were included. All four studies found no statistically significant differences in improvements on the visual analog scale. The follow-up period within the four studies ranged between 2 weeks and 3 months. No statistically significant differences were demonstrated between the two groups with regards to functional outcomes.

*Interpretation:* The studies reviewed, while limited in quantity, show that compared with corticosteroids, NSAIDs provide equivalent, if not better, pain relief from the musculoskeletal ailments assessed. Further, there is weak evidence supporting a lower recurrence rate of symptoms with NSAIDs when compared to corticosteroids. There is a need for more long-term high-quality studies on this topic.

Level of evidence: Level II (Systematic review of Level II and III studies).

#### 1. Introduction

Musculoskeletal pain is one of the most frequent chief complaints seen by family physicians, emergency physicians, and orthopedic surgeons across North America. Corticosteroids are used as a treatment method for a variety of these musculoskeletal pain conditions, varying from subacromial impingement to osteoarthritis. Corticosteroids have anti-inflammatory properties that help to reduce pain. The use of corticosteroids is, however, associated with the risk of serious adverse events. The side-effect profile for corticosteroids consists of: immunosuppression, increased blood sugar for diabetics, facial swelling, weight gain, severe depression, mania, psychosis or other psychiatric symptoms, cataracts or glaucoma, steroid-induced osteoporosis, avascular necrosis, and hepatic steatosis. 2–5

Musculoskeletal corticosteroid injections may help mitigate these risks because they have been associated with fewer adverse events. 6 Corticosteroids, as well as other medications, may be administered

through the intra-articular route to increase the intensity and duration of pain relief. Intra-articular injections of corticosteroids have demonstrated effective pain relief. Nevertheless, they have still been associated with decreased bone strength, tendon atrophy, and tendon rupture, particularly if used on Achilles tendonitis. In addition, post injection flare, skin depigmentation, subcutaneous atrophy, articular cartilage changes and increased blood glucose levels in diabetics make it difficult for diabetics to control their blood glucose, and as a result, systemic effects like osteoporosis may result. 2–5'9–16 Due to the risk of these adverse events, many physicians limit the amount of corticosteroid injections a patient will receive in an affected area. 14,15,17,18

With these extensive side-effects and limitations of use, people may want an alternative. Oral non-steroidal anti-inflammatory drugs (NSAIDs) have been a mainstay of treatment for musculoskeletal pain due to their strong anti-inflammatory properties. <sup>19</sup> When compared to intra-articular steroid injections, oral NSAIDs have demonstrated equal effectiveness in treating pain and movement restrictions in patients

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with adhesive capsulitis.<sup>20</sup> Although NSAIDs are associated with adverse events, such as the risk of gastrointestinal bleeding,<sup>36</sup> these risks may be minor and infrequent when administered via intra-articular injections, and may be less severe and less frequent than those experienced with steroid injections. Various authors have reported positive effects of intra-articular NSAID injections for a variety of musculoskeletal conditions.<sup>7,8,2</sup>1–24 Therefore, intra-articular NSAID injections may potentially provide the same relief as corticosteroid injections, with less serious adverse events.

The purpose of this systematic review is to compare intra-articular NSAID and corticosteroid administrations and determine whether NSAID injections are a safer and more effective alternative.

#### 2. Methods

#### 2.1. Search strategy

Two blinded reviewers with methodological and content expertise searched three databases (PUBMED, Medline and EMBASE) for clinical studies involving injection of non-steroidal anti-inflammatory medications (NSAIDS) or corticosteroids for any musculoskeletal pathology. The following search terms were used: "NSAID" or "Non-steroidal antiinflammatory", "Corticosteroid" or "Steroid", "Injection" or "injections". MESH and EMTREE headings were used in OVID and supplemented with free text to increase sensitivity. PUBMED was searched for articles e-published ahead of print. A reference search of relevant articles was conducted to ensure that all potential studies were included. Articles published from 1946 to April 2018 were included in this review. All identified titles and abstracts were reviewed independently and in duplicate. Disagreements regarding study inclusion were resolved by consensus discussion involving the senior author. Duplicate articles were manually excluded. Following the screening of titles and abstracts, both reviewers subsequently reviewed the full text of all studies identified during title and abstract screening, for meeting the inclusion/exclusion criteria.

#### 2.2. Inclusion and exclusion criteria

Studies were included if they: 1) compared injection of anti-inflammatory medications and corticosteroids for any musculoskeletal application. There were no restrictions made with regards to type, dose or location of NSAID or steroid. Studies were excluded if they: 1) reported no outcomes, such as review articles, technique papers, or case reports; and 2) were not written in the English language.

### 2.3. Data extraction

Two reviewers abstracted data in duplicate and kept the records in a Microsoft Excel 2011 spreadsheet. The data included: year of publication, author, sample size, study design, level of evidence, location and dose of injection, duration of follow-up, study results, and recommendations. The outcome measures were baseline and follow-up measurements of the visual analog scale (VAS), functional outcome scores (if available), and number of patients with symptomatic resolution (Tables 1 and 2).

#### 2.4. Statistical analysis

Descriptive statistics were calculated exploring the outcomes between injected NSAIDs and steroids. Inter-observer agreement for the reviewers' assessment of study eligibility was calculated with Cohen's kappa coefficient. <sup>25</sup> Based on the guidelines by Landis and Koch, a Kappa of 0–0.2 indicates slight agreement, 0.21 to 0.40 indicates fair agreement, 0.41 to 0.60 indicates moderate agreement, and 0.61 to 0.80 indicates substantial agreement. A value above 0.80 is considered almost perfect agreement. <sup>26</sup> Inter-observer agreement for assessments

of methodological quality was calculated with the Intraclass Correlation Coefficient (ICC). The Kappa and ICC were calculated using the SPSS software (SPSS Inc., Chicago, Illinois).

#### 3. Results

#### 3.1. Study identification

Our literature review yielded 2094 individual studies (384 from MEDLINE and EMBASE, 1710 from PUBMED). Following the removal of duplicates, 1871 individual studies were selected for screening. Of these, four studies met the inclusion and exclusion criteria and were included in this review.  $^{27-30}$  Detailed results of the included studies can be found in Fig. 1. Agreement between reviewers for eligibility of studies was high (Kappa = 0.89, 95% CI 0.72 to 0.98).

#### 3.2. Study characteristics

A meta-analysis was not feasible due to the heterogeneity of the data. The mean quality assessment score for the four included studies was 10.5, which was considered moderate quality. The level of agreement between the two reviewers for quality assessment was ICC = 0.78 (95% CI: 0.42 to 0.92).

#### 3.3. Study findings

Min et al.<sup>27</sup> conducted an RCT comparing Triamcinolone (40 mg) and Ketorolac (60 mg) injections in the subacromial joint space. They reported a mean improvement in pain on VAS by 0.9 in the steroid group and 1.83 in the NSAID group. They reported significant improvement in function on the UCLA shoulder rating scale for the NSAID group at 4 weeks (p = 0.03). They also reported significantly greater active abduction for the NSAID group at 4 weeks (p = 0.03). The only complication reported in the study was vasovagal syncope for the steroid group, in about 6.67% of participants.

Shakeel et al. <sup>28</sup> performed an RCT comparing Triamcinolone (20 mg) and Diclofenac (12.5 mg) in trigger finger. They reported no significant difference in functional scores at 3 months between the two groups. With regards to complications, 2% of participants in the steroid group had injection site pain and 18% had recurrence of symptoms. In the NSAID group, 4% had injection site pain, 6% had swelling, 4% had stiffness, and 2% had recurrence of symptoms.

Bellamy et al.<sup>29</sup> performed and RCT comparing Triamcinolone (80 mg) and Ketoralac (30 mg) in the setting of knee osteoarthritis with grade III Kellgren and Lawrence scale. They showed no statistically significant difference in improvement on the visual analog scale and no statistically significant difference in functional outcomes, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score at 2 week follow-up.

Aldrete et al.<sup>30</sup> performed a case controlled study comparing Indomethacin (1 and 2 mg) to Methylprednisolone (80 mg) in epidural space injection for post-laminectomy syndrome. They showed no statistically significant difference in the improvement on the visual analog scale in all three groups of methylprednisolone, indomethacin 1 mg and indomethacin 2 mg. They found no incidences of dural puncture or high sensory or motor block. They noted no typical side-effects of NSAID therapy such as rash, epigastric discomfort, or bruising.

#### 4. Discussion

This unique systematic review compared corticosteroid and NSAID intra-articular injections for the treatment of musculoskeletal conditions. The results of this review demonstrate that: 1) In the short term (2–12 weeks) duration, intra-articular NSAID injections provide equivalent, if not better, pain relief from musculoskeletal ailments, when compared to intra-articular corticosteroid injections; 2) There is

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