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Economic Impact of Ketorolac vs Corticosteroid Intra-Articular Knee Injections for Osteoarthritis: A Randomized, Double-Blind, Prospective Study

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ABSTRACT

Background: Knee osteoarthritis is a disabling disease that costs billions of dollars to treat. Corticosteroid gives varying pain relief and costs $12 per injection, whereas ketorolac costs $2 per injection, per institutional costs. The aim of this study was to compare ketorolac with corticosteroid based on pain relief using patient outcome measures and cost data.
Methods: A total of 35 patients were randomized to ketorolac or corticosteroid intra-articular knee injection in a double-blind, prospective study. Follow-up was 24 weeks. Osteoarthritis was evaluated using Kellgren–Lawrence grading. Visual analog scale (VAS) was the primary outcome measure. A query of the institutional database was performed for International Classification of Diseases, Ninth Revision codes 715.16 and 719.46, and procedure code 20610 over a 3-year period. Two-way, repeated measures analysis of variance and Spearman rank correlation were used for statistical analysis.
Results: Mean VAS for ketorolac and corticosteroid decreased significantly from baseline at 2 weeks, 6.3-4.6 and 5.2-3.6, respectively and remained decreased for 24 weeks. There was no correlation between VAS and demographics within treatments. There were 220, 602, and 405 injections performed on patients with the International Classification of Diseases, Ninth Revision codes 715.16 and 719.46 during 2013, 2014, and 2015, respectively. The cost savings per year using ketorolac instead of corticosteroid would be $2259.40, $6182.54, and $4159.35 for 2013, 2014, and 2015, respectively, with a total savings of $12,601.29 over this period.
Conclusion: Pain relief was similar between ketorolac and corticosteroid injections. Ketorolac knee injection is safe and effective with a cost savings percentage difference of 143% when compared with corticosteroid.

Knee osteoarthritis (OA) can be a disabling disease that affects up to 9 million adults in the United States [1,2]. The cost and disability associated with OA treatment can have a large impact on society. In the years 2008-2011, the estimated annual cost to treat OA and joint pain was $62.1 billion with lost wages estimated to $80.1 billion annually [3,4]. Over the next 25 years, the projected population affected with OA in the United States will increase to 67 million people [3]. With the rising cost for this disabling condition, more cost-effective treatments are needed.

Conservative treatment includes patient education, exercise, weight loss, nonsteroidal anti-inflammatory drugs, analgesic medications, bracing and/or orthoses, and intra-articular injections [5]. Intra-articular injection therapy has been studied using corticosteroids, platelet-rich plasma, and viscosupplementation [6-12]. The results are varied; however, general consensus is that corticosteroid intra-articular knee injection has been considered the gold standard [13-16]. In several studies, corticosteroid injections give varying amounts and durations of pain relief [13-17].

As an adjunct in multimodal pain control after total knee arthroplasty, ketorolac has been used successfully in the posterior

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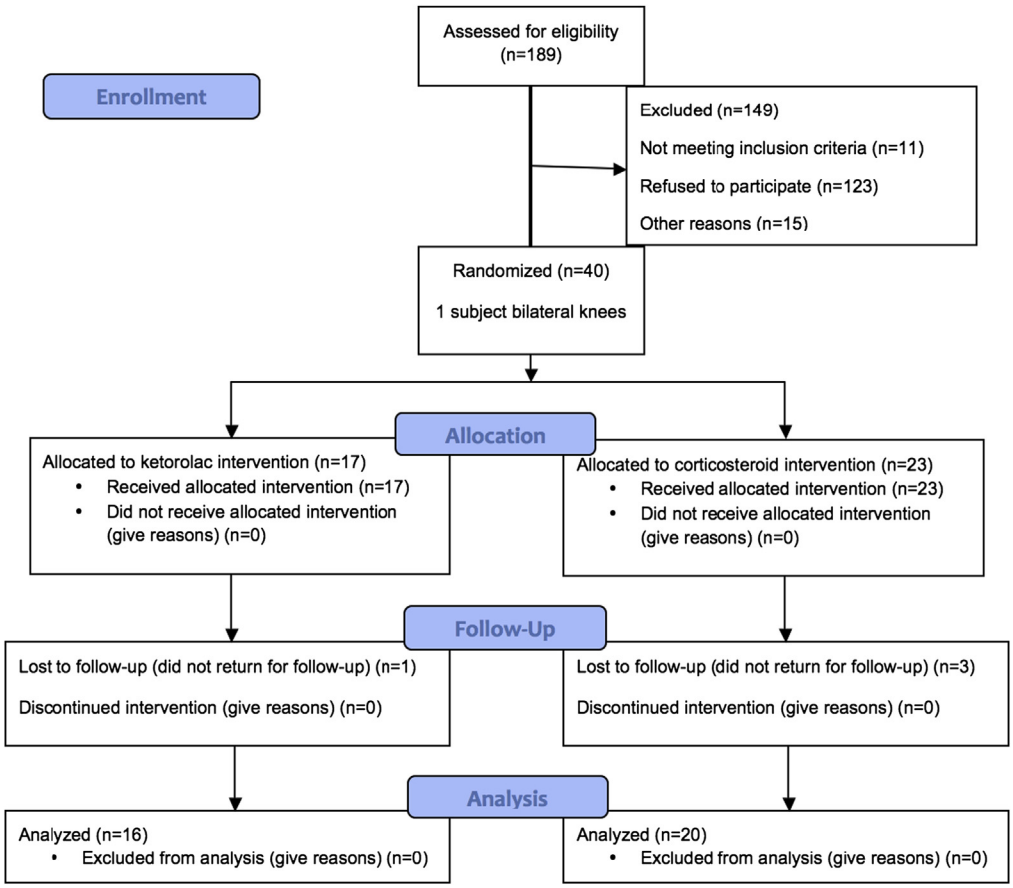

Fig. 1. Subject randomization flow diagram.

capsular injection [18]. In addition, ketorolac intra-articular knee injection has been studied as an adjunct with hyaluronic acid, but not alone in the management of knee OA [19]. Ketorolac is a nonsteroidal anti-inflammatory drug that inhibits the cyclo-oxygenase enzyme system and prostaglandin synthesis. These are key pathways involved in the inflammatory cycle of OA and targets to provide nonoperative pain management for knee OA.

To the author's knowledge, ketorolac intra-articular knee injection has not been performed as a standalone nonoperative treatment for knee OA. To determine whether ketorolac intra-articular knee injection is an appropriate adjunct in the nonoperative treatment of knee OA, we asked the following: (1) what is the effect of ketorolac compared with corticosteroid, the gold standard, with regard to the amount and duration of pain relief; (2) is there any difference in validated patient outcome measurements between both the treatment groups; (3) does body mass index (BMI) or the radiographic stage of knee OA play an effect on pain relief between the treatment groups?; and (4) what is the cost differential if any when comparing ketorolac with corticosteroid.

Materials and Methods

Inclusion and/or Exclusion Criteria

This study was designed as a prospective, double-blinded, randomized, controlled clinical trial. Institutional review board approval was obtained before proceeding with the study. This study was registered at ClinicalTrials.gov (NCT02295189). All subjects included in the study gave informed consent before enrollment. All source data were maintained per institutional review board protocol.

Inclusion criteria were an age of at least 18 years with a clinical diagnosis of knee OA. Knee OA was defined as pain in the knee with weight bearing combined with radiographic evidence of knee OA. The degree of radiographic knee OA was evaluated using the Kellgren–Lawrence (KL) grading scale [20]. The grading scale is a 0-4 scale defined as follows: KL Grade 0, no radiographic features of OA present; KL Grade 1, unlikely narrowing of the joint space, possible osteophytes; KL Grade 2, small osteophytes, possible narrowing of the joint; KL Grade 3, multiple, moderately sized osteophytes, definite joint space narrowing, some sclerotic areas, possible deformation of bone ends; and KL Grade 4, multiple large osteophytes, severe joint space narrowing, marked sclerosis, and definite bony end deformity.

Exclusion criteria were evidence or history of inflammatory or neuropathic arthropathy, insufficiency of the collateral ligaments or cruciate ligaments, current infection, recent knee intra-articular corticosteroid or viscosupplementation injection (<3 months), pregnant and/or lactating, allergy or hypersensitivity to the study medications, current use of anticoagulation medications, inability to make own decisions regarding the informed consent, and inability to read and/or understand English. All patients who satisfied the inclusion criteria and did not meet the exclusion criteria were enrolled, and consent was obtained.

Preparation and Injection

Enrolled subjects were randomized to treatment with use of a computer system by the pharmacist who prepared the injections.