Factors Associated with the Use of Hyaluronic Acid and Corticosteroid Injections among Patients with Radiographically Confirmed Knee Osteoarthritis: A Retrospective Data Analysis

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ABSTRACT

Purpose: Despite the rapid proliferation of hyaluronate (HA) and corticosteroid (CO) injections and clinical guidelines regarding their use in osteoarthritis (OA), information on the characteristics of people receiving these injections is scarce. We describe the use of injections among adults with radiographically confirmed knee OA and identify factors associated with injection use.

Methods: We used publicly available data from the Osteoarthritis Initiative (OAI), an international collaboration sponsored by the National Institutes of Health, and included participants with ≥1 radiographically confirmed knee OA (Kellgren-Lawrence grade ≥2 [definite osteophytes and possible joint space narrowing (JSN) on anteroposterior weight-bearing radiograph]) at baseline. We matched 415 participants who received at least 1 HA and/or CO injection during the 6-month interval before 1 of the first 7 annual follow-up assessments to 1841 injection nonusers by randomly selecting a study visit to match the distribution observed in the injection users. Multinomial logistic regression models were used for identifying factors associated with injection use, including sociodemographic and clinical/functional factors.

Findings: Eighteen percent of the 2256 patients identified as having knee OA had received at least 1 injection (years 1–7, 16.9%, 13.7%, 16.6%, 13.5%, 15.9%, 13.5%, and 9.9%, respectively), most commonly with CO (68.4%). HA and CO were more commonly injected in those with a higher annual household income (adjusted odds ratio [aOR] [95% CI] with HA, US ≥$50,000 vs <$25,000, 3.63; [1.20–10.99]) and less commonly in black patients (HA, 0.19 [0.06–0.55]). Greater Kellgren-Lawrence grade (grade 4 vs 2) was associated with an increased likelihood (aOR [95% CI]) of having received HA (4.79 [2.47–9.30]), CO (1.56 [1.04–2.34]), or both (4.94 [1.99–12.27]).

Implications: The receipt of HA or CO injection may be associated with higher socioeconomic positioning and indicators of greater disease severity in patients with knee OA. (*Clin Ther*. 2017;39:347–358) © 2017 Published by Elsevier HS Journals, Inc.

Key words: corticosteroids, hyaluronic acid, intra-articular injections, knee osteoarthritis, longitudinal studies.

INTRODUCTION

Thirty-seven percent of adults in the United States have radiographic evidence of osteoarthritis (OA) of the knee.[1] The prevalence of OA is increasing.[2] There

Accepted for publication January 3, 2017.
http://dx.doi.org/10.1016/j.clinthera.2017.01.006
0149-2918/$ - see front matter

is no cure for knee OA, but the guideline from the American College of Rheumatology recommends pharmacologic and nonpharmacologic treatments for relieving symptoms.[3] As a first line of defense, the guideline suggests exercise, weight loss (if needed), and/or the use of pharmacologic agents such as acetaminophen.[3] For those with radiologic evidence of OA [OARSI 2013 guidelines for knee OA: McAlindonTE, Bannuru RR, Sullivan MC, et al. OARSI guidelines for the non-surgical management of knee osteoarthritis. Osteoarthr Cartil. 2014;22: 363–388] whose pain is resistant to these treatment strategies, intra-articular injection may offer relief.

There are 2 primary types of intra-articular injections used in OA: corticosteroid (CO) injections and viscosupplementation (hyaluronic acid [HA] injections). The US Food and Drug Administration has approved 5 intra-articularly injectable CO formulations for use in knee OA.[4] CO injections reduce inflammation, which indirectly may relieve pain for up to 4 weeks. Typically, no more than 3 corticosteroid injections per year are recommended. Although there are several formulations of injectable COs available, they are thought to be similarly efficacious,[5–8] with the American College of Rheumatology guideline[3] and those from Europe[9] and Australia[10] advising the consideration of such injections for acute exacerbations or short-term relief only. HA, a naturally occurring constituent of cartilage and synovial fluid, has a different mechanism of action. HA injections enhance and maintain interarticular lubrication while potentially providing additional protection, including anti-inflammatory, analgesic, and chondroprotective effects.[11] Treatment cycles for these injections can consist of up to 5 weekly injections and may offer relief for up to 6 months; thus, HA may provide longer-term benefits compared with COs.[12] Current guidelines do not universally support the use of HA injections,[3,9,10,13,14] and some recommend against them.[15,16] Often in the presence of inconsistency in clinical guidelines such as the case with the use of HA treatment in OA,[33] non-clinical factors drive decision-making. Despite the rapid proliferation of these treatments, information about the characteristics of those receiving injections is scarce. We were unable to identify even 1 article that described the factors associated with its use.

The goals of this study were to: (1) describe the use of injections among adults with radiographically confirmed knee OA; and (2) identify factors associated with HA and CO injection use. Using retrospective data from the Osteoarthritis Initiative (OAI), an international collaboration sponsored by the National Institutes of Health, we were able to overcome the issues of temporal sequence inherent in many cross-sectional study designs. The study protocol included yearly visits. As such, we were able to identify new users of injections and extract the variables from the assessment just prior to the first visit documentation of an injection. We hypothesized that the participants receiving injections would be characterized by more severe OA symptoms than those who did not receive injections. We had no prior hypotheses regarding the characteristics of participants who would receive HA versus CO injections.

MATERIALS AND METHODS

We used the publicly available data from the OAI.[17] The original [Nevitt MC, Felson DT, Lester G. The Osteoarthritis Initiative Protocol for the Cohort Study. 2006. http://oai.epi-ucsf.org/datarelease/docs/StudyDesignProtocol.pdf. Accessed 2016] study was conducted in a prospective cohort of participants from Baltimore, Maryland; Columbus, Ohio; Pittsburgh, Pennsylvania; and Pawtucket, Rhode Island, from 2004 through 2006. The final sample included 4796 adults with established symptomatic knee OA or at high risk for developing knee OA. The present retrospective cohort study used information from the annual OAI study visits from baseline through 7 years. The annual-visit protocol included a patient questionnaire regarding the use of treatments for OA, including specific questions regarding injections of CO and HA.

The *index visit* was defined as the study visit immediately preceding the initial injection. For example, in participants in whom an injection was first reported on the year-3 visit, the index visit was defined as year-2. In injection nonusers, the index visit was selected such that the overall distribution of study visits among injection nonusers was frequency matched to those who had injections.

Measures of Injections

With respect to the information on the use of injections, participants were first asked at a study visit