Cost-effectiveness Analysis of Viscosupplementation versus Conventional Supportive Therapy for Knee Osteoarthritis in Colombia

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A B S T R A C T

Background: Treatment goals for knee osteoarthritis (OA) include preservation of mobility, control of pain, and delaying total knee replacement (TKR). **Objective:** To estimate the cost-effectiveness of viscosupplementation (hylan G-F 20) alone compared with conventional supportive therapy (CST) in the treatment of knee OA in Colombia. **Methods:** Microsimulation in patients with knee OA, modeling of clinical outcomes (disease progression, symptom improvement, TKR), and estimation of associated costs were performed (drugs, diagnostic tests, procedures, and hospitalizations). The probabilities for disease progression and clinical events were correlated with patients' characteristics. Clinical outcome information was obtained from the literature. The costs were drawn from institutional databases from health maintenance organizations and the Colombian standard tariffs handbook (ISS 2001. Agreement No. 256 of 2001. Tariffs for the health promoter Social Security EPS-ISS. Social Insurance Board of Directors. December 19, 2001). Sensitivity analyses were performed for costs and transition probabilities. **Results:** Monte-Carlo simulation for 1000 patients with knee OA showed that viscosupplementation with hylan G-F 20 delayed the occurrence of TKR by 3 years compared with CST. Western Ontario and McMaster Universities Arthritis Index scores indicate improvement in symptoms and function with hylan G-F 20. The incremental cost-effectiveness ratio for viscosupplementation is dominant, with reduction of US $576 in treatment cost in favor of hylan G-F 20, with more cost-effectiveness per quality-adjusted life-year during the first 10 years of treatment compared with CST. **Conclusions:** The results of mathematical simulation indicate that in comparison to conventional support therapies, viscosupplementation with hylan G-F 20 improved disease symptoms, joint function, and quality of life, reduced direct treatment costs, delayed TKR by 3 years, and was cost-effective in Colombia.
Keywords: cost-effectiveness, hylan GF-20, osteoarthritis, total knee replacement, viscosupplementation.

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Introduction

Osteoarthritis (OA) is the most common chronic joint disease of the cartilage. It is the sixth leading cause of "years of living with disability" globally and will be the fourth leading cause of disability by the year 2020 [1]. The incidence of OA increases with age [1,2]. The population affected by OA disability is expected to double by the year 2020 [3].

Treatment strategies for OA include the use of a stepped care strategy of intraarticular injections and total knee replacement (TKR) [4]. Treatment goals for knee OA include preservation of mobility, quality of life (QOL), control of pain, and slowing of disease progression, to delay TKR, which is costly and may not be medically desirable.

Viscosupplementation includes the injection of hyaluronan or hylan G-F 20, which has been shown to be safe and effective.

With appropriate care, viscosupplementation provides benefits for knee function, overall health, and health-related QOL at reduced levels of cotherapy [5].

Studies confirm that hylan G-F 20 viscosupplementation is more effective than conventional treatment, at no additional cost [6], and reduces the economic burden of knee OA treatment [7]. Adding one or more courses of hylan G-F 20 therapy to the standard treatment for 3 years indicated that appropriate use could delay the need for TKRs and generate savings [8–10].

In Colombia there are no data about the benefits and costs of hylan G-F 20 therapy in patients with OA and an economic evaluation is needed. The aim of this study was to determine the cost-effectiveness of hylan G-F 20 therapy compared with conventional supportive therapy (CST) in the treatment of knee OA in Colombia.

Methods

The model considered all grades of OA (Kellgren & Lawrence grades 1–4), which were stratified by ages. For the simulations, it considered a cohort of 1000 patients aged between younger than 50 years and older than 80 years. At all age groups (<50, 50–59, 60–69, 70–79, and >80 years), 59% of the patients were men and 41% were women. The age group of 70 to 79 years had the highest number of patients (357 patients). Disease severity was calculated by taking all grades of OA into consideration, and the distribution of knee OA was based on disease severity as reported in Table 1. Most of the patients (70%) were placed in grades 2 and 3 severity scale.

Simulation Methodology

A microsimulation of clinical outcomes (disease progression, viscosupplementation, symptom improvement, and frequency of TKR) was done focused on a hypothetical cohort of 1000 patients with knee OA and simulated, with annual regularity, their disability over time. Clinical data including the probability of disease progression were obtained from the published literature [10–12]. The use of hylan G-F 20 was compared with the use of CST. Treatment outcomes were simulated at different time horizons in the interval of 5 to 20 years.

In this model, functional disability is expressed in terms of scores obtained on the Western Ontario McMaster University Osteoarthritis Index (WOMAC) and then translated into quality-adjusted life-years (QALYs) [13]. The WOMAC score dimensions are pain, stiffness, and functional capacity on a scale ranging from 0 through 96.

Discrete-event simulation [14] was used considering patient's ages, sex, disease progression, and initial disease severity. Discrete-event simulation allowed modeling of different characteristics of the patients (age, sex, disease progress) over time. Patients were divided proportionally into four subgroups according to the prevalence of the OA grade according to Lussier et al. [12]. Upon entry to the model, an initial WOMAC score is randomly assigned to each patient on the basis of baseline pretreatment WOMAC scores for the population. Initial scores vary from patient to patient. Annual variation depends on clinical outcome, categorized as follows: 1) symptom improvement, 2) no change in symptoms, 3) worsening of symptoms, and 4) TKR.

The annual change in WOMAC scores for patients receiving hylan G-F 20 is estimated on the basis of results of randomized controlled trials [15–18]. The available evidence suggests that the benefit obtained by viscosupplementation with hylan G-F 20 is sustained over time [10–12,15–23]; in light of this, the WOMAC scores after the first year are assigned randomly taking into account the clinical outcome for the previous years. The information about score variation is available as reported by Raman et al. [24]. In this study, the average of the percentage change of decrease in the WOMAC scores was 9.4, 25.9, and 24.5 points on a scale ranging from 0 to 96 at 6 weeks, 6 months, and 12 months, respectively. It is assumed that the change in percentage for the scores has a normal distribution, based on kurtosis and

skewedness tests for the whole of the patient data. Because of the lack of available scientific evidence showing the distribution of WOMAC scores according to OA degrees, in order for the model to have an adjudication rule for assigning the degree of OA according to the compounded WOMAC score, an arbitrary classification was made for each of the dimensions in the scale, dividing the scale into four equal portions. This was done with the objective of assigning treatment costs according to OA degrees.

It was assumed that hylan G-F 20 was given once or twice a year (one 6-ml injection per application) [25]. CST included analgesics (nonsteroidal anti-inflammatory drugs and opioids), intraarticular corticosteroids, and arthroscopy for debridement and/or correction of associated injuries; physiotherapy; and recommendations of lifestyle changes (weight loss). In most cases, the common outcome for the terminal degenerative disease is surgical treatment with TKR.

Each replication was of 1000 patients. Each run is of N replications, allowing for a 95% confidence interval calculation [22]. The expected results include the average WOMAC score at the beginning and in the subsequent years and QALYs until the end of the stipulated time horizon.

The model was implemented using Microsoft Excel and Visual Basic macros, taking into account, in order to perform the dynamic simulation for the patients in the cohort, randomization of variables and the calculation of results derived from them.

The costs of the two treatments were taken from Sistema de Información de Precios de Medicamentos (SISMED) (Drug Information System of the Ministry of Social Protection) and "Farmaprecios" database. Other direct costs generated by medical services necessary to manage the disease (e.g., physical therapy) were also included. The accounting of medication costs has included drug acquisition and administration, pretreatment evaluation, routine laboratory parameters, and diagnostic imaging. These costs and TKR costs were taken mainly from Seguro Obligatorio de Accidentes de Tránsito (SOAT) tariff Manual 2012 and ISS 2001 tariffs [26].

Various conventional alternatives for support therapies for the knee OA treatment were considered in this study, and several simulations were performed to identify all the relevant costs and consequences for each one. Direct, average, and total costs, cost-effectiveness ratios, and incremental cost-effectiveness ratios (ICER) were all used to compare hylan G-F 20 viscosupplementation against CST.

Results of treatment were considered in certain horizons, but the reference case was predefined as 20 years of follow-up. During the simulation, the expected values for all economic and clinical outcomes were obtained for each patient. The summary of results across all patients in the cohort provides expected values for the group as a whole.

The cost-effectiveness ratio was expressed in terms of incremental cost per QALY gained compared with CST [27]. The analysis was made from the third-party payer perspective, the costs and effectiveness were discounted at an annual discount rate of 3%, and alternative rates were used as appropriate for sensitivity analysis. To address the uncertainty about model inputs, a first-order Monte-Carlo simulation was used. In a second-order Monte-Carlo simulation, the model was run for 100 replications, allowing calculation of the mean values and the 95% confidence intervals for clinical outcomes, cost acceptability curves, and cost-effectiveness ratio. The parameter variations were applied simultaneously in probabilistic sensitivity analysis on the basis of their respective estimated distribution, which includes 1) percentage variation in the WOMAC score to 6 months (which can be interpreted as efficacy); 2) health state utilities for the WOMAC interval; and 3) cost of health care services by the WOMAC interval as explained above. Sensitivity analyses were performed for costs and transition probabilities between degrees of knee OA.

Table 1 – Distribution of knee osteoarthritis based on disease severity.	
Severity scale according to Kellgren & Lawrence	% of patients [19]
Grade 1	22.4
Grade 2	37.4
Grade 3	33.5
Grade 4	6.7