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Original article

An economic evaluation of chondroitin sulfate and non-steroidal anti-inflammatory drugs for the treatment of osteoarthritis. Data from the VECTRA study☆

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ABSTRACT

Objective: Our aim was to investigate: 1) the average cost per patient with osteoarthritis treated with chondroitin sulfate compared with NSAIDs for 6 months and 2) the possible impact that the reduction NSAID use due to monotherapy with or combined administration of chondroitin sulfate treatment may have on the budget of the Spanish National Health System.
Methods: A cost-minimization model compared both treatments (efficacy equivalence assumption), used at the recommended doses and regimens during a 6-month period. Data used in the model was obtained from the VECTRA study, a retrospective study of 530 patients with osteoarthritis treated with chondroitin sulfate or NSAIDs that was conducted to determine the consumption of health care resources. The efficacy and incidence of adverse events was estimated from meta-analysis based on randomized clinical trials. Univariate sensitivity analysis was performed for the base case scenario.
Results: The overall 6-month cost per patient given chondroitin sulfate was 141 € compared with 182 € when treated with NSAIDs. If during the forthcoming 3 years, 5%, 10%, and 15% of patients currently treated with NSAIDs would gradually be replaced by treatment with chondroitin sulfate, the expected savings for the Spanish National Health System during these 3 years would be over 38,700,000 €. In addition, 2,666 cases of gastrointestinal adverse events (including 90 serious adverse events) will have been avoided for every 10,000 patients treated with chondroitin sulfate instead of NSAID. Sensitivity analysis confirmed the strength of base-case in all scenarios.
Conclusions: On the basis of these findings, chondroitin sulfate is a treatment for osteoarthritis with a lesser cost and better gastrointestinal tolerability compared with NSAIDs.

Evaluación económica del uso de condroitín sulfato y antiinflamatorios no esteroideos en el tratamiento de la artrosis. Datos del estudio VECTRA

Palabras clave:
Condroitín sulfato
Agentes antiinflamatorios no esteroideos
Agentes antirreumáticos
Artrosis
Artrosis de rodilla
Artrosis de cadera
Costes

RESUMEN

Objetivo: El presente estudio *a*) estima el coste medio de un paciente con artrosis tratado durante 6 meses con condroitín sulfato (CS) o antiinflamatorios no esteroideos (AINE), y *b*) evalúa el impacto presupuestario para el Sistema Nacional de Salud que causaría la disminución del consumo de AINE con la administración en monoterapia o conjunta de CS.
Material y método: Modelo de minimización de costes que comparó ambos tratamientos (asumiendo igualdad de eficacia), a las dosis y las pautas recomendadas, durante un período de seis meses. Los datos utilizados en el modelo se obtuvieron del estudio VECTRA, un estudio retrospectivo en el que se recogió el consumo de recursos sanitarios de 530 pacientes con artrosis tratados con CS o AINE. La eficacia y la incidencia de efectos adversos se estimaron a partir del metaanálisis de ensayos clínicos aleatorizados. Se hicieron análisis de sensibilidad simples univariantes del caso básico.
Resultados: El coste semestral por paciente tratado con CS fue de 141 €, y de 182 € en el caso de los AINE. Esto significa que, si durante los 3 próximos años el 5, el 10 y el 15% de los pacientes con artrosis tratados actualmente con AINE fueran tratados con CS, se generarían ahorros para el Sistema Nacional de Salud de

☆VECTRA is the acronym for the "Economic and Health Evaluation of Chondroitin Sulphate for the Treatment of Osteoarthritis".
◆The list of the VECTRA study researchers is shown in Annex I.

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más de 38,7 millones de euros durante este período. Además, por cada 10.000 pacientes tratados con CS en lugar de AINE se evitarían 2.666 efectos adversos gastrointestinales, de los que 90 serían graves. Los análisis de sensibilidad confirmaron la estabilidad del caso básico en todos los supuestos considerados.
Conclusiones: Comparado con los AINE, el CS es un tratamiento con menores costes y con mejor tolerancia gastrointestinal en el manejo de la artrosis.

Introduction

Osteoarthritis is one of the most common rheumatic diseases, presenting with pain, physical disability, and difficulty performing daily activities and, consequently, deteriorating the quality of life of patients. The economic and social impact of the disease is substantial, especially due to the decreased quality of life of patients, loss of productivity and increased costs arising from the use of health resources.[1-3]. Taking into account current demographic increase trends and the progressive aging of the population and the fact that osteoarthritis predominantly occurs in the elderly population, it is expected that the prevalence of osteoarthritis will increase and therefore has implications not only at the level of society in general but also on the future of the health system. Therefore, the analysis of the costs generated by osteoarthritis is increasingly a matter of major importance, primarily because the disease is a major cause of disability, both temporary and permanent, and also because of its high prevalence in Spain, where it is estimated at 10.2% of the general population (confidence interval 95%: 7.9 to 12.5)[4] and this data coincide with those in other industrialized countries.[5-8]

The goals of osteoarthritis treatment are to relieve pain, improve physical disability and, if possible, delay the progression of structural damage of the affected joints. Nonsteroidal anti-inflammatory drugs (NSAIDs) are the basic treatment of osteoarthritis, particularly in the early stages of the disease, but usually NSAIDs are associated with clinically relevant adverse effects (AE). In a survey in the UK, general practitioners and patients who were asked their view of osteoarthritis,[9] revealed that a quarter of respondents were dissatisfied with their treatment and another quarter felt that their pain was inadequately controlled. A quarter of patients, along with treatment prescribed by their doctor, were taking unneeded prescription drugs, mainly paracetamol or ibuprofen. Most doctors interviewed in the study (92%) said that the gastrointestinal safety of NSAIDs was a concern when prescribing these drugs, 24% reported prescribing low doses of NSAIDs in the hope of controlling pain without the occurrence of gastrointestinal AE (GIAE). Moreover, only 20% of osteoarthritic patients who were prescribed an NSAID had continued taking it after a year, with the onset of AE the main reason for stopping treatment.[10] Because the use of NSAIDs is not recommended for long periods of time, as in the case of osteoarthritis, and because the risk of gastrointestinal toxicity in long-term treatment increases,[11] therapeutic alternative strategies have been developed to NSAIDs, such as chondroitin sulfate (CS).

CS is a major structural component of cartilage and is classified as a slow-acting drug for the symptomatic treatment of osteoarthritis (SYSADOA), and is approved as a medicine in several European countries, and as a nutraceutical in the United States and other countries. Numerous studies have shown the clinical benefits of CS in reducing pain and improving functional ability, reducing the use of NSAIDs or paracetamol when taken together and their good tolerability, in addition to its carryover effect following the withdrawal of treatment.[12] The recommendations for the treatment of osteoarthritis based on clinical evidence, published by the *European League Against Rheumatism*[13] and the *Osteoarthritis Research Society International*,[14] also certify the efficacy and good tolerability of CS for the treatment of knee osteoarthritis.

The growing cost of drug therapies and AE has led to an increasing demand for economic studies, especially those that compare the cost of treatments with similar results (cost minimization). In this respect, to conduct an economic evaluation comparing CS with NSAIDs is relevant and it seems important to increase awareness and maximize the benefit of available medical resources in the process of decision making in the management of osteoarthritis. In a medico-economical study conducted in France,[15] the amount of NSAID prescription was reduced by 67% in patients treated with CS. The cost incurred by CS was compensated with a reduction in physiotherapy and less co-prescriptions of gastroprotective agents. In another observational study in pharmacy, use of NSAIDs and paracetamol decreased significantly in patients taking concomitant CS for long periods of time.[16] Another study showed that the CS used by patients with osteoarthritis for more than six months, induced less coprescription of NSAIDs compared with those using CS for periods of less than six months.[17] In a pharmacoeconomic analysis conducted in Spain with different drug therapies for the treatment of osteoarthritis, CS proved to be a treatment with lower costs and better gastrointestinal tolerance than ibuprofen, diclofenac sodium, celecoxib or rofecoxib.[18] On the contrary, this economic analysis is designed to evaluate the use of NSAIDs and CS in the treatment of osteoarthritis, using data from actual use of health resources obtained from a retrospective called VECTRA (Economic and Health Assessment of Chondroitin Sulfate for the Treatment of Osteoarthritis.) We had the following objectives: 1) compare the estimated average cost of a patient with osteoarthritis treated for 6 months with CS and NSAIDs, respectively, and 2) determine the budgetary impact due to NSAID co-administration CS in the National Health System (NHS).

Methods

Study design

From a retrospective study that compared the efficiency of the treatment of osteoarthritis with CS or NSAIDs (excluding selective inhibitors of COX-2) or the combination of both treatments, a deterministic pharmacoeconomic cost minimization model (for both, based on an assumption of similar efficacy), using a decision tree (Figure 1), at recommended doses and for a period of six months (time horizon) was employed. This model simulates the onset of AE, including severe gastrointestinal AE and complications of the treatments compared. The pharmacological characteristics of the model have been described in previously published studies.[16,18,19] The CS branch included the percentage of patients who, after prior treatment with NSAIDs, came to be treated with CS or the combination CS plus NSAIDs. The decision tree program was designed by TreeAge Pro 2006 Software Healthcare Inc (Williamstown, Massachusetts).

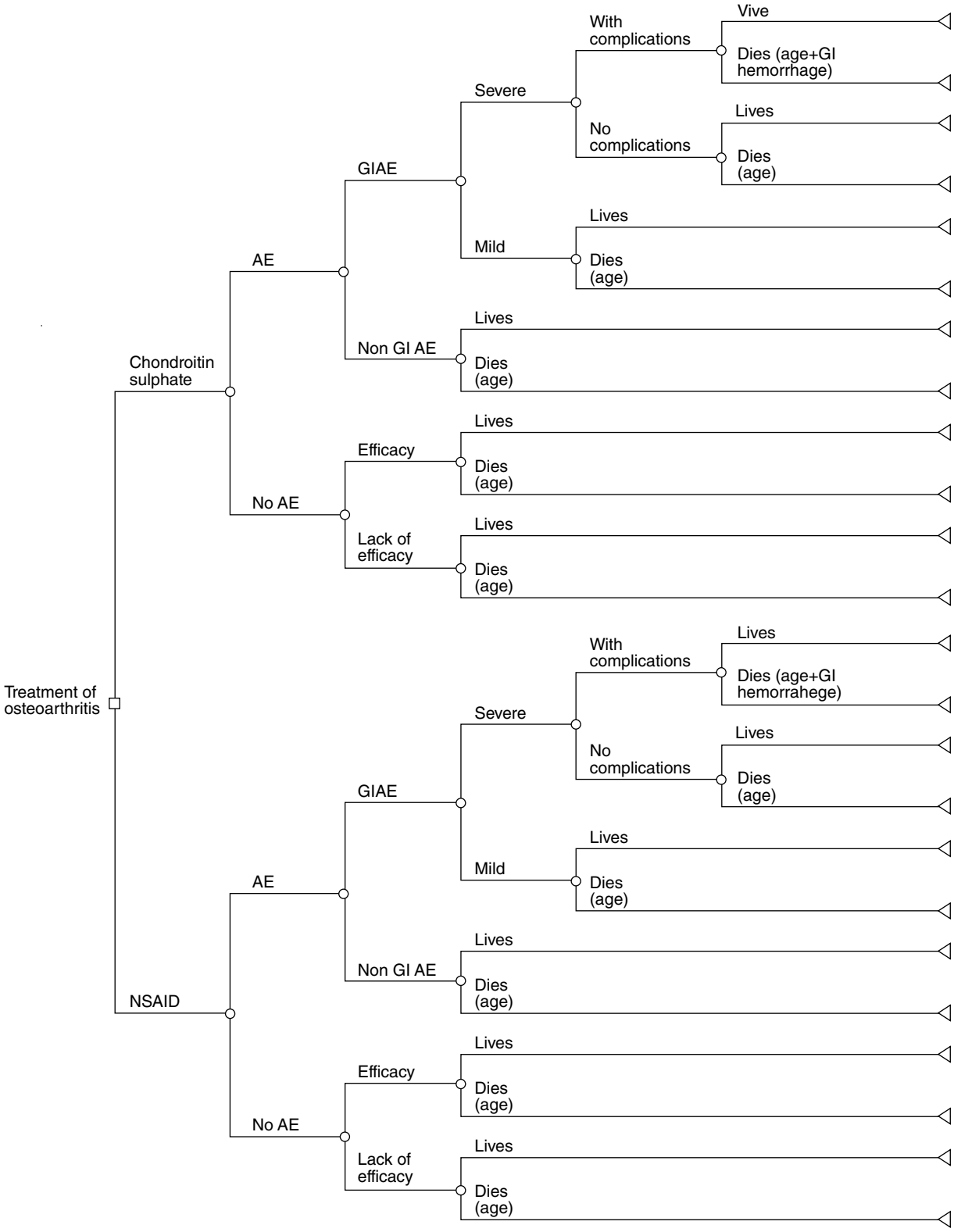

Figure 1. Treatment of osteoarthritis decision tree and its effects with chondroitin sulphate (CS) compared to non-steroidal anti-inflammatory drugs (NSAID). 24.0 and 25.4% of patients switched to CS or CS-NSAID combination, respectively, due to NSAID lack of effect. AE indicates adverse event; GI, gastrointestinal; GIAE, gastrointestinal adverse event.

Perspective and study frame

The study was done from the perspective of the NHS, considering only direct health costs. The horizon was six months.

Efficacy and adverse effects

A cost-minimization analysis was performed considering that CS and NSAIDs have comparable clinical efficacy. This assumption

Table 1
Decision tree probabilities for treatment of osteoarthritis and its effects with chondroitin sulphate compared to non steoroidal anti-inflammatory drugs

Item[a]	Treatment/ age	Mean probability	Minimal probability	Maximum probability	References
Percentage of patients with AE	CS[b]	0.0941	0.0705	0.1176	21
	NSAID[c]	0.5396	0.5200	0.5594	30
Percentage of patients with GIAE	CS[c]	0.0685	0.0514	0.0856	21
	NSAID[c]	0.5060	0.5058	0.5210	29
Efficacy rate	CS	0.78	0.60	0.95	22
	NSAID	0.83	0.80	0.87	27
Percentage of patients with severe GIAE	CS[d]	0	0	0	21
	NSAID[c]	0.0329	0.0246	0.0411	19
Percentage of complications in aptients with severe GIAE	CS[d]	0	0	0	21
	NSAID[c]	0.0099	0.0074	0.0123	19
Mortality after first episode of GI bleeding	All	0.0430	0.0190	0.1100	19, 28
Annual mortality (both genders)[e]	50 years	0.0064	0.0018	0.0046	31
	60 years	0.0073	0.0039	0.0106	31

AE indicates adverse events; NSAID, non steroidal anti-inflammatory drugs; CS, chondroitin sulphate; GI: gastrointestinal; GIAE, gastrointestinal adverse events.
[a]Probability of adverse events are those seen or estimated after 6 months of treatment.
[b]Maximum and minimum values are ±25% of mean value. In other cases, maximum and minimum values correspond to a 95% confidence interval.
[c]Combined results of all non-steroidal anti-inflammatory drugs were estimated, in the case of gastrointestinal adverse event, severe gastrointestinal adverse event and its complications using an average of those seen with naproxen, diclofenac and ibuprophen.[19]
[d]According to the Leeb metaanalysis[21] with chondroitin sulphate in monotherapy, mild gastrointestinal events were described (27 of 394 patients [6,85%], of which 18 Were epigastric pain, 7 diarrheas and 2 constipation). No severe gastrointestinal adverse events or myocardial infarctions have been described with chondroitin sulphate.
[e]Annual mortality rate (for both genders) at 44-54 and 55-64 years of age intervals, respectively, observed in the year 2000; the lower limit corresponds to the mortality rate in women and the upper one to men. We considered that mortality at 6 months represents one-half of the year.

Table 2
Results of the VECTRA study. Clinical characteristics and resources employed in 530 patients with osteoarthritis treated with chondroitin sulphate, non steroidal anti-inflammatory drugs and both

Data	CS	NSAID	CS+NSAID
No. (current treatment)	n=233	n=234	n=63
Female, %	73.39	76.07	80.95
Age, years, mean (SD)	59.29 (11.90)	63.12 (11.30)	62.03 (12.74)
Weight, kg, mean (SD)	72.40 (10.78)	73.38 (11.29)	74.04 (14.24)
Time since diagnosis, years, mean (SD)	3.92 (3.87)	4.56 (4.28)	4.56 (4.28)
*Affected localizations, mean (SD)**	1.70 (0.89)	1.91 (1.01)	2.35 (1.19)
Pain intensity, % of patients			
Mild	19.82	6.11	1.75
Moderate	61.26	68.56	68.42
Severe	18.92	25.33	29.82
Prior NSAID treatment, % of patients	51.50	–	42.86
Reasons for switching NSAID to CS or CS+NSAID, % of patients			
AE (all)	28.33	–	23,80
GIAE	24.03	–	20.63
Other AE	6.44	–	3.17
Lack of efficacy	24.03	–	25.40
Gastroprotective agents, % of patients	17.2	73.9	63.5
Use of resources due to mild-moderate AE related with prior NSAID use, % of patients			
Pharmacologic treatment	18.88	–	15.87
Additional visits	16.74	–	14.29
Hospital admission	0.00	–	1.60

AE indicates adverse events; CS, chondroitin sulphate; GIAE, gastrointestinal adverse events; NSAID, non steroidal anti-inflammatory drugs; SD, standard deviation.
*Localization: knee, hip, shoulder, hand, others.

is based on a randomized clinical trial, the only one available, that compared the efficacy of CS and diclofenac sodium.[20] The odds of clinical effectiveness, AE and fatalities due to toxicity during treatment with CS and NSAIDs, simulated in the decision tree (Table 1) were obtained from double-blind clinical trials, systematic reviews and meta-analysis published in the medical literature[20-28] by the *Food and Drug Administration*,[29] the *Canadian Coordinating Office for Health Technology Assessment*[19] and the *National Institute for Clinical Excellence*.[30] The annual mortality rate by sex and age was obtained from the National Epidemiology Center.[31]

Cost minimization analysis

The estimated cost of treating osteoarthritis with CS or NSAIDs was done through the identification and quantification of the health resources involved and then allocating a certain unit cost to those resources. Thus, we estimated the average costs for a typical patient with osteoarthritis treated with CS or NSAIDs.

The "use of medical resources" is determined by 1) the likelihood of onset of AE, obtained from a systematic review of the literature, and 2) the likelihood of change in CS or NSAID treatment, or a combination

of both, because of AE or lack of effectiveness, and resource use due to mild-moderate AE and consumption of gastroprotective drugs, and were obtained from the VECTRA study, whose results have not been previously published.

The VECTRA study is a retrospective study designed to estimate the percentage of patients with osteoarthritis taking NSAIDs and CS together with the consumption of resources associated with the the concomitant use of CS. The VECTRA study included patients of both genders, aged 18 years with radiographically diagnosed osteoarthritis in any joint and who were being treated with CS or NSAIDs. To avoid bias, the selection of patients was undertaken in a systematic way as follows: for example, suppose that a center has 30 patients available with osteoarthritis treated with NSAIDs, who should be sorted by the number of history lowest to highest, from 1 to 30. To choose the first case, a constant calculated random sampling (eg, k=n/5), where n indicated the 30 patients. Therefore, the first patient would be number 6 (30/5=6). To this obtained number we successively add the sampling value constant (k) to complete the sample size set. For example, the second case with NSAIDs would be 12 (6+6), the third would be 18 (12+6), the fourth would be the 24 (18+6) and the fifth would be 30 (24+6).

A total of 53 physicians, both hospitalists and primary care physicians in Spain, with experience in the treatment of osteoarthritis in the study agreed to participate. We asked each participant in the study to review medical records of 10 patients, five treated with CS and 5 with NSAIDs. For each patient, the physician completed a questionnaire with the following: demographic and clinical data, previous and current drug treatments, reasons for changing to CS therapy, resource consumption due to mild-moderate AE and coprescription of gastroprotective agents.

The "unit cost" means the cost of treatment of AE due to therapy andis determined according to the classification system of diagnosis related groups (Table 3). The costs of these treatments for mild-moderate gastrointestinal AE, including nausea, vomiting, dyspepsia, heartburn, epigastric and abdominal pain, diarrhea, constipation and uncomplicated peptic ulcer were obtained from the study by Tarricone et al.[32] With respect to gastrointestinal AE and to obtain a conservative estimated cost, we only considered the use of resources in the treatment of acute urticaria in primary care.[33] In addition, we calculated the half-yearly cost due to lack of efficacy of both treatments used alone. This would imply an extra medical visits to family physician/specialist. For this purpose, we asked a panel of nine clinicians what percentage of patients they believed could receive a combination of both treatments when monotherapy was not effective. In their opinion, between 27%-58% of patients would take CS and NSAIDs in combination. The dose and the maximum and minimum for 6 months treatment were obtained from the VECTRA survey data.

The acquisition costs of the treatments were obtained from the drug database.[34] Other unit costs were estimated from a database of Spanish health costs.[35] We only considered the direct medical costs. The unit costs and semi-annual costs estimated with CS and NSAIDs are summarized in Table 3. All costs are in 2007 euros.

With this data, we estimated the budgetary impact of reducing the use of NSAIDs with CS for the NHS.

Baseline case

For the "baseline case" of the study we established a 50 year old patient, a treatment duration of 6 months, 50.6% of AE with NSAIDs were gastrointestinal[29] and applied the average values of the probabilities and costs, considering only the direct healthcare costs.

Sensitivity analysis

To check the stability of the results of the baseline case and the consistency of the estimates, a simple univariate "sensitivity analysis" was made which considered the following scenarios: 1) the calculations were made with the minimum or maximum values, both of probabilities and costs; 2) we considered that 80.2% of the AE of NSAIDs are gastrointestinal, as observed in the VECTRA study; 3) 60 year-old patients were considered and 4) we considered that in the case of ineffectiveness of monotherapy with CS or an NSAID, a minimum of 27% and a maximum of 58% of patients would be treated with the combination of CS and NSAIDs.

Results

VECTRA study

The study VECTRA included 530 patients with osteoarthritis in Spain. Most patients (65.3%) had moderate pain and in 23% of the

Table 3
Unit costs and estimated process costs (euros, 2007) after 6 months of osteoarthritis treatment

Resource	Unit cost, €	Considered values	Semestral cost, €	Reference
Drug, dose (format)				
CS×400 mg (60)	19.37	–	116.22	34
NSAID[a]	–	–	56.64	34
Rheumatology visit (1)	43.11	–	–	
Rheumatology hospitalization (1 day)	382.15	–	–	35
Severe GIAE with complications[b]	–	Minimum	1,598	35
		Mean	2,916	35
		Maximum	5,227	35
				35
Severe GIAE without complications[b]	–	Minimum	944	35
		Mean	1,917	35
		Maximum	3,082	35
Mild-moderate GIAE[c]	–	–	203	32
Other non-gastrointestinal AE[d]	–	–	105	33

AE indicates adverse events; CS, chondroitin sulphate; GIAE, gastrointestinal adverse events; NSAID, non steroidal anti-inflammatory drugs.

[a]Cost calculated from non steroidal anti-inflammatory drug use in 129 patients from the retrospective study (ibuprophen, diclofenac, aceclofenac, meloxicam, naproxen, piroxicam, indomethacine, dexketoprophen, dexibuprophen, ketorolac and lornoxicam).

[b]With complications, a mean cost of the groups related to diagnosis (GRD) was considered 174 (gastrointestinal hemorrhage with complications), 176 (peptic ulcer with complications) and 180 (gastrointestinal obstruction with complications). Without complications we considered the mean cost of the GRD to be 175 (gastrointestinal hemorrhage without complications) and 181 (gastrointestinal obstruction without complications).

[c]Use of resources estimated from Spanish data from the study by Tarricone et al.[32]

[d]Estimated cost from the use of resources in the treatment of urticaria by primary care.[33]

patients pain was severe in intensity. A total of 233 patients received CS, 234 received NSAIDs and the remaining 63 patients took CS plus NSAIDs together for the treatment of osteoarthritis.

Twenty-eight point three and 23.8% of patients switched treatment to CS or a combination of CS and NSAIDs respectively, due to the onset of AE caused by NSAIDs (24.0% and 20.6% had GIAE, respectively). Twenty-for percent and 25.4% of patients changed their treatment to the combination of CS or CS plus NSAIDs, respectively, for lack of efficacy of NSAIDs. 17.2%, 63.5% and 73.9% of CS patients taking the combination of CS plus NSAIDs and NSAIDs alone, respectively, were concurrently taking gastroprotective agent (Table 2).

Cost minimization analysis

According to the "baseline case" model, in a hypothetical cohort of 10,000 patients with osteoarthritis treated with CS instead of NSAIDs, a total 2666 GIAE (of which 90 would be severe) could be prevented (Table 4).

The semi-annual cost of a patient treated with CS was € 141 compared to € 182 in the case of a patient treated with NSAIDs (Table 5). The sensitivity analysis confirmed the stability of the baseline case in all the cases considered (Table 5). Assuming a theoretical decrease in the consumption of NSAIDs as a result of combined treatment with CS, of 5%, 10%, and 15% over the next three years, respectively, savings of over 38,7 million euros were generated after three years for the Spanish NHS (Table 6, Figure 2).

Discussion

According to the VECTRA survey results, and based on an assumption of similar efficacy of the treatments compared, with results taken from the only available comparative clinical trial,[20] CS seems to be a treatment with lower costs and better gastrointestinal tolerability than NSAID for osteoarthritis. In this regard, it is important to highlight the consequences of failure due to lack of efficacy or NSAIDs toxicity. In fact, 56.7% of patients treated with CS replacement therapy began treatment with NSAIDs, in 54.4% of cases, replacement of NSAIDs was due to AE (mostly gastrointestinal problems); 69.5% of patients with AE associated with NSAID use needed additional medical consultations, with an average of 2.2 extra consultations per patient and, finally, treatment with NSAIDs was associated with greater concomitant use of gastroprotective agents (74%) compared with patients treated with CS (17%).

The results of this study corroborate those obtained previously in a Spanish pharmacoeconomic analysis published in 2004 with a similar model.[18] However, the use of health resources was obtained from a retrospective study of 530 Spanish patients with osteoarthritis, enhancing the reliability of the results.

In assessing the results of this study, we must take into account its possible limitations. First, it must be remembered that a basic assumption for the planning and design of the model was made: the relative equality of compared treatment efficacy. In our view, this assumption is the most plausible given the results of the only comparative study between CS and diclofenac sodium.[20] To try to minimize the variability of estimates, each mean value (probability of toxicity or cost) is assigned its corresponding minimum and maximum values (95% confidence interval or ±25% of mean value) to assess the potential impact of outliers on the baseline-case assumptions. Moreover, it should be noted that the limited duration of clinical trials allowed only short term reliable simulation results (six months), so it was not possible to detect significant effects of treatments on long-term survival.

The VECTRA study was not designed to detect AE, so this data was obtained from systematic reviews and meta-analysis published in the medical literature,[20-28] as well as those incurred by the *Food and Drug Administration*,[29] the *Canadian Coordinating Office for Health Technology Assessment*,[19] and the *National Institute for Clinical Excellence*.[30] It was assumed that the VECTRA study population would be similar to the general population analyzed in the meta-analysis, taking into account the selection of patients and the wide distribution of researchers in the country.

Finally, a weakness of the study lies in the fact that the assumption of similar efficacy for CS and NSAIDs, based on a single randomized clinical trial comparing its effectiveness with that of diclofenac sodium.[20]

According to the results of this model, CS appears to be an osteoarthritis treatment with lower costs and better gastrointestinal tolerability than NSAIDs. The decrease in consumption of NSAIDs with CS co-treatment could generate savings for the NHS of more than 38.7 million euros after three years and, more importantly, for every 10,000 patients treated with NSAIDs rather than CS, 2666 GIAE, of which 90 would be severe, could be avoided.

Table 4
Estimate of adverse events avoided in a cohort of 10,000 patients with osteoarthritis after 6 months of treatment with chondroitin sulphate compared to non-steroidal anti-inflammatory drugs. Basic case

AE	CS	NSAID	Cases avoided
Gastrointestinal	64	2,730	2,666
Severe gastrointestinal	0	90	90

AE indicates adverse events; CS, chondroitin sulphate; NSAID, non steroidal anti-inflammatory drugs.

Table 5
Cost of treatment a patient with osteoarthritis for 6 months with chondroitin sulfate or non-steroidal anti-inflammatory agents (euros, 2007)

Scenarios	CS	NSAID	Cost difference[a]
Mean cost[b]	141 €	182 €	–41 €
Minimum cost[b]	141 €	173 €	–32 €
Maximum cost[b]	141 €	193 €	–52 €
Minimum probability[c]	154 €	176 €	–22 €
Maximum probability[c]	130 €	189 €	–59 €
80.2% of NSAID adverse events are gastrointestinal[d]	141 €	207 €	–66 €
Age of 60 years[e]	141 €	182 €	–41 €
Minimum rescue with CS+NSAID (27%)	140 €	182 €	–42 €
Maximum rescue with CS+NSAID (58%)	143 €	183 €	–40 €

CS indicates chondroitin sulphate; NSAID, non steroidal anti-inflammatory drugs.

[a]Negative results indicate savings with chondroitin sulphate, positive results indicate savings with non steroidal anti inflammatory drugs.

[b]Values obtained that use the mean probability values and unit costs constitute the basic case for analysis; minimum and maximum values, sensitivity analysis.

[c]Values from table 2.

[d]Results of the retrospective VECTRA study.

[e]Age of 50 years in the basic case for analysis.

Table 6
Budgetary impact analysis of the prescription of chondroitin sulphate instead of non steroidal anti-inflammatory drugs for the treatment of osteoarthritis for the National Health System of Spain

Item	Valor	Reference
Analysis premise		
No. of NSAID units prescribed in Spain (2006)	41,179,000	33
Estimated percentage of prescriptions in osteoarthritis (2006)	46.5	33
No. of estimated units of NSAID prescribed for osteoarthritis (2006)	19,148,235	Calculated
No. of estimated doses per unit of prescribed drug	20 (30; 40)	33
No. on average of doses prescribed by the NHS (2006)	574.447.050	Calculated
No. of estimated NSAID dose per patient and day	1-2	VECTRA Study
No. of estimated NSAID dose per patient and year	365-730	Calculated
No. of estimated patients treated with NSAID due to osteoarthritis (NHS)	786,914-1,573,828	Calculated
Estimated percentage of NSAID substitution for CS in osteoarthritis		
Year 1	5	Estimated
Year 2	10	Estimated
Year 3	15	Estimated
No. of estimated patients to be treated with CS instead of NSAID		
1-2 doses of NSAID/day	39,346-78,691	Calculated
Year 1	78,691-157,383	Calculated
Year 2	118,037-236,074	Calculated
Year 3		
Results of the analysis		
Annual mean cost of treatment of one patient with osteoarthritis, €		
NSAID	364	Calculated
CS	282	Calculated
Actual estimated cost per treatment of osteoarthritis with NSAID (NHS), €	572,873,222	Calculated
Projected cost substituting NSAID for CS (NHS), €		
Year 1	566,420,530	Calculated
Year 2	559,967,837	Calculated
Year 3	553,515,144	Calculated
Net cost (savings for NHS) to 3rd year, €	38,716,157	Calculated

CS, chondroitin sulphate; NHS, National Health System; NSAID, non steroidal anti-inflammatory drugs.

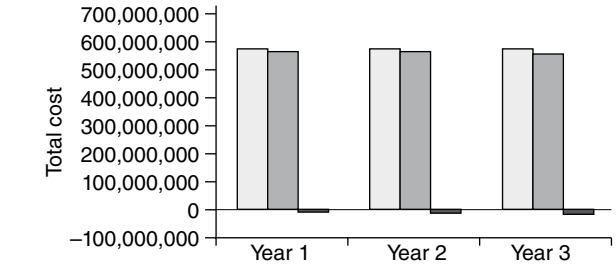

Figure 2. Results of the budgetary impact analysis for the National Health System of prescribing Chondroitin Sulphate instead of non-steroidal anti-inflammatory drugs for osteoarthritis.

Other studies have shown that the use of CS for symptomatic treatment of osteoarthritis reduces the use of NSAIDs, thereby reducing the AE potential associated with these.[15-17] Of particular interest is the study of Lagnaoui et,[16] which showed that the reduction in the use of NSAID is related to the duration of treatment with CS, being higher in patients using CS for long periods of time. This result was confirmed in the study of Taieb et al[17] in which it was found that prolonged treatment with CS reduces not only the coprescription of NSAIDs and analgesics, but also the duration of these treatments. VECTRA highlights the consequences, both health and economicwise, of failures due to lack of efficacy or toxicity of NSAIDs, as well as of reducing the incidence of AE and the savings that would be associated with the use of CS to replace NSAIDs.

The results of this study should be confirmed in a pragmatic, randomized clinical trial directly comparing the efficacy, tolerance and use of health resources with the different alternatives for the treatment of osteoarthritis.[36] Meanwhile, according to the results obtained, we can conclude that CS is an osteoarthritis treatment with lower costs and better gastrointestinal tolerability than NSAIDs.

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