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ORIGINAL RESEARCH

Cost-Effectiveness Analysis of Mometasone Furoate Versus Beclomethasone Dipropionate for the Treatment of Pediatric Allergic Rhinitis in Colombia

Carlos E. Rodríguez-Martínez · Monica P. Sossa-Briceño · Elkin Vladimir Lemos

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ABSTRACT

Introduction: Allergic rhinitis (AR) is one of the most common chronic respiratory diseases observed in the pediatric population, producing a significant morbidity, and an economic burden due to direct medical costs and indirect costs. Despite the high prevalence of AR in children and the importance of the use of topical intranasal corticosteroids for its treatment, comparative analyses of alternative treatments in pediatric patients, in terms of both cost and effectiveness are lacking.

Methods: A decision-analysis model was developed to estimate the cost-effectiveness of mometasone furoate nasal spray (MFNS) compared to beclomethasone dipropionate nasal spray (BDNS) for treating pediatric patients with AR over a 12-month period. Effectiveness parameters were obtained from a published study in which authors performed a systematic review of the literature. Cost data were obtained from a hospitaĺs bills and from the national manual of drug prices. The study assumed the perspective of the national healthcare in Colombia. The outcomes were three effectiveness measures summarized in a therapeutic index (TIX).

Results: For the base-case analysis, the model showed that compared to BDNS, therapy with MFNS was associated with lower costs (US$229.78 vs. 289.74 average cost per patient over 12 months) and a greater improvement in TIX score (0.9724 vs. 0.8712 score points on average per patient over 12 months), thus leading to dominance.

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C. E. Rodríguez-Martínez (✉)
Department of Pediatrics, School of Medicine, Universidad Nacional de Colombia, Carrera 45 No. 26-85, Bogota, Colombia
e-mail: carlos2671@gmail.com; carerodriguezmar@unal.edu.co

C. E. Rodríguez-Martínez
Research Unit, Military Hospital of Colombia, Transversal 3A No. 49-00, Bogota, Colombia

M. P. Sossa-Briceño
Department of Internal Medicine, School of Medicine, Universidad Nacional de Colombia, Carrera 45 No. 26-85, Bogota, Colombia
e-mail: mocasossa1@gmail.com

E. Vladimir Lemos
Outcomes Research Manager MSD Colombia, Calle 100 No. 7-33, piso 8, 802, Bogota, Colombia

Conclusion: The present analysis shows that in Colombia, compared with BDNS, therapy with MFNS for treating pediatric patients with AR is a dominant strategy because it showed a greater improvement in a TIX reflecting both efficacy and safety, at lower total treatment costs.

Keywords: Allergic rhinitis; Children; Cost-effectiveness; Intranasal corticosteroids; Treatment outcome; Health care costs

INTRODUCTION

Allergic rhinitis (AR) is a global health problem and one of the most common chronic respiratory diseases observed in the pediatric and adult population, with an estimated prevalence of approximately 20–40 million in the US population [1]. In Colombia a prevalence of AR symptoms has been reported ranging from 29.5% to 33.9% for the whole population, and from 25.9% to 53.8% for the pediatric population [2, 3]. Despite the fact that AR is not directly associated with a high rate of mortality or a high rate of hospitalization, the disease produces a significant morbidity. This condition has a major impact on the quality of life, sleeping habits, academic performance, daily activities, and concentration of sufferers [4]. Furthermore, in pediatric patients, improperly managed AR may contribute to the worsening of comorbid conditions, including asthma, rhino sinusitis, and otitis media [5]. The aforementioned factors lead to significant economic burden due to direct medical costs such as prescriptions and ambulatory care visits, and indirect costs such as absenteeism from school and work [6, 7].

Although there are many therapeutic options for the treatment of AR, topical intranasal corticosteroids (INS) are considered the most effective medication class for controlling symptoms of the disease [1]. INS have shown to reduce nasal congestion, rhinorrhea, sneezing, pruritus, and can also relieve ocular symptoms [8]. In Colombia, beclomethasone dipropionate nasal spray (BDNS) and mometasone furoate nasal spray (MFNS) are the two most commonly prescribed and the leading INS by market share in the country [9]; however, currently BDNS is the only INS included in Colombia's compulsory health insurance plan.

Despite the high prevalence of AR in children and the importance of the use of INS for the treatment of AR, comparative analyses of alternative treatments in pediatric patients, in terms of both cost and effectiveness are lacking. These comparative analyses are important because differences in cost of acquisition, efficacy, side effects, and therapeutic adherence between alternative treatments for AR could have a considerable impact on the control and in the tremendous economic burden of the disease. Cost-effectiveness analysis (CEA) provides a tool with which to incorporate both cost and effectiveness of alternative treatments.

The aim of the present study was to compare the cost-effectiveness of MFNS compared to BDNS for treating pediatric patients with AR in Colombia.

METHODS

Structure of the Model

A decision-analysis model was developed to estimate the cost-effectiveness of MFNS compared to BDNS for treating pediatric patients with AR. Although combination therapy with INS and antihistamines is occasionally used to treat the symptoms of AR, patients included in the model were only those

treated with a single prescription therapy of INS for symptom relief of AR. We chose BDNS because it is currently the only INS included in Colombia's compulsory health insurance plan. Additionally, MFNS, marketed by Merck Sharp & Dohme (MSD) under the brand-name Nasonex®, is—along with BDNS—the most commonly prescribed and the leading INS by market share in the country. For each of the two comparators, the model starts with a patient aged between 2 and 18 years who presents with AR and there is a probability (probability node) of improvement of symptoms. For patients whose symptoms improved, the model incorporates the probability that this improvement of symptoms has been due to improvement of nasal symptoms, ocular symptoms, or global assessment. Thereafter, the model incorporates the probability of treatment-related adverse events, and if these adverse events comprised epistaxis or not. For patients whose symptoms do not improve, the model incorporates the option (decision node) to continue treatment with a more effective INS or to send the patient for additional diagnostic and therapeutic procedures (Fig. 1). The model assumed that there would be complete compliance with either treatment measure throughout the entire year of follow-up. Although as determined by the natural history of AR it could be more appropriate to use a Markov model instead of a simple decision tree, we used the latter because we considered that using a simple decision tree it was possible to include the most important clinical events resulting from each of the two therapeutic options without unrealistic simplifying assumptions.

The model compared the one-year direct medical costs (including medical consultations, imagenology studies, and other diagnostic and therapeutic procedures for patients with no improvement of symptoms on therapy with INS, or for patients who presented treatment-

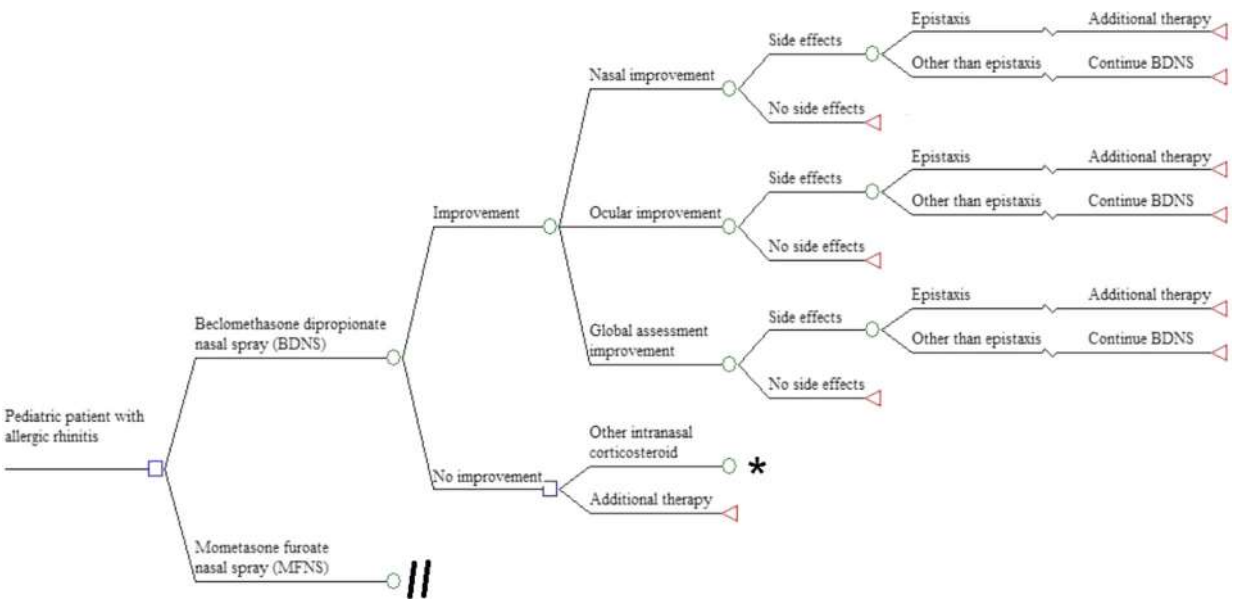

Fig. 1 Diagram of cost-effectiveness model for each treatment option. *Asterisk* For patients whose symptoms do not improve and the decision is to continue treatment with a more effective topical intranasal corticosteroid, the model follows as it is depicted for beclomethasone dipropionate nasal spray

related adverse events such as epistaxis or increased intraocular pressure) and disease outcomes from the perspective of the national healthcare system in Colombia.

Three effectiveness measures were chosen as the basis for this model: a composite total nasal symptom score (TNSS), defined as the average effect size for each of the two comparators for nasal symptoms, a composite total ocular symptom score (TOSS), defined as the average size for ocular symptoms, and a patient (or physician) global assessment (PGA).

Sources of Data

Disease Outcomes and Clinical Parameters

Assumptions regarding the probability of improvement of nasal symptoms, ocular symptoms and global assessment, the probability of treatment-related adverse events, and if these adverse events comprised epistaxis or not, were derived from the literature. Specifically, we identified a published study in which authors performed a systematic review of the literature (1966 to June 2009) to identify potentially relevant studies on efficacy and safety of several INS, including BDNS and MFNS [10]. In this study, the authors aimed to develop a therapeutic index (TIX) reflecting both efficacy and safety of these substances in a combined assessment. To develop this TIX, the authors performed meta-analyses for each single INS and for the parameters TNSS, TOSS, PGA, and epistaxis. The meta-analyses results for the different INS and the parameter TNSS, TOSS, PGA, and epistaxis were ordered and then categorized into scores from 0 to 3 using quartiles. The scores of long-term side effects and systemic ocular side effects were based on the highest level of evidence reflected by the study type of available studies and its results. The score points for the three efficacies and the three safety parameters were then summarized for each INS resulting in individual summation scores of 'sum efficacy' (ES) and 'sum side effects' (AES), which could range between a minimum of 0 and maximum of 9 points. A high ES would indicate a high efficacy and a high AES a high potential for side effects. The final TIX score was then calculated as the ratio of ES and AES with a theoretical maximum of 9 points indicating an optimal balance of a maximum efficacy and a minor potential of side effects [10]. Table 1 presents the summation scores of each parameter as well as the final TIX score for BDNS, MFNS, and for budesonide aqueous nasal spray (BANS). We included the data of BANS because, for patients whose symptoms do not improve, the model incorporates the possibility (decision node) to continue treatment with a more effective INS. Based on the summation scores of ES, the model assumed that MFNS is the next most effective

Table 1 TIX scores for each parameter, subscales and final ratio by topical intranasal corticosteroid

Parameter	BDNS	MFNS	BANS
TNSS	2	3	2
TOSS	1	2	3
PGA	1	2	3
ES	4	7	8
Epistaxis	2	1	2
Long-term side effect	3	0	2
Systemic ocular side effects	2	0	0
AES	7	1	4
TIX (ES/AES)	0.57	7	2

Table modified from [10]

AES sum side effects, *BANS* budesonide aqueous nasal spray, *BDNS* beclomethasone dipropionate nasal spray, *ES* sum efficacy, *MFNS* mometasone furoate spray nasal, *TIX* therapeutic index, *TNSS* total nasal symptom score, *TOSS* total ocular symptom score, *PGA* patient (or physicians) global assessment

INS for BDNS, and BANS is the next most effective INS for MFNS (Table 1). Probabilities of efficacy parameters were obtained based on the efficacy scores summarized in the TIX. The probability of improvement of symptoms with each one of the INS was calculated as the proportion of the maximum score for efficacy parameters with respect to the maximum possible score for efficacy parameters, and the probability of side effects with each one of the INS was calculated as the proportion of the maximum score for side effects parameters with respect to the maximum possible score for side effects parameters. Likewise, probabilities of efficacy parameters for TNSS, TOSS, and PGA were calculated as the proportion of the TIX scores for each parameter with respect to the maximum score for efficacy parameters, and probability of epistaxis was calculated as the proportion of the TIX score for epistaxis with respect to the maximum score for side effects.

Resource Utilization and Costs

As mentioned, the CEA was conducted from the perspective of the national healthcare system in Colombia and hence only direct costs were included in the analysis. In particular, the costs of medical consultations (pediatrician, otolaryngologists, allergologist, endocrinologist, and ophthalmologist), imagenologic studies (computed tomography scan of the paranasal sinuses, radiography of the paranasal sinuses, and lateral airway radiography to determine the adenoid size), as well as additional diagnostic and therapeutic procedures for patients with no improvement of symptoms on therapy with INS (Immunoglobulin E, skin prick testing, immunotherapy, impedance audiometry, endoscopic nasopharyngoscopy, adenoidectomy, septoplasty, tympanostomy tube placement, and turbinoplasty), were taken account of. Additional resources used for treatment-related adverse events (cauterization, anterior nasal packing, analgesic, topical antibiotics, and intraocular pressure measurement) were also included. All costs gathered were as close to reimbursement or true costs as possible.

Calculation of the daily therapy with INS was based on the estimated average daily dose appropriate for treating pediatric patients with AR, according to current international AR guidelines [11, 12], and the relative use of available concentrations for each medication according to current market research. The starting doses used in the present model were 2 sprays per nostril 2 times a day (400 μg total dose) for BDNS, 1 spray per nostril every day (100 μg total dose) for MFNS, and 1 spray per nostril 2 times a day (128 μg total dose) for BANS.

To determine the utilization rates of health resources and events for patients with no improvement of symptoms on therapy with INS and for patients with treatment-related adverse events, we performed a review of the literature, a consensus of experts consisting of a panel of three local pediatric otolaryngologists using the Delphi technique [13], and verified the results with a review of randomly selected medical records of 37 pediatric patients attended in the Fundacion Hospital La Misericordia with a principal diagnosis of AR (ICD-10 codes J30.1, J30.2, J30.3, and J30.4) between January 1 and December 31, 2013. The Fundacion Hospital La Misericordia is a referral hospital located in the metropolitan area of Bogota that receives patients from the most representative medical insurance companies in the city. The data number collected on health utilization were: the number of medical consultations per year (pediatrician, otolaryngologists, allergologist, endocrinologist, and ophthalmologist), the percent of patients requiring imagenologic studies (computed tomography scan of the

paranasal sinuses, radiography of the paranasal sinuses, and lateral airway radiography to determine the adenoid size), the percent of patients requiring additional diagnostic and therapeutic procedures (immunoglobulin E, skin prick testing, immunotherapy, impedance audiometry, endoscopic nasopharyngoscopy, adenoidectomy, septoplasty, tympanostomy tube placement, and turbinoplasty), and the percent of patients requiring additional resources used for treatment-related adverse events (cauterization, anterior nasal packing, analgesic, and topical antibiotics).

Unit costs of all medications were taken from the Drug Price Information System (SISMED, 2013) [9], an official database provided by the Colombian Ministry of Health and Social Protection, which represents an important primary source of medication prices in the country. Costs of INS for the model were calculated as the expected days of therapy per year multiplied by their daily cost, dosed at their recommended starting doses.

Costs were calculated in Colombian Pesos (COP) and converted to Dollars (US$) based on the average exchange rate for 2013 (1 US$ = 1868.90 COP) [14]. All the costs were adjusted to 2013 COPs before converting them to US$s. Given that the model duration was 1 year, costs and effects were not discounted. The study protocol was approved by the local ethics board. The analysis in this article is based on previously conducted studies, and does not involve any new studies of human or animal subjects performed by any of the authors.

Sensitivity Analyses

A series of one-way, two-way, and multi-way sensitivity analyses (using a tornado diagram) and the effect of alternative model specifications were examined. Data ranges in sensitivity analyses were derived from various sources: for unit costs of resources, data ranges were plus or minus 25% of the base value, because it was considered that this range represents a reasonable one for these unit costs. For the rates of resource utilization for patients with no improvement of AR symptoms and for patients with treatment-related adverse events with INS, data ranges in sensitivity analyses were derived from 95% confidence intervals (CI) from the review of the literature, the values reported in the consensus of experts, and the review of the medical records. Finally, for unit costs of all medications, data ranges in sensitivity analyses were established from the low and high values reported from SISMED (an official database provided by the Colombian Ministry of Health). In addition, a probabilistic sensitivity analysis using second-order Monte Carlo simulation was conducted to account for the uncertainties associated with the model parameters using a cohort of 10,000 trial simulations for both alternatives. This probabilistic sensitivity analysis allowed us to generate 95% uncertainty intervals (UI) around costs and effects. These were presented graphically on a cost-effectiveness plane to show the estimated joint distribution of incremental costs against incremental effects and evaluated using net benefit analysis [15]. Subsequently, a cost-effectiveness acceptability curve (CEAC) was derived from these data [16] to identify which alternative would be the most cost-effective at various thresholds of willingness-to-pay (WTP) for TIX score point. All analyses were performed with software (TreeAgePro 2012, TreeAge Software, Williamstown, MA, USA).

RESULTS

Base-Case Analysis

With respect to single INS the value of both the unit cost and the cost of daily treatment with BDNS were lower than those costs of MFNS, whereas the efficacy of MFNS was greater than the efficacy of BDNS. Likewise, the potential for side effects was higher for BDNS compared to MFNS (Table 2).

While the anterior nasal packing was the resource with the greatest unit cost for patients with drug-related adverse events with INS use, septoplasty was the resource with the greatest unit cost for patients whose symptoms did not improve with the use of INS (Table 3). Likewise, while cauterization was the resource with the greatest rate of utilization for patients with drug-related adverse events with INS, immunotherapy, and endoscopic nasopharyngoscopy were the resources with the greatest rate of utilization for patients whose symptoms did not improve with the use of INS (Table 4).

Using the base-case assumptions, the model showed that compared to BDNS, therapy with MFNS was associated with lower costs (US$229.78 vs. US$289.74 average cost per patient over 12 months) and a greater improvement in TIX score (0.9724 vs. 0.8712 score points on average per patient over 12 months), thus leading to dominance. A position of dominance negates the need to calculate an incremental cost-effectiveness ratio (Table 5).

Table 2 Probability parameters (baseline value, low value and high value) used in decision tree model

Variable	Baseline value	Low value	High value
Treatment with beclomethasone dipropionate nasal spray			
Improvement of symptoms	44.0	40.0	48.0
Improvement of nasal symptoms	50.0	45.0	50.0
Improvement of ocular symptoms	25.0	23.0	28.0
Side effects	77.0	69.0	85.0
Epistaxis	28.0	25.0	31.0
Treatment with mometasone furoate nasal spray			
Improvement of symptoms	77.0	69.0	85.0
Improvement of nasal symptoms	43.0	39.0	47.0
Improvement of ocular symptoms	28.0	25.0	31.0
Side effects	11.0	10.0	12.0
Epistaxis	100.0	0.0	0.0
Treatment with budesonide aquous nasal spray			
Improvement of symptoms	88.0	79.2	96.8
Improvement of nasal symptoms	25.0	23.0	28.0
Improvement of ocular symptoms	37.0	33.0	41.0
Side effects	44.0	40.0	48.0
Epistaxis	44.0	40.0	48.0

Probability calculations based on three efficacy and three safety parameters summarized in a therapeutic index [10]

Sensitivity Analyses

One-way, two-way, and multi-way deterministic sensitivity analyses (using a tornado diagram) showed that the cost of pediatric consultation and the cost of MFNS have the highest impact on the model outcome. However, MFNS was the dominant strategy over all the ranges of the cost of pediatric consultations and the cost of MFNS analyzed.

Table 3 Unit costs of resources for pediatric allergic rhinitis (US$, 2013)

Cost item	Baseline value	Low value	High value
Drug-related adverse events with topical intranasal corticosteroids			
Cauterization	17.81	13.36	22.26
Anterior nasal packing	28.56	21.42	35.70
Topical antibiotic	3.21	2.41	4.01
Analgesic	3.47	2.60	4.33
Seric cortisol	26.75	20.06	33.44
Diagnostic and/or therapeutic procedures[a]			
Immunoglobulin E	32.41	24.30	40.51
Skin prick testing	80.26	60.20	100.33
Immunotherapy[b]	62.02	46.51	77.52
Lateral airway radiography	18.43	13.82	23.04
CT scan of the paranasal sinuses	193.61	145.21	242.01
Impedance audiometry	6.02	4.51	7.52
Endoscopic nasopharyngoscopy	474.73	356.05	593.41
Tympanostomy tube placement	200.12	150.09	250.15
Turbinoplasty	433.26	324.95	541.58
Adenoidectomy	333.47	250.10	416.84
Septoplasty	824.84	618.63	1,031.05
Medical consultations[c]	24.08	18.06	30.10
Topical intranasal corticosteroids			
Beclomethasone dipropionate nasal spray[d]	2.34	2.29	2.76
Mometasone furoate nasal spray[e]	13.29	9.13	14.25
Budesonide aquous nasal spray[f]	43.62	37.59	46.22

CT computed tomography

[a] Diagnostic and/or therapeutic procedures for patients whose symptoms did not improve

[b] Complete monthly cost of immunotherapy

[c] Unit cost of medical consultations (pediatrician, otolaryngologist, allergologist, endocrinologist, and ophthalmologist)

[d] Unit cost of beclomethasone dipropionate nasal spray, 200 doses

[e] Unit cost of mometasone furoate nasal spray, 140 doses

[f] Unit cost of budesonide aqueous nasal spray, 120 doses

Parameter distributions used in the probabilistic sensitivity analysis are presented in Table 6. The results of the probabilistic sensitivity analysis are graphically represented as a scatter plot in Fig. 2. This scatter plot shows that MFNS tends to be associated with lower costs and a greater improvement in TIX score. Based on the results from this simulation, the 95% UI for cost per patient treated with MFNS and BDNS were US$186.87 to US$282.22 and US$238.20 to

Table 4 Rates of resource utilization for patients with no improvement of allergic rhinitis symptoms and for patients with treatment-related adverse events with topical INS

Resources	Rate of resource utilization	Range
Patients with no improvement of allergic rhinitis symptoms		
Immunoglobulin E[a]	3.7%	1.7–5.7%
Skin prick testing[a]	46.7%	40.0–51.7%
Immunotherapy[a]	50.0%	38.3–58.3%
Lateral airway radiography[a]	34.4%	31.0–37.3%
CT scan of the paranasal sinuses[a]	41.7%	37.3–46.0%
Impedance audiometry[a]	3.3%	1.7–6.7%
Endoscopic nasopharyngoscopy[a]	50.0%	44.0–55.0%
Tympanostomy tube placement[a]	0.7%	0.0–2.0%
Turbinoplasty[a]	25.0%	20.0–30.0%
Adenoidectomy[a]	7.7%	3.3–13.3%
Septoplasty[a]	2.3%	1.0–6.3%
Pediatric consultation[b]	4.3	4.0–5.0
Otolaryngologist consultation[b]	4.3	4.0–5.0
Allergologist consultation[b]	3.0	2.0–4.0
Patients with treatment-related adverse events with INS		
Epistaxis		
Cauterization[a]	4.7%	2.3–9.7%
Anterior nasal packing[a]	0.7%	0.3–2.7%
Topical antibiotic[a]	3.7%	2–7.3%
Analgesic[a]	1.3%	0.3–3%
Pediatric consultation[b]	3.6	3.0–4.0
Otolaryngologist consultation[b]	2.6	2.0–3.0
Treatment-related adverse event other than epistaxis		
Pediatric consultation[b]	3.0	2.0–4.0
Endocrinologic consultation[b]	2.0	1.0–3.0
Ophthalmologist consultation[b]	2.0	1.0–3.0
Seric cortisol measurement[c]	2.0	1.0–3.0

CT computed tomography, *INS* intranasal corticosteroids

[a] Average percentage of patients that require the diagnostic/therapeutic procedure

[b] Average number of consultations per year

[c] Average number of measurements per year

Table 5 Base-case cost-effectiveness analysis of MFNS versus BDNS for pediatric allergic rhinitis treatment

Category	Strategy	Cost (US$)	Incremental cost (US$)	Effectiveness (TIX score)	Incremental effectiveness (TIX score)	Cost/effectiveness
	MFNS	229.78	–	0.9724	–	236.31
Absolutely dominated	BDNS	289.74	59.96	0.8712	−0.1012	332.58

BDNS beclomethasone dipropionate nasal spray, *MFNS* mometasone furoate nasal spray, *TIX* therapeutic index

US$348.60, respectively. Likewise, these 95% UI for TIX scores were 0.9464–0.9897 and 0.8240–0.9131 score points, respectively. In 97.6% of the iterations, MFNS was associated with a greater improvement in TIX score and lower costs compared to therapy with BDNS. The CEAC shows that the probability that daily therapy provides a cost-effective use of resources compared to intermittent therapy exceeds 99% for all WTP thresholds (Fig. 3).

DISCUSSION

The present study shows that compared to BDNS, therapy with MFNS for treating pediatric patients with AR is a dominant strategy because it showed a greater improvement in a TIX reflecting both efficacy and safety, at lower total treatment costs. Although the variables that exhibited a significant effect on these results were the cost of pediatric consultation and the cost of MFNS, therapy with MFNS was the dominant strategy over all the ranges of the cost of pediatric consultations and the cost of MFNS analyzed. It is worth mentioning that, to the best of our knowledge, this is the first study to compare MFNS and BDNS for treating pediatric patients with AR, in terms of both cost and effectiveness.

The findings of the present study support the use of MFNS as the most efficient therapy in pediatric patients with AR diagnosis in Colombia and probably in other similar low- and middle-income countries (LMIC), at least when it is compared exclusively with BDNS. These results are important because although MFNS has a higher cost of acquisition relative to BDNS, it is associated with lower total treatment costs and better health outcomes in pediatric patients with AR. These findings should help to support the daily clinical decision-making process of choosing between a range of options for these patients. When choosing the most efficient therapy for treating pediatric AR, it is possible to impact on the significant morbidity and economic burden associated with the disease. Although traditionally it has been assumed that safety and efficacy is proven for all available INS, and that they are all equally effective in controlling symptoms of AR, our results do not support this previous assumption. Although there is no single trial which directly compares all the available INS, and our model did not include all INS currently licensed in Colombia for use in children with AR, the systematic aggregation and analysis of both efficacy and cost data in our study suggests that the choice among the different treatments available can have a great impact on the health outcomes and costs of the disease.

Our results agree with those published by Portnoy et al. [17] who found, using an evidence-based medicine approach to assess efficacy and safety in a combined parameter

Table 6 Parameter distributions used in the probabilistic sensitivity analysis

Probability distribution	Distribution parameters	Distribution parameters
Beta distribution	Alpha	Beta
Probability of improvement of symptoms		
BDNS	270.600	344.400
MFNS	84.459	25.228
BANS	47.120	6.425
Probability of improvement of nasal symptoms		
BDNS	199.500	199.500
MFNS	263.052	348.697
BANS	299.750	899.250
Probability of improvement of ocular symptoms		
BDNS	299.750	899.250
MFNS	250.600	644.400
BANS	215.247	366.502
Probability of side effects		
BDNS	84.459	25.228
MFNS	430.650	3484.350
BANS	270.600	344.400
Probability of epistaxis		
BDNS	250.600	644.400
MFNS	–	–
BANS	270.600	344.400
Gamma distribution	Alpha	Lambda
Cost of cauterization	64.072	3.597
Cost of anterior nasal packing	64.000	2.241
Cost of topical antibiotic	64.400	20.062
Cost of analgesic	64.370	18.550
Cost of seric cortisol	63.952	2.390
Cost of immunoglobulin E	64.039	1.975
Cost of skin prick testing	64.000	0.797
Cost of immunotherapy	64.000	1.031
Cost of lateral airway radiography	63.930	3.468
Cost of CT scan of the paranasal sinuses	64.006	0.330

Table 6 continued

Probability distribution	Distribution parameters	Distribution parameters
Cost of impedance audiometry	64.000	10.631
Cost of endoscopic nasopharyngoscopy	2583.447	5.441
Cost of tympanostomy tube placement	64.000	0.319
Cost of turbinoplasty	64.000	0.147
Cost of adenoidectomy	63.996	0.191
Cost of septoplasty	64.000	0.077
Cost of BDNS	396.603	169.488
Cost of MFNS	107.802	8.111
Cost of BANS	408.761	9.370

BANS budesonide aqueous nasal spray, *BDNS* beclomethasone dipropionate nasal spray, *CT* computed tomography, *MFNS* mometasone furoate nasal spray

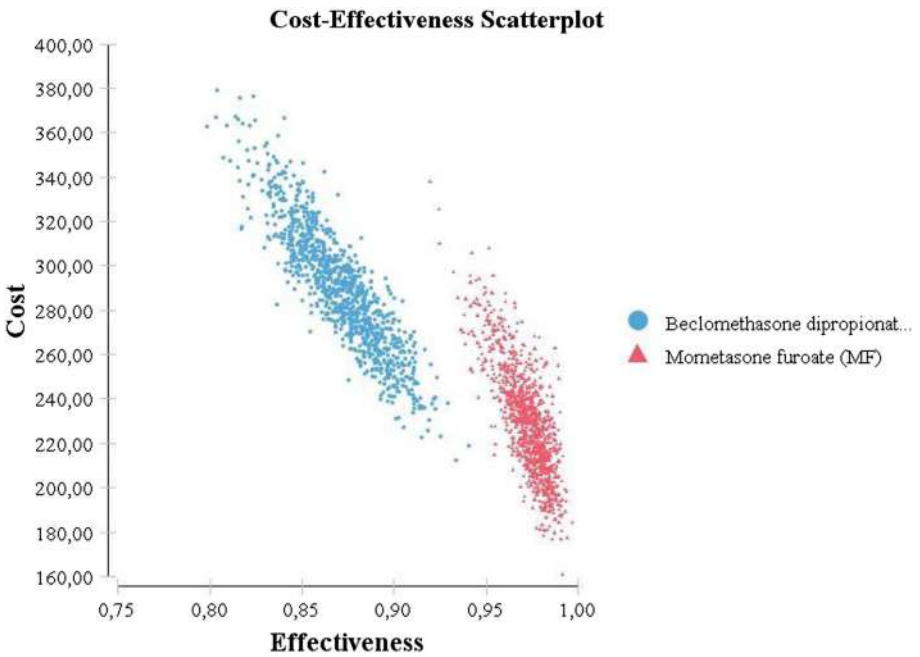

Fig. 2 Scatter plot of each iteration's cost and effectiveness values for each strategy in pediatric allergic rhinitis. The *x*-axis shows effectiveness measured as efficacy and safety parameters summarized in a therapeutic index; the *y*-axis shows costs measured in dollars (US$, 2013). Each point represents one of the 10,000 trial simulations, where each input was assigned a random value according to its probability density function

comparing different INS, the best safety/efficacy ratio for MFNS. This study, however, considered only one parameter each for safety and efficacy, did not include BDNS in the analyses, and did not incorporate costs of alternative treatments. Likewise, in agreement with our findings, there are reports that support the difference in the proportion of costs for a daily dose of BDNS

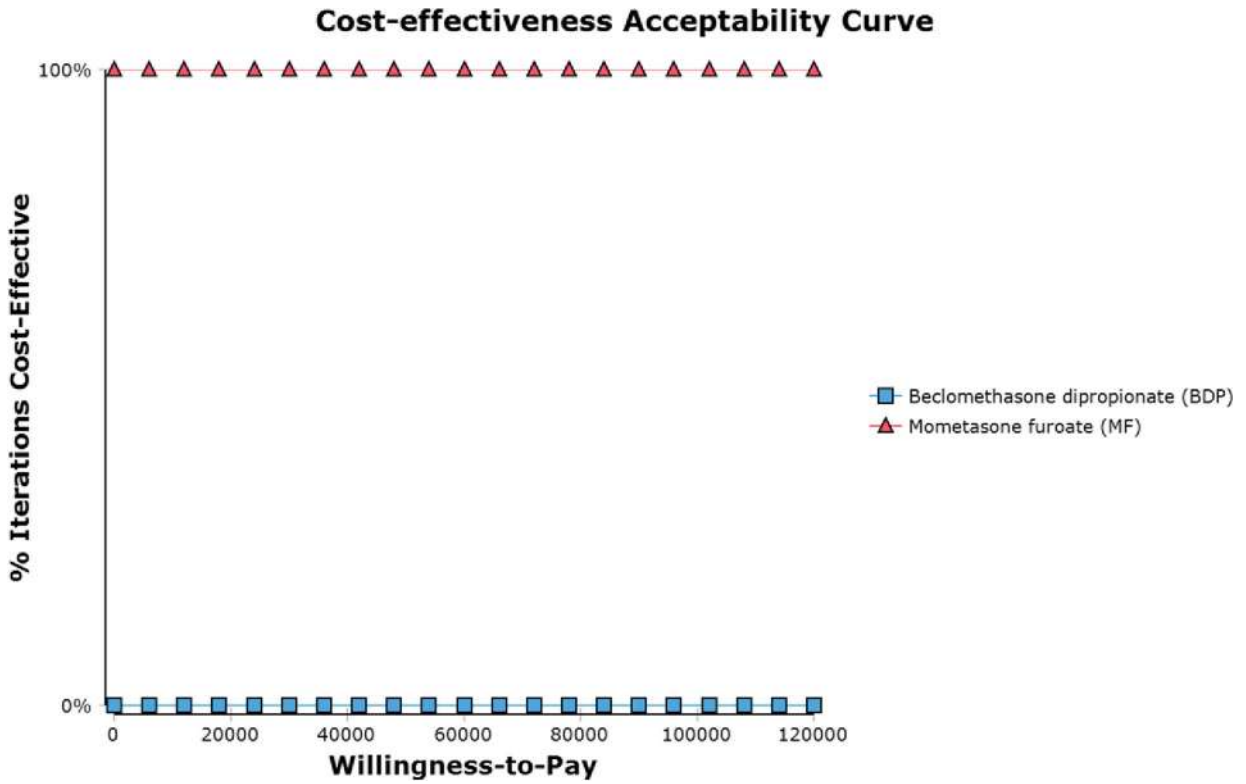

Fig. 3 Cost-effectiveness acceptability curve with MFNS versus BDNS for pediatric allergic rhinitis. The cost-effectiveness acceptability curve shows the probability of MFNS being cost-effective compared to BDNS over a wide range of WTP thresholds. This probability exceeds 99% for all WTP thresholds. *BDNS* beclomethasone dipropionate nasal spray, *MFNS* mometasone furoate nasal spray, *WTP* willingness-to-pay

compared to a daily dose of MFNS [18]. Reissman et al. [19] determined the physician prescribing patterns of the leading INS from the National Disease and Therapeutic Index database in the US, and compared economic differences resulting from these prescribing behaviors. The authors of this study concluded that BANS offers more days of treatment at a lower cost per day than other leading INS. However, unlike our study, this study did not include BDNS in the analyses, did not consider parameters for safety or efficacy of alternative treatments, and did not take into account that starting dosage of INS is different in pediatric patients compared to adult patients. For the reasons mentioned above, it is difficult to more accurately compare our results with those published in the literature.

Our model also has some limitations. First, the base-case analysis was run for 12 months instead of a complete lifetime. However, we judged a 12-month period to be enough for determining the major health and economic consequences of the use of INS in pediatric AR. Second, we did not take into account the effect of incomplete and failing adherence to therapy that typically occurs when treating chronic diseases such as AR. However, this is a conservative approach, since fewer prescribed daily doses are likely an important component of adherence to AR therapy and improved long-term outcomes [20], and there are differences in

dosing regimens between MFNS and BDNS (once daily vs. twice daily, respectively). In fact, published studies have reported a significantly greater level of adherence in patients with AR treated with MFNS compared to those treated with BDNS [21]. Third, although we assumed that differences in the results of the efficacy and safety parameters summarized in the TIX have a similar clinical significance, it's unclear whether this assumption is actually true. This is mainly because there has not been a direct comparison of all INS with regard to the efficacy and safety outcomes analyzed in the present study. Fourth, assumptions regarding the probability of improvement of nasal symptoms, ocular symptoms and global assessment, the probability of treatment-related adverse events, and if these adverse events comprised epistaxis or not, were derived from a published study in which authors only included studies up to 2009, so it is probable that this study does not reflect the current state of scientific knowledge. However, in this study, authors performed a systematic review of the literature and developed a TIX reflecting both efficacy and safety of these substances in a combined assessment. Although this fact increase the confidence in obtaining unbiased results, it would be important that future studies determine the cost-effectiveness of different INS based on more recent literature. Finally, cost data were obtained from a single clinical center and may not be representative of the whole country. However, these data were obtained from a pediatric clinic that receives patients from the most important and representative medical insurance companies in the city. Moreover, costs were subject to wide sensitivity analyses.

CONCLUSIONS

The present analysis shows that in Colombia, compared with BDNS, therapy with MFNS for treating pediatric patients with AR is a dominant strategy because it showed a greater improvement in a TIX reflecting both efficacy and safety, at lower total treatment costs. Although it is difficult to assess the clinical relevance of differences in efficacy and safety parameters summarized in the TIX, these results may help to support clinical decision making until more robust evidence is available.

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Conflict of interest. Carlos E. Rodriguez-Martinez and Monica P. Sossa-Briceño declare that they have no conflict of interest. Elkin Vladimir Lemos is an outcomes research manager in MSD Colombia.

Compliance with ethics guidelines. The analysis in this article is based on previously conducted studies, and does not involve any new studies of human or animal subjects performed by any of the authors.

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