



ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/vhri

Cost-Effectiveness of the Quantification of Enzymatic Activity in Leukocytes in Comparison to Its Nonrealization for a Rare Disease in Latin America: The Case of Mucopolysaccharidosis Type II in Colombia

Elizabeth Parody, MSc, PhD^{1,*}, Cesar A. Guevara, MD, MSc², Andrés Aguirre, MSc³, Paula M. Tello, MD⁴

¹Faculty of Natural Sciences, Universidad Icesi, Cali, Colombia; ²Faculty of Health Sciences, Universidad Icesi, Institutional physician, Foundation Valle del Lili, Cali, Colombia; ³Research Center for Social Protection and Health Economics (PROESA), Universidad Icesi, Cali, Colombia; ⁴Faculty of Health Sciences, Universidad Icesi, Cali, Colombia

ABSTRACT

Background: Mucopolysaccharidosis (MPS) type II is produced by a deficiency of iduronate-2-sulfatase (I2S). The quantification of the enzyme activity in leukocytes is used as diagnostic confirmation of MPS. **Objective:** To determinate the cost-effectiveness of the measurement of I2S enzyme activity in leukocytes compared with not carrying out the enzyme activity measurement for diagnostic confirmation of MPS II from the perspective of the Colombian health system. **Methods:** A cost-effectiveness analysis was conducted on the basis of a decision tree model. The measure of effectiveness was the correct diagnosis of cases of MPS II. The costs of I2S enzymatic quantification in leukocytes, consultation with a geneticist and with other specialists, and costs of diagnostic procedures were included. The time horizon was less than 1 year. A probabilistic sensitivity analysis was performed

using Monte-Carlo simulation with 10,000 iterations. **Results:** The incremental cost was –US \$43,145 with an incremental effectiveness of 42 cases. The probabilistic sensitivity analysis confirms the results of basal data, in which the quantification of I2S enzyme activity was less costly and more effective than the alternative. **Conclusions:** The quantification of I2S enzymatic activity is a dominant technology for the diagnostic confirmation of MPS II, compared with not making the quantification, from the perspective of the Colombian health system.

Keywords: cost-effectiveness, Hunter syndrome, iduronate-2-sulfatase, mucopolysaccharidosis.

Copyright © 2016, International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Published by Elsevier Inc.

Introduction

Mucopolysaccharidosis (MPS) is a set of disorders of the lysosomal storage produced as a result of a deficiency of the enzymes necessary for the degradation of glycosaminoglycans (GAG). The accumulation of GAG produces changes in different body systems.

MPS type II or Hunter syndrome is caused by the deficiency of iduronate-2-sulfatase (I2S), which leads to deposits of heparan and dermatan sulfate. The incidence of this type of MPS is one of the most frequent, estimated at 1 in 140,000 to 156,000 live births in Europe [1]. In the United States, the incidence is estimated at 1 in 250,000 live births [2]. The incidence in Latin America oscillates between 0.69 and 1.19 cases in 100,000 live births [3].

In Colombia, the reported frequency of MPS II is 0.45 cases per 1000 live births [4], with 4 cases reported during the period 1987 to 2008 [5]. According to the Colombian Fund for High Cost

Illnesses, there are actually 46 known cases of MPS (Fondo Colombiano de Enfermedades de Alto Costo, personal communication, October 2014).

Given the systematic involvement of the illness, early diagnosis is necessary as a means to establish therapeutic plans for the minimization of the illness impact on the personal and social functioning of the patient. Nevertheless, the diagnosis may be delayed given the epidemiological behavior of the illness, the physician's unfamiliarity with this condition, and the presence of only slight clinical manifestations in some patients.

Diagnosis includes the examination of clinical factors, biochemical parameters, and molecular characteristics. Faced with a suspicion of MPS, the concentration of GAG in urine should be measured as a first test. If elevated, the determination and quantification of its amount should be carried out with a view to guiding the request for enzymatic quantification. Given that

Conflicts of interest: The authors have indicated that they have no conflicts of interest with regard to the content of this article.

* Address correspondence to: Elizabeth Parody, Faculty of Natural Sciences, Universidad Icesi, Calle 18 No. 122-135, Cali, Colombia.

E-mail: eparody@icesi.edu.co

2212-1099/\$36.00 – see front matter Copyright © 2016, International Society for Pharmacoeconomics and Outcomes Research (ISPOR).

Published by Elsevier Inc.

<http://dx.doi.org/10.1016/j.vhri.2016.01.003>

the concentration of GAG may show a high proportion of false negatives, it is always recommendable to carry out the enzymatic measurement [1,6,7]. At present, the metabolic confirmation of the condition is made by the quantification of enzymatic activity in leukocytes, fibroblasts, or plasma.

MPS has an important impact on the health and quality of life of the patient. Because of its chronic and multisystemic character, considerable costs are generated for the health system and society in general. In the United Kingdom, the average annual cost per patient with MPS financed by the health service (hospital and other services) is £7,600 for children and £11,900 for adults [8].

Published information on costs related to this illness in Colombia could not be found. Nevertheless, it is desirable to have the tools available for decision making in the health sector, such as the economic evaluations in the Colombian context. Therefore, the objective of this study was to determinate the cost-effectiveness ratio in the quantification of I2S enzyme activity in leukocytes as compared with not making the quantification, from the perspective of the Colombian health system.

Methods

This article was developed following the Consolidated Health Economic Evaluation Reporting Standards and the CHEERS Checklist.

Population Studied

The population studied consisted of male patients of any age with clinical indications of MPS II of whatever severity. Only male patients were chosen because the illness is X-chromosome-linked. No subgroup analysis by age or by other characteristics was carried out because it appeared that no clinical characteristics or aspects related to particular diagnostic tests affected costs or outcomes.

Selection of Alternatives

The intervention was the quantification of I2S enzymatic activity in leukocytes in the Colombian health system. The comparison was the nonrealization of the quantification of enzymatic activity. In this case, given the necessity of making a diagnosis in a setting in which it was not possible to make a quantification, the diagnostic strategy most reported in the literature, and validated by clinical experts, consists in specialist consultations, diagnostic imaging, laboratory tests, and the quantification of GAG in urine.

Time Horizon and Discount Rate

The time horizon was less than 1 year, which is the period in which differences in outcomes are expected, associated with the use of quantification of I2S enzyme activity in leukocytes to confirm diagnosis of MPS type II. For this time horizon, adjustments for discount rate are not applied.

Perspective

Following methodological recommendations for the realization of economic evaluation studies in the Colombian agency for health technology assessment (in Spanish: Instituto de evaluación tecnológica en salud, IETS) [9], the perspective of the Colombian health system was selected.

Effectiveness

The effectiveness is measured as the number of cases diagnosed correctly, that is, the sum of the *true positives* and the *true negatives*. Despite being an intermediate outcome, dealing with an economic evaluation of diagnostic tests, the principal reason for this is to provide information for the making of clinical

Table 1 – Number of correctly diagnosed cases of MPS II for both alternatives evaluated in a hypothetical cohort of 100 patients with suspected MPS II for a pretest probability of 70%*.

Parameter	Intervention (quantification of I2S enzymatic activity)	The comparison (no quantification of I2S enzymatic activity)
True positive	70	32
False negative	0	38
False positive	0	6
True negative	30	24
Number of correctly diagnosed cases (true positive + true negative)	100	56

I2S, iduronate-2-sulfatase; MPS II, mucopolysaccharidosis type II.
* Source: Consultation with clinical experts.

decisions. Quality-adjusted life-year could not be quantified because of the absence of data in the literature.

For the measurement of this outcome, in accordance with the recommendations in the methodology guide, the clinical group was asked to provide estimations and ranges of sensitivity and specificity for each of the diagnostic alternatives because of the absence of this information derived from studies of diagnostic validity. The pretest probability is considered as the proportion of patients with reduced enzymatic activity given the presence of an MPS II phenotype. For this case, the experts considered this probability to be 70%. Given that the quantification of enzyme activity in leukocytes is the criterion standard method that defines the illness, a sensitivity and specificity of 100% is attributed to it. Information regarding sensitivity and specificity related to the physical examination, diagnostic imaging, and GAG in urine was absent from the literature. Therefore, 17 clinical geneticists were questioned by means of an electronic questionnaire.

The number of cases correctly diagnosed for each alternative are presented in Table 1.

Costs: Identification, Measurement, and Valuing

Because this study is from the perspective of the Colombian health system, only the direct resources of the health system were taken into account.

For the identification of the resources associated to the technologies, information was initially sought in the MPS diagnostic guides [1,10], and this information was later validated by the clinical geneticists by means of a virtual questionnaire, with the objective of appraising the use of these resources in the habitual clinical practice in the Colombian context.

The questions related to resources were principally orientated to the group that did not carry out the test of enzyme activity, that is, to which clinical specialists are patients with clinical suspicion of MPS referred and what diagnostic procedures are carried out. In accordance with this information and that from the literature, the costs related to the present technology are those of medical consultations, nonconfirmatory diagnostic procedures, and the test for GAG in urine.

For the new technology, costs of the quantification of enzyme activity (US \$192.06), the consultation with a geneticist, and the enzymatic quantification of a second arylsulfatase (arylsulfatase B, US \$74.18) are considered.

Download English Version:

<https://daneshyari.com/en/article/989960>

Download Persian Version:

<https://daneshyari.com/article/989960>

[Daneshyari.com](https://daneshyari.com)