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Cost-Effectiveness of Intracranial Pressure Monitoring in Pediatric Patients with Severe Traumatic Brain Injury: A Simulation Modeling Approach

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ABSTRACT

Objectives: To conduct an economic evaluation of intracranial pressure (ICP) monitoring on the basis of current evidence from pediatric patients with severe traumatic brain injury, through a statistical model. **Methods:** The statistical model is a decision tree, whose branches take into account the severity of the lesion, the hospitalization costs, and the quality-adjusted life-year for the first 6 months post-trauma. The inputs consist of probability distributions calculated from a sample of 33 surviving children with severe traumatic brain injury, divided into two groups: with ICP monitoring (monitoring group) and without ICP monitoring (control group). The uncertainty of the parameters from the sample was quantified through a probabilistic sensitivity analysis using the Monte-Carlo simulation method. The model overcomes the drawbacks of small sample sizes, unequal groups, and the ethical difficulty in randomly assigning patients to a control group (without monitoring). **Results:** The incremental cost in the monitoring group was Mex$3,934 (Mexican pesos), with an increase in quality-adjusted life-year of 0.05. The incremental cost-effectiveness ratio was Mex$81,062. The cost-effectiveness acceptability curve had a maximum at 54% of the cost-effective iterations. The incremental net health benefit for a willingness to pay equal to 1 time the per capita gross domestic product for Mexico was 0.03, and the incremental net monetary benefit was Mex$5,358. **Conclusions:** The results of the model suggest that ICP monitoring is cost-effective because there was a monetary gain in terms of the incremental net monetary benefit.

Keywords: brain injuries, cost-benefit analysis, decision support techniques, physiologic monitoring, probabilistic models, uncertainty.

Introduction

Severe traumatic brain injury (STBI) in children is a major cause of disability and mortality worldwide [1]. In Mexico in 2012, accidents ranked first in children aged 1 to 14 years, according to the National Institute of Statistics, Geography, and Informatics, half of which correspond to traumatic brain injury [2]. STBI is considered to be present in patients with a Glasgow Coma Scale (GCS) score from 3 to 8 points within the first 48 hours after the accident [3,4]. The health burden for children who suffer STBI is enormous because their physical and mental capacity may be greatly affected [5–7]. In addition, the associated care and rehabilitation procedures will have a financial impact on both their families and the State, and will translate into direct and indirect health costs. For example, in Germany, Sweden, and Spain, the average cost fluctuates between €7,600 and €9,000 per hospitalization, whereas the annual cost of care for the first 2 years after the injury has been estimated at more than €100,000 [8]. In the United States, the economic burden of care for patients with traumatic brain injury is substantial [9] given that the cost of hospitalization in 2006 and 2007 averaged US $21,460 ± $21,212 per patient [10]. Nevertheless, if the patient is a child, the cost will accumulate for the rest of his or her life [11]. Thus, the burden of annual hospitalization in children with this condition was more than US $1 billion in 2006 [12]. This amount did not include the cost of social service systems nor the value of the hourly work earnings that were not collected by relatives who cared for patients with post-traumatic sequelae [13,14]. To date there are no reports on the costs associated with STBI in children from Latin American countries, despite the health and economic impact of this condition.

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

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The damage caused by the impact at the time of the trauma is known as the primary lesion. In addition, secondary injury results from changes in the extracellular environment, leading to increases in the intracranial pressure (ICP), which can limit the blood supply to the brain tissue and, in turn, produce a decrease in the cerebral perfusion pressure (CPP) [15]. Nowadays, ICP monitoring is a measurable parameter that can direct treatment toward the maintenance of an adequate CPP, and it is believed to have a positive influence on survival and quality of life [16].

Nevertheless, the use of ICP monitoring for its management is not fully accepted. In the "Guidelines for the management of severe brain injury" [1], the use of ICP monitoring is mentioned as a recommendation because there is insufficient evidence to establish its effectiveness or lack thereof in pediatric patients. Hence, globally there is controversy about its use, although there are numerous class II studies that endorse it [1,17].

Furthermore, the effectiveness and cost-effectiveness of ICP monitoring in children have not been investigated directly in the Latin American region. This study attempts to provide knowledge about the value of recommending ICP monitoring in pediatric patients with STBI in Mexico. This information could be useful in other Latin American countries under similar economic conditions with respect to health care.

Data collection of patients with STBI faces several challenges [18] because it is an extremely serious condition. Usually there is a lack of uniform criteria for the selection of variables [19], sample sizes are small, and groups to be compared are unequal because of the ethical difficulty in randomly assigning patients to a control group (without monitoring) [20,21] or because physicians may refuse to monitor or not to monitor some patients [22]. This produces samples affected by uncertainty, and so clinical studies have not provided a conclusive answer about the effectiveness and cost-effectiveness of ICP monitoring.

This study aimed to assess whether ICP monitoring is cost-effective, by using a statistical model, which is a simplified way to approximate a real situation, using formal math. The inputs for the model are the probability distributions of the related costs and quality-adjusted life-year (QALY) of Mexican children with STBI graded by severity using the GCS score. The use of probability distributions in a statistical model overcomes the uncertainty related to the size of a sample, adjusts for the inequality about the severity of the primary lesion, and permits evaluating the cost and effectivenes of ICP monitoring. The purpose of this approach is to produce evidence about the value of this technology under a standard care clinical environment to support decision making in the context of public hospitals.

Methods

The approach consisted of a trial-based economic evaluation using a statistical model. A prospectively collected sample of patients with STBI aged between 1 and 15 years with a previously normal psychomotor development and without concomitant chronic diseases was obtained.

Data Collection

The study was conducted in two hospitals and the data collection period was from November 2011 to June 2014. The study was submitted to the institutional review boards of both hospitals, which gave approval (R-2011-785067 and ICD-002-6-11, respectively). Authorization to enter the study was requested from the parents or legal guardians, who signed the written informed consent form if they were willing to participate.

The follow-up period was 6 months post-trauma. All patients were being treated either at the High Specialty Medical Unit of the Mexican Social Security Institute or at the Agustín O'Horán General Hospital of the Ministry of Health of Yucatán, both of which are public, third-level hospitals located in Mérida, Yucatán, Mexico. In the former, patients are affiliated government workers or their relatives, and in the latter patients are covered by the so-called Seguro Popular (Popular Insurance), or else they are people with no medical insurance. The intraparenchymal ICP probes and monitors were obtained through funding from the Teacher Improvement Program (*Programa de Mejoramiento para el Profesorado*), for clinical and research purposes, and were made available in both hospitals free of charge.

The evaluation of each patient by a neurosurgeon was requested and, according to his clinical judgment, it was decided whether to install an intraparenchymal probe (Spiegelberg SND 13.1.53, 3PN probe, Hamburg, Germany) for ICP monitoring, thus giving rise to the study groups (monitoring group = with ICP monitoring; control group = without ICP monitoring). The intraparenchymal Spiegelberg probe has a balloon at its tip, which is filled with a small, controlled amount of air and is connected to an ICP monitor of the same brand (model HDM26.1). The system meets the specifications of the American national standard for ICP monitoring [23].

All patients with ICP monitoring were treated according to the management guidelines of the Brain Trauma Foundation [24], the main aims of which are to preserve the CPP above 60 mm Hg and the ICP below 15 mm Hg, as well as to maintain vital functions and to prevent complications of other systems and organs. Nevertheless, because this study was aimed at assessing the cost-effectiveness of ICP monitoring under normal clinical conditions, compliance of these guidelines was not strict. The control group received standard treatment on the basis of the expected pathophysiology after head trauma.

The economic evaluation of ICP monitoring was carried out from the point of view of the patient service provider/payer.

The strategies that were compared were the inclusion of ICP monitoring to guide the treatment of pediatric patients with STBI versus the standard approach, in which ICP monitoring is not used.

Costs

The cost of hospitalization included only direct medical costs and those related to clinical complications, supplies such as medicines, laboratory analyses, imaging studies (ultrasound, computed tomography scans, x-rays), surgeries, and length of stay in the pediatric intensive care unit and in the general pediatric ward. The amounts of these supplies were obtained from the clinical records, and this information was corroborated every day.

The source for the prices of medicines was the 2015 Catalog of the Mexican Social Security Institute Purchasing Department, Yucatán office (unpublished data, 2015). The costs of hospital stays, laboratory analyses, and other studies were taken from the *Official Journal of the Federation* (*Diario Oficial de la Federación*, Mexico) dated April 29, 2014 [25]. The cost of the intraparenchymal probe was the list price provided by the supplier. The ICP monitors did not generate any cost because they were loaned to the hospitals when the probes were purchased. No discount rates were applied to any of the items. All costs are reported in Mexican pesos (Mex$) (exchange rate: ~Mex $18.1 for US $1 on August 19, 2016).

Effectiveness

The measure of effectiveness was the QALY. The Health Utilities Index 2 (HUI-2) [26] was used to estimate the utilities for QALY. The HUI-2 produces a quantity on the basis of health preferences, and when it is used for children, it contains six dimensions: sensation, mobility, emotion, personal care, knowledge, and pain. Each of these dimensions has values ranging from 1 to 4 or 5 points.

A value of 1 corresponds to the healthy state, whereas the higher values represent increasing health deterioration. The total score for each patient (a vector with six values, one for each dimension) was fed to a computer program that transformed it into a utility value, under a Bayesian perspective, which has the advantage of producing lower error estimates [27,28]. The utility values for the HUI-2 range from 1 to 0, with 1 representing "healthy state" and 0 "dead." Utility measurements based on the HUI-2 were derived from a questionnaire applied to the mothers of the affected children in their own homes, at 3 and 6 months after the trauma. The questionnaire included directed questions, and the responses were verified by observing the children.

Statistical Model

The graphical representation of the clinical alternatives is shown in a decision tree (Fig. 1), which begins with the question to be answered (square symbol). The first two branches illustrate the groups to be compared, and a probabilistic node (green circle) follows each one. Each node has two branches that represent the diagnoses related with the grades of severity of the STBI. These are based on the probability of the severity associated with the damage, which is measured by the GCS ($\pi_i, i\in\{1,2\}$), with two possible outcomes: 1) GCS 3–6 representing the more severely affected patients and 2) GCS 7–8 representing the less severely affected ones. Below these branches, *Beta* represents the probability distribution of such diagnosis and # represents the complement of such distribution that forces noncoherent probabilities to sum up to 1 in each given iteration. Because the severity of STBI is a variable whose value is contained in the (0, 1) interval, the most natural distribution for these expectations is the beta family. Thus, these probabilities were transformed into a beta distribution using the Sheffield Elicitation Framework software (Department of Probability and Statistics. University of Sheffield, UK) [29]. In addition, it was assumed that the severity was distributed equally between the groups (monitoring and control), as is expected in a clinical controlled trial. Finally, in the decision tree, each of the four branches end in a red triangle node, where the names of the resulting distributions for cost and QALY are shown. These normal distributions and their corresponding parameter values are included in Table 3.

Estimation of Hospitalization Costs and QALY

For the calculation of the cost (D) of medicines (tablets, capsules, or ampoules) for a given patient k:

$$D_k = \sum_{h=1}^{r_k} a_h b_h c_h d_h,$$

where $k=1,\ldots,n_i$, in which n_i is the number of patients that belong to terminal path i; $h=1,\ldots,r_k$, where r_k is the number of medicines per patient; a_h is the box price/number of units in the box for the hth medicine; b_h is the number of units required to complete one dose (in milligrams or grams, as appropriate) of the hth medicine, c_h is the number of times the medicine was administered in 24 hours; and d_h is the total number of days that the hth medicine was prescribed.

Considering that each terminal node of the model consumes m_i supplies in quantity U_j, at unit price P_j, the total cost was

$$C_i = \sum_{j=1}^{m_i} U_j P_j + \left(\sum_{k=1}^{n_i} D_k\right),$$

and the mean cost was

$$\bar{C}_i = \frac{C_i}{n_i},$$

where $i=1,\ldots,4$ is the number of terminal paths in the tree and n_i is the number of patients that belong to i.

Likewise, the QALY (H) of patient k who survived was calculated with the following formula, adjusted to 1 year:

$$H_k = \frac{(U_3 \times 0.25)+(U_6 \times 0.25)}{0.5}.$$

For the total QALY, $Q_i = \sum_{k=1}^{n_i} H_k$, and for the mean QALY, $\bar{Q}_i = \frac{Q_i}{n_i}$. Then $\bar{C}_i$ and $\bar{Q}_i$, along with their variances, defined the normal probability distributions. Normal distributions were assumed, because symmetric distributions are a practical and convenient manner of representing the distributions of the means, as well as to allow sampling in a more efficient way.

Statistical Analysis

Probabilistic sensitivity analysis (PSA) was used to quantify the uncertainty of the data obtained from the two groups by means of a Monte-Carlo simulation. This involved sampling the density of the distributions and generating the output of the model, which consisted of probability distributions of the expected values of interest. Thus, each sampled iteration generated N different values, and as the number of iterations increased, the variance and, hence, the error of the expected values decreased. That is, the larger the number of iterations, the greater the accuracy. Consequently, the model required 15,000 iterations to produce stable values for the estimators. Increasing the number of iterations further did not produce an improvement in the expected values. The outputs were obtained using the TreeAge Pro 2013 software (TreeAge Software, Inc., Williamstown, MA).

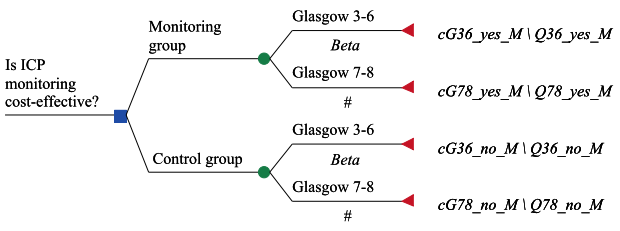

Fig. 1 – Graphical representation of the decision tree for ICP monitoring. Beta ~ be(13.6; 29.9), mean = 0.313, SD = 0.0695. ICP, intracranial pressure; Glasgow, Glasgow Coma Score. See Table 3 for details on the cost and QALY distributions.

Results

Forty-four patients were initially included, and there were no significant differences between the results from the two hospitals with respect to the means of GCS, age, cost, or QALY. Thus, the results were pooled. The general characteristics of the patients are presented in Table 1. It can be seen that the sample size was unequal in both groups. In addition, it turned out that the patients in the monitoring group were more severely affected than those in the control group, considering their GCS scores.

Table 2 presents the unit cost of each included item, as well as the corresponding source, the percentage of patients who used the item, the mean number of units used, and the average cost, for the study groups. The average cost of treatment was higher in the monitoring group than in the control group ($P = 0.002$). In addition, costs were higher and QALY values were lower for patients with lower GCS scores ($P < 0.001$). To model groups accurately, only the 33 surviving patients were included.

To obtain the probability distribution for the inputs in the decision tree (Fig. 1), first the probability of the severity of the lesion was calculated considering the GCS 3–6 scores for the control group. We set a beta distribution with parameters p and q equal to 13.6 and 29.9, respectively: $\pi \sim Be(13.6, 29.9)$. Such beta had

Table 1 – General characteristics of the patients.

Characteristic	Monitoring group (n = 14)	Control group (n = 30)	P value
Age (y), mean ± SD	9.14 ± 4.45	7.62 ± 5.05	0.34*
Sex, male (%)	9 (64)	17 (56.6)	0.68†
GCS score, mean ± SD	5.5 ± 1.74	7.03 ± 1.54	0.005*
3–6 (%)	10 (64)	9 (30)	0.02‡
7–8 (%)	4 (36)	21 (70)	
Survivors (%)	8/14 (57.2)	25/30 (83.4)	0.13‡
With GCS score 3–6	5/10 (50)	5/9 (56)	1‡
With GCS score 7–8	3/4 (75)	20/21 (95.2)	0.3‡

GCS, Glasgow Coma Scale.
* Student *t* test.
† χ^2 test.
‡ Fisher test.

a mean of 0.313 for the GCS 3–6 range and of 0.687 for the GCS 7–8 range, with a variance of 0.0048. The parameters of the distributions for costs and QALY are presented in Table 3. *cG36_yes_M* corresponds to the normal distribution of cost (*c*) for GSC 3–6 (G36) in the monitoring group (yes), which is N(516,688; 318,245), defined by its parameters (mean; SD). Likewise, *Q36_yes_M* ~ N (0.792; 0.233) defines the QALY for GCS 3–6 in the monitoring group, which is normally distributed with parameters 0.792 and 0.233. The other distributions are named in a similar fashion and correspond to the group and main diagnosis branches in Figure 1. It can be seen from the mean values that children in the monitoring group had better QALY results than those in the control group at the end of 6 months after the trauma.

The outputs for the mean values for cost and QALY in each group are presented in Table 4. The mean cost for the monitoring group was Mex$360,306, and for the control group it was Mex $356,372. The mean QALY for the monitoring group was 0.89, and for the control group it was 0.84. The incremental cost and the incremental QALY for the treatment with ICP monitoring was Mex$3,934 and 0.05, respectively. This results in an incremental cost-effectiveness ratio (ICER; ρ) of Mex$81,062.

Figure 2 is a sketch of the uncertainty of the joint distributions of the incremental cost and the incremental QALY. Note that most of the iterations are located near the center, with 60% of them to the right, and 51% in the upper quadrants. Taking into account a willingness-to-pay (WTP) value of Mex$185,866, equivalent to 1 time the per capita gross domestic product (GDP) in Mexico, it turns out that 3.4% of the iterations were below the line in the upper right quadrant. The incremental net health benefit (INHB) was 0.03 QALY, and the incremental net monetary benefit (INMB) was Mex$5,358 (~US $296.05).

The cost-effectiveness acceptability curve (CEAC) (Fig. 3) shows that it reached a maximum of 54% of cost-effective iterations, even with payments as high as Mex$500,000.

Discussion

In this study, the cost associated with the monitoring group was higher than that for the control group. This effect may be attributed to the initial severity of the patients who were to be included in the monitoring group, as has been reported in other studies [30,31], and not to the use of the ICP probe. In addition, the only child in the monitoring group who died had an initial GCS 7–8, but later had a deleterious evolution, and the probe was inserted 48 hours after the STBI. Furthermore, ICP monitoring

Table 2 – Cost of supplies in Mex$ (2015).

Supplies	Unit price	Source	Unit	Monitoring group (n = 14)			Control group (n = 30)		
				Use (%)	Mean use	Cost, mean ± SD	Use (%)	Mean use	Cost, mean ± SD
Medicines	Various	2015 Catalog of the IMSS Purchasing Department, Yucatán	Various	100	–	6,453 ± 4,245	100	–	3,238 ± 1,853
Laboratory studies	145	[25]*	Test	100	62.35	9,041 ± 5,015	100	32.4	4,698 ± 2,736
X-rays and ultrasound	582	[25]*	Study	100	6.35	3,699 ± 2,228	100	4.8	2,793 ± 1,479
CT scans	2,678	[25]*	Study	100	2.79	7,460 ± 3,384	100	2.9	7,766 ± 3,268
Surgeries	28,370	[25]*	Number	100	1.5	42,555 ± 14,185	53	0.1	17,022 ± 9,382
ICP probes	12,000	Commercial price	–	100	1	12,000	–	–	–
PICU days	31,525	[25]*	Number	100	12.21	385,055 ± 186,572	100	7.67	241,691 ± 112,762
General ward days	6,377	[25]*	Number	71	10.36	66,047 ± 62,370	83	9.87	62,919 ± 106,404
Total		[25]*				539,587 ± 255,987			340,243 ± 167,927

CT, computed tomography; ICP, intracranial pressure; IMSS, Mexican Social Security Institute; PICU, pediatric intensive care unit.
* Unit costs by level of medical attention for 2014.

Table 3 – Distributions used as inputs for costs and QALYs in the Probabilistic Sensitivity Analysis.

Cost (Mex$) in thousands, N($\bar{X}$; SD)		QALY, N($\bar{X}$; SD)
cG36_yes_M ~ N(516,688; 318,245)	\	*Q36_yes_M* ~ N(0.792; 0.233)
cG78_yes_M ~ N(289,687; 138,529)	\	*Q78_yes_M* ~ N(0.935; 0.088)
cG36_no_M ~ N(318,923; 115,687)	\	*Q36_no_M* ~ N(0.737; 0.230)
cG78_no_M ~ N(371,505; 191,366)	\	*Q78_no_M* ~ N(0.891; 0.166)

Note. Names correspond to those in Fig. 1. N = normal distribution and $\bar{X}$= mean.
QALY, quality-adjusted life-year.

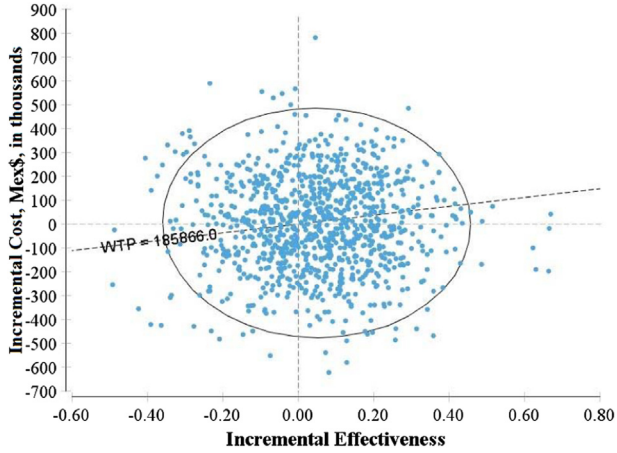

Fig. 2 – Incremental cost-effectiveness scatterplot and ellipse. Note that only 1,000 randomly chosen iterations are shown (out of a total of 15,000). WTP, willingness to pay.

proved to be a safe procedure because there were no harmful effects associated with its use, such as infection or misplacement, nor were there any ICP detection failures.

The difference in the number of patients in each group was because the decision to place the ICP monitoring system was made by the neurosurgeons, and they had a tendency to monitor the most seriously ill patients or those who had a deleterious evolution. This trend has been reported elsewhere, and it is an important consideration when making group comparisons [32].

In this study, the monitoring group had an increased consumption of resources in general. The severity of the primary lesion, however, contributed to a higher cost, and mortality was also higher in that group. Nevertheless, to produce reliable evidence about the value of ICP monitoring, the severity of the primary lesion would have to be present in the same proportion in both groups, as in a randomized trial. One disadvantage of this study is that the analysis derived from the sample used was unable to show an encouraging INHB value, as was expected. This could be due to insufficient experience in using ICP monitoring, because in the two hospitals where the sample was collected it was the first time that the health staff used this technique.

The ICER shows the additional cost per unit of QALY that could be paid if the treatment guided by ICP monitoring were to be selected. In the United States, a cost between US $50,000 and US $100,000 per additional QALY is considered cost-effective [33]. In Mexico, a reference cost that can be used as an indicator of a strategy that can be considered to be cost-effective has not yet been established. Nevertheless, the Commission on Macroeconomics and Health of the World Health Organization suggested the use of the per capita GDP as a measure to define the cost-effectiveness threshold (CET). Hence, strategies with a cost lower than 1 time the per capita GDP are highly cost-effective, those with a cost equal to up to 3 times the per capita GDP are cost-effective, and those with a cost greater than 3 times the per capita GDP are not cost-effective for a given country [34]. Under this criterion, ICP monitoring can be considered highly cost-effective, because the ICER is less than 1 time the per capita GDP in Mexico, which for the years 2011 to 2015 [35] was US $10,325, or approximately Mex$185,866.

Other interventions in Mexico that can be considered cost-effective according to the per capita GDP threshold include rotavirus vaccination, cataract surgery, antidepressants, and some strategies for secondary prevention of ischemic heart disease, which cost less than one-half of the per capita GDP per year of healthy life added. Thus, they can be considered as very cost-effective. The cost-effectiveness values for the heptavalent pneumococcal conjugate vaccine and for the early detection of breast cancer have been estimated to be between 1 and 3 times the per capita GDP. Likewise, influenza vaccination for infants and young children has not been found to be cost-effective because it exceeds 3 times the per capita GDP [36].

The per capita GDP is a gross measure that is not always appropriate in a particular country, for instance, Mexico, which has its specific budgetary constraints, health infrastructure, and disease burden. In addition, the population growth has given rise to overwhelming health care needs, for which there are insufficient funds. Therefore, a national CET value is urgently required to have an adequate and transparent decision-making system for health care allocation. Nowadays, the economic support of such strategies depends on the budget assigned to health care and the decision makers' WTP. Nonetheless, CET is not only an expression of the society's WTP for health, but it is also desirable to consider it, along with other parameters, such as the use of equity, to grant a positive recommendation [37]. For this reason, a guide for the execution of economic evaluation studies has been developed in Mexico to enable the intercomparison of diverse health strategies and then approve those that are more valuable [38]. The use of economic valuation could prevent a waste of money on strategies that do not provide health gain relative to cost, independently of other existing approaches.

The generalized idea in decision making of allocating health resources on the basis of only the ICER is still controversial. One reason for this is that precise estimates require extensive,

Table 4 – ICER results.

Strategy	Cost, mean ± SD	Incremental cost (Δ_C)	QALY, mean ± SD	Incremental QALY (Δ_E)	ICER (ρ)
Monitoring group	360,306 ± 141,178	3,934	0.89 ± 0.097	0.05	81,062
Control group	356,371 ± 136,723		0.84 ± 0.137		

ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

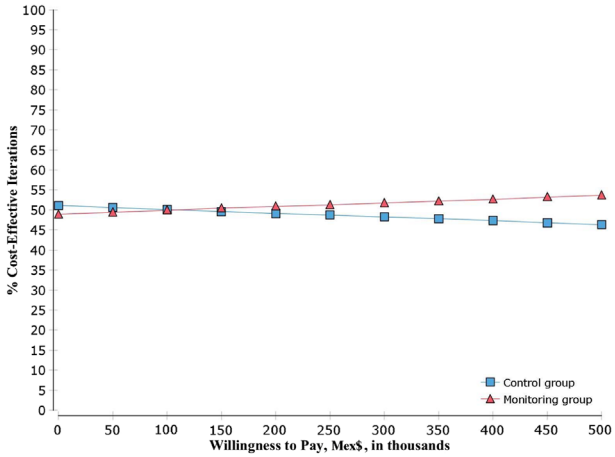

Fig. 3 – Cost-effectiveness acceptability curve. Mex$, Mexican peso.

reliable, and valid data. Another drawback is that calculating its confidence interval is very difficult. To overcome this problem, complementary analyses derived from it are recommended, such as the CEAC and the incremental net benefit. The CEAC shows the probability that an intervention will be cost-effective over a range of WTP values [39,40]. With the model presented here, there is a 50% chance that monitoring will be cost-effective with the ICER payment. The lack of superiority of ICP monitoring in improving the health results has been shown in adolescents and adults [41]. Nevertheless, if the threshold of payment is based on 1 time the per capita GDP, the INHB shows a small but non-negative health gain. INMB is a measure of efficiency representing an additional gain in monetary terms in case ICP monitoring was implemented. The incremental net benefit approach, using either the INHB or the INMB, transforms the ICER into a linear increase and offers a solid decision parameter that allows assessing the health and the monetary values of a strategy. In this case, the INMB was clearly determined in favor of implementing ICP monitoring.

It was possible to tackle the uncertainty inherent in the groups by constructing a model that overcomes problems that cannot be foreseen in the clinical setting. Thus, the cost-effectiveness model in the present case represents a valuable tool for dealing with the uncertainty from small sample size, group size disparity, and lack of random assignment to groups.

Statistical models can serve as a useful aid to reach more timely and accurate answers through the simulation of clinical scenarios that can make better use of limited information, by means of probability distributions that allow multiple simulations based on them, instead of using deterministic parameters. The results provide an explicit guide for the decision makers under conditions of uncertainty.

Conclusions

This study supports the gradually widespread knowledge stating that ICP monitoring in children with STBI does not produce serious damage, but allows taking a step forward in the management and treatment of this condition, and could be useful when considering new alternatives [42–47].

Therefore, the study presented here may serve as a guiding element to show that ICP monitoring is a reasonably efficient intervention, because implementing it will not increase the cost of care for these children and could represent a benefit for their health. The results suggest that ICP monitoring is cost-effective, given that the INHB had a positive although small value, and that there was a gain in monetary terms. The ICER value is affordable for the Mexican health system, especially when considering that this strategy could avoid more serious, long-term damage to the patients and, thus, increased expenses.

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REFERENCES

[1] Brain Trauma Foundation; American Association of Neurological Surgeons; Congress of Neurological Surgeons. Guidelines for the management of severe traumatic brain injury. J Neurotrauma 2007;24 (Suppl. 1):S1–106.
[2] El Instituto Nacional de Estadística y Geografía. Mujeres y Hombres en México 2012. Available from: http://cedoc.inmujeres.gob.mx/documentos_download/101215.pdf. [Accessed February 20, 2014].
[3] Ghajar J, Hariri RJ, Narayan RK, et al. Survey of critical care management of comatose head injured patients in the United States. Crit Care Med 1995;23:560–7.
[4] Jennett B, Bond M. Assessment of outcome after severe brain damage: a practical scale. Lancet 1975;305:480–4.
[5] Levin HS, Aldrich EF, Saydjari C, et al. Severe head injury in children: experience of the traumatic coma bank. Neurosurgery 1992;31:435–44.
[6] Stanley RM, Bonsu BK, Zhao W, et al. US estimates of hospitalized children with severe traumatic brain injury: implications for clinical trials. Pediatrics 2012;129:e24–30.
[7] Suresh HS, Praharaj SS, Indira DB, et al. Prognosis in children with head injury: an analysis of 340 patients. Neurol India 2003;51:16–8.
[8] Berg J. Economic evidence in trauma: a review. Eur J Health Econ 2004; (Suppl. 1):S84–91.
[9] McGarry LJ, Thompson D, Millham FH, et al. Outcomes and costs of acute treatment of traumatic brain injury. J Trauma Acute Care Surg 2002;53:1152–9.
[10] Farhad K, Khan HMR, Ji AB, et al. Trends in outcomes and hospitalization costs for traumatic brain injury in adult patients in the United States. J Neurotrauma 2013;30:84–90.
[11] Humphreys I, Wood RL, Phillips CJ, et al. The costs of traumatic brain injury: a literature review. Clinicoecon Outcomes Res 2013;5:281–7.
[12] Schneier AJ, Shields BJ, Hostetler SG, et al. Incidence of pediatric traumatic brain injury and associated hospital resource utilization in the United States. Pediatrics 2006;118:483–92.
[13] Johnstone B, Mount D, Schopp LH. Financial and vocational outcomes one year after traumatic brain injury. Arch Phys Med Rehabil 2003;84:238–41.
[14] Limond J, Liam Dorris L, McMillan TM. Quality of life in children with acquired brain injury: parent perspectives 1-5 years after injury. Brain Inj 2009;23:617–22.
[15] Michaud LD, Duhaime AC, Batshaw ML. Traumatic brain injury in children. Pediatr Clin North Am 1993;4:553–65.
[16] Kochanek PM, Carney N, Adelson PD, et al. Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents—second edition. Pediatr Crit Care Med 13 (Suppl. 1):S1–82.
[17] Elf K, Nilsson P, Enblad P. Outcome after traumatic brain injury improved by an organized secondary insult program and standardized neurointensive care. Crit Care Med 2002;30:2129–34.
[18] Roozenbeek B, Lingsma HF, Mass AI. New considerations in the design of clinical trials for traumatic brain injury. Clin Investig (Lond) 2012;2:153–62.
[19] Maas AIR, Harrison-Felix CL, Menon D, et al. Standardizing data collection in traumatic brain injury. J Neurotrauma 2011;28:177–87.

[20] Menon DK. Unique challenges in clinical trials in traumatic brain injury. Crit Care Med 2009;37(Suppl. 1):S129–35.
[21] Le Roux P, Menon DK, Citerio G, et al. Consensus summary statement of the International Multidisciplinary Consensus Conference on Multimodality Monitoring in Neurocritical Care. Intensive Care Med 2014;40:1189–209.
[22] O'Neil BR, Velez DA, Braxton EE, et al. A survey of ventriculostomy and intracranial pressure monitor placement practices. Surg Neurol 2008;70:268–73.
[23] Brown E. Intracranial Pressure Monitoring Devices. Arlington, VA: Association for the Advancement of Medical Instrumentation, 1988.
[24] Adelson PA, Bratton SL, Carney NA, et al. Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents. Chapter 17. Critical pathway for the treatment of established intracranial hypertension in pediatric traumatic brain injury. Pediatr Crit Care Med 2003;4(Suppl.):S65–7.
[25] Diario Official de la Federación. Distrito Federal (México): Gobierno de la República. Updated April 29, 2014. Available from: http://www.dof.gob.mx/nota_detalle.php?codigo=5342538&fecha=29/04/2014&print=true. [Accessed February 21, 2015].
[26] Torrance GW, Feeny DH, Furlog WJ, et al. Multi-attribute utility function for a comprehensive health status classification system, Health Utilities Index Mark 2. Med Care 1996;34:702–22.
[27] McCabe C, Stevens K, Roberts J, et al. Health state values for the HUI2 descriptive system: results from a UK survey. Health Econ 2005;14:231–44.
[28] Kharroubi SA, McCabe C. Modelling HUI 2 health state preference data using a nonparametric Bayesian method. Med Decis Making 2008;28:875–87.
[29] O'Hagan A, Oakley JE. The Sheffield Elicitation Framework (SHELF), version 2. 2010. Available from: http://www.tonyohagan.co.uk/shelf/. [Accessed April 6, 2016].
[30] Collins CL, Yeates KO, Pommering TL, et al. Direct medical charges of pediatric traumatic brain injury in multiple clinical settings. Inj Epidemiol 2014;1:13.
[31] Graves JM, Rivara FP, Vavilala MS. Health care costs 1 year after pediatric traumatic brain injury. Am J Public Health 2015;105:e35–41.
[32] Dawes AJ, Sacks GD, Cryer HG, et al. Intracranial pressure monitoring and inpatient mortality in severe traumatic brain injury: a propensity score-matched analysis. J Trauma Acute Care Surg 2015;78:492–502.
[33] Weinstein MC. How much are Americans willing to pay for a quality-adjusted life year? Med Care 2008;46:343–5.
[34] Marseille E, Larson B, Kazi DS, et al. Thresholds for the cost-effectiveness of interventions: alternative approaches. Bull World Health Organ 2015;93:118–24.
[35] The World Bank. GDP per capita (current US$). Available from: http://data.worldbank.org/indicator/NY.GDP.PCAP.CD. [Accessed March 26, 2016].
[36] González-Pier E, Gutiérrez-Delgado C, Stevens G, et al. Priority setting for health interventions in Mexico's System of Social Protection in Health. Lancet 2006;368:1608–18.
[37] McCabe C, Claxton K, Culyer AJ. The NICE cost-effectiveness threshold: what it is and what that means. Pharmacoeconomics 2008;26:733–44.
[38] Consejo de Salubridad General. Guía para la conducción de estudios de evaluación económica para la actualización del cuadro básico y catálogo de insumos del sector salud en México. 2015. Available from: http://www.csg.gob.mx/descargas/pdfs/2015/GCEEE_2015.pdf. [Accessed May 12, 2017].
[39] Fenwick E, Byford S. A guide to cost-effectiveness acceptability curves. Br J Psychiatry 2005;187:106–8.
[40] O'Hagan A, Stevens JM, Montmartin J. Inference for the cost-effectiveness acceptability curve and cost-effectiveness ratio. Pharmacoeconomics 2000;17:339–49.
[41] Chesnut RM, Temkin N, Carney N, et al. A trial of intracranial-pressure monitoring in traumatic brain injury. N Engl J Med 2012;367:2471–81.
[42] Guerguerian AM, Lo TY, Hutchison JS. Clinical management and functional neuromonitoring in traumatic brain injury in children. Curr Opin Pediatr 2009;21:737–44.
[43] Farahvar A, Gerber LM, Chiu YL, et al. Increased mortality in patients with severe traumatic brain injury treated without intracranial pressure monitoring. J Neurosurg 2012;117:729–34.
[44] Yuan Q, Liu H, Xing Wu, et al. Predictive value of initial intracranial pressure for refractory intracranial hypertension in persons with traumatic brain injury: a prospective observational study. Brain Inj 2013;27:664–70.
[45] Kukreti V, Mohseni-Bod H, Drake J. Management of raised intracranial pressure in children with traumatic brain injury. J Pediatr Neurosci 2014;9:207–15.
[46] Le Roux P. Intracranial pressure after the BEST TRIP trial: a call for more monitoring. Curr Opin Crit Care 2014;20:141–7.
[47] Alali AS, Gomez D, Sathya C, et al. Intracranial pressure monitoring among children with severe traumatic brain injury. J Neurosurg Pediatr 2015;16:523–32.