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Cost-effectiveness analysis of oral rehydration therapy compared to intravenous rehydration for acute gastroenteritis without severe dehydration treatment

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ABSTRACT

Background: Diarrhea causes, annually, approximately 1.7 billion cases and 760,000 deaths worldwide among children under 5 years of age, although these are preventable and treatable. This study aim to assess the cost-effectiveness for the treatment of diarrhea in emergency services in the management of children of acute gastroenteritis with non-severe dehydration.
Methods: A stochastic decision tree model considering the perspective of the Brazilian public health system was used to calculate the cost-effectiveness of the 5 interventions: oral rehydration therapy (ORT) at home, and if it fails supervised ORT; they would receive; ORT at home, and if it fails intravenous rehydration therapy (IVT). ORT at home and if it fails, the half of them will receive supervised ORT, and the other half would receive IVT; Patient receives supervised oral treatment; Patient receives IVT. Quality-adjusted life year (QALY) was used to measure the clinical outcomes.
Results: The strategy of initiating oral rehydration in children younger than 5 is the most efficient practice with a cost of $14.28 and effectiveness of 0.89 QALYs.
Conclusion: ORT is an underutilized resource for the management of children with non-severe dehydration in emergency services. The overprescribed IVT increases cost without a corresponding significant increase in effectiveness.

Introduction

Annually, approximately 1.7 billion cases of diarrhea and 760,000 deaths occur worldwide among children under 5 years of age 1, although these are preventable and treatable. Despite being a health problem that can be solved with relatively simple measures, in 2015, there were 4372 deaths and 268,590 hospitalizations due to diarrhea and gastroenteritis of presumed infectious origin, other infectious intestinal diseases and, to a lesser extent, amoebiasis, Shigellosis, cholera, typhoid and paratyphoid fevers in Brazil [1]. Among children up to 4 years of age, 35% of hospitalizations were for diarrhea and gastroenteritis of presumed infectious origin [1].

Dehydration caused by acute gastroenteritis is a condition resulting from diarrhea with or without emesis. Rehydration therapy, consisting of techniques and technologies aimed at the prevention or correction of fluid and electrolyte imbalances, is the main clinical measure regardless of the underlying cause of inflammation and irritation of the gastrointestinal tract. Technologies for the prevention or correction of dehydration fall into two categories: non-invasive technologies and invasive technologies. In the former are various oral solutions, which are usually composed of combinations of nutrients (glucose) and mineral salts. The latter includes enteral rehydration solutions administered via either orogastric or nasogastric routes and parenteral solutions infused via a venous route.

Intravenous rehydration therapy (IVT) is the most widely used invasive intervention, which is indicated in cases of suspected severe dehydration, hypovolemic shock, failure of oral therapy to restore fluid and electrolyte balance or for conditions that preclude

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the use of oral rehydration therapy (ORT) [2–4]. The recommendation of Brazilian Ministry of Health is to use ORT at home for patients with diarrhea but without dehydration; supervised ORT for patients with diarrhea and dehydration, and IVT for patients with severe dehydration.

In several countries, concerns have been raised about the need to increase adherence to ORT [5–9]. In Brazil, the scenario is not unlike that in the rest of the world. ORT is an underutilized resource for the management of children with non-severe dehydration in emergency services. This is due in part to a lack of infrastructure and insufficient resources dedicated to providing ORT in this setting [7]. Intravenous rehydration is overprescribed for reasons ranging from a lack of knowledge of clinical protocols to concerns about low adherence to ORT. Adherence to ORT can vary based on the instructions received by family members who care for the patient with dehydration. Advantages of ORT include that it is neither invasive nor traumatic to the pediatric patient and ease of administration, which does not require hospital resources [7].

Despite the advantages of ORT, there are no studies comparing the cost-effectiveness strategies for management non-severe dehydration in children. The objective of this study was to perform a cost-effectiveness analysis of ORT compared to intravenous rehydration for the treatment of acute gastroenteritis without severe dehydration in children under 5 from the perspective of the Unified Health System (SUS).

Materials and methods

The target population of the analysis was children under 5 years of age with acute gastroenteritis without severe dehydration. In the prevention of dehydration at home, the patient is instructed to maintain his/her diet, hydrate with oral rehydration solution (ORS) after each diarrheal evacuation and ingest zinc once a day for 10–14 days. Zinc administration was suggested by the WHO in 2004, and its use is related to its possibility of reducing the duration and severity of diarrheal episodes [2,10,11].

In oral rehydration administration with patient observation, in the hospital unit, the amount of oral rehydration solution is variable, compatible with the patient's seat. As initial guidance, the patient receives from 50 to 100 ml/kg to be administered in a period of 4–6 h [2,10].

The administration of intravenous rehydration is divided into two phases: (a) rapid phase and (b) maintenance and replacement phase. The rapid phase varies according to the patient's age: patients under 5 years of age receive saline solution at 0.9% for 30 min, in addition to Lactated Ringer or Polyelectrolyte Solution for 2 and a half hours. Lactated Ringer's solution is composed of sodium chloride, potassium chloride, calcium chloride dihydrate and sodium lactate, diluted in water for injection, which is based on the results obtained by the authors. The maintenance phase presents the same management for all ages and consists of the administration of 5% glycoside serum and 0.9% saline solution in a ratio of 4:1. In the replacement phase, patients receive the same sera from the previous phase, but with a ratio of 1:1 and the addition of the 10% KCl solution [2,12].

The strategies compared to treat the dehydration were: 1 — children would receive ORT at home. If it fails, they will receive supervised ORT. If it also fails, they would receive IVT; 2 — children would receive ORT at home. If it fails, they will receive IVT; 3 — children would receive ORT at home. If it fails, the half of them will receive supervised ORT, and the other half would receive IVT; 4 — patient receives supervised oral treatment. If it fails, they will receive IVT; and 5 — patient receives IVT. If it fails, they will receive IVT again.

The benefits were expressed as quality-adjusted life years (QALYs), which were calculated based on utility scores related to each event expressed in the model. There are no data in the literature on the utility effects of phlebitis with the intravenous treatment of dehydration. In this case, the value would be between the utility score of outpatient and hospital treatment. The perspective adopted was that of the Brazilian public health system. Because this is an acute condition, the horizon considered was the time required for the reestablishment of fluid and electrolyte balance, i.e., 14 days [13].

A stochastic decision tree model estimated the cost-effectiveness of different therapeutic approaches to acute gastroenteritis without severe dehydration in children under 5. The health outcomes were taken from a meta-analysis of psychometric studies that assessed the quality of life-related to various outcomes of acute gastroenteritis in accordance with previous economic evaluation analyses, especially a study produced for the National Collaborating Center for Women and Children's Health (UK) [4]. TreeAge Pro 2009 [14] simulation software was used to develop the model.

Only treatment and resolution of the acute condition were considered, and no cases of recurrent dehydration were analyzed because of the many causes of gastroenteritis and its consequences. In the IVT approach, there were no restrictions on use, although it is possible to have some barriers that preclude IVT, such as a lack of inputs, the unavailability of professionals and the inability of the health services to meet the demand for intravenous rehydration.

Mortality was not included in the simulation model as an outcome, as national data on under-five mortality from gastroenteritis are inconclusive. International studies that have evaluated the clinical consequences of the same interventions in this population have found that the number of deaths due to gastroenteritis after rehydration is not significant, especially in individuals with mild to moderate dehydration [4,15].

A diagram of the structure and variables used in the cost-effectiveness analytical model of therapeutic strategies for the treatment of acute gastroenteritis without severe dehydration is presented in Fig. 1.

A literature review produced estimates of remission and progression of diarrhea to possible outcomes. These estimates were compared and, when possible, corrected to make them more representative of the Brazilian context. Thus, national statistics on the morbidity of acute gastroenteritis and databases such as the Mortality Information System, Information System on Diseases of Compulsory Declaration, and SUS Hospital Admissions System were consulted [1,16,17].

The use of resources in each health status was represented as a function of hospital treatment, outpatient treatment, medical and nursing services, laboratory tests and medications, among others. These were based on their frequencies per event based on the guidelines for the use of resources outlined in the Primary Care Guidebook of the Ministry of Health [13] and, when necessary, a survey of specialists for more precise estimates of the resources needed, considering factors such as the average length of stay in the hospital for complications (Figs. 2 and 3).

The reimbursement amounts paid by the SUS for different items were used as measures of the above-mentioned costs (as listed in the AIH/SUS and SIA/SUS tables, including authorization for high-complexity procedures (APAC)) considering, when applicable, the differences in specialization among the health units (e.g., different payments are provided for medical consultations and hospitalizations in university units and teaching hospitals). For the cost of medicines and other items, the Price Databank of the Medication Chamber (CMED), BRASÍNDICE, the Databank of Healthcare Prices of the Ministry of Health, and the Price Databank of the Rio de

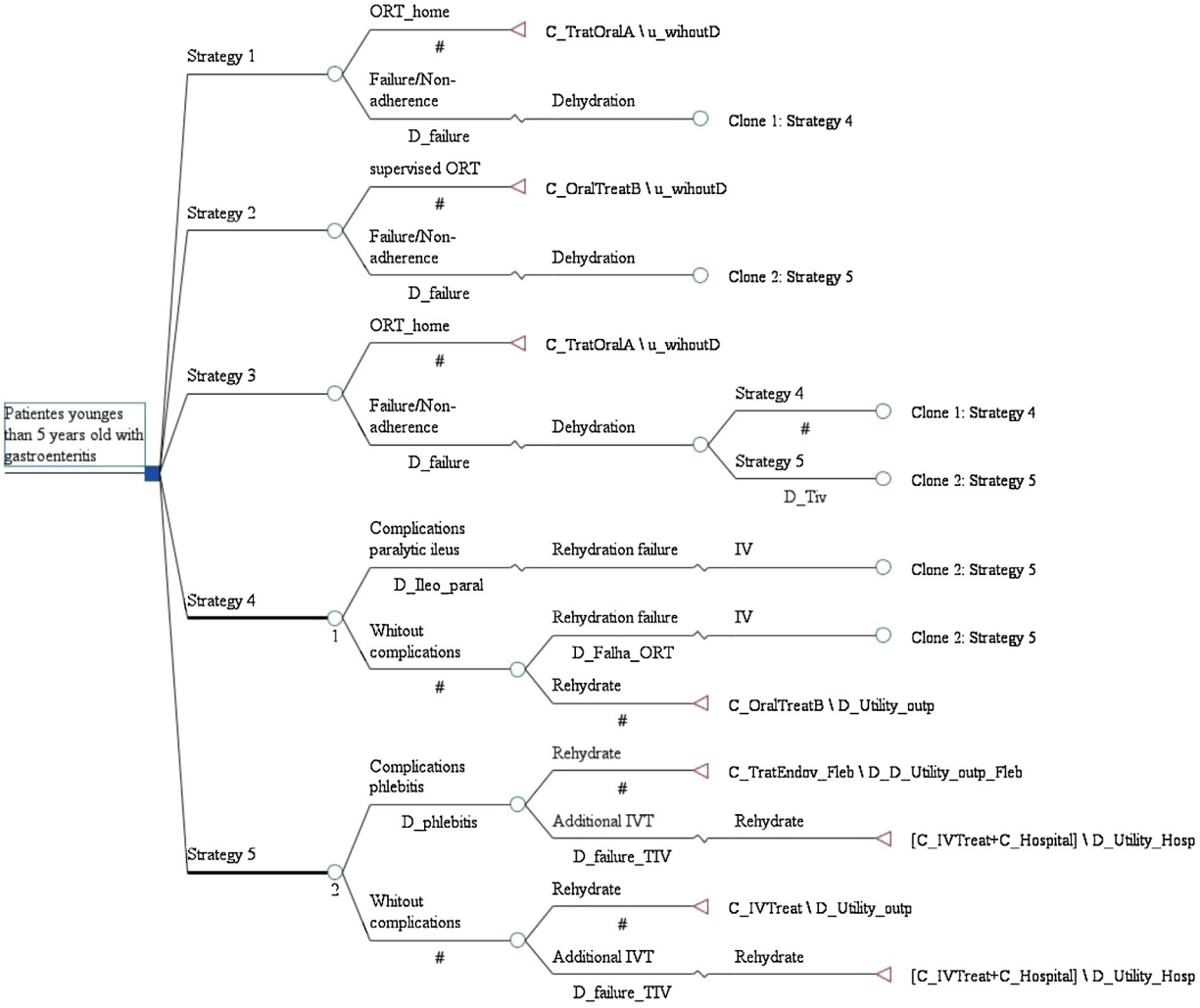

Fig. 1. Schematic representation of the simulation model for the treatment of dehydration caused by acute gastroenteritis.

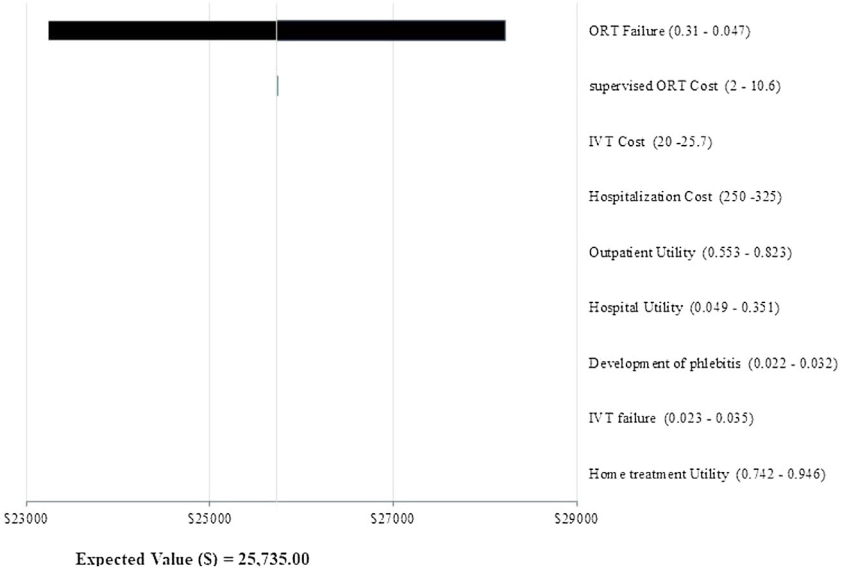

Fig. 2. Tornado chart.

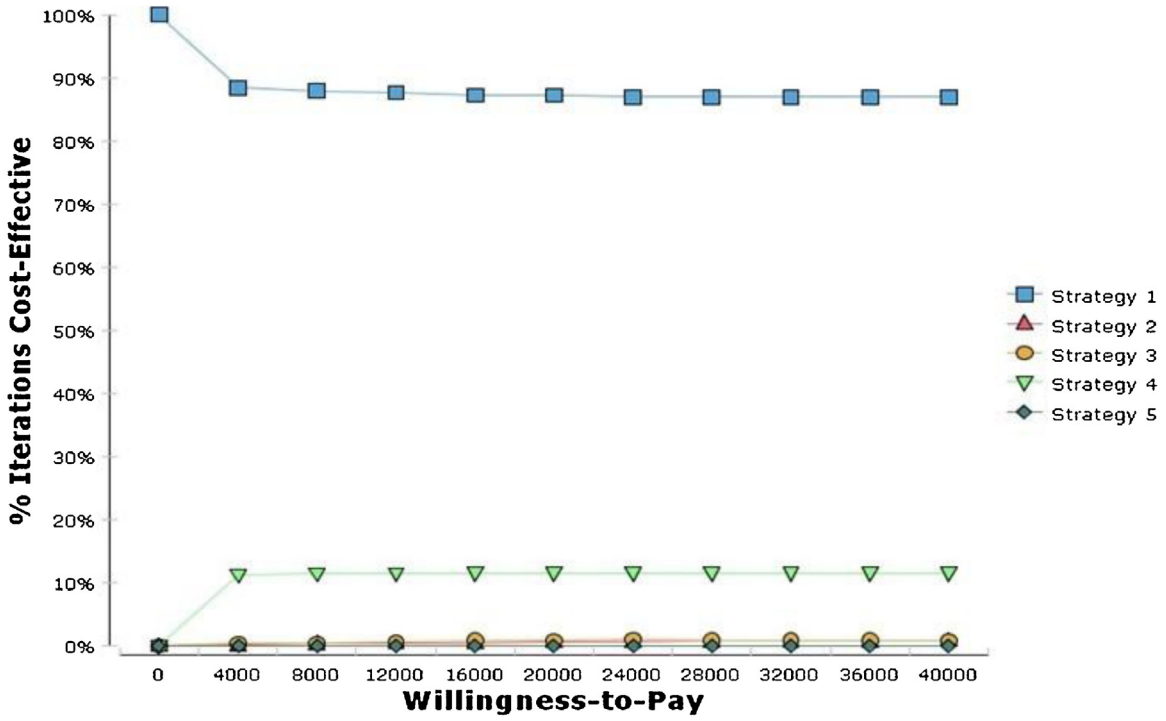

Fig. 3. Acceptability curve of the cost-effectiveness analysis for the treatment of acute gastroenteritis without severe dehydration.

Table 1
Parameters used in the simulation model.

Parameter	Mean	Distribution (range)	Sources
Costs ($)			
Medical visit	10.00	Triangular (9–12)	[1]
Nurse visit	10.00	Triangular (8–11)	[1]
Hospitalization	324.9	Triangular (300–350)	[1]
Oral rehydration solution	0.68	Triangular (0.47–0.075)	[17]
0.9% saline solution	2.37	Triangular (1.7–3.2)	[17]
Solution administration	0.63	Triangular (055–0.70)	[1]
Infusion line	1.60	Triangular (0.95–1.98)	[17]
Catheter	1.15	Triangular (1.13–1.30)	[1]
Probabilities			
Development of paralytic ileus	0.027	Beta (0.022–0.032)	[18]
Non-adherence/failure	0.50	Uniform (0.05–0.95)*	[7]
ORT failure	0.039	Beta (0.031–0.047)	[18]
Development of phlebitis	0.027	Beta (0.022–0.032)	[18]
IVT failure	0.029	Beta (0.023–0.035)	[18]
Utilities			
Hospital treatment	0.200	Normal (0.049–0.351)	[20]
Outpatient treatment	0.688	Normal (0.553–0.823)	[20]
Home treatment	0.891	Normal (0.742–0.946	[21]

Janeiro State Department (NERJ) of the Ministry of Health were consulted [1,16,17].

The parameters used in the model derived from primary and secondary studies regarding estimates of morbidity and effectiveness and from national information systems (i.e., costs) are presented in Table 1.

Sensitivity analysis

Univariate and bivariate deterministic sensitivity analyses of the model were performed, including the costs and effectiveness of the proposed treatments. In addition, a probabilistic sensitivity analysis involving an adjustment of the probability distribution of some or all the model parameters was performed.

Table 2
Cost-effectiveness of treatments for acute gastroenteritis without severe dehydration.

Therapeutic strategy	Cost (R$)	Effectiveness/QALY	ICER[a]
1	14.28	0.89	
3	16.54	0.887	Dominated
ORT	21.59	0.766	Dominated
2	25.48	0.885	Dominated
IVT	35.18	0.756	Dominated

Source: The authors.
[a] ICER — incremental cost-effectiveness ratio.

Results

The simulation of the cost-effectiveness of the strategies available for rehydration of children under 5 with acute gastroenteritis without severe dehydration revealed that Strategy 1 is most efficient as an initial therapeutic approach (Table 2). All other strategies were dominated, i.e., they had higher costs and lower effectiveness. In addition, the differences in effectiveness between Strategies 1 and 3 are very small and depend on the proportion of ORT and IVT used.

Sensitivity analysis

Univariate and bivariate deterministic analyses were performed. In the univariate analysis, a tornado chart showed that the only variable likely to affect the outcome is the probability of failure in rehydration, due either to non-compliance or to disease progression.

Due to a lack of reliable data on adherence to ORT and the progression of gastroenteritis with dehydration, all possibilities were tested on an interval of 5–95% treatment failure. The results showed that Strategy 1 remained cost-effective and dominated all alternatives.

The variable that defines the proportion of ORT and IVT use in Strategy 3 was not significant for the achieved outcome. Never-

theless, because its effectiveness is very close to that of Strategy 1, a univariate sensitivity analysis was performed to estimate its impact. For ratios ranging from 5 to 95%, there were no changes, and Strategy 1 continued to dominate all others.

Bivariate deterministic analysis of the probability of failure (due to non-adherence or progression of gastroenteritis) of home rehydration and variation in the ratio of ORT or IVT use did not change the outcome achieved in univariate analyses. Strategy 1 remained cost-effective, dominating all other strategies across the variation range analyzed.

A first-order Monte Carlo simulation confirmed the results of the main analysis (deterministic method). The following acceptability curve confirms that, regardless of the threshold adopted, Strategy 1 is more cost-effective in 95% of cases.

Discussion

There are numerous approaches to the treatment of fluid and electrolyte imbalance caused by acute gastroenteritis. Clinical trials have found no evidence of a statistically significant difference in the efficacy of rehydration using oral rehydration solution and intravenous saline solution in children [15].

An economic study produced by the National Institute for Health and Care Excellence in collaboration with the National Collaborating Center for Women and Children's Health [4] compared the cost-effectiveness of oral and intravenous rehydration therapies from the perspective of the English health system. The model adopted was based on the premise that there are no significant differences in efficacy between the two types of dehydration treatment in children under 5; therefore, it only evaluated the economic outcomes of adopting ORT or IVT through a cost-minimization study. The authors concluded that because there is no significant difference in efficacy between the two rehydration strategies, ORT, the least expensive approach, should be considered the most cost-effective treatment. The study also noted that for IVT to be cost-effective, it needed to achieve a QALY gain of approximately 3%. In the model presented here, this value would be impossible to achieve because there has always been a loss of QALYs when comparing all rehydration strategies.

The World Health Organization and the Brazilian Ministry of Health recommend that less invasive and less expensive strategies be the first therapeutic choice for cases of mild to moderate dehydration [12,13]. Although this practice is dominant in most countries worldwide, a considerable portion of pediatricians opts to use more invasive strategies to save time for staff, patients, and families [18].

The present study suggests several limitations that merit discussion. Some of them are inherent to the modeling process, which might oversimplify the process of disease progression because of its divergence from real-world circumstances. In addition, international data were used, given the scarcity of information about the disease in the Brazilian context. Different data sources were used to obtain the figures of the quality of life [20–24] and the effects of phlebitis with the intravenous treatment of dehydration.

Conclusion

The analytical decision model estimated the main costs and consequences of the rehydration strategies available in Brazil: home ORT and supervised ORT, which use an oral solution of water, glucose and salts, and IVT, which basically consists of water and electrolytes. The model results indicate that the difference in effectiveness in terms of QALYs among treatment alternatives is the variable with the greatest weight for estimating and determining the dominance of oral rehydration over intravenous rehydration.

The treatment regimen in Strategy 1 that started with oral rehydration was the most attractive from an economic standpoint, according to the results of the model and the sensitivity analysis. Initiating rehydration via the oral route in children under 5 was the most effective strategy for most combinations of values for the variables of interest. In absolute terms, initiating intravenous rehydration among children under 5 increases costs without a corresponding significant increase in effectiveness.

Finally, a review of research in epidemiology on the consequences of acute gastroenteritis in its different stages highlighted the existence of a significant knowledge gap in the world and in Brazil. At the moment, the paucity of parameters is the main barrier to the development of simulation models that are more compatible with the knowledge accumulated in clinical practice.

Competing interests

None declared.

Ethical approval

Not required.

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