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Zinc supplementation reduced cost and duration of acute diarrhea in children

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Abstract

Objective: To determine whether zinc with oral rehydration solution (ORS) is more cost effective than ORS alone in the treatment of acute diarrhea.

Study Design and Setting: Cost-effectiveness analysis among patients consulting the emergency room of a government institution.

Method: Cost of treatment and outcome of participants of a randomized trial of zinc + ORS vs. ORS alone for acute diarrhea were investigated. Included were subjects 2−59 months with diarrhea <7 days and no dehydration. The direct medical, nonmedical and indirect costs were obtained, using the societal perspective. The incremental cost-effectiveness ratio (ICER) was calculated.

Results: Sixty patients were given zinc + ORS and 57 were given ORS alone. Mean duration of diarrhea was 17 hours shorter and mean total cost of treatment was 5% cheaper in the zinc than ORS group .The ICER showed that with use of zinc, the society saves $ 2.4 per day of diarrhea <4 days and spends $ 0.03 per case of diarrhea averted <4 days from consult, although the confidence interval included the null value of zero.

Conclusion: Use of zinc with ORS reduced the total cost and duration of acute diarrhea. The ICER suggests cost effectiveness of zinc supplementation but there is a need to further assess the role of zinc supplementation in a larger population.

Keywords: Oral rehydration solution; Incremental cost effectiveness ratio; Cost effectiveness analysis; Zinc; Diarrhea

1. Introduction

Diarrheal diseases are a leading cause of childhood mortality and morbidity in developing countries and an important cause of malnutrition [1]. The majority of diarrheal deaths are caused by dehydration that can be treated with oral rehydration solution (ORS). However, ORS is unable to reduce the volume, frequency, and duration of diarrhea.

It is not clear why some episodes of diarrhea persist for a longer duration but host factors, such as nutritional deficiencies [2], which may increase susceptibility to enteric infections and delay mucosal recovery would be expected to contribute to this effect. Two well-documented determinants of diarrheal duration are low weight-for-age and decreased cell-mediated immunity. Common to both these factors is zinc deficiency [3].

Zinc is an essential trace element for humans [4]. Zinc supplementation improves immune function and reduces the incidence of diarrhea among children in developing countries [5−7]. In a meta-analysis [8] that included children <5 years old with acute diarrhea given at least 1.5 times the recommended daily allowance for zinc, those who received zinc had a 15% (95% confidence interval (CI): 8−22%) risk reduction of having diarrhea on a certain day and a 16% (95% CI = 7−26) lower probability of having an episode of diarrhea lasting >7 days Possible role of zinc includes regulation of water and electrolyte transport, improvement in the enzymatic functions of the brush borders, and enhancement of the repair of the intestinal mucosa [9,10]. While these results are encouraging, the therapeutic efficacy of zinc has important cost implications.

There are two cost effectiveness analyses that have been reported on the use of zinc in acute diarrhea. The first was done in India [11], in the context of a randomized controlled trial wherein an 8% lower cost of treatment was observed with zinc supplementation compared with ORS alone. However, both the cost of zinc and copper were

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considered as both were used for supplementation. The second study [12] used secondary data and compared the expected clinical outcomes and costs with the use of zinc + ORS vs. ORS alone. This study considered the direct medical cost alone and showed that the mean incremental cost effectiveness ratio (ICER) was reduced from US$113 for ORS alone to US$73 per disability adjusted life year (DALY) averted when ORS is combined with zinc. The results of these studies could not be directly transposed to the local setting because the cost levels differ in different settings. Furthermore, the cost may vary depending on whose perspective the cost of resources was derived.

In 2003, our institution was one of the participating sites of a randomized controlled study that assessed the acceptability of zinc supplementation in children with acute diarrhea. One group was randomized to zinc and ORS and another to ORS alone. An economic evaluation was simultaneously conducted among the patients included in our institution. This determined whether the use of zinc + ORS is more cost effective than ORS alone in the treatment of acute diarrhea.

2. Methods

This cost effectiveness analysis (CEA) was conducted in 2003 using 117 of 138 patients included in the randomized controlled trial (RCT). Both the RCT and CEA obtained ethics committee approval from the independent ethics review board of the institution. Patients were recruited at the Emergency Room (ER) of the institution and from two satellite centers (San Andres and Paco local health units) within 5 km from study site. Those recruited in the satellite centers were sent to the ER and if necessary, hydration and all laboratory work-ups were done there.

Included were children between 2 and 59 months old with diarrhea <7 days duration and no evidence of dehydration. Excluded were those with other medical illness, severe malnutrition (weight for height <-3 SD, National Center for Health Statistics) and with current intake of antibiotics or zinc supplements. After informed consent, baseline features were taken. The subjects were then randomized by block randomization with use of sealed envelopes containing the treatment assignment for each day. The day of randomization was considered day 0 of the study. The *study group* received 20 mg zinc sulfate tablet per day for 14 days along with standard WHO-ORS. The *control group* received WHO-ORS only. The zinc tablets, taken 2 hours after food intake, were dissolved in water or milk before administration or were taken as is by older children. The WHO-ORS was provided in sachet to be dissolved in a liter of clean water and consumed in 24 hours.

During follow-up visits between days 3–5 and 14–17, the presence or absence of diarrhea was ascertained through interview of caregivers. The exact day on which the stools returned to normal frequency and consistency was asked. The duration of diarrhea was computed from the day of consultation up to the time the bowel movement has returned to its normal frequency and consistency followed by a 24-hour diarrhea free period. The study personnel inspected the blister pack of zinc and counted the number of tablets left. Mothers were also asked if they have given the zinc tablets to anyone aside from the patient.

A patient was considered cured if there is cessation of diarrhea within 10 days after consult. Treatment failure was defined as the presence of any adverse drug reactions to zinc or if the duration of diarrhea was >10 days from consultation. A patient was withdrawn if he develops other medical conditions requiring antibiotic therapy or noncompliance with intake of zinc ($<80\%$ intake of recommended dose).

2.1. Cost effectiveness analysis

The prevailing cost in 2003 was used, using the local currency, pesos (P) [US$ 1 = 53 pesos, 2003). The costs considered were direct medical and nonmedical costs and indirect costs. The cost values for the components of the direct medical cost were derived mostly from the different departments of the institution.

The original cost of the hospital's ER is no longer available. Thus, the cost of the building space per patient per day was computed based on the 2003 estimate of the annual rental cost per square meter where the site of the ER is located, which is P48, 750 (US$ 92), multiplied by the approximate land area of 75 m^2 and divided by the annual number of consults (11,315). This was estimated at P323.13 (US$ 6.10) per patient per day. Cost of diagnostics was based on the charge of the institution for charity patients category B [patients with annual family income between P10,000–20,000 (US$ 189–$377)]. This was used based on an interview with the Head of the Laboratory that the charge for category B patients approximates the cost taking into consideration the operating expenses (cost of reagents and supplies) in the performance of the investigation, the use of equipment and machines and the salary of the personnel doing the procedure. The cost of medications was based on the price list of the UP-PGH Pharmacy and was used based on an interview with the Chief Pharmacist that the charge for medications in the pharmacy approximates the cost. The use of the facilities and the salary of the employees are subsidized by the government and were not considered in the computation of the cost of the drugs. The cost of personnel time was estimated based on the annual residents' (P213, 588)/nurses' (P159, 600) salary divided by the approximate time that each personnel devotes for a patient. Slack time was not accounted for. Based on informal interviews and actual observations, a resident physician spends 1 hour per patient with the time allocated as follows: history and physical examination (20 minutes), performance of necessary laboratory tests and instructions for treatment (15 minutes), reassessment after 1st and 2nd hour of hydration (10 minutes), and reassessment at end of hydration and discharge orders (15 minutes).