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Introduction

Diarrhoea remains the leading cause of death among infants and young children in low- and middle-income countries. Globally, an estimated 1.87 million children less than five years of age succumbed every year to the fluid loss and dehydration associated with diarrhoea, which approximately 19% of total child deaths. In Malaysia, acute diarrhoea is still a major public-health concern and it is mostly under-notified. The majority of diarrhoeal deaths are caused by dehydration that can be treated with oral rehydration solution (ORS). Development of an improved formula for ORS solution with reduced levels of glucose and salt (NaCl) shortens the duration of diarrhoea, reduces stool volume and reduces the need for unscheduled intravenous (IV) fluids. In 2004, the World Health Organization (WHO) and the United Nations Children's Emergency Fund (UNICEF), issued a global recommendation advocating oral zinc supplementation in addition to ORS to decrease diarrhoea deaths in the world's most vulnerable children based on the recent advances that the oral zinc treatment reduced diarrhoea duration and severity in children with diarrhoea aged six months to five years. Despite the WHO recommendation, the implementation of zinc supplementation in the management of diarrhoea has not yet been possible in all developing countries. This technology review was requested in order to review the evidence on the use of zinc supplementation as adjuvant therapy in the management of diarrhoea in children younger than five years old.

Objective/Aim

To assess the effectiveness, safety and cost-effectiveness of zinc supplementation as an adjuvant therapy in management of diarrhoea in children younger than five years old

Results and Conclusions

A total of 430 titles were identified through the OVID interface and PubMed. There were two systematic reviews (SR) and meta-analyses, one randomized controlled trial, two cost-effectiveness analyses and one cost-utility analysis were included in this review.

Effectiveness

There was good level of retrievable evidence to suggest that zinc supplementation was able to shorten the duration of acute diarrhoea by about 10 hours (mean difference -10.44 hours, 95% CI: -21.13, 0.25) although the difference was not statistically significant, and shorten the duration of persistent diarrhoea by about 16 hours (mean difference -15.84 hours, 95% CI: -25.43, -6.24). An overall 26% (95% CI: 20%, 32%) reduction in the estimated relative risk of diarrhoea lasting beyond three days was observed among zinc-treated children as well as reduction in the stool output and stool frequency. In children with signs of moderate malnutrition, the effect appears greater, reducing the duration of diarrhoea by around 27 hours (mean difference -26.98 hours, 95% CI: -14.62, -39.34). However, the evidence with regards to the benefit of zinc supplementation for children less than six months of age was unclear. Limited good level of retrievable evidence to suggest that zinc supplementation was associated with increased use of ORS and decreased use of antibiotics during acute diarrhoea. There was insufficient evidence to suggest that zinc supplementation during acute diarrhoea reduces mortality.

Safety

Good level of retrievable evidence to suggest that the use of zinc supplementation in the management of diarrhoea for children younger than five years old was safe. Most common complication reported was vomiting. However, the evidence found no difference in time to resolution of vomiting between zinc and placebo.

Cost-effectiveness

Based on the two cost-effectiveness analyses and one cost-utility analysis, zinc supplementation as an adjunct in the management of diarrhoea in children younger than five years old was found to be more cost-effective than the standard treatment. In terms of price, the price for zinc supplementation in Malaysia was unknown due to limited availability. However the price for zinc supplementation in form of syrup in Indonesia is approximately RM 10.67 per 100 ml bottle and in form of diarrhoea kit which consisted of ORS as well as 10 of 20 mg tablets of zinc sulphate in Cambodia is approximately RM 1.60 per kit.

Organizational issues

- **Hospital stay**

There was good level of retrievable evidence to suggest that zinc supplementation during acute diarrhoea was associated with reduction in the duration of hospital stay among children hospitalised for diarrhoea compared to the control groups.

- **Guidelines**

WHO and UNICEF have issued a global recommendation in 2004 which advised zinc supplementation in addition to ORS for the treatment of all diarrhoea episodes among children younger than five years of age. ESPGHAN and ESPID stated that children age more than six months in developing countries may benefit from the use of zinc in the treatment of acute gastroenteritis. However, in the regions where zinc deficiency is rare, no benefit from the use of zinc is expected

Methods

Literature search was done to search for published articles to assess the effectiveness, safety and cost-effectiveness of zinc supplementation as an adjuvant therapy in management of diarrhea in children younger than 5 years old. The following electronic databases were searched via OVID Interface: MEDLINE (1946 to present), EBM Reviews-Cochrane Database of Systematic Reviews (2005 to January 2016), EBM Reviews-Cochrane Central Register of Controlled Trials (December 2015), EBM Reviews-Database of Abstracts of Review of Effects (2nd Quarter 2015), EBM Reviews-Health Technology Assessment (4th Quarter 2015) NHS economic evaluation database (2nd Quarter 2015), Pubmed and INAHTA database. The last search was run on 20th January 2016.