### **BRIEF REPORT**

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# Role of Zinc in childhood diarrhea management: a case of Nepal

### Kadir Alam<sup>1</sup>\*, Arjun Poudel<sup>2</sup>, Subish Palaian<sup>3</sup>, Bhawesh Koirala<sup>1</sup>, Pathiyil Ravi Shankar<sup>4</sup>

<sup>1</sup>Department of Clinical Pharmacology and Therapeutics, B.P. Koirala Institute of Health Sciences, Dharan, NEPAL.
<sup>2</sup>School of Clinical Sciences, Faculty of Health, Queensland University of Technology, Brisbane, AUSTRALIA.
<sup>3</sup>Department of Pharmacy Practice, College of Pharmacy, Gulf Medical University, Ajman, UAE.
<sup>4</sup>Department of Pharmacology, Xavier University School of Medicine, Aruba, Kingdom of the NETHERLENDS.

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#### Dr. Kadir Alam, PhD,

Department of Clinical Pharmacology and Therapeutics, B.P. Koirala Institute of Health Sciences, Dharan, NEPAL. E-mail: alamkad2050@gmail.com DOI: 10.5530/jppcm.2017.1.8

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### Abstract

Diarrhea is one of the leading causes of death among children less than five years of age around the world accounting for about two million child deaths annually. One of the recent strategies made to minimize the diarrhea associated mortality in children involves the use of oral zinc in diarrhea management. The inadequacy of dietary zinc uptake is exacerbated by the net loss of zinc during diarrhea. Zinc is enlisted in WHO essential drug list under medicine for diarrhea where it is indicated in acute diarrhea as an adjunct to oral rehydration salts. Zinc is usually well tolerated. It is necessary to explore public health applications, using zinc either as a preventive measure in children or therapeutically for diarrhea.

Key words: Diarrhea, Dehydration, Mortality, Nepal, Zinc.

### INTRODUCTION

Diarrhea is one of the leading cause of death among children less than five years of age around the world accounting for about two million child death annually.<sup>[1]</sup> According to the 2004 United Nations Children's Fund (UNICEF) State of the World's Children, Nepal's mortality rate for children under five years old was 91/1000—ranking 54<sup>th</sup> of 189 countries.<sup>[2]</sup> The major cause of death in childhood diarrhea is the intense dehydration. Several treatment strategies are made to minimize the diarrhea associated mortality in children. One of the recent strategies being the use of oral zinc in diarrhea management.

### Role of zinc in diarrhea

Zinc is a nutritional supplement (mineral) usually given as zincs sulfate, zinc acetate, or zinc gluconate, which are all water-soluble compounds.<sup>[3]</sup> The association between zinc and diarrhea associated morbidity have been noted on different observational studies. It is known that increased fecal zinc loss leads to a negative zinc balance and low tissue zinc concentration among children with diarrhea.<sup>[1]</sup> Zinc deficiency is highly prevalent in children in developing countries because overall food intake as well as consumption of animal food is low and the bioavailability of zinc from fibers, phytates rich cereal based diet is limited. The inadequacy of dietary zinc uptake is exacerbated by the net loss of zinc during diarrhea.<sup>[4]</sup> Based on animal studies and cell line cultures, a possible mechanism of action of zinc has been elucidated. These findings suggest that zinc is involved in regulation of intestinal fluid transport, mucosal integrity, immunity, gene

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This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License. expression, and oxidative stress.<sup>[5]</sup>

# Studies suggesting role of zinc therapy in childhood diarrhea

Studies have been conducted in recent years studying the usefulness of zinc on both acute and persistent diarrhea. Clinical studies from India showed that regular prophylactic zinc supplementation can reduce diarrheal prevalence and diarrhea associated mortality.<sup>[6,7]</sup> Zinc supplementation during diarrhea is known to reduce the duration and severity of treated episodes.<sup>[8]</sup> One of the study from the United States have found that short course of daily zinc supplementation shortens the duration (a 15-24% reduction) and severity of episodes of diarrhea.<sup>[1]</sup> Other trials from the different parts of the world have also shown similar results. The data from these studies have been analyzed and have demonstrated the clinically important benefits of zinc as supplementation.

A community randomized trial undertaken in the nearby country Bangladesh have illustrated that the children who received zinc supplementation during and after diarrhea had 24% shorter duration of diarrhea, 15% lower incidence of diarrhea and a trend suggesting fewer diarrhea related hospital admission.<sup>[4]</sup> Further, zinc therapy may have a benefit over the oral rehydrate therapy alone which is currently recommended to prevent dehydration but does not reduce the duration of diarrhea.<sup>[9]</sup> The World Health Organization (WHO) and United Nations Children's Fund (UNICEF) recommend 10 to 20 mg of zinc per day for children with diarrhea, at least twice the recommended daily allowance.<sup>[10]</sup> Treatment of diarrhea with oral rehydration solution (ORS) reduces mortality due to dehydration. Zinc supplementation could help reduce the duration and the severity of diarrhea, and therefore have an additional benefit over ORS in reducing children mortality.<sup>[11]</sup> A systematic Cochrane review of 24 trials involving more than 9000 children have suggested that supplementation of zinc in the treatment of diarrhea might reduce the duration of diarrhea in children aged six months or more. <sup>[12]</sup>

### Zinc in WHO essential drug list

Zinc is enlisted in WHO essential drug list under medicine for diarrhea where it (zinc sulfate solid oral dosage form: 20 mg) is indicated in acute diarrhea as an adjunct to oral rehydration salts. Recent, WHO recommendations on zinc include mothers, other caregivers and health workers should provide children with 20 mg per day of zinc supplementation for 10-14 days (10 mg per day for infants under the age of six months).<sup>[13]</sup>

## Initiatives in Nepal to promote zinc therapy

In context of Nepal, since 2006 public and private sector programs are being launched to introduce zinc treatment to diarrhea management protocols. In collaboration with United States Agency for International Development's (USAID) Nepal Family Health Project, UNICEF, the Japan International Cooperation Agency, and Plan International, a public sector training program was implemented in the capital city, Kathmandu which later on introduced zinc treatment through the private sector, primarily through pharmacies, drug sellers and other service providers to the urban and peri-urban areas in Nepal.<sup>[14]</sup>

The recent National List of Essential Medicines, 2011 recommend use of zinc as dispersible tablet, equivalent to zinc 10 mg, 20 mg (scored tablets). It recommends zinc use in acute diarrhea as an adjunct to oral rehydration salts. An oral solution of zinc sulfate, 10 mg/5ml in 50- ml bottle is also listed in the list for same use.<sup>[15]</sup>

There have been studies in Nepal that studied the use of Zinc in diarrhea in children. A community based clinical trial comparing zinc with placebo on child mortality reported no significant difference from that of children receiving placebo,<sup>[16]</sup> thus questioning the usefulness of Zinc. In this study authors found Zinc to have no any effect on mortality in children younger than 12 months as well as in older children receiving zinc. Another study on zinc promotion in Nepal reported that 67.5% of children aged less than six years with diarrhea were treated with ORS, and 15.4% were treated with zinc after six month of campaign.<sup>[17]</sup>

### Zinc preparations available in Nepal

Zinc is available in Nepal as 10 and 20 mg dispersible tablets manufactured by domestic manufacturers.

### Probable side effects of Oral zinc

Zinc is usually well tolerated but it may cause vomiting in some children. Although child might vomit within 30 min after swallowing the tablet, re-administration of the tablet is suggested.

### CONCLUSION

Findings suggest the role of zinc therapy during diarrhea which can be a feasible strategy for both prevention and treatment of diarrhea. In a developing country like Nepal, zinc therapy can play a preventive role in decreasing the public health burden, though there has been a placebo controlled study that failed to confirm the effectiveness of Zinc. It is necessary to explore public health applications, using zinc either as a preventive measures in children or therapeutically for diarrhea.

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FASEB Journal 1999 A376

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