



Enhancing Zinc Use for Diarrhoea Management in India

An Advocacy Brief

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Abbreviations and Acronyms

GOI	Government of India
ORS	Oral Rehydration Solution/ Salts
UNICEF	United Nations International Children's Emergency Fund
WHO	World Health Organization
NRHM	National Rural Health Mission
ORT	Oral Rehydration Therapy
OTC	Over the Counter
ISMPs	Indian System of Medicine Practitioners
STG	Standard Treatment Guidelines
I.P.	Indian Pharmacopoeia
NFI	National Formulary of India
NLEMI	National List of Essential Medicines India
BIBCOL	Bharat Immunologicals and Biologicals Corporation Limited
MBPH	Market-based Partnerships for Health
POUZN	Point of Use Water Disinfection and Zinc Treatment project
DCGI	Drug Controller General of India

Introduction

Diarrhoea kills nearly 650 children below the age of five every day in India¹ thereby making it one of the top ten causes of mortality among infants and children below 5 years of age in India. In 2007, Government of India (GOI) introduced zinc as an adjunct to low osmolarity Oral Rehydration Solution (ORS) for more effective management and treatment of diarrhoea as recommended by UNICEF and WHO. Zinc treatment is a simple, inexpensive, and critical new tool for treating diarrheal episodes among children. Numerous trials and studies demonstrate that use of zinc in treatment of diarrhoea results in 25 percent reduction in the duration of acute diarrhoea and upto 40 percent reduction in treatment failure or mortality in persistent diarrhoea². Zinc treatment has been shown to decrease the severity of the diarrhea episode by decreasing the number of stools per day, the volume of stools per day, and the number of episodes lasting beyond 7 days³. Additionally, zinc supplementation given for 10–14 days also lowers the incidence of diarrhoea in the following 2–3 months⁴.

Although Government has made the combination therapy available through public health system under the National Rural Health Mission (NRHM), a recent survey by UNICEF in 10 cities documented that less than 1 percent of diarrhea prescriptions included zinc.

This paper analyses the Government's policy recommendations with regards to zinc use for management of diarrhea and explores reasons why the uptake of zinc is so little despite its proven success. The paper makes a case for modification in regulatory frameworks to enable a wider access to zinc through the preferred health care providers of the communities at large.

Overview of Diarrheal Disease situation in India

In India, on an average approximately 10 percent of deaths among infants and 14 percent deaths among children in the 0-4 year age group are due to diarrhoea every year. Nationally, 9 percent of children under the age of five had diarrhoea in the two weeks preceding the National Family Health Survey-3 (2005-6). Sixty percent of children with diarrhoea were taken to a health facility; 43 percent were treated with Oral Rehydration Therapy (ORT) or increased fluids, including 20 percent who received ORS. There is wide variation across the states with regard to treatment of diarrhoea with any ORT, ranging from 81 percent in Kerala and 70 percent in Himachal Pradesh to 21 percent in Rajasthan, 22 percent in Uttar Pradesh, and 25 percent in Assam⁵.

¹ Gitanjali, K. Weerasuriya. The curious case of zinc for diarrhea: Unavailable, un-prescribed and unused. *Journal of Pharmacology and Pharmacotherapeutics*. Col2, Issue 4. Oct- Dec 2011.

² Bhutta et al. Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries: pooled analysis of randomized controlled trials. *The American Journal of Clinical Nutrition*. 2000; 72(6):1516-22.

³ Zinc Supplementation for the Treatment of Diarrhea in Infants in Pakistan, India and Ethiopia. *Christa L. Fischer Walker et al. *Journal of Pediatric Gastroenterology and Nutrition* 43:357Y363. September 2006.

⁴ Bhutta Z.A., Black, R.E., Brown K. H., et al., 'Prevention of diarrhoea and pneumonia by zinc supplementation in children in developing countries: Pooled analysis of randomized controlled trials', *Zinc Investigators' Collaborative Group*, *Journal of Paediatrics*, vol. 135, no.6, December 1999, pp. 689-697.

⁵ NFHS 3 Summary of Findings

[http://www.nfhsindia.org/NFHS-3%20Data/VOL1/Summary%20of%20Findings%20\(6868K\).pdf](http://www.nfhsindia.org/NFHS-3%20Data/VOL1/Summary%20of%20Findings%20(6868K).pdf) accessed on

Box 1. UNICEF- WHO Recommendations for management of diarrheal diseases

- Prevent dehydration through the early administration of increased amounts of appropriate fluids available in the home, including ORS solution
- Continue feeding (or increase breastfeeding) during the episode and increase feeding afterward
- Recognize the signs of dehydration and take the child to a health care provider for new ORS or intravenous electrolyte solution, and familiarize themselves with symptoms requiring medical treatment (e.g. bloody diarrhoea)
- 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)

Even though ORT, especially ORS, was introduced in India in the 1980s as an effective method for managing non- complicated diarrhoea, approximately 500,000 children still died each year from dehydration due to diarrhoea, most of which could have been prevented . A Lancet study published in 2000, estimated that nearly 16 percent of all under-five deaths could be prevented just by the use of ORS.

The Response

Over the years, diarrhoea management programme in the country evolved from focusing only on WHO formula ORS at inception to introduction of zinc therapy in recent years. In 2004, the WHO and UNICEF issued a joint statement regarding the clinical management of acute diarrhoea. This statement recommended the use of zinc treatment, as well as a new formulation of oral rehydration- the low osmolarity ORS as a two-pronged approach for the treatment of acute diarrhoea in children⁶.

Global Policy recommendations:

WHO/UNICEF recommendation (Refer to Box. 1) to incorporate zinc supplementation into diarrhoea management is based on a substantial body of scientific evidence of benefits emerging from 17 efficacy studies – 12 on acute and 5 on persistent diarrhoea⁷. Together these studies have demonstrated that zinc in addition to ORS reduces both the duration and severity of acute diarrhoea in comparison to treatment with ORS alone. The study also noted significant reductions in hospitalizations from diarrhoea and overall mortality among children living in villages where zinc in addition to ORS was available compared to those living in areas where only ORS was available.

19 August 2011.

⁶ WHO UNICEF Joint Statement on Clinical Management of Diarrhoea, May 2004.
http://whqlibdoc.who.int/hq/2004/WHO_FCH_CAH_04.7.pdf

⁷ Zinc Investigators' Collaborative Group. Therapeutic effects of oral zinc and acute and persistent diarrhea in children in developing countries: pooled analysis of randomized controlled trials. *AJCN* 2000;72:1516-22

The UNICEF –WHO recommendations for management of diarrheal diseases, endorsed by the GOI, incorporate zinc supplementation as an essential component of a four pronged strategy⁸.

GOI guidelines on use of zinc

In view of the recommendations of UNICEF, WHO and the Department of Biotechnology and the proven effectiveness of the use of zinc in diarrheal disease management, on 2nd November 2006 the GOI issued a directive (Z 28020/06/2005/CH) stating that “it has now been decided to administer zinc in the national program as an adjunct to ORS in the management of diarrhea in children older than 3 months”. A brief policy note was issued along with the directive, indicating the benefits of zinc use and outlining issues related to its use and distribution.

An Expert Committee constituted by the Ministry of Health and Family Welfare, analyzed critical aspects related to dosage, side effects and risks and came to the conclusion that:

- Zinc in recommended doses has been established to be well tolerated by children with no side effects
- The window between the therapeutic and toxic dosage of zinc is large, thereby reducing any major side effects or risks resulting from over dosage.

The recommendation regarding dosage was that:

- All cases of diarrhea should receive zinc in addition to ORS
- 20 mg of Zinc Sulphate must be given daily in the form of dispersible tablets in childhood diarrhea control programme for (Children under 6 months of age must receive 10 mg daily) 14 days continuously⁹.

The Committee also recommended that as zinc supplementation is an adjunct treatment to ORT, it should always be promoted together with ORS solution or other home available fluids recommended locally for the management of diarrhoea. It did not recommend use of zinc fortified ORS in the country.

⁸ Implementing the new recommendations on the clinical management of diarrhoea : guidelines for policy makers and programme managers. World Health Organization 2006

⁹ http://mohfw.nic.in/NRHM/Documents/CH/Policy_Guidelines/GoI_Zinc.pdf

With respect to distribution, the Committee recommended that

- The Government must make it available as an Over the Counter (OTC) drug on the lines of ORS
- Both zinc and ORS should be made available at the *Anganwadi* Centres¹⁰ to facilitate early initiation of treatment and to reduce the families' expenditure on unwarranted drugs
- Availability of zinc tablets should be ensured in all parts of the country including the most remote areas.

Implications of Policy Guidelines

The policy stressed the fact that zinc should be made **“freely available and accessible round the year in every village, and all health personnel, including private practitioners and *Anganwadi* workers must be included in the network of zinc distribution.”**

The decision to allow private practitioners to be a part of the zinc distribution network is important in view of the fact that approximately 63 per cent (NFHS-II) of households where children had diarrhoea sought treatment from private healthcare practitioners and that too mostly from Indian System of Medicine Practitioners (ISMPs)¹¹.

Once these new guidelines on diarrhoea management get endorsed and included in a National Policy, with a clear mandate for implementation, and a sustainable supply of zinc and ORS is established, it would be important to review, at this stage, the practical aspects of accessibility and distribution, which in India are governed by the Drugs and Cosmetics Act 1940 and Rules 1945.

¹⁰ An Anganwadi means a courtyard, shelter or a play centre. It was started by GoI in 1975 as part of the Integrated Child Development Services program to combat child hunger and malnutrition. It is located within a village or a slum and is the focal point for delivery of all services provided under ICDS

¹¹ Saathi Bachpan Ke: End of Project report.

Provisions of regulatory framework for zinc manufacture and distribution

As mentioned above, in November 2006, The GOI included zinc in the national diarrhoea treatment guidelines and approved zinc as an OTC treatment for diarrhoea in March 2007 so as to make it widely available.

Drugs that are not prescription-only are by default presumed to be OTC. However, the Drugs and Cosmetics Act, 1940 and Drugs and Cosmetics Rules, 1945 does not define OTC drugs. Rather, the OTC status of a drug is derived from exemptions and restrictions defined under Schedules K, G and H.

As per the various schedules, ORS and zinc are not included in Schedule G¹² or Schedule H¹³ and there are no restrictions on its promotion or advertisements. Various brands of zinc and ORS can advertise freely for the appropriate claims as the Drugs and Magic Remedies Act (1954) lays no restriction on the claims made for diarrhoea management. By placing all ORS formula and zinc formulations outside these schedules, the government has made it possible to easily launch them through the OTC route. In essence, zinc and ORS can independently be promoted as OTC drugs.

However, the regulations on procurement and distribution of zinc make its accessibility in the remote areas a major problem. For instance, pricing and availability surveys in Orissa and Chhattisgarh have shown that though the availability of ORS is relatively good it is pretty dismal for zinc (see table below).¹⁴

Definition of an OTC drug as per Indian law

It is a derived definition based on 'the principle of exclusion'. Any drug which is outside the following schedule is OTC:

- *Schedule H*: list of more than 500 drugs sold on prescription only. The chemist can only dispense with a valid doctor prescription
- *Schedule G*: list of drugs which are required to be taken under medical supervision. (*companies have taken the liberty of launching such drugs as OTC with a caution mentioned on the label e.g. Benadryl*)
- *Schedule X*: list of drugs which are sedatives or central nervous system stimulants and which are likely to be misused
- *Schedule HX*: list of antibiotics drugs
- *Schedule K*: list of household remedies such as Aspirin tablets, Paracetamol tablets, Analgesic Balms, Syrups, Lozenges, Pills and tablets for cough etc. which are exempted from obtaining any sale license provided such drugs are sold in a village with a population of not more than one thousand people

¹² Schedule G gives list of drugs which are required to be taken under medical supervision. Drugs under this schedule are required to be labelled with the words "Caution it is dangerous to take this preparation except under medical supervision".

¹³ Schedule H gives names of drugs which are also known as prescription drugs. Drugs included in this schedule are required to be labelled with symbol Rx and the words "Schedule H drugs – Warning To be sold on the prescription of Registered Medical Practitioner only".

¹⁴ B. Gitanjali, K. Weerasuriya. The curious case of zinc for diarrhea: Unavailable, un-prescribed and unused. Journal of Pharmacology and Pharmacotherapeutics. Col2, Issue 4. Oct- Dec 2011.

Drug name and formulation	Chhattisgarh (availability %)		Orissa (availability %)	
	Public (N=75)	Private (N=60)	Public (N= 83)	Private (N=79)
Zinc Sulphate 20 mg dispersible tablet	29	0	2.4	3.7
ORS packet to make 1 litre solution	93	87	91.5	85.4

Unlike ORS, zinc preparations are not covered under Schedule K¹⁵. This implies that they are required to be manufactured and sold under manufacturing and selling license. This condition does not apply if they are supplied under the Health and Family Welfare Programme of the state or centre. Whereas rural stockists are not required to obtain any sale license when stocking or selling ORS of specific formulation as prescribed by the government, s/he will have to obtain wholesale drug selling license for stocking and selling zinc formulations under the Drugs and Cosmetics Rules, 1945. The same law applies to selling the product through mobile vans or health workers in rural markets.

Additionally, ORS and zinc formulations are not considered as scheduled formulations under the Drugs Prices Control Order, 1995 and therefore there are no restrictions on prices. However, keeping in mind public interest, the Central Government has the right to adjust or revise prices of such formulations in exceptional circumstances.

Analysis

Scientific studies have demonstrated that zinc is effective in diarrhoea control only when administered with ORS. However, in India licensing requirements create challenges with regard to the simultaneous availability of ORS and zinc. Licensing requirement is applicable to all categories of drugs including OTC drugs. Therefore, all drugs are required to be sold and distributed only through licensed establishments subject to the exemptions provided under Schedule K of the Drugs and Cosmetics Rules, 1945. Currently while ORS is placed under Schedule K, zinc is not.

All data indicate that a large majority of infant and children with diarrhoea are treated by private healthcare providers in the country. The private sector accounts for over 75 percent of all health expenditure, including 67 percent of all hospitals, 63 percent of all dispensaries and 78 percent of all doctors¹⁶ in India. Even the Committee under the Ministry of Health and Family Welfare that made various recommendations regarding zinc use acknowledged

¹⁵ For details of schedule K refer to Box 2 ;

¹⁶ Camille Saade. Zinc treatment for childhood diarrhoea: POUZN Public-Private Partnerships in India and Tanzania. SUZY News August 2007.

that “ currently [only] approximately 20 percent of diarrheal episodes are treated by the public health system.”

In a recent UNICEF survey of 10 Indian districts it emerged that not more than 47 percent of prescriptions for diarrhea included ORS; while “tonics”, anti-diarrheal drugs and injections continued to be prescribed in the same proportion as for ORS¹⁷. Surprisingly, although GOI is making zinc and low osmolarity ORS available through public health system under the NRHM, the survey documented less than 1 percent of prescriptions actually for zinc.

There are two significant reasons for the low uptake of zinc:

- Lack of knowledge and awareness amongst care providers on how to implement existing cost-effective interventions for diarrhea management. The challenge is to achieve greater coverage of these interventions in low-resource settings¹⁸.
- Regulations under the Drug and Remedies Act, which impose restrictions for stocking and sale of zinc, preventing single window availability of both zinc and ORS for the end users. Whereas zinc and ORS are available through the public health system, there are different regulations for ORS and zinc when it comes to stocking and sale by private providers. Given that nearly 4 out of 5 cases of diarrhea is managed outside of the public health systems, the regulations have a strong bearing on the access and use of zinc.

It must be noted that though the government stresses the promotion of the drug through the existing health system, especially the NRHM, it is not clear if zinc has been included in the ASHAs medicine kits. As per the official Ministry of Health and Family Welfare website, a list of 19 drugs is included in the ASHA drug kit. This includes Disposable Delivery Kit for clean home deliveries at home; Iron and Folic acid tablets; Punarvadu Mandur tablets (Indian System of Medicine Preparation of Iron); ORS packets; Paracetamol and Dicyclomine tablets; thermometers; cotton absorbent roll; Bandages (4 cm x 4 mts); Chloroquine tablets; condoms and oral pills (In cycles).

Additionally, the official status of zinc is not entirely clear. Even though the government approved the use of 20 mg dispersible zinc tablets for use in acute diarrhea in children in 2007, none of the publications such as the Standard Treatment Guidelines (STG), Indian Pharmacopoeia (I.P.) and National Formulary of India (NFI) mention zinc for the management of diarrhea. The IP 2007 and 2010 do not give standards for oral tablets (dispersible or otherwise) of Zinc Sulphate. The recently released NFI 2010 (preprint version) also fails to mention oral zinc¹⁹. The National List of Essential Medicines India

¹⁷ Management practices for childhood diarrhea in India. Survey of 10 districts. New Delhi: UNICEF;2009

¹⁸ Management of Acute Diarrhea: From Evidence to Policy, Shinjini Bhatnagar, Seema Alam, Piyush Gupta.
<http://www.indianpediatrics.net/mar2010/215.pdf>

¹⁹ Indian Pharmacopoeia. Government of India, Ministry of Health and Family Welfare. The Ghaziabad: Indian Pharmacopoeia Commission; 2010.

(NLEMI) lists Zinc Sulphate syrup for diarrhoea which is different from the recommendation made in the GOI directive of 2006. However, individual states like Chhattisgarh, Orissa, Tamil Nadu, and others have included dispersible zinc tablets in their recent essential drug lists, making a small but significant move in the right direction.

Currently, there are a few national and international manufacturers of zinc. Bharat Immunologicals and Biologicals Corporation Limited (BIBCOL), a public sector undertaking of the Department of Biotechnology, GOI, has been equipped with a production capacity of 240 million tablets of BIBZinC (20 mg dispersible scored tablets of Zinc Sulphate) per year²⁰. Sixteen Indian pharmaceutical companies have produced and marketed zinc for diarrheal treatment, with zinc sales increasing steadily and dramatically since October 2005²¹. Companies such as Zuventus (Zinconia), Dr. Reddy's (Z and D), Wallace (ZN), USV (Trustim), Emcure (Emzinc) have started production of oral zinc with some companies even exporting the drug. Interestingly, by the end of 2008, 89 percent of zinc sales were in syrup form, versus only 11 percent for dispersible tablets. Qualitative research conducted by POUZN²² revealed that both health professionals and caregivers preferred syrups to dispersible tablets even though the government recommendation is for dispersible tablets.

Since zinc is a relatively new product for diarrhoea control it is important to create a sustained demand to make it an attractive product for the current and new manufacturers. Presently, with the demand being low, there is a potential for some manufacturers, especially the local ones who cater specifically to the Indian market to lose interest. This will, in turn, have a bearing on its promotion and scale up.

Recommendations

MBPH²⁴ through its various programs in India works in partnership with the commercial sector to increase the provision of quality reproductive and child health products to improve the quality of life for base of pyramid population. The programs encounter limitations in distribution and promotion of many public health products due to existing regulatory barriers, including that for zinc.

Given the above analysis, MBPH recommends that suitable modifications be made in the existing regulations which currently restrict access to zinc. The Central Drugs Standards Control Organization of India under the Ministry of Health and Family Welfare in the GOI must consider bringing zinc under Schedule K drugs like ORS so that both may be made

²⁰ http://www.dst.gov.in/whats_new/press-release08/tablets-diarrhoea.htm [Accessed on 2011, July 22]

²¹ AED/POUZN: Creating a Partnership Model to Take Zinc to Scale in India

²² The Point-Of-Use Water Disinfection and Zinc Treatment (POUZN) project is a USAID Private Sector Program (PSP) initiative managed by AED. POUZN supports the use of zinc treatment with oral rehydration therapy (ORT)/oral rehydration salts (ORS) to reduce morbidity and mortality due to diarrhea.
<http://www.aed.org/annualreport/2009/Projects/resources/POUZN-India-Country-Profile-4-24-09.pdf>

²⁴ Market-based Partnerships for Health (MBPH) is a United States Agency for International Development (USAID)/India funded project being implemented in India from 2008-2012.

available through the same channels, as their effectiveness is mutually enhanced when used together.

Similarly clear provisions for oral zinc must be made in NLEMI and STG and other such official documents. States like Chhattisgarh, Tamil Nadu and Orissa have already introduced dispersible zinc tablets in the State Essential Drug list.

Training and sensitization of health care providers on the importance of zinc is required, particularly in the private sector where most cases of diarrhea go for treatment, so that they may prescribe zinc as well as educate the communities on the importance of its use. As more private providers begin to prescribe it, zinc manufacturing is likely to become a more attractive proposition for local manufacturers. In this context POUZN is making concerted efforts and lessons can be drawn from its approach of mobilizing health care providers to increase demand for/ uptake of zinc treatment. POUZN has adapted appropriate strategies for urban and rural health providers.

Zinc producers' medical representatives repeatedly contact 15,000 pediatricians, 75,000 general practitioners and over 50,000 drug sellers with messages on improved diarrhea treatment. Selected commercial partners pursue the POUZN rural strategy to expand improved diarrhea treatment in high incidence areas. POUZN has projected that 6,250,000 courses of zinc treatment will be sold by September 2010²⁵.

Additionally, based on its experience of aggressive promotion of ORS in the 1990s, the government and its allies must launch an all round promotion of zinc using popular media such as FM Radio, mobile phones, newspapers, television etc. to enhance public awareness. The focus of all such promotional activities should be the important role that zinc can play in diarrhea management and the method of its use.

Organizations working on diarrhea control and promotion of zinc have multiple entry points for advocacy including the Office of the Drug Controller General of India (DCGI), the private providers and the local manufacturers. A consortium of like minded organizations could work together to undertake such advocacy simultaneously based on their core competencies, to make zinc more easily available and thereby provide access to complete diarrhea case management in communities.

²⁵ <http://www.aed.org/annualreport/2009/Projects/resources/POUZN-India-Country-Profile-4-24-09.pdf>

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