Zinc treatment for childhood diarrhoea
A new and innovative project of ICDDR,B: Centre for Health and Population Research
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Introduction
In 2001, worldwide more than 10.8 million children under five years of age died, most of them from preventable causes and in poor countries. In Bangladesh, 330,000 children under five died in that year. The main causes of under-5 deaths are: neonatal disorders, diarrhoea, pneumonia, and malaria. WHO estimates that 13% of all under-five deaths can be attributed to diarrhoea. However, recent research has shown that this percentage may be higher, at 22% with an uncertainty range of 14-30%.

The reduction of child mortality is one of the Millennium Development Goals. The goal is to reduce under-five mortality in developing countries by two thirds between 1990 and 2015. However, at current reduction rates it is unlikely that this goal can be achieved. In 1990, the under-five mortality rate in all developing countries on average was 103 deaths per 1000 live births. By 2001, this rate had dropped to 89 on average. This is a reduction of just 14% over 11 years. The target, a reduction of under-five mortality to 34 per 1000 live births, requires increased efforts.

Jones a.o. argued recently in The Lancet that the interventions needed to achieve this Millennium Development Goal are already available, however "that they are not being delivered to the mothers and children who need them". Jones a.o. showed that level 1 interventions (level 1 = sufficient evidence of effect) are available for almost all of the major causes of under-five deaths, however, global coverage is insufficient. They categorize zinc as a level 1 treatment for diarrhoea and also as a measure to prevent diarrhoea and pneumonia, and argue that zinc as a preventative intervention could prevent up to 459,000 under-five deaths each year and as a treatment zinc could prevent almost 400,000 under-five deaths each year.

ICDDR,B’s project, Scaling Up Zinc Treatment for Young Children with Diarrhoea (SUZY), will fill this gap, first in Bangladesh and then, hopefully, worldwide. Thus, Bangladesh is about to become the starting point for an exciting and innovative project with the potential of helping to save thousand of young lives and contributing towards achievement of one of the Millennium Development Goals.

Research on zinc and diarrhoea
Zinc is a micronutrient found in foods rich in protein such as red meat, poultry, nuts and dairy products. It is essential for human growth and protection against illness and disease. Many people living in developing nations, such as Bangladesh, do not have access to sufficient amounts of zinc-rich foods. This results in zinc deficiency that can lead to growth failure and increased susceptibility to illness and death, especially among young children.

Over the past two decades, a large body of research on the role of zinc for human health has been created. ICDDR,B: Centre for Health and Population Research has been among the frontline research organizations conducting zinc research. Studies conducted at the Centre, from basic to applied research, have helped to build an evidence base for...
integrating zinc therapy into current child health practice and policies, such as the WHO recommendation for the use of zinc in the treatment of persistent diarrhoea.

Research conducted at the Centre has demonstrated, for example, that zinc supplementation in persistent diarrhoea significantly reduced the length of the recovery period in malnourished children and prevented a fall in body weight and serum zinc concentration, indicating that zinc is a beneficial therapeutic strategy in this high-risk childhood illness.\(^7\)

In a study conducted at Matlab, clusters of children were randomly assigned to receive zinc, 20 mg daily for 14 days, with each episode of diarrhoea. After two years of follow-up, the clusters receiving zinc experienced a 50% reduction in overall non-injury mortality compared to those receiving standard therapy without zinc.\(^8\)

**SUZY - Scaling Up Zinc Treatment for Young Children with Diarrhoea**

In 2002, ICDDR,B decided that the effectiveness and benefits of zinc as a treatment for childhood diarrhoea have been proven and that it is time to move to the next step: to make zinc available as a treatment to the entire under-five population. However, this requires, in addition to further research, innovative solutions for the production of zinc tablets, ways to promote the use of zinc and the establishment of a sophisticated and far-reaching distribution system.

In 2003, the Bill and Melinda Gates Foundation generously agreed to provide a grant to enable ICDDR,B to scale up zinc as a treatment for children with diarrhoea in Bangladesh. While research related to the zinc scale up project is well underway, the actual rollout is scheduled to begin in April 2004. In April, a mass marketing campaign will start to promote the use of zinc to users and providers and zinc tablets will then be available through a variety of outlets. The beginning of the rollout will also coincide with an international conference on zinc to be held in Dhaka. Tentatively, the conference will be held on 19th and 20th April 2004 at ICDDR,B headquarters in Dhaka.

**Prescribing zinc as a treatment for diarrhoea**

WHO recommends that zinc treatment be prescribed for a period of 10 to 14 days at a dose of 20 mg a day for children one to five years old (10-20 mg/day for children younger than 1 year). The product to be introduced is a 20 mg dispersible tablet that can be dissolved on a spoon with a little bit of water. The tablets will be packed in blister packs of ten. For ten days, one tablet needs to be taken a day.

This is the first time that zinc will be introduced in form of a tablet in Bangladesh. Interestingly, there are several zinc syrups available in the market. Usually, they are being prescribed to increase growth, reverse weakness, increase appetite and improve digestion. In some cases they are also used for treatment of diarrhoeal illness.

ICDDR,B decided to use tablets rather than syrup because tablets have three main advantages:

- they are less costly to produce,
- it is easier to measure the amount given, and
- tablets are easier to handle, transport and store.

**Production of zinc tablets**

The zinc tablet that will be introduced was developed by Nutriset, a French non-profit company specializing in the production of nutritional products for emergency and disaster situations. Nutriset developed the formula for the dispersible zinc premix; it is free of metallic taste. In Bangladesh, the zinc tablets will come with a taste of vanilla.

Although Nutriset will import the zinc tablets during the scale-up phase, it is planned to transfer the entire technology for the production of zinc tablets to Bangladesh. In the long term, the production of the zinc premix, the conversion into tablets and the packaging of tablets in blister packs will all be located in Bangladesh.
Nutriset and ICDDR,B are currently looking for a local partner who is interested in this technology and able to produce the zinc tablets to the required standards.

**Development of distribution systems**

ICDDR,B and its partners are working to establish an innovative distribution system for the zinc tablets. This will involve partners in NGOs, in the Ministry of Health and Family Welfare (MOHFW) and in the private sector. Currently training manuals are being developed to provide training to all those who will be involved in the distribution process. The Social Marketing Company (SMC) is well known for its work on scaling up Oral Rehydration Solution (ORS) throughout Bangladesh and has an extensive network of sales officers and sales promotion officers covering the entire country. They distribute products such as ORS and condoms to providers all over Bangladesh. This includes physicians, allopaths, homeopaths, drug sellers and pharmacists. This network will be available for the distribution of zinc tablets as well.

Zinc tablets will also be available via the facilities of the Ministry of Health and Family Welfare (MOHFW). Initially, ICDDR,B will provide MOHFW facilities with the zinc blister packs free of charge. Later, a fee will need to be considered that reflects commitment and sustainability. A further partner in the distribution of zinc tablets will be the NGO Service Delivery Program (NSDP) depot-holders. The USAID NSDP covers rural Bangladesh and has been estimated to service about 15% of the population. The NSDP relies on community/village-based health workers, known as depot-holders, as the point of entry into its health services. Depot-holders have received a modest amount of training and receive a small monthly honorarium. They make additional income through the sale of ORS, condoms, and oral contraceptive pills, as well as from referrals made to static health centres.

**Mass marketing campaign**

Like any new product, zinc as a treatment for childhood diarrhoea needs to be marketed to its target group. The Social Marketing Company (SMC) will oversee the marketing and distribution of the zinc blister packs. A tender process has just been held to identify a company that will be tasked with the development of a mass marketing campaign.

**SUZY research**

The scale-up process of zinc tablets and their introduction into the local market will be accompanied by formative and operational research informing the actual implementation process, and evaluation research, for example in form of National Coverage Surveys.

**Formative research**

Currently, formative research is being conducted to collect information needed in the initial phase of the zinc rollout. The overall aim of the formative research is to gain an understanding of key issues affecting the treatment of diarrhoeal diseases in children under 5 years of age. In a first step, the research team determines local terminologies, beliefs and concepts about childhood diarrhoea and management of diarrhoeal illness and examines local perceptions of vitamins and minerals, with a focus on zinc and the acceptability of zinc during diarrhoea episodes. The team also describes the local health system, including biomedical, traditional, religious and home care as related to health seeking behaviours for cases of diarrhoea.

Knowledge gained through the project will help, for example, to develop communication messages to be used during a mass marketing campaign, which will start in April 2004. The
formative research will also contribute to the assessment of changes in provider practices for the treatment of diarrhoea, in particular regarding the use of antibiotics, injectables and antidiarrhoeals. It is planned to present first results of the formative research component at an international conference to be held in April 2004 in Dhaka.

Safety study
Although zinc has been used in many trials and no serious side effects have been reported, there is a need for phase IV trials to identify, validate and quantify possible side effects in large patient populations. For this study, zinc therapy is being introduced at two Dhaka hospitals as part of the standard management of all children with acute or persistent diarrhoea. All children treated with zinc will be monitored, especially for excess or unusual vomiting. Based on the yearly patient attendance at the centre, it is estimated that 60000 children per year will be treated with zinc and monitored for side effects. Safety monitoring will be conducted for 12 months.

Acceptance, adherence and compliance study
This study addresses the acceptability of the dispersible zinc tablets in terms of taste and method of delivery, relative to syrup formulations already available in the market. For this study, children and caretakers who were given zinc tablets will be followed to investigate whether or not the children are receiving the zinc following discharge from hospital, for how long and what factors influence adherence to diarrhoea management instructions. For the acceptance, adherence and compliance study, the research team will enrol 1600 children.

Evaluation
The scaling up project will be accompanied and supported by an immediate evaluation of its the overall performance and impact. Several research projects will contribute to the overall impact evaluation. National coverage surveys will be undertaken in rural and urban populations within each of the 6 divisions of Bangladesh to evaluate caretaker treatment practices, service utilization and equity and changes in these areas. The study will be carried out in both slum and non-slum areas in Dhaka and Chittagong. Surveys are also planned in six districts, one from each division.

The most important question to be answered is whether or not the scaling up activities are having the desired effect; to what extent are children with a diarrhoeal illness receiving zinc and what impact is this having on antibiotic and ORS use. Closely connected to this is the question of disparities (equity) based upon income status, gender, type of provider seen, and where children live.

In addition, longitudinal, repeat observational studies of incident cases of childhood diarrhoea will be conducted in two sub-districts where ICDDR,B conducts routine demographic surveillance; in one rural sub-district (Mirsarai) and in one urban sub-district (Kamalapur in Dhaka).

Specifically, this study aims to:
• monitor the proportion of children under five receiving zinc treatment during diarrhoeal episodes,
• document changes in provider and caretaker practices,
• document caretaker expectations, satisfaction and acceptance of zinc as a treatment,
• document provider satisfaction and acceptance of zinc treatment protocols,
• determine what influence the zinc treatment protocol has on other services and activities carried out by Ministry of Health and Family Welfare (MOHFW) staff and depot-holders under the NGO Service Delivery Program,
• estimate the health impact of the zinc treatment protocol.
• determine the value added, in terms of coverage and impact, of training village-based depot holders to dispense zinc for diarrhoeal illness.

The various research projects will provide valuable information for national health policy and service delivery in the private, public and NGO sectors. In addition, they will help international policy makers to decide
Review Article

about a global roll-out of zinc treatment scale-up based on ICDDR,B's experience in Bangladesh.

Acknowledgement
For further information about the SUZY project and for updates on the research projects and the roll-out, please visit the newly established homepage of the Scaling Up Zinc Treatment for Young Children with Diarrhoea at http://www.icddrb.org/activity/SUZY. The homepage will also provide information on the international conference on zinc tentatively to be held on 19th and 20th April 2004 in Dhaka.

References