Program Experience with Micronutrient Powders and Current Evidence

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Abstract

The efficacy of micronutrient powders (MNP) in the treatment of anemia in moderately anemic children aged 6–24 mo has been clearly demonstrated. The evidence of the effectiveness of MNP in large-scale programs, however, is scarce. This article describes the program experience and findings of large-scale MNP distribution in refugee camps and in an emergency context in Bangladesh, Nepal, and Kenya. The MNP contained 15–16 micronutrients as per the WHO/World Food Programme/UNICEF joint statement, whereas the iron content was reduced to 2.5 mg from NaFeEDTA in a malaria-endemic area in Kenya. Hundreds of thousands of children aged 6–59 mo and pregnant and lactating women were targeted to consume MNP either daily or every other day over an extended period of time. Extensive social marketing campaigns were undertaken to promote regular use of the product. A number of studies were embedded in the programs to assess the impact of MNP on the nutritional status of target beneficiaries. Some improvements in anemia prevalence estimates were observed in particular subgroups, but other results did not show significant improvements. A significant decrease in the prevalence of stunting was observed in Nepal and Kenya but not in Bangladesh. Diarrhea episodes decreased significantly among children receiving MNP in Nepal. A key challenge is to ensure high MNP acceptance and adherence among beneficiaries. Investigation of non-nutritional causes of anemia is warranted in settings with high compliance but no improvement in hemoglobin status. Further investigation into the most appropriate manner to use MNP in malaria endemic settings is warranted.

MNP: An Innovative Strategy

In recent years, point-of-use fortification of home-prepared meals with supplements in the form of powders, crushable tablets, and lipid-based spreads has received growing attention as a promising approach to tackling micronutrient deficiencies.

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Abbreviations used: Hb, hemoglobin; MNP, micronutrient powder; PLW, pregnant and lactating women; RNI, Recommended Nutrient Intake; WFP, World Food Programme; UNHCR, United Nations High Commissioner for Refugees.
development. The target group may be expanded to include children aged 25–59 mo depending on program duration, needs, and availability of resources.

Ample scientific evidence supports the efficacy and bioavailability of MNP, primarily among moderately anemic children aged 6–24 mo, in a variety of settings (2). Conclusions from the meta-analysis of all efficacy trials conducted in controlled settings indicated that MNP containing 10–12.5 mg of iron were as effective as iron drops in treating anemia and resulted in better acceptance (2). Additionally, the use of MNP reduced the risk of anemia by nearly 50% (2). However, evidence of the effectiveness of MNP in large-scale program settings is scarce.

To date, MNP programs have been conducted in many different countries across several regions. Worldwide, >80 MNP programs have been implemented in development settings, in refugee camps, and as part of an emergency response. Most programs have been carried out at a subnational or pilot scale, targeting children under 5 y. Despite the large number of MNP programs, information about impact evaluation is scarce. However, limited available information indicates a positive MNP impact in program settings (3–5). Anemia prevalence in children aged 6–59 mo fell from 46 to 25% after 26 mo of MNP distribution in a large-scale program implemented through the Integrated Nutrition Program in Mongolia (4). MNP were also successfully used in an emergency setting in Indonesia, where over 28 million sachets were distributed to ~200,000 infants and children aged 6 mo to 12 y who had been affected by the tsunami and earthquake. Within 5 mo, program coverage reached 90% and anemia prevalence was 25% less among the MNP recipients compared to those who had not received MNP (5).

The UN WFP and DSM started the Improving Nutrition Improving Lives public-private partnership in April 2007. As part of this partnership, large-scale MNP distribution programs have been implemented in several countries to improve the nutritional status of target beneficiaries, mainstream and learn about MNP, and assess MNP impact under program conditions. The aim of this paper is to briefly review the recent large-scale MNP program experience and the data collected during the impact evaluation.

### Large-Scale MNP Programs

Most MNP programs within the WFP-DSM partnership have been implemented with the UNHCR either in the context of refugee camps or emergency response (Table 1). MNP programs in Bangladesh have been conducted as part of the Cyclone Sidr response (targeting 101,000 under-fives and 59,000 PLW), food- and cash-for-work activities implemented in response to the high food prices (targeting 14,500 children aged 6–24 mo and 6000 PLW), and programming in the Rohinga refugee camps. Two MNP programs are in progress in Nepal: one in the Bhutanese refugee camps (targeting 8500 children aged 6–59 mo) and another as part of the high-food price emergency response (targeting >114,000 children aged 6–59 mo). In Kenya, an MNP program at the Kakuma camp targeted 55,000 refugees of all ages (Table 1).

The recommended dose of MNP is either one sachet per child per day or every other day, taking into account the micronutrient content of general food rations received and regular diet (Table 1). The alternate-day dosing scheme aims to provide approximately one-half of the RNI of micronutrients every day through regular MNP intake. Two sachets every other day are distributed to PLW, providing an amount of micronutrients close to one RNI for this particular population group (Table 1). It is assumed that this population is simultaneously receiving iron-folic acid supplements. In general, consumption of 90 sachets by a child within a flexible timeframe of 90–180 d is considered sufficient to improve micronutrient intake to approach recommended levels. Although a minimum of 60 doses (consumed over a 2–4 mo period) has also been found efficacious in reducing anemia (6), these findings occurred in controlled settings with increased communication with beneficiaries and this level of intake may not be sufficient for all micronutrients.

The implementation of MNP programs is a fairly complex process, necessitating alignment of stakeholders; government permission (unless programs are government initiated); ethical approval; resource mobilization; training of local health workers; formative research; packaging design, production, procurement, and distribution of MNP; program monitoring; and impact evaluation (J. van Hees, personal communication). Experience with each of these components and lessons learned are outside the scope of this document but are being documented elsewhere (J. van Hees, personal communication). The conceptual approach for determining the micronutrient formulation in different settings is briefly discussed below.

The micronutrient composition was determined based on the WHO/WFP/UNICEF joint statement regarding prevention and control of micronutrient deficiencies in populations affected by emergency (1). The joint statement recommends 15 micronutrients for inclusion in the formulations. MNP formulations remained fairly consistent across the WFP-DSM partnership programs with minor variations accounting for factors such as malaria endemicity, availability of fortified foods, vegetable consumption (vitamin K), and consumption of iron absorption inhibitors such as tannins in tea and phytate (Table 2). In the refugee camps in Nepal, Bangladesh, and Kenya, standard food rations including fortified blended food, vitamin A-fortified oil, and iodized salt were provided. In addition, refugee children aged 0–59 mo received vitamin A capsules every 6 mo. Accordingly, the vitamin A content of MNP was reduced to 25% of the recommended amount in the joint statement and iodine to 33%. Vitamin K was added in the formulation, because intake was assumed to be low due to the low green leafy vegetable consumption in refugee camps. Vitamin C content was doubled to enhance iron absorption and mitigate the effect of tannins in tea and phytic acid in cereals and legumes.

The risk of untargeted iron supplementation in malaria-endemic areas among preschool children is well known (7,8), although its generalizability has been questioned. Furthermore, how to define when an area is endemic to malaria is unclear. Untargeted home fortification with MNP containing low levels of iron but with a constant bioavailability, together with iron absorption enhancers such as ascorbic acid, was assumed to be safer in malaria-endemic areas. Hence, at the Kakuma refugee camp in Kenya where malaria is endemic, the iron content was reduced to 2.5 mg in the form of NaFeEDTA. This form of iron was chosen because of its constant bioavailability despite the presence of iron absorption inhibitors. This would likely lead to an invariable supply of iron regardless of the type of local food to which MNP were added at home (9,10). In a theoretical calculation, either a 10 or 15% absorption rate was applied to the 2.5 mg iron from NaFeEDTA, and 5% to iron provided from daily intake of corn-soy blend, which was assumed to be the main dietary source of iron for the refugees to whom the MNP would be provided (Table 3). Consequently, the additional
<table>
<thead>
<tr>
<th>Program area</th>
<th>Bangladesh</th>
<th>Nepal</th>
<th>Kenya</th>
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<tbody>
<tr>
<td>Program area</td>
<td>4 southern coastal districts: Barguna, Bagerhat, Patuakhali, Pirojpur</td>
<td>3 districts (Rajshahi, Nawabganj, Naogaon), northeast Bangladesh and 2 districts (Patuakhali, Bholai), southwest Bangladesh</td>
<td>Jhapa district, southeast Nepal</td>
</tr>
<tr>
<td>Program area</td>
<td>3 districts (Rajshahi, Nawabganj, Naogaon), northeast Bangladesh and 2 districts (Patuakhali, Bholai), southwest Bangladesh</td>
<td>17 food-insecure districts throughout Nepal</td>
<td>Turkana district, northwest Kenya</td>
</tr>
<tr>
<td>Program area</td>
<td>Cox’s Bazar district, southeast Bangladesh</td>
<td>Bhutanese refugee camps</td>
<td>Kakuma refugee camp</td>
</tr>
<tr>
<td>Target beneficiaries</td>
<td>5000 children 6–59 mo of age</td>
<td>14,500 children 6–24 mo of age</td>
<td>8500 children 6–59 mo of age</td>
</tr>
<tr>
<td>Target beneficiaries</td>
<td>2000 adolescents 1200 PLW</td>
<td>6000 PLW</td>
<td>&gt;14,000 children 6–59 mo of age</td>
</tr>
<tr>
<td>Target beneficiaries</td>
<td>114,000 children 6–59 mo of age</td>
<td></td>
<td>55,000 refugees, all ages</td>
</tr>
<tr>
<td>Target beneficiaries</td>
<td></td>
<td>114,000 children 6–59 mo of age</td>
<td></td>
</tr>
<tr>
<td>Program duration</td>
<td>Since Jul 2008</td>
<td>Since Mar 2010</td>
<td>Since Sep 2009</td>
</tr>
<tr>
<td>Design of impact evaluation</td>
<td>Aug 2008 – Jan 2009</td>
<td>Cross-sectional survey at endline in the intervention vs. comparison group</td>
<td>Cross-sectional survey in the intervention vs. comparison group at baseline and endline</td>
</tr>
<tr>
<td>Design of impact evaluation</td>
<td>Follow-up of cohort</td>
<td>Follow-up of cohort</td>
<td>Follow-up of cohort</td>
</tr>
<tr>
<td>Main impact evaluation outcomes: anemia</td>
<td>Anemia prevalence among children under five decreased from 64% to 48% after a 6-mo period</td>
<td>No differences in anemia prevalence among children under 5 y between intervention vs. control areas after 7 mo. However, anemia prevalence prior to the MNP distribution may have been higher among children in the intervention vs. control area, resulting in the negation of the potential positive impact of MNP</td>
<td>Prevalence of moderate anemia (Hb 70–100 g/L) among children under 5 y decreased from 19% in 2007 to 14% in 2010 (P &lt; 0.05), whereas the proportion of mild anemia (Hb 100–110 g/L) did not significantly change (24% in 2007, 26% in 2010).</td>
</tr>
<tr>
<td>Main impact evaluation outcomes: anemia</td>
<td>Not yet available</td>
<td>Not yet available</td>
<td>No change in anemia prevalence among children under 5 y following 1 y of MNP intervention (56 vs. 60%). Iron status, as assessed by serum transferrin receptor level, improved after adjusting for age (24.1 ± 0.5 vs. 20.8 ± 0.7 nmol/L; P &lt; 0.001).</td>
</tr>
</tbody>
</table>

1 Hb, hemoglobin; MNP, micronutrient powder; PLW, pregnant and lactating women; WFP, World Food Programme.
amount of low-dose iron in the MNP, together with iron derived from the corn-soy blend, was assumed to help fulfill the iron needs of the most vulnerable population groups such as young children (Table 3). The zinc content in Kakuma was reduced to 2.5 mg in order not to be higher than the iron content.

Impact Evaluation in Large-Scale MNP Programs

A number of studies have been nested in large-scale programs to assess the potential impact of MNP on the nutrition and health status of the beneficiaries. Study design varied across programs, depending on factors such as program design and implementation (e.g., blanket coverage, availability of a comparison group, possibility to conduct a baseline measurement) (Table 1). In some cases, a cohort of children was followed prospectively, whereas in other settings, population-based representative cross-sectional surveys were conducted periodically to assess the impact of MNP. The main outcome assessed was Hb concentration as a proxy indicator of micronutrient deficiencies; nutritional status assessed by anthropometric measurements; and morbidity in the prior 2 wk as an indicator of general health status.

### TABLE 3

<table>
<thead>
<tr>
<th>Child age, y</th>
<th>Daily absorbed iron requirement</th>
<th>Estimated daily absorbed iron from food sources</th>
<th>Estimated daily absorbed iron from MNP</th>
<th>Total daily absorbed iron</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median 95% percentile</td>
<td>5%</td>
<td>10%</td>
<td>15%</td>
</tr>
<tr>
<td>1–3</td>
<td>0.46 0.58</td>
<td>0.25 0.29</td>
<td>0.25 0.27</td>
<td>0.5–0.62</td>
</tr>
<tr>
<td>4–6</td>
<td>0.5 0.63</td>
<td>0.36 0.38</td>
<td>0.25 0.37</td>
<td>0.61–0.73</td>
</tr>
</tbody>
</table>

2 Total daily requirement of absorbed iron to support growth and balance basal iron losses.  
3 Based on a daily corn-soy blend intake of 40 g (1–3 y) or 60 g (4–6 y) with iron content (from fortification and the ingredients themselves) of 12 mg/100 g; note that absorption of iron from other food consumed is not included.  
4 MNP containing 2.5 mg iron from NaFeEDTA.  
5 Not including the absorption-enhancing effect of ascorbic acid and NaEDTA on intrinsic iron.  
6 Values represent the median of the total daily requirement for absorbed iron.  
7 Values represent the 95% percentile of the total daily requirement for absorbed iron.  
8 Assuming a 5% iron absorption rate.  
9 Assuming 10% of the iron from MNP is absorbed.  
10 Assuming 15% of the iron from MNP is absorbed.
Anemia
At the Rohinga refugee camps in Bangladesh where a cohort of children who had received MNP was followed, anemia prevalence decreased from 64 to 48% (P < 0.001) after a 6-mo period (February to April 2009) compared to baseline (August to October 2008) (Nasima Akhter, Helen Keller International, personal communication). The positive effect of MNP on anemia was corroborated by the first 2 annual cross-sectional nutrition surveys conducted in the camps, which showed a reduction of anemia among under-fives from 47% in 2008 to 29% in 2009 (P < 0.001) (Helen Keller International, personal communication). However, in the 2010 nutrition survey, the prevalence of anemia among children under 5 y increased to 49% (K. Bougma, personal communication). This increase may have occurred due to a decrease of the acceptability and reduction in the number of people who picked up MNP following the introduction of peanut-flavored, lipid-based nutrient supplements to children in the camp during the lean season for a period of 5 mo (Dorothy Gazarwa, UNHCR, personal communication). Regardless, the increase in anemia among children using MNP in this population is concerning and needs to be further examined, because it has programmatic implications.

In the Cyclone Sidr response MNP program in Bangladesh, a cross-sectional survey was conducted both in the intervention area and in a comparison area where MNP was not distributed. Anemia prevalence did not differ among children under 5 y between these two areas after a 7-mo period of MNP intervention (11). However, the results require more careful interpretation, because anemia prevalence was higher among adolescent girls in the intervention area than in the comparison area, although no adolescents in either area received MNP. This implies that anemia prevalence prior to the MNP distribution may have been higher among children in the intervention area than in the control area, resulting in the negation of the potential positive impact of MNP. However, the observed anemia prevalence after 7 mo of intervention was still very high at 79%. In the same program, anemia prevalence was found to be lower among lactating mothers who consumed ≥75% of the distributed MNP sachets compared to those who had an adherence rate <75% (50 vs. 61%, P = 0.06) (11).

In the Bhutanese refugee camps in Nepal, the overall prevalence of anemia among children aged 6–59 mo remained relatively constant between January 2007, prior to the MNP distribution (43%), and May 2010 (40%), after a 26-mo period of MNP distribution (12). The prevalence of moderate anemia (Hb = 70–100 g/L) decreased from 19% in 2007 to 14% in 2010 (P < 0.05), whereas the proportion of mild anemia (Hb = 100–110 g/L) did not change significantly (24% in 2007; 26% in 2010) (12).

At the Kakuma refugee camp in Kenya, a malaria-endemic area, a cohort of children under 5 y was prospectively followed. Anemia prevalence did not significantly change following 1 y of MNP intervention, after adjusting for age (56 vs. 60%). Iron status, as assessed by serum transferrin receptor level, improved after adjusting for age (24.1 ± 0.5 vs. 20.8 ± 0.7 nmol/L; P < 0.001) (13).

Stunting
According to cross-sectional nutrition surveys conducted at the Damak refugee camp in Nepal, there has been a clear downward trend in stunting, with a decline in prevalence from 39% in 2007 to 23% in 2010 (P < 0.05) (12). Accordingly, the height-for-age Z-score has steadily improved over the past 3 y. In the Cyclone Sidr response program in Bangladesh, stunting prevalence was reported to be lower among children who had consumed ≥75% of the distributed sachets compared to those with a compliance rate of <75% (40 vs. 52%; P < 0.05) (11). In the cohort study conducted at the Kakuma refugee camp in Kenya, stunting prevalence among children under 5 y was reduced from 12 to 7% (P < 0.05) after a 1-y period. However, the prevalence of stunting remained constantly high (~70%) with no significant improvement since 2008 at the Rohinga refugee camps in Bangladesh (Helen Keller International, personal communication; K. Bougma, personal communication). Although most previous research examining the impact of multiple micronutrient supplementations on stunting found no significant improvement (14–16), our evidence collected from various settings indicates a potential positive effect of MNP on stunting. The extended duration of supplementation and enrolment of young children (starting from 6 mo of age) who are most vulnerable to impaired linear growth may have contributed to the positive findings in our programs. In addition, the differences in the root causes and baseline levels of stunting in each setting and the extent to which other interventions are implemented in parallel may explain the variations in findings.

Diarrhea
Data from Bhutanese refugee camps in Nepal showed a significant reduction in the 2-wk cumulative incidence of diarrhea over the past 3 y. The proportion of children who reported having diarrhea in the prior 2 wk decreased from 30% in 2007 to 18% in 2009 and further to 13% in 2010 (2009 vs. 2010; P < 0.05) (12). Although the reduction may be attributed to other ongoing interventions at the camp, the additional zinc supplied from MNP may have been a protective factor. Data from cross-sectional surveys in Bangladesh did not show a significant reduction in 2-wk cumulative incidence of diarrhea (20.1% in 2009 vs. 19.2% in 2010), but adherence to MNP may have decreased in 2010 (see above). Data on diarrhea morbidity was not available for the Kakuma program.

Acceptability
The self-reported acceptability of MNP and adherence were variable. MNP was well accepted by the program beneficiaries, leading to a high compliance rate in Bhutanese refugee camps and the Cyclone Sidr response program (11,12). Various positive perceived benefits of MNP have been reported as well. In the Bhutanese refugee camps, for instance, the majority of the care takers reported perceived improvement in their children’s health, appetite, and energy level after consuming MNP (F. Husain and O. Bilukha, unpublished results). On the other hand, in the Rohinga refugee camps in Bangladesh, only ~40% of children were reported to have regularly consumed MNP in 2010 despite the high MNP pick-up rate (90%) at the food distribution centers (Dorothy Gazarwa, UNHCR, personal communication). At the Kakuma refugee camp in Kenya, MNP was not well accepted by the beneficiaries, with a collection rate at distribution points of ~45–50%. Various factors associated with the product and program implementation, such as inappropriate packaging, superficial formative research, insufficient social marketing, and inadequate staff training, seem to have contributed to the low collection rate (17). The low compliance of MNP may partially explain the lack of change in anemia prevalence following 1 y of intervention. It may also be difficult to attribute the improvement of iron status to MNP due to the relatively low MNP pick-up rate (as described above). However, similar findings from previous studies on home fortification and
the proven bioavailability of NaFeEDTA in high-phytate diets support the effect of MNP intervention (Richard Semba, Johns Hopkins University School of Medicine, personal communication).

In summary, evidence from two programs (in Bhutanese camps in Nepal and a Kakuma refugee camp in Kenya) suggests a potential positive impact of MNP on stunting. In Bhutanese camps in Nepal we also saw a decrease in diarrhea morbidity. Although some improvements in anemia were observed in particular settings, other results did not show significant improvement as measured by Hb levels. Context-specific characteristics such as food consumption, nutrient intake, causes of micronutrient deficiencies, implementation of various interventions occurring at different times, and acceptance of and adherence to MNP when distributed at a large-scale vary widely and affect the impact of MNP programs. However, it should be noted that in many cases the impact evaluation was carried out only among those who received MNP without a proper comparison group, and we thus cannot rule out other factors as being responsible for the observed improvement (or lack of improvement) in various outcomes. Efforts to monitor program implementation and acceptance and assess the impact of MNP are essential to understanding the effectiveness of individual programs (14).

Three considerations are particularly important. Hb concentration can be affected by micronutrient status; other nutritional conditions; non-nutritional factors such as inflammation, infection, thalassemia, worm infestation, and malaria; and other causes. Consequently, anemia may not be appropriate as a stand-alone indicator to assess the effectiveness of MNP. Assessment of MNP adherence in a program context is challenging. Triangulation of different sources of information, such as observation of remaining sachets and questioning, may provide the best possible information. Efforts to address how to better scale-up and monitor MNP distribution and uptake are needed. Implementation of MNP programs in complex and evolving environments is complicated. Impact evaluation requires careful design and planning and needs to be taken into account from the outset of the program, although this may not be feasible in emergency. Follow-up of the same cohort over time is likely to be better than multiple sets of cross-sectional assessment, and availability of a proper comparison group and baseline measurement are critical.

Multiple interventions are often being introduced according to need and funding that may affect the outcomes measured, both positively and negatively. Finally, more research needs to be done on providing iron in malaria-endemic areas. The quality, assumptions of bioavailability, potential role of NaFeEDTA as an iron fortificant, and definition of when a locale is malaria endemic all need further clarity to improve the response of preventing anemia in such settings.

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Literature Cited