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Micronutrient dietary supplements - A new fourth approach

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SUMMARY. Currently the three main widely used strategies to control micronutrient deficiencies are food diversification, fortification, and consumption of medicinal supplements. In Tanzania a fourth strategy has been evaluated in school children, and is to be studied in pregnant and lactating women. The dietary supplement comes in the form of a powder used to prepare a fruit flavored drink. Children consumed for six months 25 grams per school day attended, the powder being added to 200 ml of water. The dietary supplement provides between 40 and 100 percent of the RDA of 10 micronutrients, which includes iron, vitamin A and iodine. Unlike medicinal supplements it provides the multiple vitamins and minerals in physiologic, not megadoses. In a well conducted randomized double blind placebo controlled trial, a dietary supplement in the form of a fortified powder fruit drink produced statistically significant differences not only in vitamin A and iron status, but also in the growth of young school age children.
Key words: Multiple supplementation, Ferrochel, nutritional deficiencies, fortified beverage.

RESUMEN. Suplementación dietética de micronutrientes – Un cuarto nuevo enfoque. Hasta este momento, las tres estrategias mas frecuentemente utilizadas para el control de las deficiencias de micronutrientes son: diversificación de alimentos, fortificación y consumo de suplementos medicinales. En Tanzania, una cuarta estrategia fue evaluada en niños escolares y se estudiará en mujeres embarazadas y en mujeres lactantes. El suplemento dietético se prepara como un polvo usado para preparar una bebida con sabor a naranja. Los niños estudiados consumieron durante seis meses, 25 gramos del polvo disueltos en 200 mL de agua por día de asistencia a la escuela. El suplemento provee entre 40 y 100% del RDA de 10 micronutrientes entre los cuales se encuentra hierro, vitamina A y yodo. Contrario a los suplementos medicinales, la bebida provee vitaminas y minerales en cantidades fisiológicas y no en dosis mayores. En una prueba de campo bien efectuada, randomizada, doble ciega con control de placebo, la bebida fortificada produjo diferencias estadísticamente significativas, no solo en la condición nutricional con relación a hierro, vitamin, a A y yodo, sino también en el crecimiento de los niños estudiados.
Palabras clave: Suplementación múltiple, Ferrochel, deficiencias nutricionales, bebida fortificadas.

INTRODUCTION

Malnutrition is increasingly recognized as a very prevalent and important health problem in many countries, a problem that has serious long-term consequences for the child and may adversely influence development itself. That more than 2,000 million people live at risk of diseases related to micronutrient deficiencies-most commonly vitamin A, iron, and iodine-and that most of these people are women of childbearing age and young children in developing countries, are facts that are often stated and much studied (1). Malnutrition in its severe and not-so-severe forms still remains a significant cause and determinant of mortality, short- and long-term morbidity, and permanently lost productivity and intellectual capacity in societies which can ill afford such losses and costs.

Despite these devastating consequences, the range of methods by which micronutrient deficiencies are addressed have remained much the same and almost consistently fall into one of the following categories (2).

Food diversification - in some cases this will simply come about by increasing overall food intake while in other cases it comes about through behavioral change which increases the consumption of nutrient rich foods. This may be affected through diversifying household and/or regional food production strategies to ensure that foods rich in the nutrients identified as deficient become available.

Food fortification. The deliberate addition of a specific nutrient to a food vehicle which is identified as being widely consumed in adequate quantities by populations at risk of the deficiency. The classic examples being the iodization of salt; and the fortification of milk with vitamin A and vitamin D.

Medicinal supplements. (a) periodic administration of large doses of a specific micronutrient, such as vitamin A or iodine, which either provide some protection from a prolonged period of deficient intake or treats a deficiency which has already resulted in clinical symptoms, or (b) medicinal amounts far above the RDA for the nutrient, for example iron and folate supplements during pregnancy.

These methods are, for the most part, technically easy and cost-effective given the economic gains which can be

achieved. Significant achievements in reducing micronutrient malnutrition have been made using them.

Each of these three standard approaches has its disadvantages and limitations. Most people agree that food diversification offers the best long term approach that is likely to be sustainable. But often it requires major changes either in agricultural production, including home gardens, or in higher incomes for the poor, allied with nutrition education. So in many non-industrialized countries progress is slow, and in some African countries with a deteriorating economic situation, food diversification is unlikely to substantially reduce micronutrient deficiencies in the near future.

Conditions for fortification vary depending on the nutrient and the foods eaten in a country. In some countries several commonly eaten foods do pass through commercial processing where fortification is feasible. Salt iodination has greatly reduced iodine deficiency disorders in many countries. But in many non-industrialized countries it is difficult to find a suitable food vehicle to fortify with iron or vitamin A. A suitable food has to be consumed regularly by those at risk of the deficiency who are often children and women in poor families. Especially in rural areas those suffering from micronutrient deficiencies may purchase few manufactured or processed foods.

Medicinal supplements are of two kinds. First there are those taken in pharmacological doses daily or at frequent intervals, and second those prescribed to be consumed in large doses at intervals of 4 to as long as 24 months. Ferrous sulfate and folate are examples of the former, and vitamin A and lipiodol (containing iodine) are examples of the latter. Medicinal supplementation is dependent on a delivery system which is often relatively costly if the supplement is to reach those at risk. Other problems include poor compliance which is common with iron prescribed during pregnancy, and low participation rates for example when massive dose vitamin A supplements are offered over time.

A World Bank review of micronutrient programs (3), found that three common problems arising from the implementation of any or all of these strategies were: (i) the lack of appropriate consumer demand; (ii) the lack of appropriate delivery infrastructure with adequate access for poor women and isolated populations; and (iii) the lack of honest, efficient and technically competent enforcement systems for food fortification. Furthermore, a key feature of successful programs was consistently found to be "supply": that is supply of the food itself or seeds and other necessary inputs to allow dietary diversification; supply through secure access to fortified foods via appropriate food vehicles in adequate quantities; and/or supply through cost-effective, professionally prescribed and readily available medicinal supplements.

Dietary supplements - it's been done before

Micronutrient dietary supplements offer a fourth approach, and one which can control deficiencies using a single intervention.This approach is unique since it delivers micronutrients that fill the nutritional gap via a vehicle that is, or becomes well accepted by the target group. The supplementation of diets with a specific food substance high in one or more micronutrients recognized as potentially deficient in the regular diet is not a new concept. Not so long ago children in industrialized or industrializing countries received a regular dose of cod-liver oil to stave off the effects of vitamin A and D deficiencies. At the turn of the century, rickets, the consequence of prolonged deficient vitamin D intake or lack of sunshine was very common amongst children in the poor communities of industrialized cities where the diets comprised a small range of foods and there was limited access to outdoor areas and thus direct sunlight. In some countries, on the shelves of remote, small rural and urban shops, one can still find bottles of Haliborange - a concoction of halibut oil high in vitamins A and D or of Ribena, to provide vitamin C. In many countries north and south similar products, some labeled as "tonics," provide micronutrient supplements. However these tonics often do not include those minerals and vitamins most lacking in local diets. Often, this is a very costly way of providing micronutrients to target groups that have limited income.

In Europe and North America, the promotion of cod-liver oil and other healthful dietary supplements empowered mothers with affordable options to prevent rickets in their children and where such solutions were not affordable those dietary supplements were available free of charge through public health clinics. The development of better health care systems, affordable and diversified food supplies and a growing appreciation of the health benefits of outdoor play presumably also underlay the decline of rickets in industrialized countries (4). Unfortunately, the concept of regular dietary supplement consumption has not been translated from industrialized countries to the populations of non-industrialized countries which continue to be at risk, or suffer from micronutrient deficiencies.

Trial of a micronutrient supplement in Tanzania

In Tanzania a randomized double blind placebo controlled trial of a multiple-micronutrient fortified dietary supplement in school children has been completed (5). A similar trial has been planned to assess the feasibility and efficacy of a similar micronutrient dietary supplement in pregnant and lactating women.

Micronutrient deficiencies including iron deficiency anemia, vitamin A deficiency and iodine deficiency disorders are recognized as important public health problems in

Tanzania (6). The project was a collaborative study involving the Tanzania Food and Nutrition Centre, Cornell University, UNICEF, the Micronutrient Initiative and the Procter and Gamble Company.

The dietary supplement used was a fortified powdered fruit drink. It was developed and produced especially for this project by scientists at the Procter and Gamble Company in Cincinnati, Ohio, USA. The product tested consisted of 25 grams of a fine white powder in individual serving sachets. One sachet contained 5.4 mg of iron from bis-glycinate chelate, 1750 IU of vitamin A, 45 μg of iodine, 5.25 mg of zinc, 72 mg of ascorbic acid, 0.6 mg of riboflavin, 0.14 mg of folic acid, 3 μg of vitamin B_{12}, 0.7 mg of vitamin B_6 and 10.5 mg of vitamin E. Nutrient and product stability evaluations demonstrated the product is stable up to one year.

In the Mpwapwa District of Dodoma Region 830 children attending 6 primary schools participated in the study. A baseline examination included the collection of clinical, biochemical and anthropometric data. Eligible children were then randomly assigned to one of two groups either to receive one sachet of the micronutrient dietary supplement each school day attended, or to consume a non-fortified product, identical in appearance and taste. The research team, schoolteachers, and participants were blinded. Six months later a final examination was conducted on 775 children.

The results, in terms of measures of iron and vitamin A status, plus anthropometric findings are being published elsewhere (5). In summary there were no significant differences at the baseline in serum retinol levels, nor in terms of measures of iron status (including hemoglobin, hematocrit, zinc protoporphyrin, and serum ferritin).

Six months later there were highly significant differences between the two groups always in favor of the micronutrient supplemented children. In the group with mild and moderate anemia (less than 11g/dL hemoglobin), there was a significant increase in hemoglobin only in the group that received the fortified dietary supplement (by 0.92 g/dL) as compared to that of the placebo group (by 0.02 g/dL). This was confirmed by a significant increase in ferritin in the treatment group (by 16μg/L) versus the placebo group (by 2 μg/L). Also, low serum vitamin A levels were significantly lowered in the fortified group but not in the non-fortified group. There was a significant decrease (by 50%) in vitamin A deficiency as expressed by serum retinol of <20 μg/dL in the group that received the micronutrient fortified beverage.

Somewhat surprisingly, although weight, height and BMI did not differ between groups at the baseline, the fortified group, at follow-up, had gained significantly more in all three parameters as compared with the non-fortified group. The highly significant gains attributable to micronutrient supplementation were weight gain of 0.55 kg, height gain of 0.57 cm, and BMI (Body Mass Index) of 0.88 (wt/ht2).

This trial suggests that the micronutrient supplement was effective in improving iron and vitamin A status, as well as growth of children. The supplement was extremely popular. The fact that primary school children would not, compared to pre-school children or pregnant and lactating women, usually be considered the prime beneficiaries of such a mechanism, is recognized. However, the benefits of the school setting in providing a secure delivery mechanism (schoolteachers prepared the drink and supervised consumption) and thus high compliance were considered critical for this initial trial. A trial with pregnant women is planned.

Some principles and considerations relating to this approach

The objective of the trial in Tanzania was to deliver adequate levels of bioavailable iron, stable vitamin A and iodine via a beverage that children find highly palatable, and that is of low cost. The multiple nutrient fortified powder fruit drink delivers nutrients, taste, convenience and affordability all together. The dietary supplement strategy recognizes some of the key principles incorporated in one or all of the three commonly used intervention methods discussed above: behavioral change via social marketing; diversification of food intake; supply of specific vitamins in specific foods; and regular doses of vitamins and minerals specific to regionally or locally recognized deficiencies. These are the underlying mechanisms by which micronutrient deficiencies are addressed. Just as food diversification seeks to create a supply, demand and taste for a new food item so should the promotion of a dietary supplement; and, just as medicinal supplements aim to provide a significant (albeit pharmacological) dose of specific nutrients a well developed supplement could do the same.

Important factors in the development and promotion of a dietary supplement include:

Nutrient composition

A single serving of the product should deliver adequate levels of three critically needed (iron, vitamin A and iodine) micronutrients.

Product acceptance

The addition of the micronutrients should not affect the accepted taste and color of the vehicle. The preparation as well as the consumption of the product have to be culturally accepted. It should not replace, but rather complement other foods and beverages.

Product shelf life and nutrient stability

The stability of the nutrients added and the product shelf life should be evaluated in a condition that mimics the envi-

ronment under which it will be stored and prepared for consumption.

Product efficacy

For a dietary supplement to have an impact on the micronutrient status of the population who consume the product, the nutrients have to be bioavailable. Thus, the ability of the fortified product to improve micronutrient status should be demonstrated by carrying out a well designed clinical study.

Product package and convenience

The product should be of a kind that can be transported easily to poorly accessible remote areas and from stores to homes, and should not be bulky. It should be easy to prepare and serve in the home. The package should be strong and air tight.

Quality assurance and surveillance

The product should be made by following an established quality assurance program. The quality of the starting materials and the process of making the product determines the quality of the finished product. To make sure that the product is delivering the micronutrients claimed in the package at the time of consumption, monitoring should be done by a third party such as a regulatory agency.

Affordability

This is key to success of the dietary supplement strategy. It should be within the economic reach of the target groups. The cost of the product should reflect the value of the product. This has to be recognizable by the targeted consumer.

Raising awareness

The reality is that many of the populations suffering from micronutrient deficiencies are not aware of the problem. For the consumers to make an informed decision in choosing between a fortified and similar but unfortified products, they have to be educated about the prevalence, consequences and prevention of micronutrient malnutrition. Through schools, social marketing and media, the benefits of the product and the consequence of micronutrient malnutrition have to be communicated to the consumers and the professionals.

Partnerships

To accomplish all these elements, a partnership has to be established among the key players, which includes government agencies, industry, international agencies, non-government organizations and the scientific community. Each organization has expertise and these often complement each other. The goal is to succeed in accomplishing a common goal, which is combating micronutrient deficiency by leveraging each stake holder's strength.

Reviewing some of the problems identified with the other approaches to micronutrient deficiencies, the dietary supplement may potentially overcome some of these. Where sufficient appreciation and desire for the food item is generated - developed through commercial marketing strategies - supply should be ensured through market demand. Political will and external, public resources are not necessary inputs although they could be of benefit in generating a rapid development of demand and supply or for ensuring access through subsidies and/or free supply where income is not sufficient. The argument for a contribution from commercial manufacturers to the cost of subsidies and for social-marketing type promotions should not be overlooked given the potential for longer term sales development.

As with the dietary supplement practices of old, this approach can empower mothers and families with a healthful, care-giving practice which they control and can, ideally, access with security and at reasonable cost. Importantly, it is technically possible to include several micronutrients within a single food item, thus the process of addressing a situation where there are several deficiencies is simplified - a clear advantage over current fortification and medicinal supplementation strategies.

CONCLUSION

Tanzania is currently taking steps to address the serious problems of iron, vitamin A and iodine deficiencies. Wisely a variety of strategies are being used. Among the interventions being used are iron and folate supplements routinely administered to pregnant women; programs are in place to deworm children in part to reduce anemia; fermentation and germination or grains is being advocated to improve iron utilization and to reduce the action of phytates; vitamin A supplements administered to high risk children in many health units; efforts to increase the production and consumption of carotene rich foods; legislation in place to ensure iodination of salt from the major manufacturers; and other actions to address diseases such as malaria which influence nutritional status.

This study is considered an important first step in testing and further developing the mechanism of dietary supplementation for addressing micronutrient deficiencies. A distinction is being made here between medicinal supplements such as ferrous sulphate tablets and dietary supplements. Differences include the fact that medicinal supplements are taken under medical supervision and control, whereas dietary supplements for children are controlled by the mother or family, and for the pregnant woman by the mother herself. Another important difference is that this dietary supplement provided physiological "doses" of each nutrient, where medicinal supplements provide doses of micronutrients much above the RDA.

It is not expected or intended that this approach will replace current programs and strategies but instead that it will provide policy-makers, health-planners, and more importantly mothers and families, with an additional option. The decision on which strategy should be pursued or promoted, and how public dollars should be directed for nutrition interventions must be assessed on a case by case basis. Moreover, consistent with current understandings and experiences which show that no single approach will be effective in all settings and at all times, the development of a 'fourth option' can provide an effective means to fill the gaps left by other approaches. It should be noted that the Procter and Gamble Company developed and supplied the supplement as a prototype for this project. The product is not available in the marketplace.

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