Are Biofortified Staple Food Crops Improving Vitamin A and Iron Status in Women and Children? New Evidence from Efficacy Trials

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ABSTRACT

Biofortification is the breeding of crops to increase their nutritional value, including increased contents of micronutrients or their precursors. Biofortification aims to increase nutrient levels in crops during plant growth rather than during processing of the crops into foods. Emerging research from 8 human trials conducted in the past decade with staple food crops that have been biofortified by traditional plant breeding methods were presented in this symposium. Specifically, data from 6 efficacy and 2 effectiveness trials were discussed to assess the effects of regular consumption of these enhanced staple crops on improving population vitamin A and iron status and reducing the burden of micronutrient deficiencies in targeted populations living in South Asia, Sub-Saharan Africa, and Latin America. Biofortified food crops appear to have a positive impact on nutritional and functional health outcomes, as the results from the trials suggest. Additional implementation research will be needed to ensure maximization of the beneficial impact of this intervention and a smooth scaling up to make biofortification a sustainable intervention in public health. The challenge for the global health community remains how to take this efficacious intervention and implement it at large scale in the real world. Adv. Nutr. 5: 568–570, 2014.

Background

Biofortification is the breeding of crops to increase their nutritional value, including increased contents of micronutrients or their precursors. Biofortification aims to increase the nutrient density in crops during plant growth rather than during processing of the crops into foods.

This symposium was proposed to foster a better understanding of results from recent and emerging research from human efficacy trials conducted in the past decade with staple food crops that were biofortified by traditional breeding methods. Data from 6 efficacy trials assessing whether regular consumption of these enhanced staple crops could improve population vitamin A and iron status and reduce the burden of vitamin and mineral malnutrition in target countries in South Asia, Sub-Saharan Africa, and Latin America were presented. Mineral- or carotenoids-biofortified staple food crops for human nutrition provided the academic community with recently generated information on the potential of these crops (beans, rice, pearl millet, cassava, and maize) as a complementary intervention to control and prevent iron and vitamin A deficiencies and improve functional outcomes, particularly cognitive performance and physical and brain activity.

Symposium Proceedings

The symposium was structured to present preliminary findings from 6 efficacy trials and 2 effectiveness trials, as well as the considerations on implementation. Six experts spoke to the specific objectives of the symposium, focusing primarily on their research results and conclusions.

Provitamin A–Biofortified Crops: Maize and Cassava

Vitamin A deficiency remains a nutritional concern in Sub-Saharan Africa. Over the past decade, conventional plant
breeding efforts yielded maize hybrids (“orange” maize) and yellow cassava to contain higher concentrations of β-carotene (10–15 μg/g fresh weight) which gives the biofortified crops their yellow/orange color. The body converts β-carotene into vitamin A. The results from an efficacy trial with biofortified orange maize were presented by Dr. Palmer.

A large-scale trial was designed to test whether regular consumption of biofortified orange maize could be an efficacious public health intervention. The trial was performed between 2012 and 2013 in the rural farming district of Mkushi, in Zambia’s Central Province, by researchers from the Johns Hopkins Bloomberg School of Public Health, Tropical Diseases Research Centre in Zambia, and the Zambian National Food and Nutrition Commission. Children aged 4–8 y were grouped into clusters of ~15–25 each, which were then randomly assigned to either white (n = 50) or orange (n = 50) maize meal. Data on socioeconomic status, dietary intake, morbidity, and anthropometry were collected. Similarly, venous blood was collected to measure serum retinol, β-carotene, C-reactive protein, and α-1-acid glycoprotein. Pupillary responsiveness to light stimuli was tested in a subsample of children (n = 542) using a portable dark adaptometer. Outcomes were measured at baseline and at a 6-mo follow-up assessment. The intervention provided 200 g (dry weight) of maize flour, 6 d/wk for 6 mo, served to 1024 participating children as morning porridge and mid-day nshima with relish following standardized recipes.

Participant children were marginally malnourished; although half had serum retinol < 1.05 μmol/L, only ~10% were deficient (as defined by ≤0.70 μmol/L serum retinol and adjusted for inflammation). After 6 mo, with 90% follow-up, serum β-carotene was ~0.3 μmol/L greater in the orange maize group than in the white maize group. However, neither mean serum retinol concentration nor prevalence of vitamin A deficiency (as defined by ≤0.70 μmol/L serum retinol) differed between the groups. Post hoc analyses revealed no interaction between baseline deficiency and treatment. Pupillary responsiveness increased significantly across all light stimuli. After adjustment for baseline differences, children in the orange maize clusters had a 2.2 (95% CI: 1.0, 4.6) greater odds of improved pupillary function.

In this context of the marginally deficient population, regular biofortified maize consumption significantly increased serum β-carotene concentrations, with no additional improvement in vitamin A status. Additionally, children who consumed orange maize were twice as likely to have improved visual function. The authors concluded that regular biofortified maize consumption could provide an important safety net, i.e., a safe and effective delivery mechanism for provitamin A that could be converted to vitamin A as needed by the body.

**Iron-Biofortified Crops: Common Beans, Rice, and Pearl Millet**

In this section, the effects of improvements in iron status as a result of biofortification interventions were examined with respect to physical and brain activity and cognitive performance. Data from the first meta-analysis assessing the effect of consuming iron-biofortified staple food crops on the iron status of individuals from 4 efficacy trials was also presented.

**Changes in physical performance in response to iron-biofortified pearl millet and beans.** Dr. Haas and Ms. Luna examined the impact of 2 iron-biofortification interventions on 2 measures of physical performance: 1) the effects of the interventions on maximum aerobic power (VO₂max); and 2) net energetic efficiency at 2 submaximal workloads. In 135 Indian adolescent boys and girls, significant improvements in serum ferritin (P = 0.04) and total body iron (P = 0.01) after 4 mo of consuming iron-biofortified pearl millet compared with low-iron controls were observed. After 6 mo, the high-iron group also significantly improved (P = 0.04) the net efficiency of work, measured as energy expended at 60% of maximum work rate minus energy expenditure at 0 workload on a cycle ergometer. There was no significant difference between treatment groups in VO₂max (P = 0.25), and there was no significant association between change in iron status and change in performance in this sample. In a sample of 136 female Rwandan university students consuming either iron-biofortified or control beans for 4 mo, the high-iron group had significant improvements in hemoglobin (P < 0.01), serum ferritin (P = 0.015), total body iron (P = 0.024), and VO₂max (P = 0.038) but not energetic efficiency at 60% of maximum work output. There was a significant positive relation between hemoglobin and VO₂max with analysis of repeated measures taken throughout the study period (P < 0.001).

To the authors’ knowledge, these studies are the first to demonstrate the effects of iron biofortification of a staple crop on iron status and selected measures of physical performance. These preliminary results support previous research that shows that VO₂max is primarily limited by low hemoglobin and oxygen transport (1), whereas work efficiency appears to be limited by total body iron status, which in turn affects oxygen transport and muscular tissue energy metabolism.

**Effects of consuming biofortified staple food crops on iron status: meta-analysis of women and children from 4 countries.** Drs. Finkelstein, Mehta, and Haas presented findings from a meta-analysis of 4 randomized trials on the effects on iron status of iron-biofortified staple food crops: 1) iron-biofortified rice in 191 adult religious nuns in Manila, Philippines (2); 2) iron-biofortified pearl millet in 246 adolescents in Sarole Pathar, India (J. Finkelstein, J. Haas, S. Udipi, unpublished data); 3) iron-biofortified beans in 234 female university students in Butare, Rwanda (J. Haas, J.B. Gahutu, M. Lung’aho, unpublished data); and 4) iron-biofortified beans in 568 male and female primary school students in Oaxaca, Mexico (J. Haas, S. Villalpando, T. Shamah, unpublished data). In each of these studies, iron status, inflammation (as measured by C-reactive protein and α-1-acid glycoprotein concentrations), and anthropometric indices were evaluated at baseline and end line. Primary endpoints included the following: 1) hemoglobin concentration; 2) serum ferritin concentration; 3) serum transferrin receptor concentration; and 4) total body iron. Anemia and iron deficiency were common: 34% of participants were anemic (18–44%) and 50% were iron deficient (11–71%) at baseline. Iron-biofortification interventions improved indicators of iron status, including hemoglobin and serum ferritin.
concentrations and total body iron, and significantly increased the likelihood of resolution of iron deficiency. The effects of iron-biofortification interventions on iron status were greatest among individuals who were iron deficient at baseline.

Findings suggest that iron-biofortification approaches are efficacious in improving iron status in women and children, with the additional potential to benefit iron-deficient individuals. A systematic analysis to include dose–response and plausibility analyses, other iron-fortification interventions, and the effects of iron-biofortification interventions on functional outcomes is now being performed.

**Changes in perceptual and cognitive performance and associated brain dynamics in response to iron-biofortified pearl millet and beans.** Drs. Murray-Kolb and Wenger presented and discussed the impact of iron-biofortified pearl millet and beans on measures of perceptual and cognitive performance and associated brain dynamics, as measured using electroencephalography (EEG). These data are drawn from the same studies in which changes in physical performance were assessed (as presented by Dr. Haas). A set of 5 widely used laboratory tasks was administered to subsamples of participants in each of the 2 intervention studies. These tasks were designed to assess a particular aspect of perceptual and cognitive functioning linked to brain areas in which variations in iron status were shown to produce variations in activity. Three of the 5 tasks, namely a simple reaction time task, a go/no-go task, and the attentional network task, assessed a set of potential effects in attention, ranging from low- to high-level alerting. These 3 tasks were the focus of the presentation.

With respect to changes in behavior, reliable reductions in reaction times and reliable improvements in measures of alerting, orienting, and selection as a function of experimental group and changes in blood iron markers were observed in both the simple reaction time and go/no-go tasks in both studies. With respect to changes in brain dynamics, reliable increases in the amplitudes of early components of the event-related potentials (segments of the EEG referenced to the onset of task stimuli) and reliable changes in the spectral power components of the EEG indicative of the ability to deploy focused attention as a function of experimental group and changes in blood iron markers were observed in all 3 tasks in both studies.

According to the speakers, these studies are the first of their kind to be able to document changes in both behavior and brain dynamics to changes in iron status as a function of provisions of a biofortified crop. In addition, because these data were obtained from participants whose physical activity was also measured, these studies allow for an examination of parallel changes in perceptual and cognitive performance, brain dynamics, and physical performance.

**Effectiveness Trials: Measuring the Impact and Cost Effectiveness of Biofortification**

Effectiveness studies are considered the ultimate proof of concept of biofortification as an efficacious and cost-effective population-level nutrition intervention. These studies are designed to measure the causal impact of interventions delivering planting material of biofortified crops on various outcomes, including adoption, diffusion and consumption of biofortified crops, and micronutrient status by assessing changes in relevant micronutrient intake and biomarkers. Effectiveness studies may also investigate the cost-effectiveness of different delivery interventions to inform recommendations for scaling up those that are found to be most effective and least costly.

Dr. Birol summarized the results of the 2 effectiveness studies conducted in Uganda (3) and Mozambique (4) by a large, multidisciplinary research team, led by the International Food Policy Research Institute. This study investigated the effectiveness of 2 delivery models for disseminating planting material for a vitamin A–biofortified sweet potato, namely orange sweet potato. Evidence from Uganda showed that delivery of orange sweet potato resulted in significantly increased vitamin A intakes among children and women and improved vitamin A status among some children. In Mozambique, delivery of orange sweet potato resulted in increased vitamin A intakes, with orange sweet potato providing almost all of the total vitamin A intakes for children. These effectiveness studies also showed that the less expensive, less intensive delivery model was as effective as the more intensive and hence more expensive delivery model in reaching these outcomes. The most effective and least expensive delivery model tested cost $15–20 per disability-adjusted life year averted, which is considered highly cost effective by World Bank standards.

A recent publication in *The Lancet* (5) stated that “The feasibility and effectiveness of biofortified vitamin A-rich orange sweet potato for increasing maternal and child vitamin A intake and status has been shown,” and “Evidence of the effectiveness of targeted agricultural programs on maternal and child nutrition, with the exception of vitamin A, is limited...and rigorous effectiveness assessments are needed.” Plans are currently under way to implement effectiveness studies for iron-biofortified beans and pearl millet and vitamin A–biofortified cassava and maize, whose efficacy was established.

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**References**