Are there Potential Risks from Rice Fortification with Iron?

Commentary

Crystal Karakochuk
Faculty of Land and Food Systems,
University of British Columbia

Rice fortification as a public health strategy

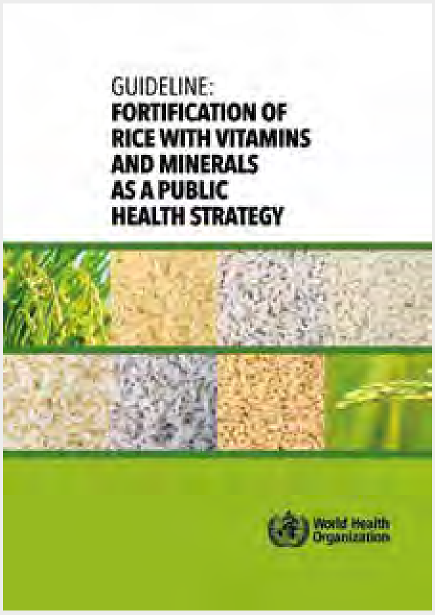
There is no doubt that food fortification is an effective public health nutrition strategy to prevent micronutrient deficiencies at the population level. Rice is a common staple food in many African countries and is well suited for fortification because it is widely consumed and acceptable.[1] Further, rice fortification is not limited to iron. Fortification of rice with multiple micronutrients has potential benefits beyond the reduction of micronutrient deficiencies. For example, fortification of rice with other micronutrients (e.g., vitamin A or zinc) can also benefit erythropoiesis and prevent anemia.

Authors of a systematic review (updated in 2017, including 16 studies) summarized the evidence on the efficacy of rice fortification:[2]

- Fortification of rice with iron (alone or in combination with other micronutrients) probably improves iron status by reducing iron deficiency (nine studies, moderate-certainty evidence) but may make little or no difference to the risk of anemia (seven studies, low-certainty evidence).
- Fortification of rice with other micronutrients (vitamin A or folic acid) may reduce vitamin A or folate deficiency (five studies, low-certainty evidence and one study, very-low-certainty evidence, respectively).
- Fortification of rice with iron (alone or in combination with other micronutrients) may increase hookworm infection (one study, low-certainty evidence).

This evidence has supported the development of the 2018 WHO recommendations for rice fortification as a public health strategy (**Figure 1**).

FIGURE 1: Global WHO recommendations for rice fortification (2018)



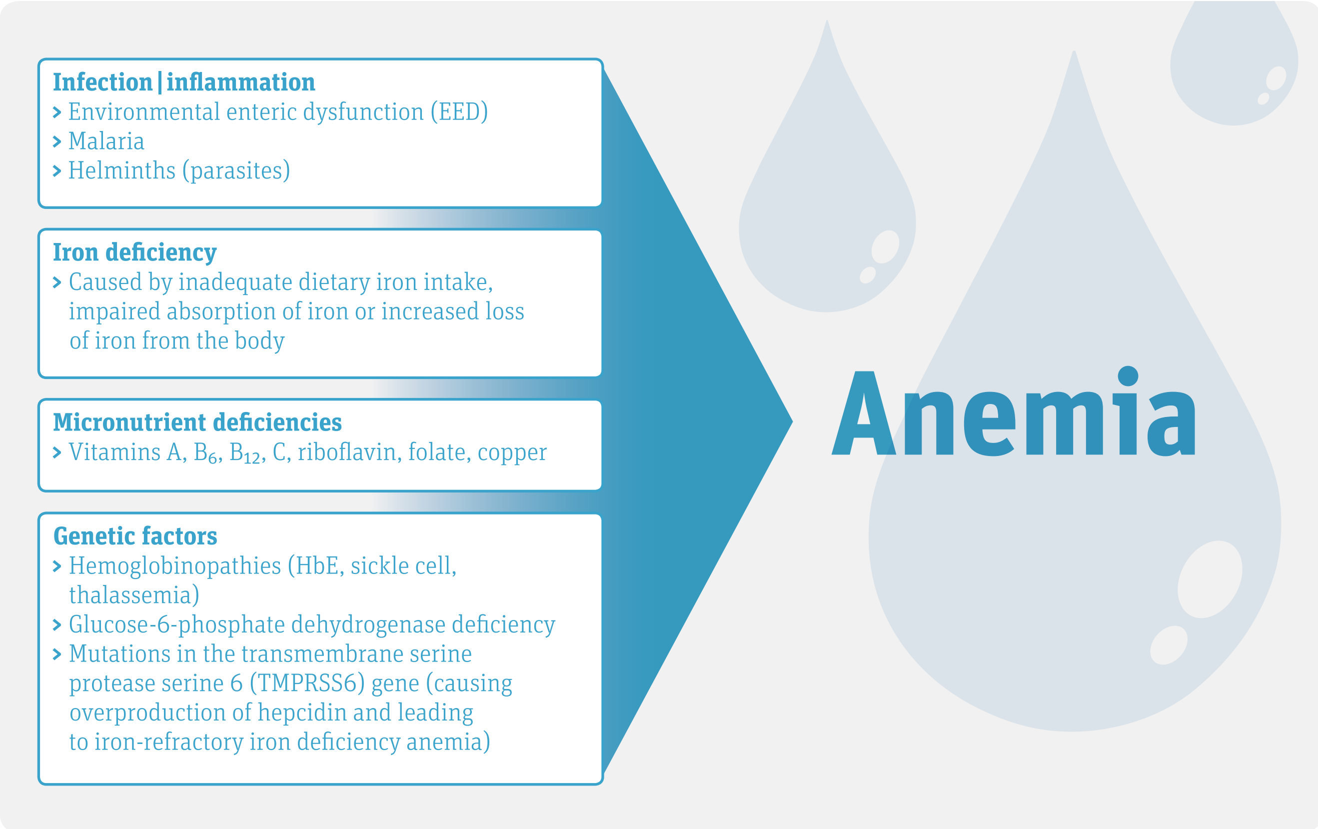
In 2018, WHO released a guideline on fortification of rice as a public health strategy

Emerging concerns regarding excess iron

However, concerns have emerged as to whether or not there is potential harm regarding the risk of excess iron in some populations, particularly in iron-replete individuals or among those with genetic hemoglobinopathies and/or infections such as malaria, pneumonia, or diarrhea.

Rice fields outside of Dili, Timor-Leste

FIGURE 2: Potential causes of anemia



Preparation of rice in a WFP school feeding site in Rwanda

Iron is an essential mineral in the body. It is required for oxidative energy metabolism, erythropoiesis and oxygen transport, as well as other important functions. Iron deficiency is associated with an increased risk of adverse health outcomes, especially in infants, children and pregnant women. However, at the same time, iron is potentially harmful, especially in the presence of oxygen, as it catalyzes the formation of highly reactive oxygen species via the Fenton reaction. Excess iron can cause intestinal injury, oxidative stress, DNA and cellular damage (e.g., DNA strand breaks) and increased susceptibility to pathogen growth.[3,4,5]

> "Iron is an essential mineral in the body. However, at the same time, iron is potentially harmful, especially in the presence of oxygen"

We highlighted these concerns in a recent *Sight and Life* magazine article – "Iron supplementation in iron-replete populations: Is there an emerging concern?"[6] We cited several recent surveys across Africa that showed low prevalence rates of iron deficiency among women and children. Rather than iron deficiency, genetic hemoglobinopathies (e.g., sickle cell disease) and infection (e.g., malaria) are common in many African countries and can be major contributors to anemia. If iron deficiency is not the cause of the anemia then, at best, iron interventions are a waste of resources and, at worst, they may cause harm. Thus it is imperative to determine the major causes of anemia in a population in order to develop appropriate and effective public health strategies to prevent, reduce and treat anemia.

The potential harm of rice fortification with iron

Consumption of iron-containing micronutrient powders have shown some potential for adverse effects in infants and children. In recent studies in Kenyan children, provision of micronutrient powders including iron (12.5 mg iron as ferrous fumarate) showed increased abundances of enteropathogens (including *Shigella, E. Coli* and *Clostridium*) and increased gut inflammation (increased fecal calprotectin concentrations), as compared to the same micronutrient powder without iron.[7] We highlight that novel ways to mitigate the adverse effects of iron-containing micronutrient powders on the gut microbiota have since been proposed, such as the inclusion of prebiotic galacto-oligosaccharides to micronutrient powders.[8] These promising approaches require further research.

> "We speculate that rice fortification would have a lower potential for harm as compared to other iron interventions"

We speculate that rice fortification would have a lower potential for harm in iron-replete individuals and populations with a higher burden of infectious disease, as compared to other iron interventions such as oral iron supplementation or home fortification with iron-containing micronutrients. This is because the doses of daily iron are typically lower and the consumption of the iron fortificant is limited to the amount of rice an individual can consume. In addition, the iron is incorporated in the food matrix, which reduces the potential for non-transferrin-bound iron accumulation in the blood.

Lastly, fortified rice can be one of multiple iron interventions in a population and this needs to be assessed at the time of program design and implementation in order to minimize the risk of excess iron intake.

Conclusion

The efficacy of rice fortification likely varies by population and context, and also depending on the proportion of anemia that is due to iron deficiency rather than other causes. The potential harm of rice fortification is expected to be low, given the low daily dose of iron and the limit of how much rice can be consumed by an individual. More research is needed to ascertain if there is potential harm presented by iron-fortified rice (or excess iron) and if this harm translates to adverse outcomes of biological or clinical significance.

References

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