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IRON FORTIFICATION: HEALTH RISKS OF EXCESSIVE IRON INTAKE

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Typically, a chosen food staple like wheat or rice, or even salt, is fortified to provide up to two thirds (10 mg/day) of the iron requirement of adult women, and almost the entire daily requirement of men. | Photo Credit: The Hindu

Iron is an essential mineral required for many bodily functions, including the formation of hemoglobin, but can be harmful when taken in excess. One of the methods suggested for the treatment of iron deficiency anemia is fortification of food with iron. Typically, a chosen food staple like wheat or rice, or even salt, is fortified to provide up to two thirds (10 mg/day) of the iron requirement of adult women, and almost the entire daily requirement of men. Thus, excess consumption of iron can occur if one habitually consumes a balanced quality diet to begin with or exceeds limits for consumption of the fortified food (as can occur with staples like rice or wheat) or if two fortified foods are simultaneously consumed.

In addition, when combined with additional iron supplemental interventions like weekly iron folic acid supplements (such as in the National Iron Plus Initiative programme), this can lead to an excess of iron intake for women. There is a defined level of iron intake beyond which the risk of adverse events begins to increase. This is called the ‘tolerable upper limit’ of intake, and is set at 40 mg/day.

While this is relevant for populations with normal iron stores, it can be especially deleterious for populations who have iron overload states like patients with thalassemia and other hemolytic anemias, hemochromatosis, and chronic liver disease, which have impaired iron excretion mechanisms.

Once iron is absorbed, it is thought that its excretion is steady and very small, except when bleeding takes place, as with menstrual bleeding. Thus, women can ‘excrete’ iron from the body, but men cannot, unless they have some form of pathological or abnormal bleeding. This makes men particularly vulnerable to excess iron intake.

Iron transactions in the body are complex. Recent studies using stable isotopic iron to accurately understand iron balance (absorption and excretion), conducted in the U.S. and Africa, showed that with fortification, there is an increased excretion of iron in children, such that the body tries to rid itself of the excess absorbed iron. It is not known exactly how, or through what route, this extra excretion takes place. It is likely that the extra iron is lost through the intestine,

where cells of the intestinal lining exfoliate or drop off, and thereby deposit their iron into the intestine lumen for excretion, or through the urine. We do not know the consequences of this form of body iron loss, nor of the crosstalk between body iron stores and this excretion. Nevertheless, beyond the excess stores, the net effect of iron provision through fortification, on haemoglobin formation, is likely to be lower than thought.

As stated above, to the extent that the body can, it will try to regulate iron absorption. Nevertheless, the excess iron in the fortified diet can remain unabsorbed. Typically, it is expected that just 5-10% of the ingested iron, from the iron salt that is added, is absorbed. The rest passes on through the intestine and reaches the large intestine (colon) prior to excretion. Studies have shown that unabsorbed iron can lead to inflammation in the gastrointestinal lining and disrupt the colonic microbiota with long term consequences. This is due to a proliferation of iron-living bacteria in the colonic microbiome, and a reduction of beneficial strains like lactobacteria, with the appearance of some bacterial strains that could be pathogenic. This irritation of the lining may present itself clinically as abdominal cramps, constipation, or diarrhoea.

In addition, the irritation of mucosa can also lead to gastrointestinal blood loss, as has been described in endoscopic studies of patients on iron supplementation. An excess of iron in the gastrointestinal tract can impair absorption of other minerals such as zinc and copper, which are also essential for the body and lead to other deficiencies.

A more pressing worry is that excess iron has been closely linked to many chronic comorbidities like diabetes. Diabetes risk is increased in subjects with increased dietary iron intake and with higher iron stores (represented by high levels of a storage molecule called ferritin) even in the absence of markers of inflammation. This is attributed to many causes, including oxidative damage and beta cell destruction by reactive oxygen species (ROS) which could lead to decreased insulin secretion. Iron can generate ROS and lead to oxidative stress in the body.

Oxidative stress can, in turn, lead to damage to cells, protein, and DNA with long term consequences. This chronic oxidative stress leads to the impairment of mitochondrial -oxidation of long chain fatty acids. This abnormal fat oxidation leads to excessive serum triglyceridemia and excessive accumulation of triglycerides in muscle and liver tissues. This is relevant for India.

An analysis of data on blood biomarkers of chronic disease risk (like glucose and lipids) from the Comprehensive National Nutritional Survey in Indian adolescent children aged between 10-19 years of age, showed that for every 10mcg/L increase in serum ferritin, which reflects the storage state of iron, the risk of having high fasting serum glucose, total cholesterol, triglycerides and hypertension increased proportionately. A scenario analysis of these data showed that if an additional 10mg of iron/day were provided (by fortification), the prevalence of high fasting serum glucose could increase by 2-14% across different socioeconomic groups.

In very high amounts, iron also has a role to play in the hepatic stellate cell (HSC) activation and excessive deposition of extracellular matrix in the liver. This can lead to liver fibrosis, with subsequent progression to cirrhosis. When liver iron concentration (LIC) exceeds a threshold of 60 µmol/g, HSC function starts to deteriorate, and cirrhosis can occur at LIC levels above 250 µmol/g.

Even though iron fortification has been successful in addressing iron deficiency, it is important to consider the dangers of consuming too much iron. Rather than adopting mandatory iron fortification programmes where unsupervised high iron intakes are instituted across a diverse population, it is imperative to develop individualised strategies and ensure thorough monitoring

to detect any adverse events at the earliest. There is no doubt that some segments of the population need the extra dietary iron but not all.

Eventually, precision in public health is essential if we are to avoid the risk of iron overload and the potential for long-term chronic illnesses due to excess iron. As a public health strategy, the pendulum should not swing all the way to the other side.

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