Landmark Malawi trial boosts iron levels in pregnant women

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The World Health Organization (WHO) currently recommends oral iron taken twice daily as the standard of care in developing nations, but adherence to this treatment is poor.

The finding, driven by a collaboration between Australian and Malawian researchers, paves the way for more effective health policies to reduce the global health burden of anemia, which remains one of the most avoidable causes of illness and death in resource-poor nations. The research is published in *The Lancet*.

Iron deficiency is a major public health burden in resource-poor countries and a key precursor to anemia—a condition affecting nearly half of all pregnancies in Africa. It occurs when a person lacks oxygen-carrying red blood cells (hemoglobin) and iron.

While the WHO recommends oral iron tablets taken twice daily for pregnant women in sub-Saharan Africa, less than 30% of the population consumes this recommended dose.

Ferric carboxymaltose (FCM) is a 15-minute iron infusion treatment widely given to iron-deficient pregnant mothers in developed countries.

In efforts to find more effective ways of treating iron-deficient patients, WEHI researchers worked with Malawian scientists at the Training Research Unit of Excellence and Kamuzu University of Health Sciences to compare FCM to standard-of-care oral iron.

Half of the Malawian women (431) in their second trimester received FCM, while the other half took standard-of-care oral iron.

Professor Sant-Rayn Pasricha, a leading anemia expert and Division Head in WEHI's Population Health and Immunity Division, said the trial was four times larger than the one conducted to bring FCM onto the market.

"When we first set out to do this trial, people thought we were trying to achieve the impossible," said Professor Pasricha, who is also a

hematologist.

"We proved that FCM can not only be safely administered in a complex resource-limited setting like Malawi, but can also reduce the iron deficiency component of anemia by around 60%—a significantly better result than the oral iron currently recommended in these populations.

"The results show women who received FCM throughout the trial had a substantial reduction in iron deficiency and iron deficiency anemia during their third trimester, at delivery and 4-weeks post-partum.

"This will open a whole new field of research that was previously thought impossible and could help transform health policies in vulnerable communities.

"I'm tremendously excited that a medicine widely used in high-income nations might have an application to help women in Sub-Saharan Africa and other resource-poor settings. Our next task is to identify those women who have the best chance of benefiting from the IV treatment."

Unique health challenges

Pregnant women with anemia are at elevated risk of complications, including post-partum hemorrhage, stillbirth and low birthweight.

Despite the substantial improvements in iron levels, the trial found FCM was not superior to oral iron in reducing the overall burden of anemia in pregnant women and did not reduce incidences of low birthweight or anemia in women at the time of delivery.

Researchers say this is because anemia can be driven by more than iron-deficiency in developing nations.

"For example, conditions like malaria and HIV, which are common in parts of Sub-Saharan Africa, can drive up inflammation in the body and prevent access to stored iron," Professor Kamija Phiri, a leading epidemiologist and Director of the Training and Research Unit of Excellence, said.

"Additionally, hemoglobinopathies—a group of inherited blood disorders predominantly affecting red blood cells—are common in the region and cause anemia."

Professor Pasricha says the results emphasize the urgent need for new mechanisms to address these unique health challenges.

"Over half of participants had inflammation in their bodies, despite testing negative for malaria," he said.

"With some parasites able to hide in the placenta during pregnancies, it is likely that current tests are not sensitive enough to help us understand a mother's complete health status and flow-on risks to her unborn child.

"While you can do a blood test to detect determinants of anemia, like ferritin, in developed nations, there is no such tool in place for these parts of the world to measure iron status.

"Our study shows there is an urgent need for field-friendly testing capabilities for iron status and causes of anemia, which will provide critical insight into how and where medicines like FCM should be used."

With FCM remaining an expensive treatment option, researchers hope the promising results of the trial can encourage philanthropic efforts to further research the intervention and make it more accessible to women in low-income settings.

The research team is currently tracking the mothers involved in this study and their babies to assess whether the intervention will impact on anemia prevalence, post-partum depression and child neurodevelopment.

More information: Sant-Rayn Pasricha et al, Ferric carboxymaltose versus standard-of-care oral iron to treat second-trimester anaemia in Malawian pregnant women: a randomised controlled trial, *The Lancet* (2023). DOI: 10.1016/S0140-6736(23)00278-7

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