Letter to the Editor

Response to “Efficacy of oral iron therapy in geophagic women with iron deficiency anaemia residing in Botshabelo, South Africa”

The Editor,

We read the recent paper by Mogongoa1 on efficacy of oral iron therapy in geophagic women with interest. The author must be congratulated on a detailed study. In summary, the study divided 84 geophagic women with iron deficiency anaemia into two groups, one which stopped geophagia, and one which continued with geophagia, while receiving oral iron supplements. After ten weeks of gradually escalating doses of oral iron the participants’ average iron status and haemoglobin had not improved significantly. Response to iron therapy was defined as a rise of the haemoglobin concentration by 2 g/dL within three weeks.2 In the group that had stopped geophagia 9.3% (4/43) participants had an increase of 2 g/dL in haemoglobin over the ten weeks, while in the group that continued with geophagia only one participant (2.9% = 1/35) had a similar improvement. The author concluded that “oral iron therapy was not effective in geophagia cases of iron deficiency anaemia” in the abstract and “in this study oral iron therapy was not effective for the correction of iron deficiency anaemia in geophagic Botshabelo females” in the conclusions. We wish to point out that this conclusion might not be entirely correct.

The author attributed the apparent lack of efficacy of oral iron therapy to a number of possible factors which included that geophagic soils reduce iron absorption1 by a number of ways, after ten weeks of gradually escalating doses of oral iron the participants’ average iron status and haemoglobin had not improved significantly. Response to iron therapy was defined as a rise of the haemoglobin concentration by 2 g/dL within three weeks.2 In the group that had stopped geophagia 9.3% (4/43) participants had an increase of 2 g/dL in haemoglobin over the ten weeks, while in the group that continued with geophagia only one participant (2.9% = 1/35) had a similar improvement. The author concluded that “oral iron therapy was not effective in geophagia cases of iron deficiency anaemia” in the abstract and “in this study oral iron therapy was not effective for the correction of iron deficiency anaemia in geophagic Botshabelo females” in the conclusions. We wish to point out that this conclusion might not be entirely correct.

The author attributed the apparent lack of efficacy of oral iron therapy to a number of possible factors which included geophagic soils reduce iron absorption1 by a number of ways, and that daily iron supplementation resulted in increased hepcidin production that inhibits iron absorption.3 The author also mentions that ten weeks of oral iron supplementation might not be sufficient to correct iron deficiency anaemia.

Clearly geophagia is a complex phenomenon. We want to discuss issues that may have influenced the results and their interpretation.

1. The inclusion criteria were stringent. The participants all had to have a haemoglobin of below 10.5 g/dL. This makes their anaemia moderate (8.0–10.9 g/dL) or even severe (below 8.0 g/dL) according to the 2011 WHO criteria.4 The participants had to have a serum ferritin below 15 µg/L.5,6 Therefore the participants had a marked iron deficiency. We suggest that they probably required prolonged oral supplementation to correct the iron deficiency.

2. The specific cause of the iron deficiency in each participant had not been diagnosed. It is critical to diagnose the specific cause of iron deficiency.7 There might have been participants who had ongoing blood loss for other reasons, apart from geophagia. The most common causes of iron deficiency anaemia include insufficient dietary intake, chronic blood loss and malabsorption.9 Common medical conditions known to reduce iron absorption include H. pylori infections, atrophic gastritis, coeliac disease and inflammatory bowel disease. Conditions like heavy menstrual bleeding, helminthic infections, gastrointestinal bleeding, and the use of salicylates and nonsteroidal anti-inflammatory drugs, promote ongoing blood loss.10,11 In order for replacement therapy to be successful, the underlying causes for the iron deficiency need to be identified and treated.

3. Factors in the participants’ diet other than geophagia may have influenced their absorption of the oral iron. Several recognised inhibitors of iron absorption commonly form part of the diet. These include calcium, tannins (in tea and coffee) and phytates (in cereals), as well as frequently used drugs such as proton pump inhibitors.12,13 Oral iron is also best absorbed on an empty stomach, which is why study participants from recent trials involving oral iron therapy1 were instructed to take iron supplementation following periods of fasting. It is not clear at which time of day the study participants took the oral iron supplements, and whether they were told to avoid taking them with food. In the group that continued with geophagia it might be interesting to know at which times of day they consumed the soil. The timing of the taking of the supplements, food and geophagic soil may have influenced the amount of iron absorbed by individual participants.

4. The author’s paper does not provide information whether participants had systemic conditions that might have influenced their iron absorption. It is mentioned that there are other laboratory results that were not discussed in the author’s paper. If any of the participants had chronic inflammatory conditions or chronic infectious diseases their iron absorption might have been reduced by the accompanying increase in hepcidin secretion.14

5. Although the daily dosing regimen followed in this study is supported by previous recommendations,1,15 increasing evidence suggests that a single dose of oral iron on alternate days results in better iron absorption. The author quotes Stoffel et al.4 Stoffel et al.4 confirmed the work of previous authors,13,16 who demonstrated improved iron absorption and lower hepcidin levels with single, alternate day dosing compared to consecutive day and divided dosing. A single dose of iron supplement on alternative days is becoming increasingly the accepted dose because it reduces the adverse effects of oral iron without delaying the response.17

6. The author’s study assessed the response to oral iron replacement by measuring red cell indices (haemoglobin, mean cell volume and mean cell haemoglobin [MCH]), as well as by serum ferritin, serum iron, total iron binding capacity and...
transferrin saturation. The presence of a reticulocyte response is reliable for assessing response early after initiation of oral iron therapy. Another useful parameter for assessing iron absorption is the reticulocyte haemoglobin content (CHr or Re-He depending on the automated analyser used) which increases within days of starting iron replacement therapy, even before the MCH, and serves as a surrogate marker for response of anaemia to iron therapy. Therefore we suggest that the author may also have used these indicators to monitor the response to oral iron supplements.

7. The author used an increase in of 2 g/dL in haemoglobin within three weeks as a criterion for adequate response to iron supplementation, but the source is a textbook which is not peer reviewed. The goals of iron supplementation in iron deficiency anaemia remain the normalisation of the haemoglobin concentration, as well as the replenishment of body stores. The 2011 guidelines state that haemoglobin concentration should rise by 2 g/dL after 3–4 weeks, and if there is lack of response the cause should be investigated. Patients should be followed up for three months to a year. More recent authors suggest that response to treatment should only be evaluated at 4 to 8 weeks, or even at three months. It is only if poor compliance, continued blood loss, malabsorption, a misdiagnosis or multiple diagnoses have been excluded that other treatment options should be considered. Compliance was good in the author’s study. Therefore we suggest that the treatment should have been continued for much longer than ten weeks and probably at least three months.

8. Unfortunately the soil consumed during geophagia in urban areas of South Africa often contains heavy metals, like lead, and toxins. Such substances may contribute to the anaemia and impede response to treatment. It is not clear if such contaminants were excluded in the author’s study, even though the author states that blood was tested for “selected minerals.”

Therefore we conclude that the author’s claims that “oral iron therapy was not effective in geophagia cases of iron deficiency anaemia” and “in this study oral iron therapy was not effective for the correction of iron deficiency anaemia in geophagic Botshabelo females” cannot be confidently deduced from the author’s study design or results. It might be necessary to use radiolabeled isotopes of iron in order to elucidate the interplay of geophagia, iron deficiency and oral iron supplementation, in a similar way in which they have been used to study iron absorption recently.

Conflict of interest
The authors declare no conflict of interest.

Yours sincerely

Marius Coetzee and Anneke van Marle

Department of Haematology and Cell Biology, University of the Free State, South Africa

References