Obesity-related inflammation, hepcidin and iron absorption

Project 411

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Background Many transition countries are struggling with the double burden of malnutrition. Iron deficiency is more prevalent in overweight and obese (OW/OB) subjects compared to their normal weight counterparts. This association is likely a result of adiposity-related inflammation which increases hepcidin and decreases iron absorption. Whether weight loss can normalize this condition sufficiently to increase iron absorption is unclear. The aim of this study was therefore to investigate, in obese subjects, whether weight loss as a result of restrictive bariatric surgery, can improve the inflammatory state and hepcidin concentrations sufficiently to normalize iron absorption.

Subjects and methods Fourty three obese subjects (baseline BMI>35kg/m2) were recruited before undergoing restrictive bariatric surgery (gastric banding or sleeve gastrectomy). The baseline measurements for the study were carried out 6 weeks after surgery was completed and the endpoint measurements another 6 months later. At those time points, fractional iron absorption was determined by measuring the incorporation of stable iron isotopes (57Fe and 58Fe) into erythrocytes 14 days after oral and intravenous administration. Also on both time points blood samples were collected for the determination of iron status (serum ferritin, transferrin receptor), inflammatory markers (CRP, IL6, leptin) as well as hepcidin. Weight, height as well as body composition (using DXA) was further determined in all subjects at both time points.

Results and Discussion Of the 43 subjects originally recruited 38 have completed the study. During the six months between baseline and endpoint assessments a substantial weight loss of 18% in average was achieved and body fat was reduced by 20%. At the same time, the inflammatory markers CRP, IL6 and leptin were significantly reduced ($p<0.005$) and with this hepcidin concentrations decreased by 33% ($p=0.001$). Despite those changes, no improvement in iron absorption could be detected (7.34% at baseline and 8.03% at endpoint; $p=0.341$).

Transferrin receptor decreased significantly from baseline to endpoint ($p=0.003$), indicating an improvement in iron status. At the same time, serum ferritin concentrations also decreased significantly ($p<0.001$) which, under normal circumstances, would indicate a deterioration of iron status. However, as serum ferritin is an acute phase protein which increases in parallel with inflammation, this decrease can be attributed to the reduction in inflammation over the intervention and therefore has to be considered as an artefact concerning iron status.

Iron status is one of the main regulators of iron absorption with an improvement resulting in reduced absorption. Thus, the improvement in iron status may potentially have counteracted an effect due to the reduction in inflammation. However, as the improvement was within the normal range of iron status and not from deficient to normal, we would not expect this to greatly influence iron absorption in this case.

Conclusion In conclusion, the results of this study indicate that despite a significant reduction in BMI and %body fat as well as a significant decrease in inflammation, the effect was not sufficient to affect iron absorption. This demonstrates that sub-clinical inflammation as seen in overweight already affects iron absorption at a relatively low level without further impact at higher concentrations and thus, only a complete elimination of inflammation would be effective in bringing iron absorption back to normal.