Evaluation of the validity of a novel isotope dilution method to assess the iron status and its changes in Swiss women

Project: 510

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Background: Estimates of dietary iron requirements by the World Health Organization (WHO) and the US Institute of Medicine (IoM) are derived by factorial modeling of iron excretion data from men. Direct quantification of long-term iron absorption and iron loss i has not regularly been performed in women and data about are scarce.

Objective: We assessed long-term iron absorption and iron loss in healthy Swiss women during different iron interventions versus a control period where each subject acted as her own control.

Design: We recruited 55 women of reproductive age who have participated in a former stable isotope study at the Laboratory of Human Nutrition of ETH Zürich. It can be assumed that one year post administration the isotopic label of the subject has equilibrated with total body iron. After uniform labelling, absorption of iron is proportional to the rate of decrease in the isotopic tracer concentration in circulation, while loss of iron is proportional to the rate of decrease of the isotopic tracer amount. We followed subjects for a pre-intervention period of 3 months, a 3-months intervention period and a 3-monhts post-intervention period. During intervention period, iron-deplete women (n=27) I) received an iron intervention supplementing 50 mg iron as FeSO4 daily for 3 months, or II) an intravenous Ferinject® injection providing an amount of iron calculated according to the Ganzoni formula, and iron-replete women (n=28) consumed iron fortified almond biscuits providing 16 mg iron as ferrous sulphate daily. Pre- and post-intervention periods served as control periods. Venous blood samples were collected at beginning, mid-point and end of both control periods and monthly during the intervention period and the isotopic composition of all blood samples was analyzed to determine the dilution of the isotopic label. Data on dietary iron intake, menstrual blood losses and physical activity was collected through questionnaires during each period.

Results: Forty-eight subjects completed the study. Median [IQR] daily iron absorption was similar to WHO estimates for iron requirements (1.46 mg/d) during pre-intervention control period. During intervention it 2.3-fold to 3.66 [3.11;4.44] mg/d in the oral iron supplemented study arm and 1.7-fold to 1.97 [1.50;2.54] mg/d in the study arm receiving iron fortified biscuits. No quantification of iron absorption and iron loss was feasible in the study arm receiving intravenous iron. Surprisingly, iron losses substantially increased with consumption of oral iron supplements (from 0.94 [0.11;1.48] mg/d to 2.38 [1.18;3.29] mg/d), while iron losses remained rather constant in the study arm consuming iron fortified biscuits (1.15 [-0.70;2.29] mg/d and 1.56 [1.14;2.38] mg/d, respectively). Furthermore, after iron intervention,

iron absorption decreased to 0.94 [0.63;1.37] mg/d and 1.11 [0.73;1.40] mg/d in the iron supplementation and iron fortification study arms, respectively, maintaining subjects in negative net iron balance. No significant correlation could be detected between iron dilution rates in the body and dietary (iron intake) and lifestyle (menstrual blood losses, physical activity) factors.

Conclusions: Our study raises the question of substantial increases in iron losses during oral iron supplementation. This should prompt the investigation of the pathophysiologic mechanisms responsible, and, potentially, development of new iron formulations. In general, long-term studies measuring dilution of equilibrated stable iron isotopes may provide a reference method for evaluating programs of iron fortification and supplementation