Iron Deficiency in Young Women: Causes, Consequences and Solutions

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Abstract

Background

Iron deficiency is the most common nutritional deficiency worldwide and premenopausal women are at particular risk. Iron deficiency without anaemia is associated with a number of health consequences, including impaired work performance and possible impairments to self-perceived health and well-being, and increased fatigue. Research into iron deficiency and possible causes, consequences and solutions could help to improve the quality of life for many premenopausal women.

Objectives

This research aimed to investigate the causes, some of the consequences and a possible solution to iron deficiency in premenopausal women. Objectives were to determine the relative validity and reproducibility of an iron food frequency questionnaire (FeFFQ) developed to identify iron-related dietary patterns; to identify the most important determinants of suboptimal iron status and investigate the relative importance of dietary patterns among these determinants; to determine the relationship between iron status and self-perceived health, well-being and fatigue; and to investigate the effectiveness of a dietary intervention using an iron-fortified breakfast cereal and milk consumed with either high or low ascorbic acid, lutein and zeaxanthin-rich fruit to improve iron status in women with low iron stores.

Method

In a validation study, premenopausal women (n=115) completed the FeFFQ twice, one month apart to assess reproducibility and a four-day weighed diet record (4DDR) to assess validity. Dietary patterns from both FeFFQs and the 4DDR were identified using factor analysis and agreement between diet pattern scores were compared using correlation coefficients, Bland and Altman analysis, cross-classification and the weighted κ- statistic. In a cross-sectional study, 375 premenopausal women completed the FeFFQ (from which dietary patterns were identified) and a dietary practices questionnaire. They also completed a health and demographic questionnaire including questions regarding possible determinants of iron status, as well as a validated blood loss questionnaire. In a second cross-sectional study, 233 female university students completed the SF-36v2 General Health Survey and Multidimensional Fatigue Symptom Inventory-Short Form (MFSI-SF) questionnaire to investigate self-perceived health, well-being and fatigue. In both cross-sectional studies, a blood sample was taken to determine iron status (serum ferritin (SF), haemoglobin (Hb), C-reactive protein (CRP)). In a randomised controlled trial (RCT), 69 women with low iron stores (SF≤25μg/L, Hb≥115g/L) received an iron-fortified breakfast cereal (16 mg iron as ferrous sulphate) meal and either kiwifruit (intervention) or banana (control) every day for 16 weeks. Iron status (SF, Hb, CRP, and soluble transferrin receptor) was assessed at baseline and end.

Results

Two dietary patterns ('healthy'; 'sandwich & drinks') were identified from the FeFFQs and 4DDR. Correlation coefficients between the FeFFQ and 4DDR diet pattern scores (validity) were 0.34 ('healthy'), and 0.62 ('sandwich & drinks'), both $P<0.001$. Correlation coefficients between the two FeFFQs (reproducibility) were 0.76 for both dietary patterns ($P<0.001$). Determinants of suboptimal iron status (SF<20μg/L) included blood donation in the past year (odds ratio (OR) 6.7, [95% confidence interval (CI) 3.1, 14.7]; $P<0.001$), being Asian (5.2 [2.4, 11.2]; $P<0.001$), having children (2.7 [1.4, 5.3]; $P=0.003$), previous iron deficiency (2.1 [1.1, 3.9]; $P=0.027$), longer duration of menstrual period (1.3 [1.1, 1.6]; $P=0.01$), and following either a 'milk & yoghurt' (1.4 [1.1, 1.9]; $P=0.014$), or a 'meat & vegetable' (0.6 [0.4, 0.8]; $P=0.002$) dietary pattern. Current iron status was not a determinant of self-perceived health, well-being or fatigue after controlling for other variables. In the RCT, iron status improved significantly ($P<0.001$) in the kiwifruit group (SF from baseline to end (median [25^{th}, 75^{th} percentile]) (17.0 [10.5, 22.0]μg/L to 25.0 [20.0, 32.0]μg/L; $P<0.001$)) compared to the banana group (16.5 [10.0, 20.8]μg/L to 17.5 [12.3, 22.8)]μg/L; $P=0.086$).

Conclusions

The FeFFQ was found to be a reproducible and reasonably valid tool for identifying iron-related dietary patterns. Following a 'meat & vegetable' dietary pattern reduced the risk, while following a 'milk & yoghurt' dietary pattern increased the risk of suboptimal iron status. The strongest predictors of suboptimal iron status were blood donation and Asian ethnicity, followed by parity and previous iron deficiency. Both dietary patterns were stronger predictors of suboptimal iron status than duration of menstrual period. Iron status had no effect on self-perceived health, well-being or fatigue. Consumption of an iron-fortified breakfast cereal with kiwifruit compared to banana improved iron status in women with low iron stores. Modification of dietary patterns and blood donation practices, as well

as the consumption of an iron-fortified breakfast cereal with an ascorbic acid, lutein, zeaxanthin-rich fruit may contribute to improved iron status in women with low iron stores.

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Approval has been obtained from the Massey University Human Ethics Committee (Southern A) for all research described in the thesis.

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Abbreviations

aa	Ascorbic acid
AGP	α_1-acid glycoprotein
B	Baseline
BFI	Brief Fatigue Inventory
BLU	Blood Loss Unit
BMI	Body Mass Index
CI	Confidence Interval
CRP	C reactive protein
DcytB	Duodenal cytochrome B reductase
4DDR	4-Day Diet Record
df	Degrees of freedom
DHQ	Diet History Questionnaire
DMT1	Divalent Metal Transporter 1
DP	Dietary Pattern
DR	Diet Record
DRI	Dietary Reference Intake
E	End
EDTA	Ethylene Diamine Tetraacetic Acid
FAO	Food and Agriculture Organization of the United Nations
FeFFQ	Iron Food Frequency Questionnaire
FFQ	Food Frequency Questionnaire
Fe^{2+}	Ferrous iron
Fe^{3+}	Ferric iron
FR	Food Record
FSS	Fatigue Severity Scale
GHQ	General Health Questionnaire
Hb	Haemoglobin
HCP1	Haem Carrier Protein 1
HNRU	Human Nutrition Research Unit
IBC	Iron Binding Capacity
ID	Iron Deficiency

IDA	Iron Deficiency Anaemia
IFNHH	Institute of Food Nutrition and Human Health
IUD	Intra-Uterine Device
KMO	Kaiser-Meyer-Olkin
LOA	Limits Of Agreement
MBL	Menstrual Blood Loss
MCS	Mental Component Summary
MFSI-SF	Multidimensional Fatigue Symptom Inventory – Short Form
MFP	Meat/fish/poultry
n	number
n/a	not applicable
NaFeEDTA	Sodium iron ethylenediaminetetraacetate
nd	Not detectable
NHANES	National Health and Examination Nutrition Survey
NS	Non Significant
NZ	New Zealand
OCP	Oral Contraceptive Pill
OR	Odds Ratio
PASW	Predictive Analytics SoftWare
PCDB	Placebo Controlled Double Blind
PCS	Physical Component Summary
PFS	Piper Fatigue Scale
POMS	Profile of Mood States
Psa-V	*Psuedomona's Syringae* pv. *Actinidiae*
RBC	Red Blood Cell
RCT	Randomised Controlled Trial
RDA	Recommended Dietary Allowance
RDI	Recommended Dietary Intake
RNI	Recommended Nutrient Intake
RPC	Randomised Placebo Controlled
RPCDB	Randomised Placebo Controlled Double Blind
SD	Standard Deviation
SF	Serum Ferritin

SF-36	SF-36v2 Health Survey
SLS-Hb	Sodium lauryl sulphate-Hb
SNP	Single Nucleotide Polymorphism
SPI	Short Performance Inventory
SPSS	Statistical Package for the Social Sciences
SST	Serum Separator Tube
sTfR	Soluble Transferrin Receptor
t	t-statistic
TfR	Transferrin Receptor
TIBC	Total Iron Binding Capacity
TS	Transferrin Saturation
UK	United Kingdom
USA or US	United States of America
VAS	Visual Analogue Scale
VT	Vitality
WHO	World Health Organization
WISE	Women's Iron Status and Education
y	years