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ORIGINAL ARTICLE

Post-prandial iron absorption in humans: Comparison between HFE genotypes and iron deficiency anaemia

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Summary
Background & aims: Measurement of serum iron increase after ingestion of a meal could be an efficient method of comparing post-prandial iron absorption between groups of individuals. We determined whether the rise in post-prandial serum iron is increased in fully treated patients with hereditary haemochromatosis (HFE C282Y+/+; HH) compared to iron deficiency anaemia (IDA), iron-replete heterozygous subjects (HFE C282Y+/−) and iron-replete controls (HFE C282Y−/−).
Methods: Serum iron increase was measured over 4 h after a meal containing 13.1 mg non-haem iron.
Results: Post-prandial increase in serum iron was similar in treated HH versus IDA ($P = 0.54$), but greater than control subjects ($P < 0.0001$). In five HH patients, using ^{58}Fe as a tracer, the rate of iron absorption was increased ($P < 0.05$) and serum non-transferrin bound iron showed a tendency to increase ($P = 0.06$). Serum iron curves did not differ for heterozygous subjects and controls ($P = 0.65$).
Conclusions: Using the serum iron method we found a comparable increase in post-prandial iron absorption in treated HH and IDA compared with controls. While post-prandial iron

Abbreviations: HH, hereditary haemochromatosis; IDA, iron deficiency anaemia; NTBI, non-transferrin bound iron; KCL, King's College London; PPI, proton pump inhibitor; EDTA, ethylene diamine tetraacetic acid; NTA, nitrilotriacetic acid; IREG1, iron regulated gene-1; DMT1, divalent metal transporter-1; Dcyt*b*, duodenal cytochrome-*b*; $FeSO_4$, ferrous sulphate.

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absorption in the group heterozygous for the C282Y mutation was modestly increased relative to controls, this difference was not statistically significant.

Introduction

The utilisation of iron for the synthesis of haemoglobin, 14 days after the administration of an iron dose, has been used extensively to investigate factors affecting dietary iron bioavailability and disorders of iron absorption.[1–3] This method is technically demanding and the commonly applied assumption that 80% of iron entering the portal vein is utilised for the synthesis of haemoglobin is questionable in certain conditions, such as in hereditary haemochromatosis (HH), where the rate of iron utilisation for haematopoiesis may be reduced.[4]

Measurement of serum iron concentrations immediately before and 1 h following ingestion of an iron dose offers a reliable and easy means of evaluating iron absorption in patients in a clinical setting.[5] Serum iron increase following ingestion of a meal containing 13.1—100 mg iron also provides a good estimate of dietary iron bioavailability in healthy iron-replete subjects and individuals with iron deficiency anaemia (IDA).[6,7] This method could be a rapid and low-cost means of comparing dietary iron absorption between different groups of individuals, including patients with HH. In addition, assessing the changes in serum iron increase after ingestion of an iron-rich meal could improve our understanding of the kinetics of iron transport across the duodenal enterocyte and the origin of circulating non-transferrin bound iron (NTBI) in HH.

Here we used the serum iron method to compare post-prandial iron absorption between four groups, namely: patients with HH (HFE C282Y+/+), subjects with IDA, iron-replete heterozygous carriers of the C282Y mutation of the *HFE* gene (HFE C282Y+/−) and iron-replete controls (HFE C282Y−/−). The main aims of this study were to determine whether the rise in post-prandial serum iron is increased, firstly, in fully treated patients with HH to the same extent as in IDA and, secondly, in iron-replete heterozygous subjects (HFE C282Y+/−) when compared with iron-replete controls. We also aimed to determine whether the rate of iron absorption is greater in HH compared with controls, and if post-prandial appearance of NTBI is increased in HH as is the case in IDA subjects.[8]

Materials and methods

Subjects

Heterozygous subjects, controls and women with IDA were recruited from King's College London (KCL). HH patients were outpatients of the Institute of Liver Studies, King's College Hospital. These studies were approved by KCL Research Ethics Committee and the Local Research Ethics Committee, King's College Hospital.

A screening questionnaire was used to ascertain personal information such as details of medications, allergies, general and recent health, including acute infection or inflammation. Blood was drawn for measurement of serum ferritin, transferrin saturation, full blood count and for the determination of the C282Y and H63D mutations of the *HFE* gene. Study participants included: 14 healthy white males (HFE C282Y−/−), 12 male HH patients (HFE C282Y+/+), seven healthy HFE C282Y heterozygous subjects (HFE C282Y+/−; four females, three males), and 10 women with IDA but who were otherwise healthy (Table 1). None of the volunteers were a blood donor. HH patients were fully treated and received maintenance venesection treatment to maintain their iron stores within normal limits as shown by a serum ferritin of ~50 μg/l. At least 2 months had elapsed between the last venesection treatment and the time of the iron absorption test. The iron burden at diagnosis was calculated by assuming that 600 ml whole blood contains ~0.25 g iron and noting the volume of blood removed by the initial course of phlebotomy leading to a reduction in serum ferritin to ~50 μg/l and a transient fall in haemoglobin to be between 12 and 13 g/dl. On an average the iron burden was 14.6 ± 1.9 g. Transferrin saturation was determined in controls and HH patients at baseline as previously described.[9]

Subjects with known gastrointestinal disease or other serious illnesses, and those who were taking prescription

Table 1 Subject characteristics

Group	*n*	Sex	Age (years)	Haemoglobin (g/l)	Serum ferritin (μg/l)
Controls (HFE C282Y−/−)	14	M	45.6 ± 3.1^{a}	150 ± 3.0^{a}	115 ± 15^{a}
HH patients (HFE C282Y+/+)	12	M	57.4 ± 3.4^{b}	$133 \pm 4.6^{b,c}$	94.3 ± 16^{a}
Heterozygotes (HFE C282Y+/−)	7	3 M, 4 F	30.1 ± 2.2^{c}	$144 \pm 6.6^{a,c}$	64 ± 22.2^{a}
IDA	10	F	21.1 ± 0.7^{c}	118.7 ± 0.7^{b}	9.9 ± 1.7^{a}

Mean (±S.E.) age, haemoglobin and serum ferritin concentrations in four study groups.
HH, hereditary haemochromatosis; IDA, Iron deficiency anaemia; M, Male; and F, Female.
Values within each parameter are statistically significant at the level of $P < 0.05$ where superscript letters are different.