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ORIGINAL ARTICLE

Oral ferrous fumarate or intravenous iron sucrose for patients with inflammatory bowel disease

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Abstract

Objective. Iron therapy may reinforce intestinal inflammation by catalysing production of reactive oxygen species. The effects of oral ferrous fumarate and intravenous iron sucrose on clinical disease activity and plasma redox status were investigated in patients with inflammatory bowel disease (IBD). ***Material and methods***. Nineteen patients with iron deficiency anaemia and Crohn's disease (11) or ulcerative colitis (8) were included in a crossover study. The patients were randomly assigned to start treatment with ferrous fumarate (Neo-fer®) 120 mg orally once daily or iron sucrose (Venofer®) 200 mg intravenously 3 times during a period of 14 days. Clinical disease activity assessment and blood and faecal analysis were performed on days 1 and 15. ***Results***. Following oral ferrous fumarate clinical disease activity ($p = 0.037$), general well-being score (i.e. patients felt worse) ($p = 0.027$) and abdominal pain score ($p = 0.027$) increased, while no changes were seen following iron sucrose treatment. C-reactive protein (CRP) and faecal calprotectin were unchanged after both treatments. As compared with iron sucrose, ferrous fumarate increased Crohn's disease activity index (CDAI) scores of general well-being ($p = 0.049$), whereas alterations in clinical disease activity ($p = 0.14$) and abdominal pain score ($p = 0.20$) did not differ. Ferrous fumarate did not significantly alter plasma malondialdehyde (MDA) or plasma antioxidants. Iron sucrose increased plasma MDA ($p = 0.004$) and decreased plasma vitamin C ($p = 0.017$) and betacarotene ($p = 0.008$). ***Conclusions***. Oral ferrous fumarate, but not intravenous iron sucrose, increased clinical disease activity in IBD patients. Intravenous iron sucrose increased intravascular oxidative stress.

Key Words: *Anaemia, antioxidants, ferric compounds, ferrous compounds, inflammatory bowel diseases, iron, iron deficiency, malondialdehyde*

Introduction

Iron is an essential element that is involved in many biological functions, such as energy metabolism, DNA synthesis, oxygen transport and storage, growth and immune defence. However, free iron may be harmful because it is a powerful catalytic agent in the generation of highly reactive oxygen species (ROS).

One-third of patients with inflammatory bowel disease (IBD) suffer from recurrent anaemia [1,2]. Iron deficiency and anaemia of chronic diseases are the most common causes of anaemia in IBD [3]. Available compounds for oral iron supplementation, generally ferrous salts, are associated with frequent gastrointestinal side effects, leading to poor compliance. Most of the ingested ferrous iron is not absorbed but passed on to the ileum and colon, sites of inflammation in Crohn's disease and ulcerative colitis. There it can react with superoxide ($O_2^{\bullet -}$) and hydrogen peroxide (H_2O_2) from activated neutrophils in the inflamed mucosa, leading to production of the hydroxyl radical ($OH^{\bullet}$). Hydroxyl radicals are extremely reactive and can attack any cell component and cause oxidative damage and lead to the production of other ROS [4]. The pro-oxidative imbalance created by this overproduction of ROS may enhance intestinal injury, as demonstrated in animal models of IBD [5–8].

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Parenteral iron formulations are ferric hydroxide carbohydrate complexes, similar to ferritin in chemical form and structure [9]. These formulations contain iron in a non-ionic form, making it less toxic [9]. In addition, the parenteral route of administration does not favour to intestinal iron accumulation. Intravenous administration of iron hydroxide sucrose complex (iron sucrose) has a good safety profile and response rate in IBD-associated iron deficiency anaemia [10–13]. However, there are no previous data on the pro-oxidant potential of iron sucrose in IBD.

By monitoring increases in lipid peroxidation and loss of antioxidants in body fluids, one may gain evidence of ongoing oxidative stress. Malondialdehyde (MDA) is an end-product of non-enzymatic, oxidative degeneration of polyunsaturated fatty acids. Plasma MDA is a frequently used index for assessing lipid peroxidation *in vivo*.

The aim of this study was to evaluate the effects of oral ferrous fumarate and intravenous iron sucrose on clinical disease activity and plasma redox status, and to compare the two treatment modalities.

Material and methods

Patients

Nineteen patients with Crohn's disease (CD) or ulcerative colitis (UC) and iron deficiency anaemia were recruited from our outpatient clinics and included in a crossover study. Inclusion criteria were iron deficiency anaemia, defined by B-haemoglobin <12 g/dl in females and <13 g/dl in males and S-ferritin <50 µg/l. A negative serum pregnancy test at screening and a medically acceptable form of contraception throughout the study were required for all females of childbearing potential. Exclusion criteria were iron therapy or blood transfusions during the 6 weeks before inclusion, indications of haemolysis, deficiency of cobalamin or folic acid, renal disease, cancer, infliximab therapy and recent start of azathioprine therapy. Written informed consent was obtained from each patient and the Regional Committee for Medical Research Ethics approved the study protocol.

Study design

In this randomized, non-blinded, crossover trial each treatment period lasted 14 days, separated by a washout period of at least 6 weeks (range 6 weeks–16 months). Iron deficiency had to be reconfirmed before the start of the second treatment period.

Medications

Ferrous fumarate (Neo-fer®, Nycomed Pharma, Norway or Erco-fer®, Orion Pharma, Finland), corresponding to 120 mg Fe^{2+}, was given orally once daily for 14 days (days 1 to 14). During the course of the study, registration of Neo-fer tablets was withdrawn from the market for economic reasons, hence 6 patients were given the synonymous drug Erco-fer.

Iron sucrose (Venofer®, Vifor International Inc., Switzerland), corresponding to 200 mg Fe^{3+}, diluted in 250 ml of 0.9% sodium chloride solution was given intravenously 3 times during 14 days (days 1, 5 and 10).

Clinical disease activity

Disease activity was recorded before (day 1) and after (day 15) iron therapy. Clinical disease activity was assessed with the Harvey-Bradshaw Simple Index of Crohn's Disease Activity [14] for patients with CD. The Harvey-Bradshaw Simple Index is based on five items: general well-being, abdominal pain, stool frequency, abdominal mass and extra-intestinal complications. Maximum score is 25 and scores of ≥ 5 indicate active CD. For patients with ulcerative colitis, the Simple Clinical Colitis Activity Index [15] was recorded. The Simple Clinical Colitis Activity Index is based on six items: general well-being, stool frequency day and night, urgency of defecation, blood in stool and extraintestinal complications. Maximum score is 20 and scores of ≥ 4 indicate active ulcerative colitis.

The Harvey-Bradshaw Simple Index and the Simple Clinical Colitis Activity Index are similar regarding design and clinical significance of a given change in score. To allow pooling of results from patients with CD and UC, disease activity scores were calculated as actual score divided by maximum score.

All patients completed the Crohn's Disease Activity Index (CDAI) diary card [16] the week before the start of iron therapy and during the second week of iron therapy. The CDAI diary card implies daily recording of general well-being, abdominal pain and number of liquid or very soft stools. Because patients often misunderstood the last item, the total number of stools was also recorded. The sum of daily registrations yields a score for each symptom. The higher the score, the more the patient is troubled.

Laboratory investigations

Blood samples were collected after an overnight fast on day 1 and day 15.

Routine laboratory investigations included B-haemoglobin, B-reticulocyte count, E-mean corpuscular

volume, B-erythrocyte count, B-leucocyte count, B-platelet count, S-ferritin, S-iron, S-total iron binding capacity, S-transferrin receptor, S-C-reactive protein (S-CRP), B-erythrocyte sedimentation rate (B-ESR), S-protein and S-albumin.

Plasma MDA [17], plasma aminothiols [18], plasma vitamins A, E and C [19] and plasma beta-carotene [20] were measured by high-performance liquid chromatography (HPLC) as described elsewhere.

Stool samples were collected the day before the start of iron therapy and on day 14, and stored at −20°C until analysis of faecal calprotectin by PhiCal Test (Eurospital S.p.A., Trieste, Italy). Briefly, approximately 0.1 g of thawed faeces was mixed with 5 ml extraction buffer in a closed tube for 30 min on a shaker. After centrifugation, a sample from the supernatant was tested with an enzyme immunoassay specific for calprotectin. Results are expressed as mg calprotectin/kg faeces. Values above 50 mg/kg are regarded as a positive PhiCal test [21].

Statistical analysis

Differences between means were evaluated with Student's *t*-test for paired comparisons, and the mean of differences and 95% confidence interval (CI) are given. Scores were analysed using the Wilcoxon matched-pairs test, and median and range are given; *P*-values less then 0.05 were considered statistically significant. Data were analysed using the GraphPad Prism 4 for Windows (GraphPad Software Inc., San Diego, Calif., USA) statistical software package.

Results

Nineteen patients (Table I) were randomly assigned to start treatment with oral ferrous fumarate (5 CD, 4 UC) or intravenous iron sucrose (6 CD, 4 UC). Two patients, one male with CD and one female with UC, stopped treatment with ferrous fumarate after 6 days because of side effects. Data from these two patients are not included in the analysis. Hence, all data and analyses presented are based on the 17 patients who finished the study.

At inclusion none of the parameters differed significantly between patients starting with ferrous fumarate and patients starting with iron sucrose (data not shown).

Clinical disease activity and adverse events

Clinical disease activity scores are presented in Table II. Treatment with ferrous fumarate increased clinical disease activity ($p = 0.037$) (Figure 1). The CDAI diary general well-being score increased (i.e. patients felt worse) from 3.5 (0–13) to 5 (0–16) ($p = 0.027$) and abdominal pain score increased from 4 (0–12) to 6.5 (0–14) ($p = 0.027$). The total number of stools did not alter. Intravenous iron sucrose had no influence on clinical disease activity ($p = 0.92$) (Figure 1), CDAI diary general well-being scores, abdominal pain score or total number of stools.

Table I. Patient characteristics. Range for age, number of patients for all others.

	Crohn's disease	Ulcerative colitis
Female	7	6
Male	4	2
Age (years)	18–46	18–45
Disease location		
Terminal ileum	3	
Colon	5	
Ileocolon	2	
Proximal GI	1	
Total colitis		3
Subtotal colitis		2
Distal colitis		3
Medication		
5-ASA	6	7
Sulphasalazine	2	
Steroids	5	3
Azathioprine	4	1

Abbreviation: GI = gastrointestinal.

As compared with iron sucrose, ferrous fumarate increased the CDAI scores of general well-being ($p = 0.049$), while alterations in clinical disease activity ($p = 0.14$) and abdominal pain score ($p = 0.20$) did not differ significantly.

Two patients stopped treatment with ferrous fumarate after 6 days because of side effects. They both reported an intolerable increase in abdominal pain and diarrhoea, which abated after withdrawal of treatment. All patients completed the treatment with iron sucrose. One female with CD had a temperature above 39°C the night after the first infusion, but subsequent infusions were uneventful. Five patients reported feeling tired the same day and the day after iron infusion.

Routine laboratory investigations

Routine laboratory investigations are summarized in Table III. Both ferrous fumarate and iron sucrose had significant effects on biochemical markers of iron metabolism and erythropoiesis. However, changes were more pronounced after iron sucrose, and B-haemoglobin was significantly increased only by iron sucrose. Ferrous fumarate increased B-reticulocyte count by 0.021 10^{12}/l (CI 0.005 to 0.036; $p = 0.014$), E-mean corpuscular volume by

Table II. Clinical disease activity and faecal calprotectin. Median (range).

Parameters	Before Ferrous fumarate	After Ferrous fumarate	Before Iron sucrose	After Iron sucrose
Harvey-Bradshaw Simple Index in Crohn's disease patients	3.5 (1–7)	5 (2–6)	4 (2–5)	4 (1–5)
Simple Clinical Colitis Activity Index in ulcerative colitis patients	1 (0–3)	1.5 (0–4)	1 (0–4)	1 (0–3)
Calprotectin (normal <50 g/kg)	86 (9–414)	87 (8–507)	98 (9–603)	100 (10–790)

1.6 fl (CI 0.7 to 2.5; $p=0.002$) and S-ferritin by 13 μg/l (CI 7 to 19; $p=0.0006$), and decreased S-transferrin receptor by −0.18 mg/l (CI −0.28 to −0.08; $p=0.002$) and S-total iron binding capacity by −5 μmol/l (CI −8 to −2; $p=0.003$). Iron sucrose increased B-haemoglobin by 0.7 g/dl (CI 0.2 to 1.2; $p=0.007$) and B-reticulocyte count by 0.050 10^{12}/l (CI 0.033 to 0.068; $p<0.0001$), E-mean corpuscular volume by 2.3 fl (CI 1.6 to 3.0; $p<0.0001$), S-ferritin by 110 μg/l (CI 85 to 134; $p<0.0001$) and S-iron by 4.5 μmol/l (CI 1.7 to 7.3; $p=0.004$), and decreased S-transferrin receptor by −0.30 mg/l (CI −0.53 to −0.07; $p=0.015$) and S-total iron binding capacity by −11 μmol/l (CI −13 to −8; $p<0.0001$). Three patients had an increase in B-haemoglobin of ≥2.0 g/dl after treatment with iron sucrose.

In Table III, it can be seen that levels of B-haemoglobin, S-ferritin, S-transferrin receptor and S-iron differ at the start of the two treatments. The differences are due to the more pronounced effect of iron treatment in the group of patients starting with iron sucrose as compared with those starting with ferrous fumarate. At inclusion, none of these parameters differed significantly between patients starting with ferrous fumarate and patients starting with iron sucrose.

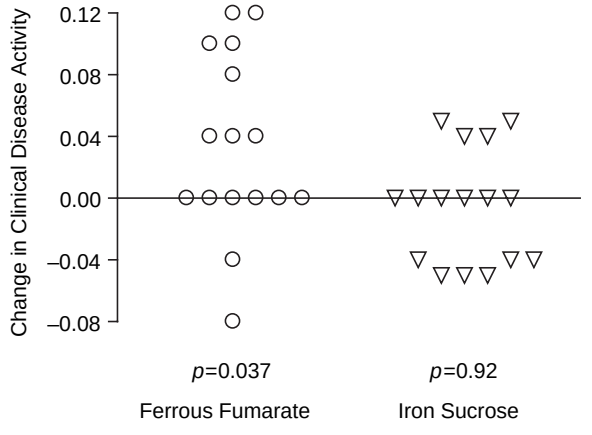

Figure 1. Change (=posttreatment score−pretreatment score) in clinical disease activity index scores shown for individual patients. *P*-values indicate the probability that change=zero for each treatment. The Harvey-Bradshaw Simple Index was used for patients with Crohn's disease and the Simple Clinical Colitis Activity Index for patients with ulcerative colitis. Disease activity is expressed as actual score divided by maximum score (25 for the Harvey-Bradshaw Simple Index and 20 for the Simple Clinical Colitis Activity Index).

MDA, vitamins and aminothiols

Ferrous fumarate insignificantly increased plasma MDA by 49 nmol/l (CI −40 to 138; $p=0.26$) (Figure 2) and decreased plasma vitamin C by −3.9 μmol/l (CI −9.9 to 2.0; $p=0.18$) and plasma betacarotene by −0.15 μmol/l (CI −0.32 to 0.02; $p=0.08$). Treatment with iron sucrose significantly increased plasma MDA by 92 nmol/l (CI 34 to 148; $p=0.004$) (Figure 2) and decreased plasma vitamin C by −7.8 μmol/l (CI −14.0 to −1.6; $p=0.017$), plasma betacarotene by −0.12 μmol/l (CI −0.20 to −0.04; $p=0.008$). Plasma vitamins A and E, and plasma glutathione, plasma cystein and cysteinyl-glycine were unchanged after both treatments (Table IV). Alterations in plasma MDA (Figure 2), plasma vitamin C, plasma betacarotene (data not shown) did not differ significantly between treatments. None of the plasma parameters was significantly correlated to disease activity indices, calprotectin or CRP (data not shown).

Faecal calprotectin

Data are presented in Table II. No significant change in calprotectin was observed after treatment with ferrous fumarate ($p=0.14$) or iron sucrose ($p=0.14$).

CD patients with elevated S-CRP

During ferrous fumarate treatment, three of four CD patients with elevated S-CRP had a further increase in S-CRP, and plasma antioxidant defence was weakened in all four (data for individual patients not shown). No such changes in S-CRP were seen following iron sucrose treatment.

Discussion

After 2 weeks of oral ferrous iron therapy there was an increase in clinical disease activity in patients with IBD. The patients experienced deterioration in general well-being and abdominal pain. Intravenous

Table III. Routine laboratory investigations. Median (range) for CRP, mean (SEM) for all others.

Parameters	Before Ferrous fumarate	After Ferrous fumarate	Before Iron sucrose	After Iron sucrose	Normal values
S-CRP (mg/l) median (range)	<10 (<10–96)	<10 (<10–141)	<10 (<10–84)	<10 (<10–73)	<10
B-ESR (mm/h)	23 (4)	22 (4)	25 (4)	21 (4)*	Female <20 Male <15
B-haemoglobin (g/dl)	11.6 (0.4)	11.8 (0.3)	10.6 (0.3)	11.3 (0.2)*	Female 11.6–16.0 Male 13.2–16.6
B-reticulocyte count (10^{12}/l)	0.044 (0.003)	0.064 (0.007)*	0.045 (0.004)	0.095 (0.009)*	0.030–0.100
E-mean corpuscular volume (fl)	82 (3)	84 (2)*	80 (3)	82 (3)*	80–102
B-erythrocyte count (10^{12}/l)	4.5 (0.2)	4.5 (0.2)	4.3 (0.2)	4.4 (0.1)	Female 3.7–5.5 Male 4.0–5.8
B-leucocyte count (10^9/l)	5.9 (0.5)	5.9 (0.5)	5.8 (0.4)	5.8 (0.4)	3.5–11.0
B-platelet count (10^9/l)	371 (30)	356 (29)	396 (31)	354 (27)	140–400
S-ferritin (μg/l)	19 (4)	32 (3)*	12 (3)	122 (13)*	Female 15–160 Male 25–200
S-transferrin receptor (mg/l)	2.07 (0.16)	1.89 (0.16)*	2.58 (0.41)	2.27 (0.33)*	0.84–1.54
S-iron (μmol/l)	11.6 (2.1)	15.5 (2.4)	6.1 (1.2)	10.6 (1.3)*	9.0–33.0
S-total iron binding capacity (μmol/l)	73 (4)	68 (3)*	76 (4)	66 (3)*	49–85
S-protein (g/l)	71 (1)	71 (2)	71 (1)	70 (1)	62–76
S-albumin (g/l)	42 (1)	41 (1)	41 (1)	40 (1)	39–47

Abbreviations: CRP = C-reactive protein; ESR = erythrocyte sedimentation rate.
*Significantly different from pretreatment values ($p < 0.05$). B-haemoglobin, S-ferritin, S-transferrin receptor and S-iron differ at start of the two treatments. The differences are due to the more pronounced effect of iron treatment in the group of patients starting with iron sucrose as compared to those starting with ferrous fumarate. At inclusion, none of these parameters differed significantly between patients starting with ferrous fumarate and patients starting with iron sucrose.

iron sucrose had no influence on clinical disease activity or specific clinical symptoms.

There are few data in the medical literature about tolerance to oral ferrous iron therapy in IBD. We previously showed that gastrointestinal side effects of oral ferrous fumarate, such as diarrhoea, gastrointestinal pain and nausea, were more pronounced in patients with active CD compared with healthy controls [22]. Others have reported iron intolerance in as many as 25% of IBD patients [23]. De Silva et al. found equal intolerance to ferrous sulphate in IBD and non-IBD patients [24].

We previously showed that one week of ferrous fumarate supplementation decreased plasma antioxidants in patients with active CD [22]. In the present study, we were not able to confirm these findings. However, the patients scored less on clinical disease activity indices and had higher levels of plasma antioxidants, indicating less active disease in the present as compared to the previous study [22]. A certain degree of intestinal inflammation may be necessary to give recognizable changes in plasma parameters. Indeed, 3 out of 4 CD patients with elevated S-CRP had a further increase in S-CRP, and deterioration in plasma antioxidant status was observed in all four patients, after ferrous fumarate treatment.

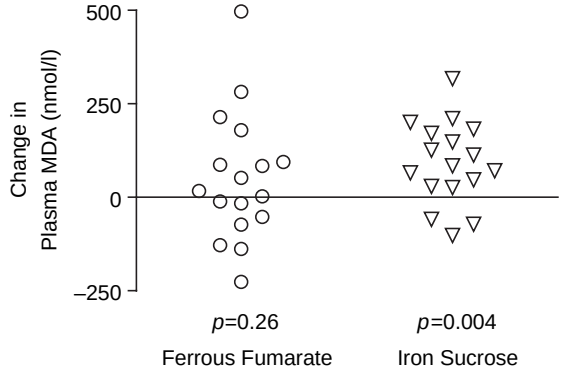

Figure 2. Change (=post-treatment score − pretreatment score) in plasma malondialdehyde (MDA) shown for individual patients. *P*-values indicate the probability that change = zero for each treatment.

The noxious effect of oral iron has been clearly demonstrated in animal models of IBD. Oral as well as rectal ferrous sulphate supplementation lead to an increased production of pro-inflammatory cytokines in the colonic mucosa of IL-10 knock-out mice, but not in control animals [6]. Oral iron supplementation increased the severity of colitis judged by histology [5,25] and increased colonic and plasma lipid peroxides and decreased plasma antioxidant vitamins [5] in dextran sulphate sodium colitis in Wistar rats. Healthy control rats on iron supplementation had normal colonic histology [5,25] and lipid peroxide levels [5]. It seems therefore that pre-existing inflammation is necessary for overt damage to occur with therapeutic doses of oral ferrous iron.

Intravenously administered iron sucrose is taken up by the reticuloendothelial system where it is

Table IV. Plasma levels of malondialdehyde (MDA), vitamins C, E and A, betacarotene and aminothiols. Mean (SEM).

Parameters	Before Ferrous fumarate	After Ferrous fumarate	Before Iron sucrose	After Iron sucrose
MDA (nmol/l)	670 (59)	719 (81)	532 (42)	624 (40)*
Vitamin C (μmol/l)	52.0 (5.7)	48.1 (6.2)	52.5 (6.5)	44.7 (5.9)*
Vitamin E (μmol/l)	22.3 (1.2)	21.5 (1.0)	23.1 (1.7)	22.3 (1.5)
Vitamin A (μmol/l)	1.6 (0.1)	1.6 (0.1)	1.6 (0.1)	1.7 (0.1)
Betacarotene (μmol/l)	0.90 (0.16)	0.75 (0.12)	0.87 (0.16)	0.76 (0.15)*
Glutathione (μmol/l)	5.26 (0.50)	5.31 (0.51)	5.10 (0.32)	4.57 (0.41)
Cysteine (μmol/l)	216 (8)	221 (7)	206 (8)	196 (8)
Cysteinyl-glycine (μmol/l)	21.1 (1.0)	22.4 (1.2)	20.9 (0.9)	19.8 (1.0)

*Significantly different from pretreatment levels ($p < 0.05$).

metabolized and stored [26]. Iron is then gradually released into the circulation where it combines with transferrin for transportation to the bone marrow [26]. However, parenteral iron agents contain a small fraction of labile iron capable of exerting a biological impact prior to cellular uptake, estimated to 2–6% of total iron and varying according to the sequence: iron dextran <iron sucrose <ferric gluconate [27,28]. Transferrin scavenges most of this labile iron [27], but some is bound to serum albumin, citrate and other undefined, negatively charged ligands [29]. This non-transferrin-bound iron (NTBI) has the potency to become redox active [30]. Appearance of catalytically active NTBI in serum was demonstrated after infusion of 100 mg iron sucrose to haemodialysis patients in three recent studies [31–33]. NTBI reached maximum levels 1–3 h after the iron infusion and was cleared from the circulation after 2–3 days [31,32]. Furthermore, infusion of 100 mg iron sucrose to patients with chronic renal failure gave significant elevations in plasma levels of MDA, reaching maximum levels within 30 min after start of the infusion [33–35]. Increases in MDA concentrations were significantly related to NTBI concentrations [33]. The extent of NTBI is likely to be dose dependent [33]. Following intravenous iron therapy we found increased plasma MDA and decreased plasma vitamin C, and beta-carotene, but no concurrent increase in S-CRP and clinical disease activity, suggesting increased biological oxidative stress without any obvious influence on intestinal inflammation. Since we gave a relatively high total dose of 600 mg iron sucrose over a period of 10 days, NTBI may explain our findings of increased plasma MDA levels and decreased plasma radical scavenger levels 5 days after the last infusion.

The increase in oxidative stress observed after treatment with intravenous iron may occur independently of existing inflammation, as infusion of 100 mg iron sucrose to healthy volunteers increased oxygen radical formation, assessed by whole-blood electron spin resonance [36]. On the other hand, pre-existing inflammation reinforced the harmful effects of intravenous iron [37].

The clinical implications of the increased oxidative stress in IBD patients after intravenous iron sucrose are currently unknown. It has been proposed that the increased oxidative damage after intravenous iron may contribute to the higher incidence of atherosclerosis in haemodialysis patients with end-stage renal disease [35,37]. Concerns regarding atherosclerosis are less in IBD, since they receive intravenous iron for only short periods. However, even if intravenous iron administration does not favour to intestinal accumulation, influence on intestinal inflammation cannot be ruled out.

When designing this study, single doses of 200 mg iron sucrose were chosen, as this is the dose used in previous studies of intravenous iron therapy in patients with IBD [11–13]. Intravenous iron sucrose at 200 to 600 mg a week is also the recommended treatment for iron deficiency anaemia in IBD patients [3]. In the light of the findings regarding intravenous iron-related oxidative stress, we may have to reconsider our dose regimens, and give smaller and or less frequent iron infusions.

It is likely that intravenously administered iron exerts its catalytic properties mainly in the intravascular compartment. This is not the case following oral iron administration. As most orally administered iron is not absorbed, the intestinal mucosa is heavily exposed to the iron load. In the present study, MDA and vitamins were measured in plasma. Apparently, changes in the gastrointestinal tract have to be substantial to be recognized in plasma, while intravascular changes are more readily recognized. Plasma MDA and vitamins may not be appropriate parameters for estimation of oxidative stress in the gut. Furthermore, faecal calprotectin is not a product of lipid peroxidation and does not necessarily relate to the production of free radicals in the mucosa.

Both oral ferrous fumarate and intravenous iron sucrose gave a significant increase in the blood reticulocyte count and a decrease in the serum

transferring receptor, indicating a response to therapy. Changes in the haematologic parameters were more pronounced after intravenous iron sucrose. Moreover, blood haemoglobin increased significantly only after treatment with iron sucrose, confirming the efficacy of this iron compound. However, the duration of the treatment periods was too short for proper evaluation of efficacy on anaemia.

In summary, this study showed that oral ferrous fumarate, but not intravenous iron sucrose, increased clinical disease activity in patients with IBD, whereas iron sucrose increased intravascular oxidative stress. Present evidence suggests that oral ferrous iron should be given with caution to IBD patients. Intravenous iron sucrose is effective and well tolerated. However, intestinal inflammation and especially acute flare-ups should be actively treated before giving iron sucrose.

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