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Effects of ferrous sulphate and non-ionic iron–polymaltose complex on markers of oxidative tissue damage in patients with inflammatory bowel disease

K. ERICHSEN*,†, R. J. ULVIK†,‡, T. GRIMSTAD§, A. BERSTAD*,†, R. K. BERGE† & T. HAUSKEN*,†
*Department of Medicine and †Institute of Medicine, University of Bergen, Bergen; ‡Laboratory of Clinical Biochemistry, Haukeland University Hospital, Bergen; §Department of Medicine, Stavanger University Hospital, Stavanger, Norway

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SUMMARY

Background: Iron deficiency is a common complication of inflammatory bowel disease. Oral iron therapy may reinforce intestinal tissue injury by catalyzing production of reactive oxygen species.

Aim: To compare the effects of ferrous sulphate and non-ionic iron–polymaltose complex on markers of oxidative tissue damage and clinical disease activity in patients with inflammatory bowel disease.

Methods: Forty-one patients with inflammatory bowel disease and iron deficiency were randomized to treatment with ferrous sulphate 100 mg twice a day or iron–polymaltose complex 200 mg once a day for 14 days.

Results: Following ferrous sulphate, plasma malondialdehyde increased ($P = 0.02$), while urine 8-isoprostaglandin $F_{2\alpha}$ and plasma antioxidants did not change significantly. Iron–polymaltose complex did not change plasma malondialdehyde, urine 8-isoprostaglandin $F_{2\alpha}$ or plasma antioxidants. Comparing the two treatments, changes in plasma malondialdehyde tended to differ ($P = 0.08$), while urine 8-isoprostaglandin $F_{2\alpha}$ and plasma antioxidants did not differ. Neither ferrous sulphate nor iron–polymaltose complex altered clinical disease activity indices.

Conclusions: Ferrous sulphate increased plasma malondialdehyde, a marker of lipid peroxidation. Comparing treatment with ferrous sulphate and iron–polymaltose complex, changes in plasma malondialdehyde tended to differ. Clinical disease activity was unchanged after both treatments.

INTRODUCTION

Iron deficiency is a common complication of inflammatory bowel disease (IBD). Chronic intestinal bleeding may exceed the amount of iron that can be absorbed from the diet, resulting in a negative iron balance.[1] Intravenous iron sucrose is recommended for the treatment of iron deficiency anaemia.[1] However, there is some uncertainty about how to treat patients with iron deficiency and haemoglobin in the normal range. Compounds for oral iron supplementation, generally ferrous (Fe^{2+}) salts, are associated with frequent gastrointestinal side effects, leading to poor compliance.

Reactive oxygen species (ROS) are produced in excess by neutrophils in inflamed intestinal mucosa and are thought to contribute significantly to the tissue injury in IBD.[2] As free iron is a strong catalyst of ROS production, oral ferrous iron therapy may even be harmful to IBD patients. Oral ferrous iron supplements are poorly absorbed and lead to high faecal iron concentrations,

Correspondence to: Dr K. Erichsen, Department of Medicine, Section for Gastroenterology, Haukeland University Hospital, N-5021 Bergen, Norway. E-mail: kari.erichsen@helse-bergen.no

and a significant fraction of faecal iron is available for catalytic activity.[3] When iron meets the inflamed intestinal mucosa it may increase ROS production and thereby aggravate tissue damage, as demonstrated in animal models of IBD.[4, 5]

The newer compound iron-polymaltose complex is a ferric (Fe^{3+}) hydroxide–carbohydrate complex similar to parenteral iron formulations. It contains iron in a non-ionic form, making it less toxic.[6] In blood donors, side effects were less frequent and compliance was better with iron–polymaltose complex when compared with ferrous sulphate.[7] Evidence for the use of iron–polymaltose complex in IBD patients is lacking.

The aim of this study was to compare the effects of oral ferrous sulphate and oral iron–polymaltose complex on markers of oxidative tissue damage and clinical disease activity.

METHODS

Patients

Patients were recruited from out-patient clinics at Haukeland University Hospital and Stavanger University Hospital between February 2004 and November 2004. Eligibility criteria included patients with ulcerative colitis (UC) or Crohn's disease (CD) in active or quiescent stage, and iron deficiency defined by E-mean corpuscular volume <80 fL or S-ferritin <15 μg/L or S-soluble transferrin receptor >1.54 mg/L. Exclusion criteria included iron therapy or blood transfusions during 6 weeks before inclusion, azathioprine treatment initiated <2 months before inclusion, infliximab treatment, cobalamin or folic acid deficiency, pregnancy, cancer and renal disease. Written informed consent was obtained from each patient and the Regional Committee for Medical Research Ethics approved the study protocol.

Study design

This study was a prospective, non-blinded, randomized trial with two parallel treatment groups. Patient numbers were assigned sequentially as the patients entered the study and randomization was performed according to a computer-generated randomization list. Randomization was performed in two strata, one for CD and the other for UC. Investigators and patients were not blinded to study drug assignment during the study period, although investigators were blinded to drug assignment during analysis of laboratory parameters.

Medications

Ferrous sulphate enteric-coated tablets (Nycoplus Ferro-Retard®; Nycomed Pharma AS, Asker, Norway), each tablet corresponding to 100 mg Fe^{2+}, one tablet (100 mg) was taken in the morning and one tablet (100 mg) in the evening between meals for 14 days.

Iron hydroxide polymaltose complex tablets (Maltofer Filmtablets®; Vifor International Inc., St Gallen, Switzerland), each tablet corresponding to 100 mg Fe^{3+}, two tablets (200 mg) were taken in the morning with meal for 14 days. Administration of study drugs were in accordance with the manufacturers recommendations.

Haukeland Hospital Pharmacy prepared and stored the packages of study medication and delivered them to the patients. Compliance was assessed by pill count from returned packages and was performed by the pharmacy. Satisfactory compliance was defined as the consumption of at least 80% of the study medication.

Laboratory investigations

Blood samples were collected after an overnight fast on day 1 and 15. Plasma malondialdehyde (MDA), plasma vitamins A, E and C, plasma beta-carotene, and plasma aminothiols were measured by high-performance liquid chromatography (HPLC) as previously described.[8, 9]

Routine laboratory investigations included B-haemoglobin, B-reticulocyte count, E-mean corpuscular volume, E-mean corpuscular haemoglobin, E-mean corpuscular haemoglobin concentration, B-erythrocyte count, B-leucocyte count, B-platelet count, reticulocyte haemoglobin (CHr), hypochromic red cells (HYPO), S-ferritin, S-iron, S-total iron binding capacity, S-soluble transferrin receptor, S-C-reactive protein (S-CRP), B-erythrocyte sedimentation rate (B-ESR), S-protein and S-albumin.

Urine samples were collected in the morning of day 1 and 15 and analyzed for creatinine. Butylated-hydroxy-toluene (BHT) was added to 2 mL of urine to give a final concentration of 20 mmol/L. The samples were then stored at −80 °C until analysis of urine 8-isoprostaglandin $F_{2\alpha}$ (8-iso-$PGF_{2\alpha}$) by gas chromatography–mass spectrometry. The method used is based on the procedure reported by Nourooz-Zadeh *et al.*,[10] but

modified for urine matrix by omitting the initial alkaline hydrolysis step and adopting the solid-phase protocols published by Lee *et al.*[11]

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). Results are expressed as mg calprotectin/kg faeces. Values above 50 mg/kg are regarded as positive PhiCal test.[12]

Clinical disease activity

Clinical 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 CD activity for patients with CD.[13] The Harvey–Bradshaw Simple Index is based on five items: general well being, abdominal pain, stool frequency, abdominal mass and extraintestinal complications. Maximum score is 25 and scores of ≥5 indicate active CD. For patients with UC, the Simple Clinical Colitis Activity Index was recorded.[14] It is based on six items: general well being, stool frequency day and night, urgency of defaecation, 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 Disease Activity Index (CDAI) diary card[15] the week before start of iron therapy and during the 2 weeks of iron administration. The CDAI diary card implies daily recording of general well being, abdominal pain and number of liquid or very soft stools. Total number of stools was also recorded. The sum of seven daily registrations yields a score for each symptom. The higher score, the more the patient is troubled. The study drug administration period was 14 days and therefore the average score of the 2 weeks is applied for the analysis. Patients also recorded presence of nausea before and during iron treatment.

Patients who discontinued study drug treatment because of worsening of symptoms were included in analyses of clinical disease activity and symptom scores. Their disease activity scores were increased by two points, and symptom scores were increased by one point per day.

Objectives and outcomes

The primary objective of the study was to compare the effects of oral ferrous sulphate and oral iron–polymaltose complex on markers of oxidative tissue damage. The primary outcome measures were plasma MDA and urine 8-iso-$PGF_{2\alpha}$. The secondary objective was to compare the impact of the two iron formulations on clinical disease activity and specific symptoms. The duration of treatment was too short to be a study of efficacy on correction of iron deficiency.

Statistical analysis

For blood, urine and faecal parameters, differences within and between groups were evaluated with Student's *t*-test for paired and unpaired comparisons. Mean of differences and 95% CI were given. Clinical disease activity indices and symptom scores were analyzed using Wilcoxon matched pairs test for paired comparisons and Mann–Whitney test for unpaired comparisons. Median and range are given. Differences between proportions were evaluated with Fisher's exact test. Two-tailed *P*-values <0.05 are considered statistically significant. Data were analysed using the GraphPad Prism 4 for Windows (GraphPad Software Inc., San Diego, CA, USA) statistical software package.

RESULTS

Forty-one patients (Table 1) were randomized to treatment with either ferrous sulphate ($n = 21$) or iron–polymaltose complex ($n = 20$). Thirty-seven patients went through the trial according to the protocol. In these 37 patients, pill count revealed similar compliance in patients treated with ferrous sulphate [100% (82–100)] and iron–polymaltose complex [100% (86–100)] ($P = 0.88$). Three patients (one CD and two UC) discontinued ferrous sulphate treatment after 1, 4 and 5 days respectively, and one patient (CD) discontinued iron–polymaltose complex treatment after 1 day. They all experienced intolerable increase in stool frequency, abdominal pain and nausea. These patients are excluded from the analyses of laboratory parameters, but included in the analyses of clinical disease activity and symptom scores. No patients declined participation because of adverse effects of earlier courses of oral iron therapy.

For patients using concurrent medications (Table 1), average steroid dose was 7.5 mg/day, average

Table 1. Patient characteristics. Median (range) for age, number of patients for all others

	Ferrous sulphate	Iron–polymaltose complex
CD/UC	13/8	11/9
Female/Male	13/8	12/8
Age	41 (17–69)	31.5 (16–68)
Disease location CD*		
terminal ileum	2	2
colon	4	1
ileocolon	3	4
upper GI	4	4
Disease location UC		
distal colitis	1	2
subtotal colitis	3	3
total colitis	4	4
Concurrent medication		
5-ASA	13	11
Sulphasalazine	1	2
Steroids	7	5
Azathioprine	6	6
None	1	5

CD, Crohn's disease; UC, ulcerative colitis; GI, gastrointestinal tract; 5-ASA, 5-acetylsalicylic acid.
* Disease location for CD as defined by the Vienna classification for CD.

5-acetylsalicylic acid (ASA) dose was 1.9 g/day, and average azathioprine dose was 112.5 mg/day. Dosing was similar in the two treatment groups. Concurrent therapy was not changed during the study period.

At inclusion no parameter differed significantly between patients treated with ferrous sulphate and with iron–polymaltose complex. Effects of iron treatments were similar in CD and UC patients, and therefore results from CD and UC patients were pooled.

Markers of oxidative stress

Urine 8-iso-$PGF_{2\alpha}$ tended to increase by 194 pg/mg creatinine (CI −58 to 447; $P = 0.12$) after iron sulphate treatment, while no alteration was seen after iron–polymaltose complex treatment ($P = 0.56$) (Table 2). Plasma MDA increased significantly by 95 nmol/L (CI 18–171; $P = 0.02$) after iron sulphate, and again no alteration was found after iron–polymaltose complex ($P = 0.16$) (Figure 1). Plasma vitamins A, C and E, beta-carotene, glutathione, cysteine, cysteinyl-glycine and homocysteine were unchanged after both treatments (Table 2). Comparing treatment with ferrous sulphate and iron–polymaltose complex, the changes (from before to after treatment) in plasma MDA tended to differ ($P = 0.08$), while changes in urine 8-iso-$PGF_{2\alpha}$ ($P = 0.28$) did not differ. Also, the mean plasma MDA values of the two groups were significantly different after treatments ($P = 0.007$), with higher MDA levels in the ferrous sulphate group (Table 2). None of the urine or plasma parameters correlated to clinical disease activity indices, faecal calprotectin or CRP (data not shown).

Cinical disease activity and symptoms

At the beginning of iron treatment clinical disease activity scores were similar in patients receiving ferrous sulphate [CD 3 (0–8) and UC 1 (0–7)] and patients receiving iron–polymaltose complex [CD 2 (0–10), UC 2 (0–5)]. Defined by these indices 6 of 21 patients in the ferrous sulphate group and 3 of 20 patients in the iron–polymaltose complex group had active disease.

Table 2. Markers of oxidative stress

	Ferrous sulphate		Iron–polymaltose complex	
	Before	After	Before	After
Urine 8-isoprostaglandin $F_{2\alpha}$ (pg/mg creatinine)	417 (46)	629 (124)	396 (46)	434 (64)
P-malondialdehyde (nmol/L)	294 (25)	395 (25)*	275 (21)	300 (19)
P-vitamin A (μmol/L)	1.7 (0.2)	1.8 (0.2)	1.6 (0.1)	1.9 (0.3)
P-vitamin C (μmol/L)	60.9 (6.0)	58.6 (5.4)	61.3 (5.1)	54.5 (5.5)
P-vitamin E (μmol/L)	30.2 (1.8)	29.3 (1.5)	29.3 (1.6)	28.3 (1.7)
P-beta-carotene (μmol/L)	0.67 (0.09)	0.67 (0.10)	0.59 (0.13)	0.57 (0.09)
P-glutathione (μmol/L)	5.05 (0.48)	5.08 (0.54)	5.22 (0.30)	5.43 (0.43)
P-cysteine (μmol/L)	203 (11)	199 (13)	211 (11)	209 (11)
P-cysteinyl-glycine (μmol/L)	16.7 (1.1)	16.6 (1.2)	18.7 (0.9)	18.5 (1.1)
P-homocysteine (μmol/L)	4.87 (0.59)	4.58 (0.47)	6.53 (1.16)	6.04 (0.94)

Values are expressed as mean (SEM).
* Significantly different from pre-treatment level ($P < 0.05$). Data from four patients who discontinued iron treatment are not included in the table.

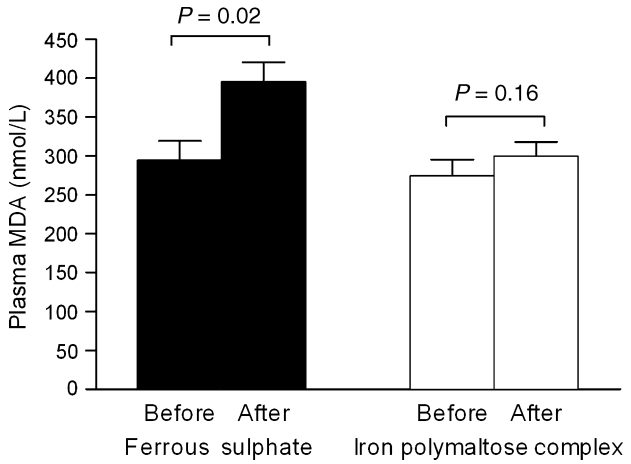

Figure 1. Effect of ferrous sulphate and iron–polymaltose complex on plasma levels of malondialdehyde in patients with inflammatory bowel disease. Results are expressed as mean ± SEM. *P*-values given are for paired comparisons.

Clinical disease activity remained largely unchanged with both ferrous sulphate ($P = 0.45$) and iron–polymaltose complex ($P = 0.80$) (data not shown). The alterations (from before to after treatment) did not differ between treatments ($P = 0.81$).

During ferrous sulphate treatment the total number of stools per week increased [from 19 (7–106) to 24 (7–55); $P = 0.009$]. During iron–polymaltose treatment the total number of stools per week did not change (from 17 (7–46) to 17 (6–66); $P = 0.25$). Comparing the two treatments, the alterations in stool frequency did not differ ($P = 0.40$). Neither ferrous sulphate nor iron–polymaltose complex influenced general well being or abdominal pain scores (data not shown). Increase in nausea was reported by 9 of 21 patients receiving ferrous sulphate and 7 of 20 patients receiving iron–polymaltose complex ($P = 0.75$).

Routine laboratory investigations and calprotectin

Routine laboratory investigations are presented in Table 3. Neither ferrous sulphate nor iron–polymaltose complex increased B-haemoglobin. Only ferrous sulphate had significant impact on biochemical markers of iron deficiency, with increase in CHr by 1.9 pg (CI 0.01–3.8; $P = 0.049$), S-ferritin by 12 μg/L (CI 6–17; $P = 0.0003$) and B-reticulocyte count by 0.016×10^{12}/L (CI −0.004 to 0.036; $P = 0.10$), and decrease in HYPO by −2.5% (CI −4.6 to −0.3; $P = 0.03$), S-soluble transferrin receptor by −0.21 mg/L (CI −0.31 to −0.11; $P = 0.0005$) and S-total iron binding capacity by −7 μmol/L (CI −10 to −4; $P < 0.0001$). Iron–polymaltose complex increased only B-reticulocyte count (0.016×10^{12}/L with CI 0.001–0.030; $P = 0.03$).

No significant change in faecal calprotectin was observed after treatment with ferrous sulphate [from 237 (59) to 242 mg/kg (57)] or iron–polymaltose complex [from 500 (105) to 527 mg/kg (81)].

DISCUSSION

Malondialdehyde and 8-iso-$PGF_{2\alpha}$ are products of non-enzymatic, oxidative degeneration of polyunsaturated fatty acids, and are frequently used markers of lipid peroxidation.[16] Ferrous sulphate treatment for 2 weeks significantly increased plasma MDA, and tended to increase urine 8-iso $PGF_{2\alpha}$. No such changes were found following treatment with iron–polymaltose complex. Comparing ferrous sulphate and iron–polymaltose complex, the changes in MDA tended to differ. Because of wide variations in MDA levels, a type II error cannot be excluded. Also, the mean plasma MDA values of the two groups were significantly different after treatments, with highest MDA levels in the ferrous sulphate group.

There is growing evidence that oral ferrous salts may enhance intestinal tissue damage in IBD. The finding of increased plasma MDA following ferrous sulphate treatment coincide with our previous findings of decreased plasma antioxidants in patients with active CD, but not in healthy controls, following 1 week of ferrous fumarate supplementation.[17] Furthermore, oral supplementation of ferrous salts and other ionic iron compounds lead to increased intestinal inflammation assessed by histology,[4, 5, 18–20], and increased levels of colonic[4, 5, 18, 20] and plasma lipid peroxides and plasma 8-isoprostanes,[18] in rats with experimental colitis. Taken together, current evidences suggest that caution should be exercised in the use of ferrous salts in IBD patients.

There are few data in the medical literature comparing the pro-oxidant potential of ferrous iron compounds and stable complexes with ferric iron. In healthy subjects with low iron stores, treatment with ferrous sulphate, but not iron–polymaltose complex, increased the susceptibility of lipoproteins to oxidative modification.[21] In children with iron deficiency anaemia there was no convincing difference in the effects of ferrous sulphate and iron–polymaltose complex on plasma antioxidants

Table 3. Routine laboratory investigations

Parameter	Normal	Ferrous sulphate		Iron–polymaltose complex	
		Before	After	Before	After
B-haemoglobin (g/dL)	Female (11.6–16.0) Male (13.2–16.6)	13.1 (0.4)	13.3 (0.3)	12.5 (0.3)	12.5 (0.3)
B-haematocrit (%)	Female (36–46) Male (37–49)	41 (1)	42 (1)	39 (1)	40 (1)
E-mean corpuscular volume (fL)	80–102	86 (1.6)	87 (1.3)*	84 (1.8)	85 (1.6)
E-mean corpuscular haemoglobin (pg)	27–35	27 (0.8)	28 (0.8)*†	27 (0.7)	27 (0.7)
E-mean corpuscular haemoglobin concentration (g/dL)	31.0–36.0	31.8 (0.4)	32.0 (0.3)	31.6 (0.3)	31.2 (0.3)
Reticulocyte haemoglobin (pg)	>28	29.3 (0.8)	31.1 (0.7)*	29.1 (0.8)	29.5 (0.7)
Hypochromic red cells (%)	<5	10.4 (3.6)	8.8 (3.2)*	10.3 (3.0)	10.6 (2.8)
B-erythrocyte count (10^{12}/L)	Female (3.7–5.5) Male (4.0–5.8)	4.8 (0.1)	4.8 (0.1)	4.7 (0.1)	4.7 (0.1)
B-reticulocyte count (10^{12}/L)	0.030–0.100	0.068 (0.006)	0.084 (0.007)	0.059 (0.006)	0.075 (0.008)*
B-leucocyte count (10^9/L)	3.5–11.0	6.5 (0.5)	6.3 (0.4)	6.9 (0.6)	7.0 (0.7)
B-platelet count (10^9/L)	140–400	324 (23)	306 (21)	347 (18)	343 (21)
S-total iron binding capacity (μmol/L)	49–85	81 (2)	74 (2)*†	77 (2)	77 (2)
S-iron (μmol/L)	9.0–33.0	11.1 (2.0)	14.2 (2.2)	8.8 (0.8)	8.9 (1.5)
S-ferritin (μg/L)	Female (15–160) Male (25–200)	13 (2)	25 (3)*†	13 (2)	13 (2)
S-soluble transferrin receptor (mg/L)	0.84–1.54	1.95 (0.18)	1.77 (0.13)*	2.08 (0.24)	2.03 (0.21)
B-erythrocyte sedimentation rate (mm/h)	Female <20 Male <15	11 (2)	10 (2)	22 (3)	20 (3)*
S-C-reactive protein (mg/L)	<10	7 (2)	6 (2)	12 (3)	11 (2)

Values are expressed as mean (SEM).

* Significantly different from pre-treatment level ($P < 0.05$).

† Significantly different change compared with iron–polymaltose complex ($P < 0.05$). Data from four patients who discontinued iron treatment are not included in the table.

and markers of lipid peroxidation.[22] Another iron complex, ferric maltol, produced less lipid peroxidation than ferrous sulphate *in vitro*.[23]

In healthy subjects the difference in pro-oxidant potential of ferrous salts and iron–polymaltose complex has been ascribed mainly to different mechanisms of absorption. Ferrous iron is absorbed rapidly leading to an increase in serum iron and fast distribution of iron to the tissues, whereas iron from iron–polymaltose complex is absorbed and distributed slowly.[21] In patients with IBD the setting is different as iron is thought to do more harm within the intestinal lumen at the surface of the inflamed mucosa. What happens with the different iron compounds when they pass through the gastrointestinal tract is therefore of importance.

Most of ingested iron is not taken up, but passed on with the faecal stream. To participate in reactions leading to ROS production, iron must be either freely water-soluble or loosely bound to small organic compounds, and only a fraction of the total iron concentration in faeces is in such states.[3] However, even low-dose ferrous sulphate supplementation markedly increases the concentration of weakly bound iron in faeces.[3]

Iron–polymaltose complex has a high complex stability, comparable to that of iron sucrose used for intravenous application.[6] Release of iron from ferric hydroxide preparations occurs at low rate, and a significant increase in the concentration of weakly bound iron in faeces is therefore not likely to occur following intake of iron–polymaltose complex. This reasoning coincide with our findings of alterations in plasma MDA and urine 8-iso-PGF2 after treatment with ferrous sulphate, but not iron–polymaltose complex, in IBD patients. The lower changes in iron parameters after iron–polymaltose complex may also be related to the slow release of iron from the complex.

IBD patients were more prone to side effects during oral ferrous iron intake as compared with healthy controls.[17] So, even if iron–polymaltose complex has a low side effect profile in healthy subjects,[7] some more

complaints might be observed in IBD patients. Interestingly, ferric trimaltol, another ferric iron complex not commercially available, corrected iron deficiency and had a low incidence of side effects in IBD patients intolerant to ferrous compounds.[24]

In the present study, we found no difference in the tolerability of ferrous sulphate and iron–polymaltose complex in patients with IBD. Three of 21 patients discontinued ferrous sulphate treatment, while one of 20 patients discontinued iron–polymaltose complex treatment, because of side effects. About one third of patients in both groups experienced more nausea during treatments, while neither of treatments gave more abdominal pain. Changes in stool frequency did not differ between treatments. However, stool frequency increased in patients taking ferrous sulphate. This is in accordance with our previous finding that ferrous fumarate therapy increased stool frequency in patients with CD.[17] In the same study, healthy controls experienced decreased stool frequency. Lower gastrointestinal side-effects during ferrous iron therapy appear not to be dose related,[25] and the reason for changes in stool frequency is unknown.

In two previous studies, we found aggravation of abdominal pain following ferrous fumarate treatment in IBD patients.[17, 26] In the present study, enteric coating of the ferrous sulphate tablets may have prevented this side effect.

Faecal calprotectin is an unspecific marker of intestinal inflammation.[27] At inclusion the ferrous sulphate group had lower calprotectin levels as compared with the iron–polymaltose complex group. The difference was however not statistically significant and it is not clear whether the difference has any clinical significance.

The duration of the treatment periods was too short for proper evaluation of efficacy on correction of iron deficiency. Only ferrous sulphate treatment influenced biochemical markers of iron metabolism, but neither ferrous sulphate nor iron–polymaltose complex increased blood haemoglobin.

It is not possible to demonstrate the bioequivalence of iron–polymaltose complex and iron salts by applying the usual methods of determining the area under the curve of serum iron.[28] This is because iron–polymaltose complex has an absorption behaviour completely different from that of iron salts.[28] Iron–polymaltose complex shows no serum iron increase after administration.[28] However, using the twin-isotope technique the total iron uptake from iron–polymaltose complex and ferrous salts was found to be similar.[29,30] Two studies with treatment duration of 3–6 months demonstrated that iron–polymaltose complex was as efficient as ferrous sulphate in correcting blood haemoglobin levels in iron deficiency anaemia, but iron–polymaltose complex did not increase serum ferritin to the same extent as ferrous sulphate.[7,21] To find out whether iron–polymaltose complex has a role in the treatment of iron deficiency in patients with IBD a study of longer duration is needed.

In summary, ferrous sulphate increased plasma MDA, a marker of lipid peroxidation, supporting the notion that ferrous iron may aggravate oxidative tissue damage. No change in redox status was found after treatment with iron–polymaltose complex. Comparing treatment with ferrous sulphate and iron–polymaltose complex, changes in plasma MDA tended to differ. Clinical disease activity was unchanged after both treatments.

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