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IRON ABSORPTION IN PATIENTS WITH DERMATITIS HERPETIFORMIS

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Abstract. Iron absorption has been studied in patients with dermatitis herpetiformis (DH). Four patients out of 20 had iron deficiency, defined as absence of or only traces of haemosiderin in bone marrow smears. These four had adequate absorption of ferrous iron. The iron deficiency in at least 3 of them was ascribed to increased iron loss. The results indicate that, although having a mild to moderate malabsorption syndrome, DH patients can be expected to exhibit adequate absorption of orally administered iron. Explanations of a negative iron balance other than defective absorption should therefore be sought.

Key words: Anaemia; Dermatitis herpetiformis; Iron absorption; Iron deficiency

Most patients with dermatitis herpetiformis (DH) have an associated gluten-sensitive enteropathy (9, 22, 25, 30). The intestinal changes in DH are most evident in the proximal part of the jejunum (19). This part of the gastrointestinal tract is the principal site of iron absorption (31) and an increased frequency of iron deficiency might be expected to occur among such patients.

Iron deficiency is a common finding in any population and thus it is necessary to compare the findings in DH with a control group in order to be able to evaluate an increased frequency of iron deficiency. Such an evaluation must include a considerable number of patients with DH. However, DH is an uncommon disease and the investigations reported on the frequency of iron deficiency are not conclusive, as the groups were small and lacked controls (7, 8, 9, 19, 22, 25). Direct studies on the absorption of iron in patients with DH have, to our knowledge, not been reported. In the present study the absorption of ferrous iron was studied with a whole-body counter technique in 21 patients with DH.

PATIENTS

Twenty-one patients with DH, consecutively chosen from the Outpatient Clinic of the Department of Dermatology in Göteborg, aged 18–71 years, were included in the study (Table I). The diagnosis for each patient was based on typical clinical findings, skin biopsies and a therapeutic response to diaminodiphenylsulphone (DDS) treatment (Dapsone®; ICI-Pharma AB, Sweden). At the time of investigation 11 patients were being treated with DDS. Two women had had oral iron therapy for some weeks during the last year (cases 15 and 18). No patients had any dietary restrictions.

METHODS

All haematological determinations were made on venous blood drawn in the morning without stasis after 15 min rest in the supine position. All patients had fasted overnight.

Haptoglobin

Haptoglobin was measured by a nephelometric immunoprecipitation method (27). Values between 0.3 and 1.8 g/l haemoglobin-binding capacity are considered normal.

Serum iron and TIBC

The serum iron was determined according to the Panel Method (17) and TIBC by the method of Herbert et al. (16).

Bone marrow haemosiderin

The bone marrow smears were stained according to Hansen & Weinfeld (14). The grading of bone marrow haemosiderin was made according to Lundin et al. (21). The identities of the smears were unknown to the examiner.

Table I. *Sex, age, Dapsone®, (DDS-)treatment and haptoglobin in 21 patients with dermatitis herpetiformis (DH)*

Patient no.	Sex	Age (y.)	Duration of DH (y.)	DDS (mg/day)	Haptoglobin (g/l)
1	♂	60	30	–	1.0
2	♂	53	20	–	–
3	♂	25	2	–	1.5
4	♂	24	3/4	–	0.4
5	♂	18	7	–	1.0
6	♂	66	1/2	–	1.4
7	♂	55	35	100	0.2
8	♂	63	1/2	50	1.0
9	♂	58	8	100	1.1
10	♂	26	7	100	<0.2
11	♂	30	11	50	<0.2
12	♂	71	2	100	1.1
13	♂	50	8	170[a]	<0.2
14	♀	36	5	–	0.8
15	♀	24	1	–	1.3
16	♀	66	1	–	0.7
17	♀	52	1/6	–	1.4
18	♀	44	16	150	0.5
19	♀	54	7	100	0.3
20	♀	65	9	50	0.7
21	♀	55	11	50	<0.2

[a] Diasone® (aldosulphone sodium).

Iron absorption

The iron absorption was measured from a small dose of ferrous ascorbate. After fasting overnight the patients received 0.56 mg of iron as ^{59}Fe-labelled ferrous sulphate ($FeSO_4 \cdot 7H_2O$, analytical grade, Merck Co.)+17.6 mg ascorbic acid together with 125 ml of tap water (including rinsings) (15). The absorption was measured in a shadow shield whole body counter with four 6″×2″ thallium-activated sodium iodide crystals. Data on this whole body counter have been reported earlier (12). A background value was obtained immediately before the dose was given. The patient was measured again 30 min after ingestion of the dose. The retention measurement was made not less than 14 days after the administration of the dose. The total activity of ^{59}Fe retained from the absorption measurements in the patients was less than 2 μCi. None had had any iron treatment during the last 2 weeks before the investigation.

Serum vitamin B_{12} and folate

The B_{12} content in serum was assayed with *Euglena gracilis* strain Z according to Anderson's modification (1). The serum folate level was assayed with the aid of *Lactobacillus casei* (ATCC 7469) according to a modification described by Hansen (13). Serum B_{12} values below 100 pg/ml are regarded as low and values between 100 and 150 pg/ml as subnormal. Serum folate below 1.0 ng/ml are regarded as low and values between 1.0 and 1.7 ng/ml as subnormal.

Gastric acid secretion

The gastric secretion was determined after pentagastrin stimulation, as described previously (2). The intragastric position of the tube was controlled fluoroscopically.

D-xylose absorption

An oral dose of 25 g (13 patients) or 5 g (8 patients) D-xylose was given to fasting patients. The amount of D-xylose excreted in the urine during the next 5 hours was

Table II. *Haematological and iron absorption data in 13 male patients with dermatitis herpetiformis*

Patients 1–6 have not been treated with Dapsone®. N.D.=not done

Patient no.	Haemoglob. conc. (g/100 ml)	MCHC (%)	Serum iron conc. (μg/100 ml)	TIBC (μg/100 ml)	Bone marrow haemosid.	Iron abs. (%)
1	14.4	32	156	307	II	17
2	14.1	34	81	234	II	44
3	16.2	33	97	297	II	30
4	15.7	33	125	268	II	39
5	13.8	34	137	290	II	55
6	13.6	33	139	380	0	87
Mean	14.6	33.2	122.5	296.0		45.3
S.E.M.	0.4	0.3	11.5	19.9		9.9
7	15.2	30	191	332	I	61
8	12.9	32	118	294	II	46
9	15.1	31	141	367	I	40
10	13.8	33	171	285	II	25
11	12.2	33	136	254	I	32
12	14.7	32	125	333	I	N.D.
13	13.2	32	99	240	I	34
Mean	13.9	31.9	140.1	300.7		39.7
S.E.M.	0.4	0.4	11.9	17.3		5.2

Table III. *Haematological and iron absorption data in 8 female patients with dermatitis herpetiformis*
Patients 14–17 have not been treated with Dapsone®. N.D.=not done

Patient no.	Haemoglob conc. (g/100 ml)	MCHC (%)	Serum iron conc. (μg/100 ml)	TIBC (μg/100 ml)	Bone marrow haemosid.	Iron abs. (%)
14	13.7	33	88	262	I	50
15	12.7	33	48	397	0	53
16	13.2	35	37	310	trace	74
17	14.2	34	103	331	I	20
Mean	13.5	33.8	69.0	325.0		49.3
S.E.M.	0.3	0.5	15.8	28.0		11.1
18	11.1	31	115	246	II	53
19	11.5	33	102	361	0	45
20	12.8	31	125	346	II	18
21	11.7	34	104	341	N.D.	53
Mean	11.8	32.3	111.5	323.5		42.3
S.E.M.	0.4	0.8	5.3	26.2		8.3

measured according to Roe & Rice (24), as modified by Kerstell (20). An excretion of more than 4.9 g and 1.2 g respectively is considered normal.

Lactose tolerance test

An oral dose of 100 g lactose was given. A glucose rise in blood (measured by an *o*-toluidine method) of more than 25 mg/100 ml is considered normal (26).

Faecal fat excretion

Faecal fat excretion was measured by the method of van de Kamer et al. (29). The patients were on an ordinary ward diet and 0.2 litre cream was added each day. Faeces was collected over a 3-day period. Normally the faecal fat excretion is less than 7 g daily.

RESULTS

Haemoglobin and serum iron concentrations

In females, the mean haemoglobin concentration value was significantly lower ($p<0.05$) in those treated with DDS (11.8 g/100 ml) than in those without treatment (13.5 g/100 ml) (Table III). The corresponding values in males were 13.9 and 14.6 g/100 ml, but this difference was not statistically significant (Table II).

Two of the 13 males showed a haemoglobin concentration below 13.0 g/100 ml and 3 of the 8 females had values below 12.0 g/100 ml (Tables II and III). All patients with subnormal haemoglobin values had been treated with DDS (Table I). None of the men had a serum iron concentration below 60 μg/100ml. Two women had serum iron concentrations below 60 μg/100 ml and they showed signs of iron deficiency, defined as absence or traces of haemosiderin in the bone marrow smears (Table III). In females the serum iron concentration was significantly higher in DDS-treated than in non-treated patients.

Bone marrow haemosiderin

One man lacked haemosiderin in the bone marrow smear. He had had occult gastrointestinal bleeding some years earlier. Three of 7 women lacked or had only traces of haemosiderin (Table III).

Iron absorption

Four patients (one male and three females) with iron deficiency defined as absence or traces of haemosiderin in bone marrow smears had an average absorption of 65% (range 45–87%). The corresponding value for patients having haemosiderin grades I–II was 38% (range 17–61%) (Tables II and III).

Serum vitamin B_{12} and folate

Two men and one woman had serum vitamin B_{12} values between 100 and 150 pg/ml. None showed vitamin B_{12} values below 100 pg/ml. One man and two women had serum folate values below 2 ng/ml (Table IV).

Gastric acid secretion

Nine patients (5 men and 4 women) had achlorhydria (less than 1.0 mEq/h) and 3 had low gastric acid secretion values (below 10 mEq/h).

Table IV. *Serum vitamin B_{12} and folate, gastric acid secretion, d-xylose test, lactose test and faecal fat excretion in 21 patients with dermatitis herpetiformis*

N.D.=not done

Patient no.	Serum vit. B-12 (pg/ml)	Serum folate (ng/ml)	MAO[a] (mEq/h)	D-xylose g/ 25 g	D-xylose g/ 5 g	Lactose[b] (mg/100 ml)	Faecal fat excretion (g/day)
1	320	3.5	0	4.7		39	10.0
2	150	4.3	0	2.9		28	18.8
3	310	5.6	19.2	4.7		88	9.2
4	480	2.2	18.2		1.3	42	8.4
5	340	2.7	N.D.		1.6	72	3.3
6	280	7.0	13.7		0.9	55	9.7
7	420	2.9	0	3.6		124	10.3
8	200	2.7	0.2	3.0		42	N.D.
9	180	4.6	3.1	6.8		100	12.4
10	360	2.4	25.5	4.8		62	2.1
11	540	6.1	6.7		1.1	34	8.1
12	160	2.8	0.4	4.2		73	2.6
13	140	0.8	4.7		2.6	N.D.	28.2
14	330	0.9	20.5		1.1	12	12.4
15	345	6.9	N.D.		0.9	33	5.2
16	105	2.9	0	3.1		48	2.0
17	565	2.9	0	5.5		62	10.9
18	160	0.8	19.1	4.7		48	12.5
19	410	4.0	0.8	4.6		20	8.3
20	460	9.8	0	6.7		120	6.7
21	N.D.	N.D.	10.3		1.2	40	3.2

[a] Gastric acid secretion. Maximal acid output=MAO.
[b] Lactose tolerance test. Maximal glucose rise.

D-xylose test and lactose tolerance test

Ten of 13 patients showed *d*-xylose test (25 g) below 4.9 and 4 out of 8 patients had a *d*-xylose test (5 g) below 1.2. Two out of 20 patients had a pathological lactose tolerance test (below 25 mg 100 ml) (Table IV).

Table V. *Earlier studies on iron deficiency in patients with dermatitis herpetiformis (DH)*

No. of patients with iron deficiency	Methods	Authors
3/9	Fe/s, TIBC	Berg et al. (3)
0/14	Fe/s	Brow et al. (4)
No difference between controls and DH pats	Fe/s	Cream & Scott (7)
5/12	Fe/s, TIBC, STP	Fry et al. (8)
2/7	Fe/s, TIBC, STP	Fry et al. (9)
0/6	Fe/s, TIBC	Johnson & Alpert (19)
3/29	Bone marrow haemosiderin	Marks et al. (22)
7/24	Fe/s	Shuster et al. (25)

Faecal fat excretion

Thirteen of 20 patients had a faecal excretion exceeding 7 g/day.

DISCUSSION

Decreased iron absorption and increased frequency of anaemia have been observed in patients with non-tropical sprue (5, 6, 32). Patients with DH also have a gluten-sensitive enteropathy but the gastrointestinal lesions are usually less extensive and more patchy than in patients with non-tropical sprue (4). The reported frequencies of iron deficiency in DH are divergent (Table V). No studies on the iron absorption in patients with DH have been published.

Five of 21 patients (2 men and 3 women) in the present series showed subnormal haemoglobin concentration values (below 13.0 g/100 ml in men and below 12.0 in women). All of them had been treated with DDS. This drug frequently induces haemolysis (10, 11), which might at least partly explain the reduction in haemoglobin concentration. A contributory factor might be iron deficiency in one female (No. 19) and a B_{12}/folic acid deficiency in one subject (No. 18).

Four (20%) patients showed iron deficiency, defined as absence or traces of haemosiderin in bone marrow smears. These patients had a mean absorption of 65% of the test dose. The remaining 16 patients, having haemosiderin grades I–II, absorbed an average of 38%. These values indicate a normal regulation of the iron absorption and no malabsorption of inorganic iron could be detected when comparing these results with earlier studies in normal and iron-deficient subjects who were given the same iron test dose (15, 23).

A mild to moderate steatorrhoea occurred in more than 50% of the patients (Table IV). Furthermore a reduction of the *d*-xylose absorption was a common finding (Table IV). These results indicate a malabsorption in a large proportion of the patients, and are thus in agreement with earlier findings (4). However, no malabsorption of iron could be detected by the absorption studies with ferrous iron. This indicates that the absorptive area in the proximal parts of the intestine was only moderately reduced. In patients with extensive non-tropical sprue a pronounced malabsorption of inorganic iron has been reported (5).

All 3 patients with an iron absorption below 20% in the present study had achlorhydria (Table IV) but this would probably affect the absorption of ferrous iron only to a minor extent (23). However, it is possible that HCl is of greater importance in the absorption of food iron (18, 28).

The present study does not rule out that food iron absorption might be reduced in patients with DH, but this seems unlikely as the majority of patients had had DH more than 7 years without any indications of iron deficiency.

The main cause of iron deficiency in the present subjects could not be ascribed to defective absorption. An increased loss of iron was the likely explanation in at least 3 of the 4 subjects. One man had had gastrointestinal bleeding some years ago and 2 women were still menstruating. The remaining woman had, however, no history of any recent blood loss and she had entered the menopause.

The present study thus indicates that iron deficiency in a patient with DH should not primarily be ascribed to deficient intestinal absorption of iron. Other explanations of the negative iron balance should therefore be sought. Patients with DH can generally be expected to have an adequate absorption of orally administered iron.

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