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Multicentre Double-Blind Clinical Trial of Iron Protein Succinylate in Comparison With Iron Sulfate in the Treatment of Iron Deficiency Anaemia

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Summary

This prospective, double-blind, controlled, multicentre trial was carried out to evaluate the efficacy and tolerability of iron protein succinylate (ITF 282) in comparison with iron sulfate in the treatment of iron deficiency anaemia. 174 patients (98% females) with iron deficiency anaemia were randomised to receive either two iron protein succinylate tablets per day (60mg iron each; n = 86) or one ferrous sulfate controlled-release tablet per day (105mg iron; n = 88); both treatments were scheduled to last 60 days. The course of all laboratory efficacy variables (Hb, Hct, RBC, etc.) during the treatment period showed good therapeutic activity of both ITF 282 and iron sulfate. After 2 months of treatment, the haematochemistry data indicated a satisfactory recovery of iron metabolism in both groups of patients: plasma iron increased from 38 to 75 μg/dl with ITF 282 and from 38 to 66 μg/dl with iron sulfate; the transferrin saturation rate increased from 9 to 21% with ITF 282 and from 9 to 19% with iron sulfate. The circulating haemoglobin increased from 9.98 to 12.08 g/dl with ITF 282 and from 9.92 to 12.21 g/dl with iron sulfate. The differences between the treatments were not statistically significant. A marked clinical improvement in anaemic symptoms (paleness, asthenia, tiredness) was observed with both treatments. The general tolerability was favourable with both treatments; however, ITF 282 appeared to be better tolerated than iron sulfate when gastrointestinal symptoms were taken into account. This trial showed that ITF 282 is an interesting, novel approach to iron treatment.

Iron protein succinylate (ITF 282) is an iron derivative that has been recommended for the oral treatment of iron deficiency anaemia. In ITF 282, iron is bound to milk succinylated proteins to form an iron-protein complex. This organic iron compound, which is highly soluble in water, is capable of forming a precipitate at pH <4, but it becomes soluble again at a higher pH.[1] Furthermore, the preparation is not digested by pepsin, but is hydrolysed by pancreatin at neutral pH. Because of these characteristics, the iron contained in ITF 282 remains in the proteic shell in the stomach, and thus does not cause gastric mucosal damage. The release of iron from ITF 282 and the subsequent iron

absorption occur later in the duodenal lumen as a consequence of the rise in pH.[2,3]

The clinical efficacy and tolerability of ITF 282 in a daily dosage of 120mg iron have already been proven in comparison with well-referenced iron derivatives in two large, controlled, double-blind clinical trials, including about 1100 adult patients and 500 children affected with iron deficiency anaemia.[4,5]

The aim of the present study was to confirm the effectiveness and tolerability of ITF 282 in comparison with iron sulfate in the treatment of iron deficiency anaemia.

Patients and Methods

Patients

This was a phase III, double-blind, controlled, multicentre study comparing the efficacy and tolerability of ITF 282 with iron sulfate in the treatment of iron deficiency anaemia of mild to moderate severity.

About 180 adult patients (aged 18 to 65 years) with this condition were initially recruited for the trial. Pregnant women aged 18 to 38 years were included if the pregnancy was at least 13 weeks advanced.

The following criteria were used for the diagnosis of iron deficiency anaemia: haemoglobin (Hb) between 7 and 11 g/dl, and at least two of the following: plasma iron or ferritin lower than normal values; iron binding saturation lower than 18%, or total iron binding capacity above normal values.

Patients with hyposideraemic anaemia possibly linked to inflammatory disorders or to cancer were excluded from the present study. Patients requiring potentially interfering drugs, such as intravenous iron, ascorbic acid, antacid or H_2-blocking drugs were not allowed to take part in the trial.

Each selected patient was informed of the aim of the study, and gave her/his written consent. The study protocol was approved by the Ethics Committee of the 'Hopital Intercommunal' of Creteil (Paris, France).

Methods

In each participating centre, enrolled patients were to be treated for 60 days with either ITF 282 or iron sulfate, according to a randomisation list.

The 'double dummy' method was used to achieve treatment blindness:

- Patients treated with ITF 282 took 1 tablet of iron protein succinylate (60mg iron) and 1 placebo tablet of iron sulfate in the morning before lunch, and 1 tablet of ITF 282 in the evening before dinner.
- Patients treated with iron sulfate took 1 tablet of slow-release iron sulfate (105mg iron) and 1 placebo tablet of ITF 282 in the morning before lunch, and took 1 placebo tablet of ITF 282 in the evening before dinner.

Any other interfering drugs (see 'Patients' section above) were avoided during the study.

The patients' medical histories and present symptoms were registered before treatment initiation (baseline); clinical features and treatment tolerability were checked after 15 days (D15), after 30 days (D30), and at study termination (D60). Symptoms and signs associated with iron deficiency were evaluated at each visit: skin and mucosal pallor, asthenia, effort dyspnoea, effort angina, tiredness, dysphagia, and headache.

The symptom severity was recorded by the physician by means of a descriptive score allocated by the physician: absent (= 0), mild (= 1), moderate (= 2), intense (= 3), severe (= 4).

Monitoring of biological data for drug efficacy was performed at baseline, and then repeated at D15, D30 and D60. The following biological data were measured: erythrocytes, haematocrit, haemoglobin, mean corpuscular volume of erythrocytes (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), blood iron, ferritin, total iron binding capacity (TIBC), transferrin saturation, and reticulocytes.

At the beginning and end of treatment, some laboratory safety variables were checked: leucocytes with differential count, platelets, total bilirubin, blood urea, fasting blood sugar, creatinine,

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uric acid, total proteins, total cholesterol, triglycerides, aspartate aminotransferase (AST), alanine transferase (ALT), alkaline phosphatase, sodium, potassium and chloride.

Treatment tolerance was evaluated by the following:

- Collecting adverse events spontaneously reported by patients or observed by the investigator.
- Asking the patients nonleading questions, such as: 'did you experience anything unusual since the last visit?'
- Submitting a checklist to the patients for completion at each visit during treatment. The checklist included most recurrent symptoms usually observed during iron treatment, such as: nausea, regurgitations, vomiting, heartburn, gastric pain, gastric heaviness, meteorism, abdominal pain, diarrhoea and black stools. As some of these symptoms are common findings in pregnant women, a separate analysis on the checklist excluding pregnant women was included in the study protocol.

At the end of the trial, the physician's rating of the efficacy and tolerability was expressed as: 'nil', 'poor', 'fair', 'good' or 'very good'.

Statistical Analysis

Parametric data collected in this trial were analysed with analysis of variance (ANOVA) with multiple comparisons, or with Student's t-test for independent groups. Nonparametric statistics were performed with the Wilcoxon signed-rank test (to test the hypothesis of no difference between paired observations) and with the Mann-Whitney rank-sum test for independent samples. The data of the contingency tables were analysed with Yates' χ^2 test.

All statistical analyses were performed using the statistical package PCSM (Programme Conversationnel de Statistiques pour les Sciences et le Marketing) version 5. A p value < 0.05 was considered to be statistically significant.

Results

Patient Population and Study Course

174 patients were recruited in the 5 participating centres: 86 in the ITF 282 group, and 88 in the iron sulfate control group. These two groups were comparable with respect to all the monitored demographic and clinical characteristics. Almost all enrolled patients were female (170 of 174; 98%): one-third of them were pregnant. No significant differences were observed in demographic and clinical features, including concomitant diseases and treatments (table I).

After enrolment, 1 patient in the ITF 282 group and 1 patient in the control group asked to be dismissed from the trial (consent withdrawal); furthermore, before the first control visit, 2 patients in the reference group dropped out and one was hospitalised (for reasons not related to the trial).

During the trial, 1 patient in the ITF 282 group and 1 in the reference group withdrew because of poor tolerability; 2 other patients in both treatment groups withdrew for reasons not related to the treatment. At D15, D30 or D60, 18 patients in the ITF 282 group and 15 in the reference group had incomplete laboratory evaluations; 9 patients in the ITF 282 group and 5 in the reference group had incomplete clinical evaluations (symptom scores).

As the statistical package used could not perform ANOVA that included in the calculations cases with missing data, analysis of laboratory efficacy data was made on 64 patients treated with ITF 282 and 66 patients treated with iron sulfate.

The assessment of clinical symptom scores was made in 73 patients in the ITF 282 group and 76 patients in the reference group. However, final evaluations of drug efficacy and tolerability of all patients, if available, were included in this report.

Treatment Efficacy

The course of the laboratory efficacy variables during the treatment period demonstrated good therapeutic activity of both ITF 282 and iron sulfate.

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Table I. Patients' clinical characteristics

Cause of anaemia	ITF 282 (%) [n = 86]	Iron sulfate (%) [n = 88]	Statistic[a]
Pregnancy	34 (40)	23 (26)	
Puerperium	18 (21)	22 (25)	
Metrorrhagia/menorrhagia	11 (13)	17 (19)	
Gastrointestinal bleeding	1 (1)	1 (1)	
Surgical intervention	1 (1)	2 (2)	
Haematoma	1 (1)		
Haemorrhoids	1 (1)		
Diet – poor in iron		1 (1)	
Not defined	19 (22)	22 (25)	
Bleeding patients			
Genitourinary bleeding	17 (19.8)	25 (28.4)	
Gastrointestinal bleeding		1 (1.1)	NS
Other	5 (5.8)	5 (5.7)	
Patients with one or more concomitant diseases	32 (37)	36 (41)	NS
Patients with one or more associated treatments	35 (41)	45 (51)	NS
Concomitant diseases			
ORL	2 (2.3)	1 (1.1)	
Respiratory		1 (1.1)	
Cardiovascular	5 (5.8)	7 (8.0)	
Gastrointestinal	4 (4.7)	1 (1.1)	
Metabolic/endocrine	3 (3.5)		
Nervous system	1 (1.2)	2 (2.3)	
Psychiatric	3 (3.5)	6 (6.8)	

a Yates' χ^2.

Abbreviations: ITF 282 = iron protein succinylate; NS = nonsignificant; ORL = otorhinolaryngology.

The biological data (table II) indicate a recovery of iron metabolism (plasma iron, transferrin saturation rate) and improvement in anaemia (erythrocytes, haemoglobin, MCV) in both groups of patients. No significant difference in serum iron concentration was observed between the 2 treatment groups on admission, while a marked increase in circulating iron was observed following initiation of treatment that was both early and intense. Increases in serum iron levels of approximately 96 and 72% were observed with ITF 282 and iron sulfate, respectively, at final assessment, compared with baseline. The statistical analysis showed a time-related effect ($p < 0.0001$), with increases in serum iron between baseline and D15, and between D15 and D30, with no difference between treatments.

No significant changes in mean ferritin values were observed during the study period; ferritin levels remained stable regardless of the administered treatment, despite a wide variability both within and between subjects.

No statistically significant difference in red blood cell numbers was observed between the 2 treatment groups on admission. An increase in the number of erythrocytes was observed from the second assessment (D15), lasting throughout the whole study period, and reaching up to 16% with ITF 282 and 17% with iron sulfate at D60, in comparison with baseline. The statistical analysis showed a time-related effect, with a significant increase in red blood cell numbers between baseline and D15, between D15 and D30, and between D30 and D60, but no difference between treatments.

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Table II. Biological data (mean ± SD)

Parameter	Time	ITF 282 (n = 64)	Iron sulfate (n = 66)	Statistic[a]
Plasma iron (μg/dl)	Baseline	38.31 ± 15.2	38.3 ± 13.1	
	D15	56.41 ± 26.6	56.6 ± 25.4	A: NS
	D30	67.41 ± 39.0	64.0 ± 31.8	B: NS
	D60	75.1 ± 32.8	65.7 ± 27.6	C: $p < 0.0001$
Ferritin (μg/L)	Baseline	34.5 ± 82.2	33.1 ± 58.0	
	D15	35.6 ± 86.2	38.8 ± 33.1	A: NS
	D30	33.2 ± 57.0	36.1 ± 50.8	B: NS
	D60	33.5 ± 64.2	33.4 ± 30.6	C: NS
Transferrin saturation rate (%)	Baseline	9.4 ± 4.2	9.2 ± 3.9	
	D15	15.7 ± 9.5	18.7 ± 14.9	A: NS
	D30	19.5 ± 12.6	19.4 ± 10.5	B: NS
	D60	20.8 ± 10.1	19.0 ± 9.0	C: $p < 0.0001$
Erythrocytes ($\times 10^6/mm^3$)	Baseline	3.67 ± 0.52	3.65 ± 0.55	
	D15	3.90 ± 0.48	3.99 ± 0.50	A: NS
	D30	4.07 ± 0.56	4.18 ± 0.55	B: NS
	D60	4.26 ± 0.59	4.26 ± 0.55	C: $p < 0.0001$
Haemoglobin (g/dl)	Baseline	9.98 ± 0.86	9.92 ± 0.86	
	D15	10.72 ± 0.98	11.06 ± 0.90	A: NS
	D30	11.41 ± 1.19	11.73 ± 1.09	B: NS
	D60	12.08 ± 1.30	12.21 ± 1.20	C: $p < 0.0001$
MCV (μm^3)	Baseline	84.0 ± 8.9	83.2 ± 8.5	
	D15	84.7 ± 7.9	84.5 ± 7.0	A: NS
	D30	85.1 ± 7.2	85.5 ± 6.0	B: NS
	D60	86.0 ± 6.5	87.0 ± 5.1	C: $p < 0.0001$

a ANOVA. Sources of variation: A = interaction treatment-time; B = treatment; C = time.

Abbreviations: D15 = 15 days after treatment initiation; D30 = 30 days after treatment initiation; D60 = study termination; ITF 282 = iron protein succinylate; MCV = mean corpuscular volume of erythrocytes; NS = nonsignificant.

No significant difference in haemoglobin concentration was observed between the 2 treatment groups on admission; the circulating haemoglobin concentration increased markedly in both groups, up to normal values at D60. The 2 treatments provided a similar improvement in haemoglobin concentration, without any clinical or statistical difference between treatments: the statistical analysis showed a time-related effect ($p < 0.0001$) with a significant increase between baseline and D15, between D15 and D30, and between D30 and D60.

An increase in haematocrit was observed from the second assessment (D15) and lasting throughout the whole study period. The statistical analysis showed a time-related effect, with a significant increase in haematocrit values between baseline and D15, between D15 and D30, and between D30 and D60, but no difference between treatments.

Microcythemia was not systematically present in all patients' assessments. A moderate increase in both MCV and MCH was observed during the trial in both treatment groups. The statistical analysis showed a time-related effect, with a significant increase in MCV between baseline and D15, between D30 and D60, but no change between D15 and D30, and a significant increase in MCH between baseline and D15, between D15 and D30, and between D30 and D60. For both MCV and MCH, no difference was observed between treatments.

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A marked overall improvement in the clinical symptoms of anaemia (table III) was observed with both treatments, starting from D15 and lasting throughout the whole study period. No significant difference was observed between the 2 treatments.

At the end of the study, the investigators were asked to give an overall (biological and clinical) evaluation of drug effectiveness (table IV).

In most cases, the treatment with ITF 282 was regarded as excellent (75%), and only in a small

Table III. Anaemia symptom scores[a] (mean ± SD)

Parameter	Time	ITF 282 (n = 73)	Iron sulfate (n = 76)
Skin and mucosal paleness	Baseline	1.78 ± 0.88	1.72 ± 0.81
	D15	1.31 ± 0.83	1.09 ± 0.83
	D30	0.82 ± 0.75	0.75 ± 0.75
	D60	0.47 ± 0.60	0.45 ± 0.64
Asthenia	Baseline	2.16 ± 0.96	2.00 ± 0.94
	D15	1.48 ± 0.99	1.39 ± 0.85
	D30	0.93 ± 0.75	0.92 ± 0.90
	D60	0.63 ± 0.80	0.51 ± 0.70
Tiredness	Baseline	2.22 ± 0.92	2.01 ± 1.01
	D15	1.49 ± 0.88	1.39 ± 0.85
	D30	0.96 ± 0.72	1.00 ± 0.88
	D60	0.66 ± 0.82	0.66 ± 0.79

a Only the symptoms with baseline mean scores higher than 1.00 were included in this table.

Statistics: *Within treatment* – Wilcoxon signed-rank test between paired observations. D15, D30 and D60 in comparison with baseline: $p < 0.001$ for all comparisons. *Between treatments* – Mann-Whitney rank-sum test for independent samples. The analysis was performed on the decrease of symptom scores (baseline – D60) in the 2 groups: p = nonsignificant for all symptoms.

Abbreviations: D15 = 15 days after treatment initiation; D30 = 30 days after treatment initiation; D60 = study termination; ITF 282 = iron protein succinylate.

Table IV. Investigators' final evaluation of drug efficacy and tolerability

	ITF 282		Iron sulfate		Statistic[a]
Drug efficacy	**(n = 84)**		**(n = 83)**		
Excellent	26	75%	26	68%	NS
Good	37		30		
Moderate	18	21%	16	19%	
Poor	1	4%	8	13%	
None	2		3		
Drug tolerability	**(n = 84)**		**(n = 84)**		
Excellent	59	95.5%	50	90.5%	NS
Good	17		26		
Moderate	7	8.5%	6	7%	
Poor			2	2.5%	
None	1	1%			

a Yates' χ^2.

Abbreviations: ITF 282 = iron protein succinylate; NS = nonsignificant.

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minority of cases as insufficient (4%). Conversely, the treatment with iron sulfate was considered insufficient in a higher number of cases (13%). Nevertheless, no statistically significant differences were observed between the 2 treatments.

Drug Safety and Tolerability

As mentioned in the 'Patients and Methods' section, drug tolerability was evaluated in 2 ways: firstly, by collecting adverse events spontaneously reported by patients or elicited by the investigator with a nonleading question, and secondly by presenting a checklist to each patient for completion.

Reported adverse events: Overall, 8 patients in the ITF 282 group (9% of the patients evaluated for tolerability in this group) and 9 patients in the reference group (11%) spontaneously reported adverse events related to the treatment; most were related to the gastrointestinal tract (table V).

All spontaneously reported adverse effects but one were of mild to moderate severity, and disappeared spontaneously while continuing the treatment or shortly after treatment termination; in only 1 case (nausea, vomiting and diarrhoea with iron sulfate) was drug treatment withdrawn because of poor tolerability.

None of the reported reactions could be classified as severe or potentially harmful, according to current definitions.

Statistical analysis did not show any statistically significant difference in the incidence of spontaneously reported adverse effects between the 2 treatments.

Checklist: Answers given by patients on the checklist about gastrointestinal symptoms were analysed:

- including all evaluable patients, and then,
- excluding the pregnant women.

The number of patients who gave positive answers on the checklist during 1 of the 3 control visits (D15, D30, D60) is shown in table VI: fewer patients in the ITF 282 group gave at least 1 positive answer during 1 of the 3 check visits in comparison with the reference group.

The statistical analysis comparing the number of patients who gave at least one positive answer in the 2 groups showed a borderline significant difference ($p = 0.053$) in the total population, and a significant difference ($p < 0.05$) in the subpopulation that excluded pregnant women.

A further analysis was performed by separating 'gastric' symptoms from abdominal symptoms in the checklist. The results of this analysis showed

Table V. Reported adverse effects

	ITF 282 (n = 85)	Iron sulfate (n = 84)	Statistic[a]
No. of patients reporting adverse reactions	**8 (9%)**	**9 (11%)**	NS
Total no. of adverse reactions	**11**	**15**	NS
Gastrointestinal	8	14	
Constipation	3		
Diarrhoea	1	4	
Gastralgia	1	2	
Soft stool/black stool	2		
Anal pain		1	
Nausea/vomiting	1	4	
Abdominal discomfort		2	
Dyspepsia		1	
Other	3	1	
Skin rash		1	
Dizziness	1		
Asthenia	1		

a Yates' χ^2.

Abbreviations: ITF 282 = iron protein succinylate; NS = nonsignificant.

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Table VI. Tolerability checklist: percentage of patients giving at least 1 positive answer during the trial (at D15, D30 or D60)

	ITF 282	Iron sulfate	Statistic[a]
Total population	(n = 85)	(n = 84)	
Percentage of patients giving 1 or more positive answers	36.5	51	p = 0.053
For gastric symptoms	26	41	p < 0.05
For abdominal symptoms	29	38	NS
Nonpregnant patients	(n = 52)	(n = 64)	
Percentage of patients giving 1 or more positive answers	27	47	p < 0.05
For gastric symptoms	15	34	p < 0.05
For abdominal symptoms	23	34	NS

a Yates' χ^2.

Abbreviations: D15 = 15 days after treatment initiation; D30 = 30 days after treatment initiation; D60 = study termination; ITF 282 = iron protein succinylate; NS = nonsignificant.

Table VII. Tolerability checklist: percentage of patients giving positive answers for each symptom (at least once during the trial, at D15, D30 or D60)

Symptom	Total population			Nonpregnant patients		
	ITF 282 (n = 85)	iron sulfate (n = 84)	statistics[a]	ITF 282 (n = 52)	iron sulfate (n = 64)	statistics[a]
Nausea	14	24	NS	8	17	NS
Vomiting	7	5	NS	6	2	NS
Heartburn	9	14	NS	6	9	NS
Gastric pain	12	20	NS	11	19	NS
Gastric reflux	11	17	NS	2	9	NS
Epigastric pressure	14	19	NS	8	14	NS
Meteorism	18	24	NS	13	20	NS
Abdominal discomfort	22	27	NS	17	22	NS
Diarrhoea	14	23	NS	10	25	p < 0.05

a Yates' χ^2.

Abbreviations: D15 = 15 days after treatment initiation; D30 = 30 days after treatment initiation; D60 = study termination; ITF 282 = iron protein succinylate; NS = nonsignificant.

that, both in the total population and in pregnant patients, gastric symptoms were significantly less frequent ($p < 0.05$) in the ITF 282 group (table VI).

The results of tolerability assessment of iron treatment made by evaluating the positive answers to each item of this checklist are shown in table VII: by considering both total population and the subgroup of nonpregnant patients, the frequency of positive responses to each symptom (with the exception of vomiting) is lower for ITF 282 patients. The difference between treatments did not reach statistical significance, except for the symptom of diarrhoea in nonpregnant patients (10% in the ITF 282 group, 25% in the iron sulfate group; $p < 0.05$).

From a clinical point of view, all positive answers (but one) in the checklist were related to mild symptomatology not interfering with patients' quality of life nor with treatment institution; only 1 patient in the ITF 282 group, marking off on the checklist for nausea, vomiting, diarrhoea and abdominal discomfort, asked for drug withdrawal at D15.

At the end of the study, the investigators were asked to provide their overall evaluation of tolerability according to a 5-score rating (table IV).

Overall tolerability was regarded as excellent in 70% of cases with ITF 282, as opposed to 59.5% with iron sulfate; the statistical analysis did not show any difference between treatments.

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The analysis of laboratory safety data at study termination did not show any clinically or statistically significant difference in comparison with the baseline evaluation in both study groups.

Discussion

The clinical efficacy of iron sulfate in the treatment of iron deficiency is widely recognised, up to the point that iron sulfate is considered to be the reference drug for the treatment of sideropenic anaemia.[6]

The results of this trial are consistent with the known clinical profile of iron sulfate, and the findings on the clinical efficacy and tolerability of ITF 282 tend to confirm the recently published clinical results obtained with iron protein succinylate in larger populations of adult[4] or paediatric[5] anaemic patients.

In this comparative trial, 120mg iron given as ITF 282 proved to be as effective as 105mg iron as iron sulfate in correcting iron deficiency and increasing the most significant haematological variables.

As a direct consequence of the normalisation of the haematological picture obtained with both treatments, both ITF 282 and iron sulfate appear to effectively manage the clinical symptoms of iron deficiency and provide almost complete remission at the end of the treatment.

Adverse effects of iron treatment are usually gastrointestinal, and include heartburn, nausea, upper gastric discomfort, constipation and diarrhoea. In many instances, both the frequency and the severity of the symptoms tend to be exaggerated. Functional gastrointestinal symptoms are common in the absence of any medication; furthermore, they are greatly influenced by suggestion.

Nevertheless, in this trial a few patients spontaneously reported adverse effects in both treatment groups.

Patients given ITF 282 experienced greater gastrointestinal tolerability than those given iron sulfate: only 8 gastrointestinal adverse effects were reported by patients treated with iron protein succinylate, while 14 gastroenteric reactions were reported in the iron sulfate group.

Because of the biochemical properties of iron protein succinylate, iron is not released in the stomach, so it cannot exert its irritating action on the gastric mucosa. The present clinical trial results confirm the relevance of these properties. In fact, when patients were directly asked by means of a checklist about undesirable effects in their upper (gastric) and lower digestive tracts, a lower positive response rate for gastric symptoms was found, both in the total evaluable population and in non-pregnant patients; in both populations the difference with iron sulfate was statistically significant.

Conclusion

Correction of anaemia was observed during the study period in both treatment groups, with a statistically significant increasing trend in the haematological parameters assessed. No significant difference in efficacy between treatments was observed. Taking into consideration the difference between the 2 dosage forms, it can be concluded that according to the final results of this comparison trial, ITF 282 (120mg iron) proved to be as effective as the reference drug iron sulfate (105mg iron) in the oral treatment of iron deficiency anaemia.

Overall, ITF 282 seemed to be better tolerated than iron sulfate when gastrointestinal symptoms were taken into account.

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