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Original article

Efficacy and tolerability of a novel food supplement (Turbofer®) containing microencapsulated iron in liposomal form, in female iron deficiency anaemia

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Summary. *Introduction:* According to the WHO, iron deficiency and related iron deficiency anaemia (IDA) are the most prevalent nutritional disorders worldwide. Anaemia occurs in all age racial and ethnic groups. The goal of treatment of anaemia is to increase the amount of oxygen that blood can carry by raising the red blood cell count and/or Haemoglobin level and to treat the underlying cause of the anaemia. *Objectives:* To evaluate the efficacy of a novel food supplement, Turbofer®, formulated with microencapsulated iron in liposomal form, on the capacity to raise Haemoglobin and Haematocrit levels, the most important indicators of IDA in the study population. Tolerability was also evaluated. *Materials and methods:* 30 subjects, post-menopausal females, were enrolled in an open multi-center study. The subjects were administered Turbofer®, twice daily, independently by food intake, for eight weeks. The subjects included suffered from iron deficiency anaemia (Haemoglobin < 11,5 g/dl) and had already been treated with other iron supplements or drugs experiencing side effects. Laboratory tests were performed at visit 1 (baseline) and visit 2 (eight weeks after beginning treatment) together with registration of side effects (signs and symptoms) caused by previous and actual iron treatments by means of Gastrointestinal Sign and Symptoms Score. *Results:* The mean level of Haemoglobin at the beginning of the study was 10.65 ± 0.59 and 12.77 ± 1.08 at the end of the study. This increase is highly significant ($p<0.00001$). Also the value of Haematocrit showed a highly significant rise ($p<0.00001$) from 33.32 ± 2.78 to 38.95 ± 2.92 in the population study. There were no dropouts and Turbofer® was very well tolerated by all subjects, with a marked decrease of the gastrointestinal symptoms compared to previous iron treatments. *Conclusion:* 8 weeks of Turbofer® daily supplementation significantly rise the Haemoglobin and the Haematocrit level. Microencapsulated iron in liposomal form improves iron absorption leading to high bioavailability: as a result, Haemoglobin increase quickly and Turbofer® treatment does not cause the stomach upset and constipation associated with the use of other iron tablets, that is often responsible for the poor compliance.

Key words: iron deficiency anaemia, iron, Haemoglobin, Haematocrit

Introduction

The World Health Organization (WHO) considers iron deficiency the number one nutritional disorder in the world. As many as 80% of the world's population may be iron deficient, while 30% may have iron deficiency anaemia (IDA) (1, 2).

Anaemia, defined as a low blood Haemoglobin concentration, has been shown to be a public health problem that affects low-, middle- and high-income countries and has significant adverse health consequences, as well as adverse impacts on social and economic development (3).

Although the most reliable indicator of anaemia at the population level is blood Haemoglobin concentration, measurements of this concentration alone do not determine the cause of anaemia. Anaemia may result from a number of causes, with the most significant contributor being iron deficiency. Approximately 30%- 50% of cases of anaemia are considered to be due to iron deficiency (1-3).

Even though anaemia occurs in all ages, racial, and ethnic groups, women of childbearing age, pregnant women, preterm and low birth weight infants, older infants and toddlers, and teenage girls are at greatest risk of developing iron deficiency because they have the greatest need for iron (4-7).

The goal of treatment of IDA is to increase the amount of iron providing oral iron supplements to restore normal storage levels of iron, ferritin and to replenish Haemoglobin deficits. Consequently, the amount of oxygen that blood can carry increases by raising the red blood cell count and/or Haemoglobin level. Moreover, it is important to treat the underlying cause of the anaemia.

Tolerance of oral iron treatments is generally low and the frequency and severity of side effects, especially gastrointestinal (GI) (i.e., nausea, vomiting, dyspepsia, constipation, diarrhea, dark colored stools, abdominal distress) often leads to poor compliance (4).

Turbofer® is formulated with microencapsulated iron pyrophosphate in liposomal form, a water dispersible micronized source of iron that has been microencapsulated to enhance iron absorption and to reduce both GI side effects and undesirable organoleptic attributes. Turbofer® contains 14 mg iron in liposomal form, 80 mg vitamin C, 2.5 mcg vitamin B_{12} and 200 mcg folic acid in sticks with orodispersable granulate which directly dissolves in the mouth without the need for water and therefore suitable also for those who have trouble swallowing

An open multicentre clinical study has been conducted to demonstrate efficacy and tolerability of Turbofer®.

The study has been carried out in accordance with the ICH Topic E6 (R1)(CPMP/ICH/135/95) Guideline for Good Clinical Practice and the principles enunciated in the Declaration of Helsinki and the approval by an Institutional Ethics Committee.

Methods

30 subjects, post-menopausal female, 45-65 years of age, were enrolled according to the following inclusion criteria:

- iron deficiency anaemia (Haemoglobin <11.5 g/dl);
- subjects able to provide written informed consent;
- subjects already treated with other iron supplements or drugs that experienced side effects (not including allergy) related to iron administration.

Subjects were instructed to take the food supplement, twice daily, once in the morning and once in the evening, independently by food intake as Turbofer® has no interaction with food.

The treatment lasted eight weeks, with a week washout period from other possible treatments containing iron. Out of 30 patients, 20 remembered the previous iron therapy as in Table 1.

During the 2 visits, baseline (Visit 1) and end of study (Visit 2), eight weeks after the beginning of the treatment, laboratory tests were performed together

Table 1. Previous treatment of Iron

Patients	Iron salt
12	Iron Sulphate
5	Iron Gluconate
2	Iron Saccharate
1	Iron Polymaltose

with registration of side effects (signs and symptoms) caused by previous (Visit 1) and Turbofer® (Visit 2) iron treatments by means of Gastrointestinal Sign and Symptoms Score.

Results

Efficacy

The results of the study have been analyzed by descriptive statistics (means, standard deviations and percentages) using the Student t-test for paired samples with a significance value of p <0.05:

- **Haemoglobin**: almost all subjects show a highly relevant Haemoglobin increase (Fig. 1).
  The mean level at the beginning of the study was 10.65 ± 0.59 g/dl and 12.77 ± 1.08 g/dl at the end of the study, after 8 weeks of Turbofer® supplementation: this increase was highly significant (p<0.00001) and higher than the planned level of significance.
- **Haematocrit**: almost all subjects show a relevant Haematocrit increase (Fig. 2).
  The mean level % at the beginning of the study was 33.32 ± 2.78 and 38.95 ± 2.92 at the end of the study, after 8 weeks of Turbofer® supplementation: this increase was highly significant (p<0.00001) and higher than the planned level of significance.

Tolerability

Turbofer® was very well tolerated by all subjects: no patient discontinued the treatment due to side effects.

The following outcomes were registered:

- Turbofer® significantly (p<0.05) reduces the occurrence of the following symptoms: nausea, vomiting, bloating, abdominal cramps, early satiety, acid eructation/ heartburn, sickness, loss of appetite, retrosternal discomfort, epigastric or upper abdominal pain, constipation (Fig. 3).
  9 out of the 12 symptoms reported with previ-

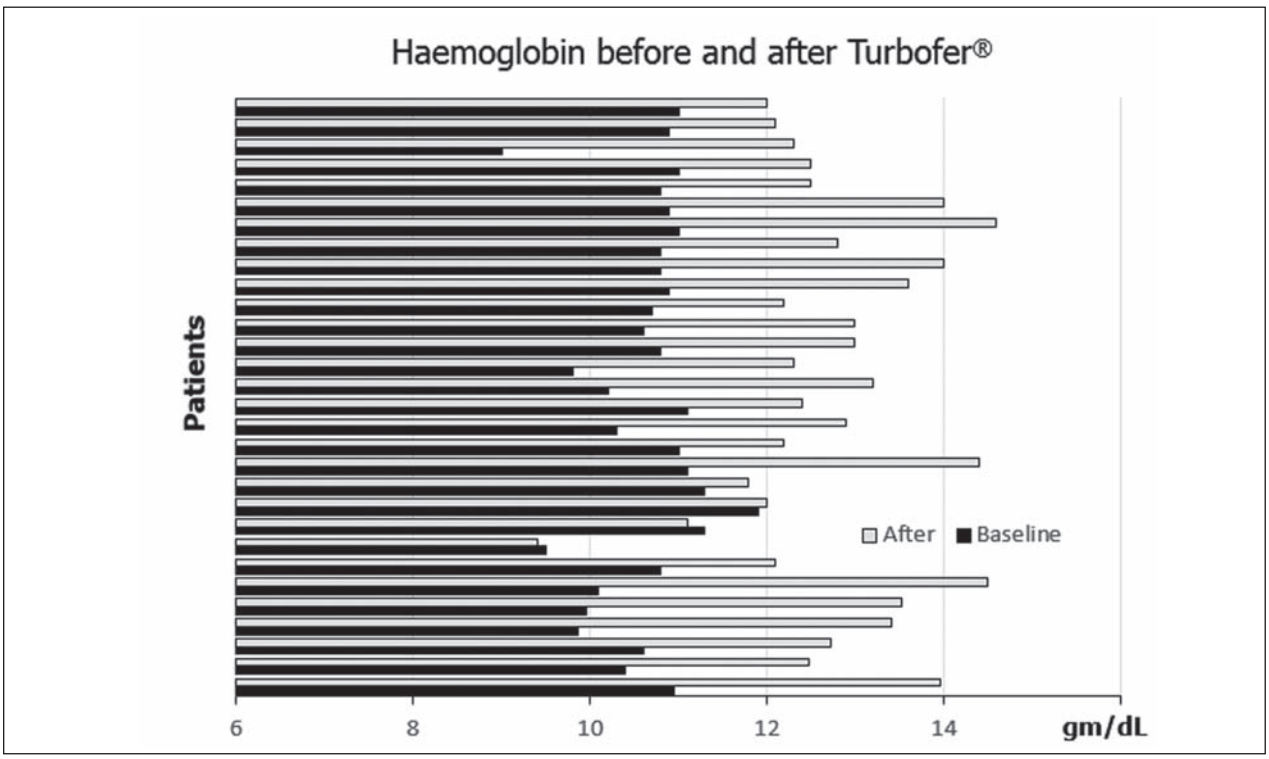

Figure 1. Haemoglobin measurements per patient at Baseline and After 8 weeks of Turbofer® supplementation (g/dL)

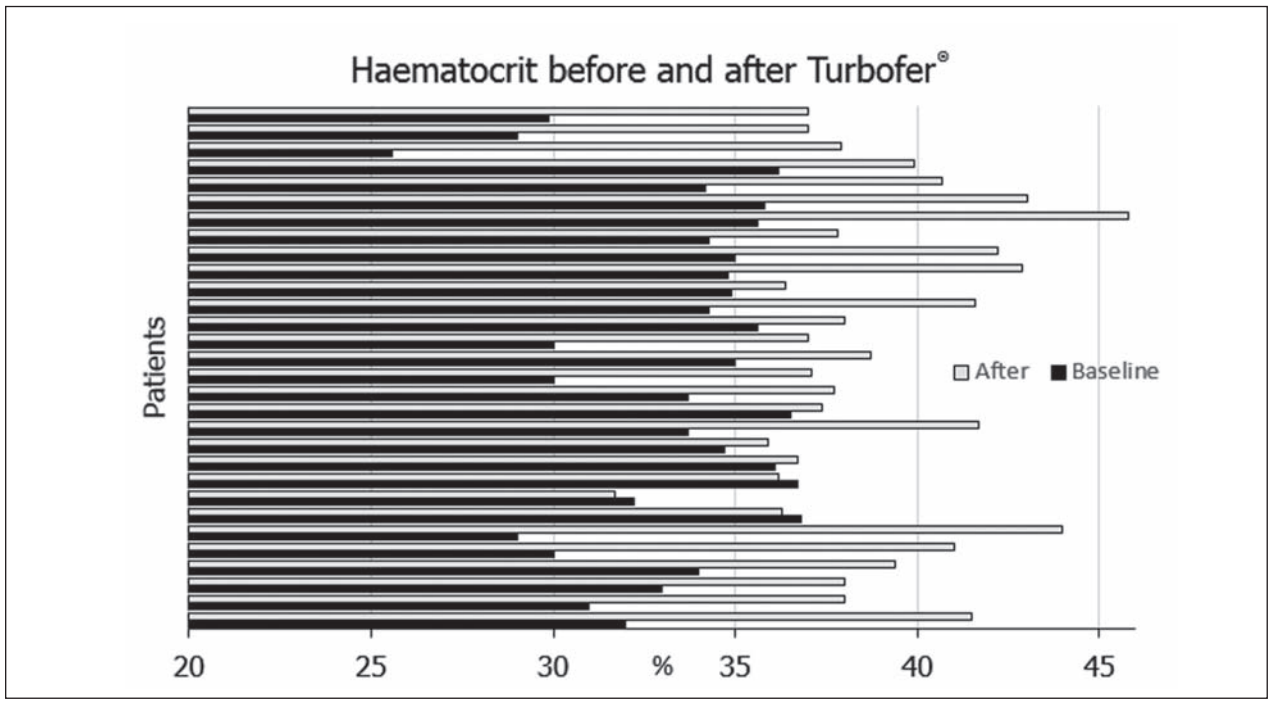

Figure 2. Haematocrit measurements per patient at Baseline and After 8 weeks of Turbofer® supplementation (%)

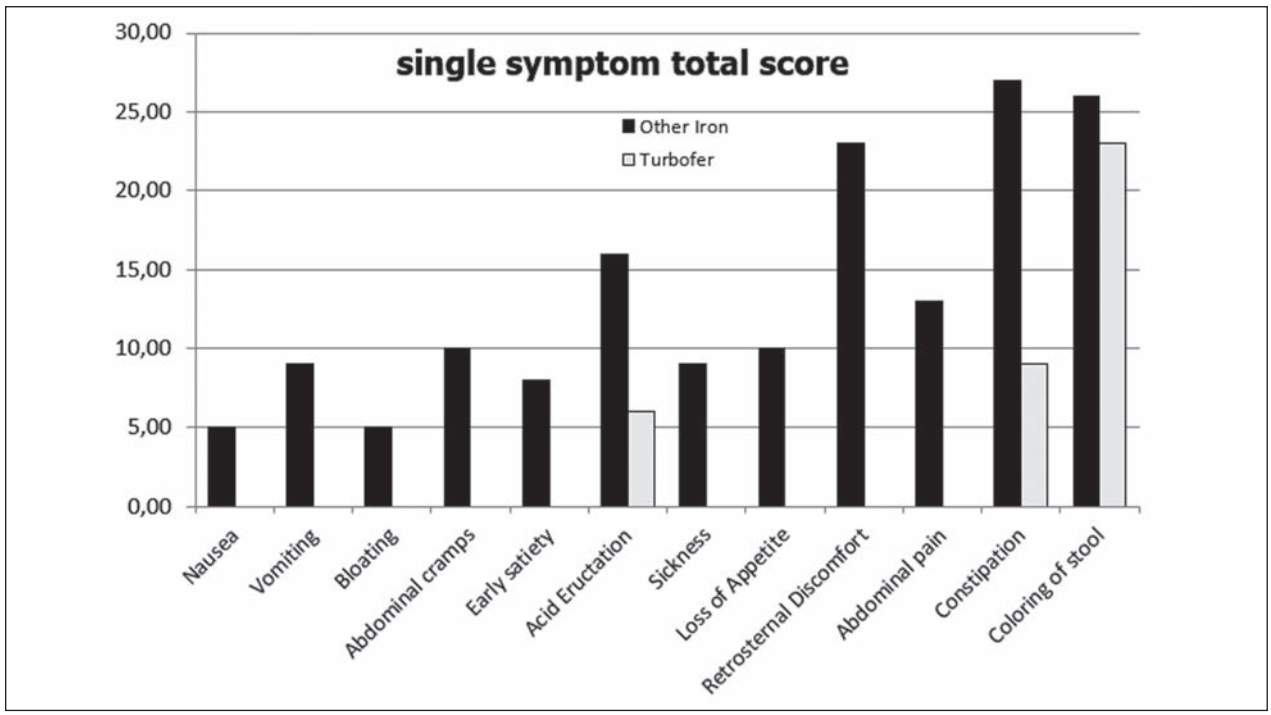

Figure 3. Outcomes for all single side effect total score from previous iron treatment to the end of 8 weeks of Turbofer® supplementation

ous iron therapy were not reported with Turbofer® supplementation.

- The Signs and Symptoms mean Average Total Score was 6.19 with previous iron treatment. After 8 weeks of Turbofer® the Signs and Symptoms mean Average Total Score was 1.46 (Fig. 4), significatively reduced.
- Ten patients reported "epigastric pain" with previous iron treatment, pain that did not occur with Turbofer® (Fig. 5). Noteworthy, epigastric pain is the most frequent side effect usually related to other iron treatments, leading to poor compliance and to discontinue treatment.

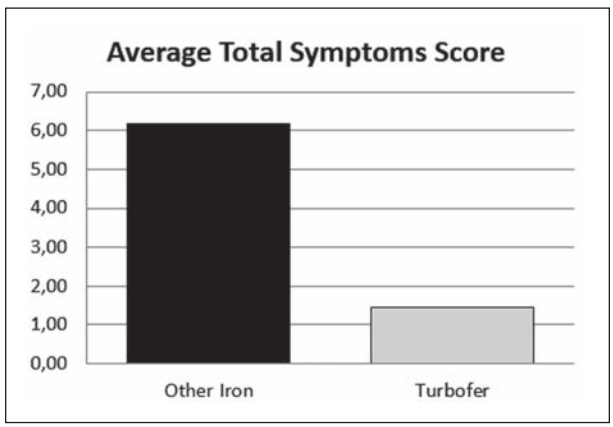

Figure 4. Signs and Symptoms Average Total Score per patient. From previous iron treatment to the end of 8 weeks of Turbofer® supplementation

The most frequent side effect recorded with Turbofer® was stool coloring that has been evaluated as mild in a 5-points Likert scale. This side effect has no impact on bowel function or on treatment efficacy.

Conclusion

In this study 8 weeks of Turbofer® daily supplementation significantly rises the Haemoglobin and the Haematocrit level in female iron deficiency anaemia.

Microencapsulated iron in liposomal form improves iron absorption leading to high bioavailability: as a result, Haemoglobin (a measure for circulating iron) increases significantly and quickly.

Turbofer® significantly reduces the occurrence of the gastrointestinal signs and symptoms caused by other iron treatments and registered at baseline. Noteworthy, epigastric pain, which is the side effect more

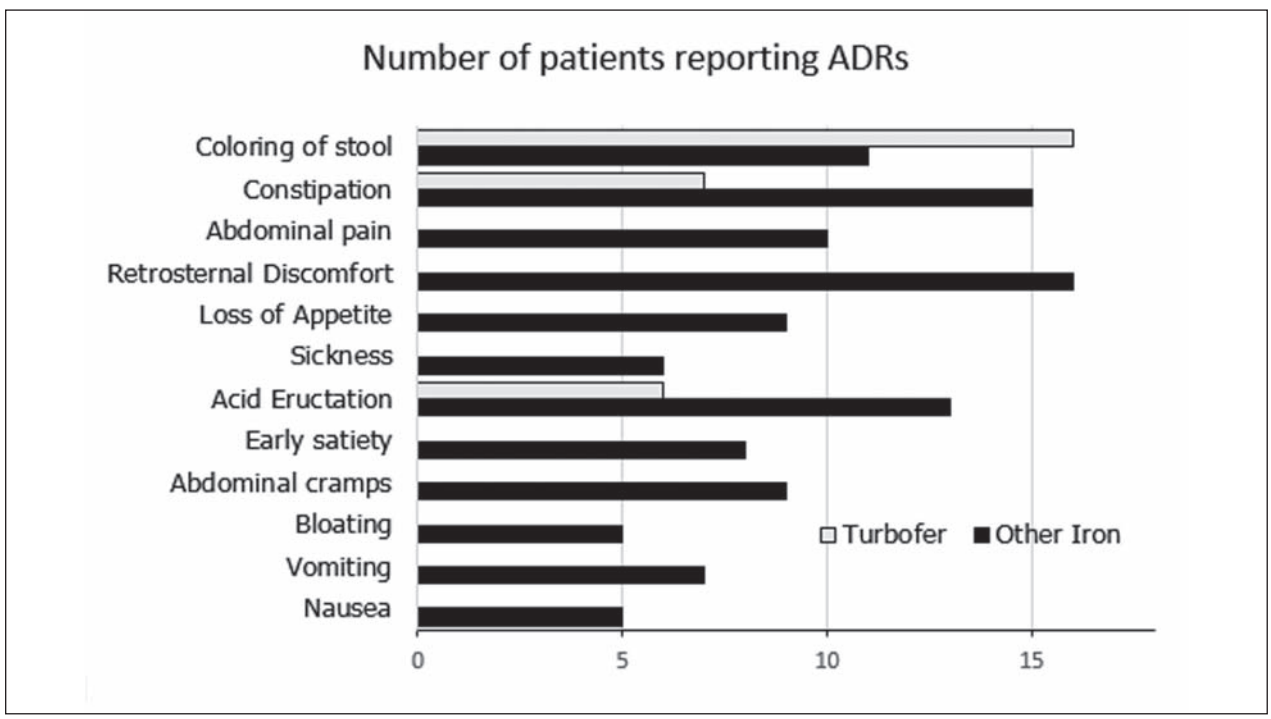

Figure 5. Number of patients per side effects at Baseline (previous iron treatment) and After 8 weeks of Turbofer® supplementation

frequent related to other iron treatments, disappeared during Turbofer® daily supplementation. The only side effect registered, coloring of stools, had no impact on bowel function.

Due to the Turbofer® high safety profile, no drop-out for treatment related reason was registered.

It is important to underline the fact that problems of adherence limit the effectiveness of iron supplementation programs with reports suggesting adherence rates of 40-60% in the treatment and prevention of iron deficiency anaemia (8).

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References

1. Worldwide prevalence of anaemia 1993-2005 - Geneva, World Health Organization, 2008.
2. Kassebaum NJ, Jasrasaria R, Naghavi M, Wulf SK, Johns N, Lozano R, Regan M, Weatherall D, Chou DP, Eisele TP, Flaxman SR, Pullan RL, Brooker SJ, Murray CJ. A systematic analysis of global anemia burden from 1990 to 2010. Blood 2013; Dec 2.
3. WHO. The global prevalence of anaemia in 2011. Geneva: World Health Organization; 2015.
4. Low M, Farrell A, Biggs BA, Pasricha SR. Effects of daily iron supplementation in primary-school-aged children: systematic review and meta-analysis of randomized controlled trials. CMAJ 2013; 185(17): E791-802.
5. Horowitz KM, Ingardia CJ, Borgida AF. J Womens Health (Larchmt). Anemia in pregnancy. Clin Lab Med 2013; 33 (2): 281-91.
6. Goddard AF, James MW, McIntyre AS, Scott BB; British Society of Gastroenterology. Guidelines for the management of iron deficiency anaemia. Gut 2011; 60 (10): 1309-16.
7. Viteri FE. Iron supplementation for the control of iron deficiency in populations at risk. Nutr Rev 1997; 55: 195-209.
8. United Nations Children's Fund. Preventing iron deficiency in women and children: technical consensus on key issues. New York: United Nations Children's Fund; 1998.

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