

## Pharmacoeconomic Efficacy Of Ferrous And Ferric Iron Supplements In The Territory Of The Republic Of Uzbekistan.

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### ABSTRACT

*Research objective: to conduct a clinical and economic analysis on the efficacy of ferrous and ferric iron supplements in the treatment of iron deficiency anemia in the outpatient settings of the Republic of Uzbekistan.*

*Material and research methods. The analysis was carried out in 3 outpatient settings of the Bukhara region of the Republic of Uzbekistan in the period from 2018 to 2020. The study included 220 patients with moderate iron deficiency anemia (Hb 70-90 g/l). Pregnant women were excluded from the study. As an investigational sample the most common ferrous and ferric iron supplements in the form of tablets and capsules were selected. For assessment of the clinical efficacy, we studied the dynamics of decrease of general anemia syndrome manifestations, the dynamics of decrease of sideropenic syndrome manifestations, Hb level increase and the severity of adverse reactions. For determination of the economic expediency of supplements administration, the cost-effectiveness ratio was calculated.*

*Results and discussion. The analysis of the dynamics of clinical and laboratory parameters showed that the ferrous IS administration resulted in more pronounced Hb level increase in blood compared to ferric IS. The study of the dynamics of general anemia syndrome manifestations using the VAS showed that the ferric IS administration contributed to a significantly more pronounced dynamics of symptoms. It was revealed that the ferric IS provides both sufficiently high Hb level increase and high tolerability for patients.*

*Conclusion. The analysis of the ferrous and ferric IS on the territory of the Republic of Uzbekistan showed that both supplements have approximately same degree of clinical and laboratory efficacy. Along with this, ferrous iron supplement demonstrated a higher Hb level increase in a month of therapy due to the high iron bioavailability. The market analysis established that ferrous iron supplement was less expensive compared to ferric one. However, ferric iron supplements had a significant advantage defining its efficacy, expressed by severity of*

*side effects. This fact clears expenses and proves their relevance in the market of iron supplements.*

*Key-words: ferrous iron supplement, ferric iron supplement, Hb level, iron deficiency anemia, clinical and laboratory efficacy.*

## **INTRODUCTION**

It is considered that a replacement therapy with iron supplements (IS) used in the treatment of iron deficiency anemia (IDA) is a complex and multifaceted direction. It requires the physician to know many important factors which should be considered when assigning and monitoring the treatment to achieve optimal clinical effect [1,2]. For many years, the IDA therapy included the use of ferrous ( $\text{Fe}^{2+}$ ) iron supplements, mainly in the form of ferrous sulfate. Ferrous sulfate supplements were the “gold standard” of the IDA treatment, as they had fast absorption [3,4,5]. For this reason, most of the IS are based on this active substance. Ferrous gluconate, ferrous chloride and ferrous fumarate have an estimated absorption rate of 10-15 % [6,7].

However, the world experience in the treatment of IDA showed that the use of ferrous iron supplements 5–8 mg/kg per day in most patients leads to the development of side effects. Therefore, this fact may serve as a basis for drug discontinuation, dose reduction and treatment break [5]. For this reason, today worldwide there is a tendency to replace ferrous ( $\text{Fe}^{2+}$ ) iron supplements with less toxic ferric ( $\text{Fe}^{3+}$ ) iron supplements [7]. The creation of new supplements based on ferric hydroxide polymaltose forced specialists to change the tactics and treatment course for IDA.

The results of pharmacoeconomic studies allow to obtain the necessary information on the use of these drugs in the treatment of certain diseases, which contribute to achieve the optimal clinical effect with minimum costs. For this reason, physicians should assess the benefits of drugs not only from a material point of view, but also from the point of view of the quality of treatment, rapid improvement of the patient's quality of life and the absence of complications [8,9,10]. Physicians are obliged to know the economic component of the issue, and explain to patients the benefits of treating IDA using certain IS.

## **RESEARCH OBJECTIVE**

Research objective is to conduct a clinical and economic analysis on the efficacy of ferrous and ferric IS in the treatment of IDA in outpatient settings of the Republic of Uzbekistan.

## **MATERIAL AND RESEARCH METHODS**

The investigation was carried out in 3 outpatient settings of the Bukhara region of the Republic of Uzbekistan in the period from 2018 to 2020. The study included 220 patients with moderate IDA (Hb 70-90 g/l). There were 175 women and 45 men, aged 18 to 48 years. Pregnant women were excluded from the study. In most cases, alimentary anemia and inflammatory diseases of the gastrointestinal tract were the etiological factors in the development of IDA.

For investigational IS we selected the most common used drugs in the region's drug stores – ferrous and ferric iron supplements in the form of tablets and capsules. Depending on the IS intake, the patients were divided into 2 groups: the group 1 included 120 patients who

took ferrous IS; the group 2 included 100 patients who took ferric IS. In both cases, the patients took IS during 1 month with a regimen of 1 capsule 2 times a day.

For assessment of the clinical efficacy, we studied the following criteria for the treatment of IDA: the dynamics of decrease of general anemia syndrome (GAS) manifestations, the dynamics of decrease of sideropenic syndrome (SPS) manifestations, increase in Hb level and the severity of adverse reactions when taking IS. For assessment of the dynamics of GAS and the severity of adverse reactions, we used a modified visual analogue scale (VAS), according to which the patients evaluated their own condition on a 10-point scale. To assess the SPS we applied a modified scale for assessing objective signs on a 14-point scale.

Besides, to determine the economic expediency of supplements, the cost-effectiveness ratio was calculated using the formula:

$$CER = DC + IC / Ef$$

where CER is the cost-effectiveness ratio (shows the costs per unit of efficacy); DC - direct costs; IC - indirect costs; Ef is the efficacy of treatment.

Statistical analysis was carried out using standard office programs Microsoft Excel 2018. In addition, we applied methods of medical variation statistics, which included the calculation of indicators of the arithmetic mean of the studied indicator (M) and standard deviation ( $\sigma$ ) for relative values (frequency, %) and standard error of the mean (m). The statistical significance of the obtained data when comparing the mean values was determined by the Student's test (t) calculating the error probability (P). The distribution (by the kurtosis criterion) and the equality of the general variances (F-test) were checked. The confidence level  $P < 0.05$  was taken as statistically significant changes.

## RESULTS AND DISCUSSION

The analysis of the dynamics of clinical and laboratory parameters showed that the ferrous IS administration resulted in more pronounced Hb level increase in blood compared to ferric IS ( $P < 0.05$ ). At the same time, a proven and significant increase in Hb level after a month of treatment was established in both survey groups (Table 1).

The study of the dynamics of GAS manifestations by the method of the subjective assessment of the patients' state using the VAS showed that ferric IS administration contributed to a significantly more pronounced dynamics of symptoms ( $P < 0.05$ ). Evaluation of the IDA symptoms showed that there were no significant differences in the dynamics of SPS in both groups. Using both drugs we noted a similar positive dynamics of relief. The most pronounced and statistically significant differences were presented by the severity of side effects when administering IS. The Table 1 shows that the severity of side effects of ferric IS was significantly lower compared to ferrous IS.

**Table 1**  
**Clinical and laboratory dynamics in patients of groups 1 and 2**

Indicator		Group 1 Ferrous IS	Group 2 Ferric IS
Hb (g/l)	Initially	83,4±11,1	85,1±8,3

	After treatment	114,2±4,5*	111,3±7,6*
	Dynamics	26,1±9,4^	25,6±6,7
GAS (points)	Initially	5,8±0,7	5,9±1,4
	After treatment	3,6±0,7*	3,6±0,7*
	Dynamics	2,05±0,1^	2,35±0,15
SPS (points)	Initially	8,9±2,1	8,7±0,7
	After treatment	4,8±3,5*	4,9±1,4*
	Dynamics	3,65±0,1	3,8±0,04
Side effects (points)		6,9±0,3^	4,2±1,1

Note: \* - differences in comparison with the initial indicators are statistically significant (P <0.05); ^ - differences in comparison with similar indicators of group 2 are statistically significant (P <0.05);

Comparison of ferrous and ferric IS in the form of tablets showed that the content of elemental iron in 1 tablet of both groups supplements in all cases was equal and amounted 100 mg. The prices of supplements are presented equivalent to US dollars. For this reason, the cost of one ferrous IS tablet averaged \$ 0.123±0.021, while the cost of 1 ferric IS tablet was \$ 0.183±0.035. At the same time, the dosage regimen, considering the IDA severity, was the same for both supplements. This fact led to the consumption of a large actual dose of elemental iron by the patient when taking the ferric IS. If to calculate the dosage according to the regimen: 1 tablet or capsule 2 times a day, then ferrous IS administration during a month-therapy was more economical - \$ 7.4 ± 1.23, while ferric IS costed \$ 11.2±1.16 (Table 2).

**Table 2**

Pharmacoeconomic indicators of ferrous and ferric IS for 2020  
(considering the cheapest price of IS)

Name	Ferrous IS	Ferric IS
Dosage form	Tablets	Tablets
Active substance	Ferrous sulfate	Ferric hydroxide polymaltose
Content of Fe (mg)	100	100
Price per 1 unit (\$)	0,123±0,021	0,183±0,035
Consumption of the supplement (1 patient per month)	60 tablets	60 tablets
IS cost for a month of treatment (\$)	7,4±1,23	11,2±1,16
Active dose of elemental Fe received by the patient for a month of therapy (mg)	6000	6000

The Fig. 1 shows the results of calculating the cost-effectiveness ratio (CER) according to the main clinical criterion for the treatment of IDA, which is Hb level increase. The graphs show that the use of ferrous IS was more economical in 39%, than the use of ferric IS.

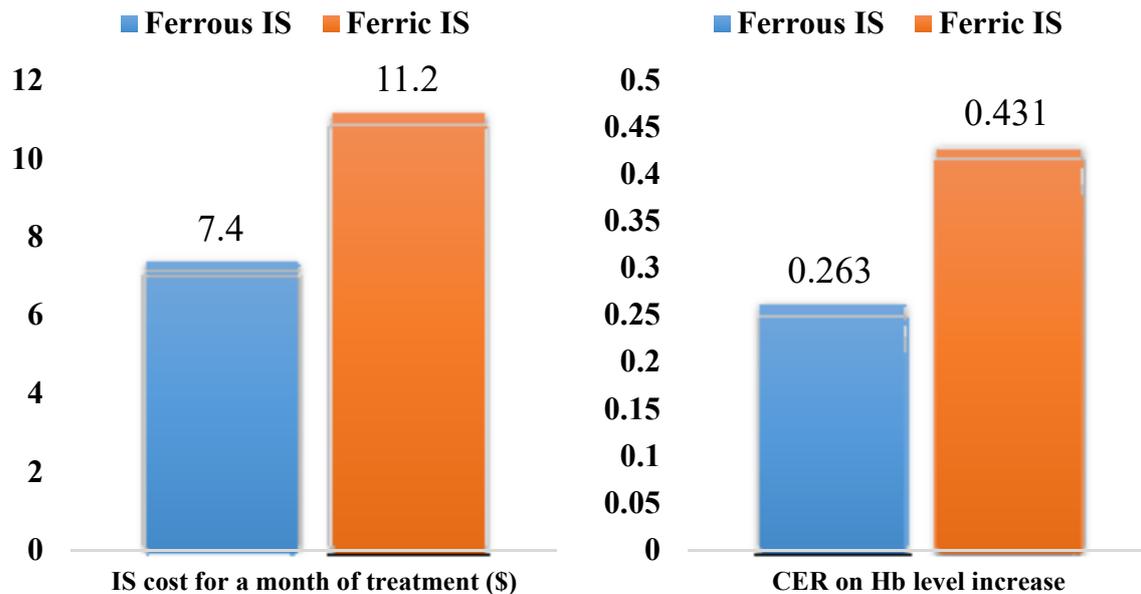


Fig. 1. "Cost-effectiveness" ratio of ferrous and ferric IS

Despite the significant difference in CER, it should be noted that this ratio was calculated considering only the clinical criterion for the Hb level increase. If to take into consideration other important aspects of the ferrotherapy efficacy, it becomes clear that the ferric IS provides both sufficiently high Hb level increase and high tolerability for patients. This is due to the fact that the severity of side effects is 20% lower than while administration of ferrous IS.

## CONCLUSION

Summarizing above stated, we may conclude that:

- the pharmaco-economic comparative analysis of the most common ferrous and ferric IS on the territory of the Republic of Uzbekistan showed that both supplements have approximately same degree of clinical and laboratory efficacy, despite the fact that ferrous iron supplement demonstrated a higher Hb level increase in a month of therapy due to the high iron bioavailability;
- ferrous iron supplement is less expensive compared to ferric one. However, ferric iron supplements have a significant advantage defining its efficacy, expressed by severity of side effects. This fact clears expenses and proves their relevance in the market of iron supplements today.

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