

METHOD FOR ASSESSING THE PHARMACOECONOMIC EFFICIENCY OF IRON PREPARATIONS

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Annotation

The results of pharmaco-economic analyzes indicate the need to use those iron preparations in the treatment of IDA, allowing the patient to receive optimal treatment. In this regard, doctors should be aware of the benefits of iron preparations, not only from a material point of view, but also in terms of the quality of treatment, a rapid improvement in the patient's quality of life and the absence of complications. Doctors are obliged to fully understand the economic component of the issue and explain to patients the benefits of treating IDA with certain iron preparations.

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Relevance. According to the WHO, about 1 billion people on earth are iron deficient. Even in the developed countries of Europe and North America, 7.5-11% of all women of childbearing age suffer from iron deficiency anemia, and 20-25% have latent tissue iron deficiency. A significantly higher frequency of iron deficiency anemias is also observed in Uzbekistan. This is due to a number of social, medical and household reasons. [1,2].

Purpose of the study. Comparative analysis of the pharmaco-economic efficiency of iron preparations (IPs) Fe (II) and Fe (III) on the example of Gynotardiferon and Ferrum Lek in an outpatient setting.

Materials and methods. The study included 40 patients with IDA of moderate severity (hemoglobin level 90-70 g / l). The age of the patients was from 18 to 40 years, 36 women and 4 men. All patients underwent outpatient treatment. Among 40 patients, 22 took Ferrum Lek, 18 Gino-tardiferon. Assessment of general anemic syndrome (GAS). To assess the clinical efficacy of iron therapy, the study used our own modification of the commonly used visual analogue scale (VAS) to determine the intensity of subjective manifestations of general anemic syndrome (see figure 1).

Evaluate the presence and severity of the following symptoms: weakness, increased fatigue, dizziness, headaches (more often in the evening), shortness of breath on exertion, palpitations, syncope, flashing "flies" in front of the eyes with a low level of blood pressure, often there is a moderate increase temperature, often drowsiness during the day and poor falling asleep at night, irritability, nervousness, conflict, tearfulness, loss of memory and attention, loss of appetite

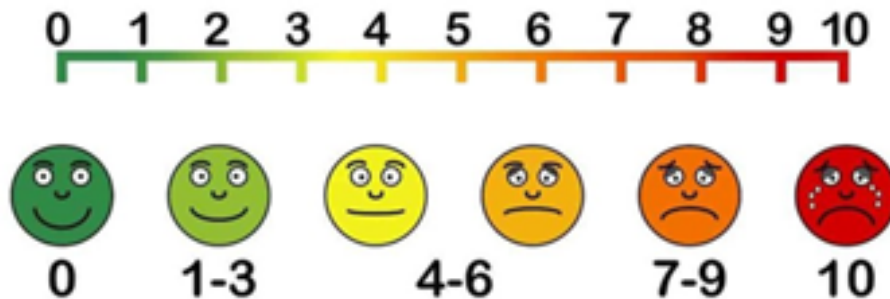


Figure 2.1. Visual analogue scale for assessing general anemic syndrome.

The subjective symptoms of GAS mainly included manifestations of asthenic syndrome: weakness, increased fatigue, dizziness, headaches (more often in the evening), shortness of breath on exertion, palpitations, syncope, flashing "flies" in front of the eyes at a low level arterial pressure, there is often a moderate increase in temperature, often drowsiness during the day and poor sleep at night, irritability, nervousness, conflict, tearfulness, decreased memory and attention, impaired appetite. The advantage of this method was that it is suitable for use by both adults and children. During treatment, patients were provided with questionnaires, in which they were asked to determine their subjective assessment of the severity of these symptoms. The questionnaire contained a scoring system with 6 grades of severity. According to the test conditions, the patient had to assess his condition with an exact figure.

One of the main criteria for the effectiveness of IPs is the severity of side effects during their intake. For a subjective assessment of the severity of side effects from the use of iron preparations, patients were also provided with a similar questionnaire based on the VAS principle (see fig. 2). The questionnaire included the following symptoms: nausea, vomiting, diarrhea, constipation, abdominal pain, heartburn, dark stools, darkening of the gums and tooth enamel, and headache.

Evaluate the presence and severity of the following symptoms after starting iron supplementation: nausea, vomiting, diarrhea, constipation, abdominal pain, heartburn, dark stools, darkening of the gums and tooth enamel, headache

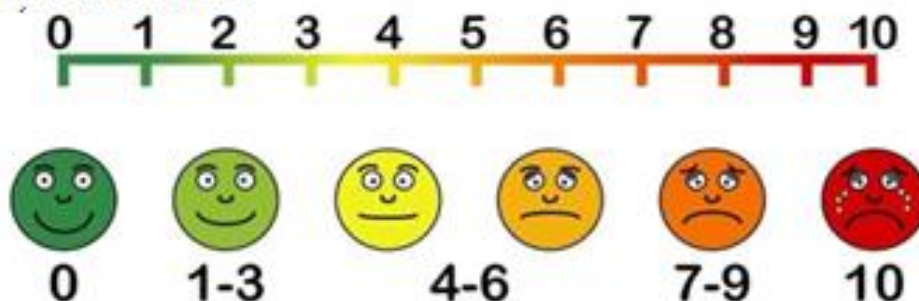


Figure 2. Visual-analogue scale for assessing side effects when taking iron supplements.

Assessment of the objective manifestations of sideropenic syndrome (SPS). To assess the sideropenic syndrome in patients, a specially developed scale was also used to assess its main objective manifestations (see Table 1).

Table 1. A scale for assessing the objective manifestations of sideropenic syndrome.

1	Changes in the skin and its appendages (dryness, peeling, slight cracking, pallor). Hair is dull, brittle, "split", turns gray early, falls out intensely, changes in nails: thinning, brittleness, transverse blackening, sometimes spoon-like concavity (koilonychia).	0	1	2
2	Changes in the mucous membranes (glossitis with atrophy of the papillae, cracks in the corners of the mouth, angular stomatitis).	0	1	2
3	Changes in the gastrointestinal tract (atrophic gastritis, mucus atrophy of the esophagus, dysphagia). Difficulty swallowing dry and solid food.	0	1	2
4	The muscular system. Myasthenia gravis (due to weakening of the sphincters, an imperative urge to urinate appears, the inability to hold urine while laughing, coughing, sometimes bedwetting in girls). The consequence of myasthenia gravis can be miscarriage, complications during pregnancy and childbirth (decreased contractility of the myometrium).	0	1	2
5	Addiction to unusual smells.	0	1	2
6	Perversion of taste. It is expressed in the desire to eat something slightly edible.	0	1	2
7	Tendency to tachycardia, hypotension.	0	1	2

To assess the sideropenic syndrome after examining the patient and assessing each symptom, the total score was calculated.

The results of the study were evaluated using the method for small samples [2]. Partial calculation of statistical characteristics was carried out using the XL program. Differences in the groups were assessed by Student's t-test and considered significant at $p < 0,05$.

Research results. Table 2. demonstrates the pharmacoeconomic characteristics of the studied IPs. In the Ferrum Lek preparation, the content of elemental iron (III) polymaltose was 100 mg. At the same time, the cost of 1 Ferrum Leka tablet was 2100 soums. If the calculation is carried out according to the reception scheme: 1 tablet 2 times a day, then the costs for 1 month of therapy were equal to 126,000 soums. If we analyze the economic characteristics of a representative of iron preparations Fe (II) Gynotardiferon with iron sulfate as an active ingredient and folic acid as an excipient, then at the cost of 1 tablet of 1800 soums, the cost of a monthly course of ferrotherapy was 108,000 soums. It should be noted that in less expensive representatives of the group, the content of elemental iron in 1 tablet is equal to 100 mg, while in this preparation it is equal to 80 mg.

Table 2. Pharmacoeconomic analysis of solid oral iron preparations based on the average cost of drugs in the Republic of Uzbekistan.

Name	Ferrum Lek	Gyno-tardiferon
Dosage form	Tablets	Tablets
Active substance	Iron (III) hydroxide polymaltose	Iron sulfate
Fe content	100 mg	80 mg
Additional component		Folic acid 350 mkg
Price for 1 unit (sum)	2100	1800
Consumption of the drug for 1 patient per month	60 tablets	60 tablets
The cost of iron supplements for 1 month of treatment (sum)	126000	108000

When analyzing the pharmacoeconomic efficiency in terms of the increase in Hb levels, the total cost of treatment during a month's course of ferrotherapy, which included the cost of IPs itself, was taken as a basis. Analysis of the increase in the level of Hb hemoglobin in the groups of patients showed that a more pronounced dynamics within 1 month of therapy was achieved in the groups taking the drug

Gyno-tardiferon. The calculation of the CER index, where the level of Hb growth was taken as the indicator of "efficiency", showed that the use of this drug Fe (II) was more effective.

Table 3. Analysis of pharmacoeconomic efficiency in terms of the increase in hemoglobin levels.

The drug and n patients	Original Hb level (g / l)	Hb level at the end of treatment (g / l)	Hb gain (g / l)	CER
	M±m	M±m	M±m	
Ferrum Lek n=72	85,1±6,36	106,6±11,3*	21,5±4,9	5860
Gyno-tardiferon n=32	85,4±15,5	108,1±16,9*	22,7±1,4	4757

Note: * - differences compared with the initial indicators are statistically significant (P <0.05);

The severity of GAS, its dynamics in patients and the calculation of the cost-effectiveness indicator based on this treatment criterion are presented in Table 4.5. The table demonstrates that almost all patients before treatment had an average GAS severity in the range of 5-7 points on the VAS, which corresponded to the Hb level with a moderate IDA. Repeated questioning showed that all patients showed a statistically significant decrease in GAS intensity (P <0.05). A more significant dynamics of subjective symptoms was determined in the group of patients receiving Ferrum Lek preparations (a decrease in the severity of symptoms by more than 2 points). The effectiveness of other IPs Fe (II) was less pronounced.

The calculation of CER by the indicator of the dynamics of GAS also showed that the use of Ferrum Lek turned out to be more effective.

Table 4. Analysis of pharmacoeconomic efficiency by the dynamics of GAS.

The drug and n patients	GAS before treatment (points according to VAS)	After GAS treatment (VAS score)	Dynamics	CER
	M±m	M±m	M±m	
Ferrum Lek n=22	5,9±1,4	3,6±0,7*	2,3±0,7	54782
Gyno-tardiferon n=18	6,1±2,1	4,4±2,1*	1,7±0,3	63529

Note: * - differences compared with the initial indicators are statistically significant (P <0.05);

Table 5. Analysis of pharmacoeconomic efficiency on the dynamics of SPS.

The drug and n patients	SPS before treatment (points)	SPS after treatment (points)	Dynamics	CER
	M±m	M±m	M±m	
Ferrum Lek n=22	8,7±0,7	4,9±1,4*	3,8±0,7	33157
Gyno-tardiferon n=18	9,1±0,7	5±2,1*	4,1±1,4	26341

Note: * - the differences compared to the initial indicators are statistically significant (P <0.05);

The severity of SPS, its dynamics in patients and the calculation of the "cost-effectiveness" indicator based on this criterion of treatment are presented in Table 5. The table shows that almost all patients before treatment had an average severity of SPS in the range of 7-9 points by 14 points scale, which corresponded to the Hb level and the degree of IDA. Repeated questionnaires showed that all patients showed a statistically significant decrease in the intensity of the SPS (P <0.05). A more significant dynamics of subjective symptoms was determined in the group of patients receiving IPs Fe (II).

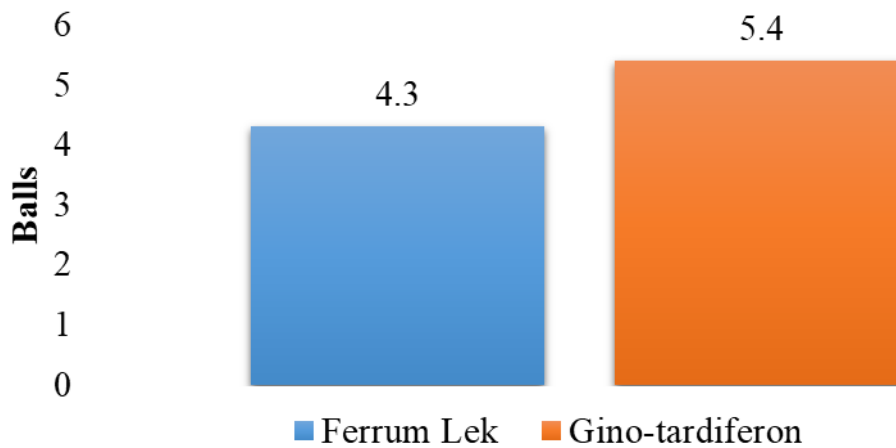


Figure 3. The severity of side effects of iron preparations.

Figure 3 shows a comparative characteristic of the severity of side effects of the considered IPs. It can be seen from the graph that Ferrum-Lek had a significantly lower severity of side effects.

Assessment of the economic feasibility of using drugs by the cost-effectiveness ratio according to the formula:

$$\text{CER} = \text{DC} + \text{IC} / \text{Ef}$$

showed that, in general, the use of a representative of IPs Fe (III) Ferrum Lek showed more optimal overall values of effectiveness in the treatment of IDA.

Conclusion. Thus, the results of the study of the clinical and economic analysis of IPs for oral administration in the form of solid dosage forms showed that all patients received a favorable clinical effect while taking IPs. A significant decrease or disappearance of signs of anemia and sideropenia along with an increase or normalization of the hemoglobin level was obtained both in patients taking IPs Fe (III) and IPs based on Fe (II). However, the most important in this study were the magnitude and rate of increase in the level of hemoglobin when using these IPS. In this aspect, it was shown that the intake of Fe (II) in the form of iron sulfate was more effective.

It should be noted that in the case of tableted IPs, the increase in Hb when taking the drug was significantly higher in Fe (II). At the same time, attention is drawn to the fact that there was a superiority both in the magnitude of the increase in Hb and in its rate. The more pronounced effectiveness of preparations of iron (II) salts in comparison with preparations of iron-containing complexes, apparently, is due to different bioavailability. This fact has been repeatedly confirmed by the results of studies by foreign researchers.

Another objective clinical criterion of the effectiveness of IPs in the treatment of IDA in the study was the severity of the sideropenic syndrome. Its severity was evaluated in points. The results of the assessment in dynamics showed that despite the fact that all patients showed positive dynamics of symptoms during therapy, when using iron Fe (II), the dynamics of relief of symptoms was significantly more significant.

If we evaluate the economic efficiency of therapy with IPS against the background of only objective indicators, it becomes clear that therapy with IPs Fe (II) is much more effective and cheaper than therapy with IPs Fe (III). Analysis of the relative cost of treatment, taking into account the average prices of IPS for the country at the moment, has shown that even therapy with the most expensive IPS Fe (II) is cheaper for a patient in comparison with the therapy with the cheapest IPs Fe (III) by an average of 20-25 thousand sums.

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