The Problem of Correction of Asthenic Syndrome With Iron Deficiency Anemia

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Abstract: *To evaluate the effect of iron preparations (IP) on the level of somatic health and AS in women of fertile age with iron deficiency anemia (IDA). Were examined 30 women with a diagnosis of IDA in age from 18 to 49 years, before and after the course ferrotherapy. To assess the exchange of iron was performed a general and biochemical blood test. To determine and establish the severity of asthenic syndrome (AS) were used the asthenic state scale (ASC) and MFI-20. A quantitative analysis of the level of somatic health was carried out by the express-system of G.L. Apanasenko. The operability was determined using a treadmill-test using a standard procedure. The received data was processed using the «Microsoft2010» and «SPSS24» application software. After the course of IP all patients had an increase in iron metabolism, while 41.6% of women had complaints of weakness and decreased working capacity. According to the results of ASC and MFI-20 was diagnosed the preservation of AS after the course of ferrotherapy in more than 50% of cases, half of the patients had hemoglobin normalization. The analysis of working capacity and level of somatic health in dynamics showed improvement of all investigated parameters after a course of substitution therapy, while it is noted that the level of somatic health is still «low» and corresponds to 2 points, with the initial one - 0 points. IP that affect the replenishment of iron deficiency in the body cannot fully influence the degree of severity of asthenia and the adaptive capabilities of the body, which may justify the appointment of additional medicines for correction of AS.*

Keywords. *Fertile age; iron deficiency anemia; asthenic syndrome; iron preparations*

1. Introduction

At present, iron deficiency is a nationwide medical and social problem in the healthcare system of various countries and it is actively studied by scientists and practicing doctors of leading domestic and foreign medical universities and clinics [1-3]. In the world, according to WHO, there are about 1 billion people suffering from iron deficiency anemia, i.e. each 5th-6th inhabitants of the planet. In Kazakhstan, more than 45% of women of childbearing age suffer from iron deficiency anemia (IDA) and 30% of women have latent iron deficiency [4, 5]. Today, the incidence of IDA tends to decrease, if in 2009 it was identified 2314.0 people per 100 thousand population, then in 2015 - 1753.7 [6]. For many years, the «gold standard» for the treatment of IDA is ferrous sulfate [7, 8]. Despite the expressed efficacy in reducing iron levels, it practically does not affect the manifestations of asthenic syndrome (AS) (weakness, headache, decreased working capacity), which is leading in IDA [9, 10].

Despite the fact that the issues of IDA therapy have been studied in detail in different categories of the population, the problem of correction of cognitive disorders, disturbances of the psychoemotional background and traditional manifestations of AS in the form of weakness and decreased working capacity due to chronic cerebral hypoxia in IDA remains unresolved [11-15].

Goal. To assess the effect of IP on the level of somatic health and the degree of severity of AS in women of fertile age with IDA on the background of a 4-week course of IP.

Objectives of the research.
1. To study the effect of IP on the parameters of iron metabolism in women of fertile age with IDA.
2. To estimate the frequency and severity of AS in women of fertile age with IDA after a course of ferrotherapy.

3. To assess the level of somatic health in women of fertile age with IDA after a course of ferrotherapy.

4. To assess the level of working capacity in women of fertile age with IDA after the course of ferrotherapy.

2. Methods

The study group consisted of 30 women with diagnosed IDA at the age from 18 to 49 years, the average age was 29,1 ± 2,2 years. The criteria for inclusion in the study were: age 18-49 years; verified diagnosis of IDA; the presence of informed consent of the patient to participate in the study. Exclusion criteria: age is less than 18 and older than 49 years; the presence of an infectious disease, a febrile state; the presence of cancer, chronic somatic diseases in the acute stage, chronic diseases in the stage of decompensation; all types of diabetes mellitus.

Anemia of mild severity (Hb 90-109 g / l) was observed in 22 patients (the average level Hb 103 g / l); Anemia of medium severity (Hb 70-89 g / l) - in 8 people (the average level of Hb 79.5 g / l). The serum iron level initially averaged 14.8 mmol/l and 9 mmol/l, the total iron binding capacity (TIBC) was 36.3 mmol/l and 43.6 mmol/l, ferritin - 22.8 mmol/l and 12.8 mmol/l, according to the degrees of gravity.

The substitution therapy was carried out with an iron preparation (IP) for 4 weeks (Sorbifer Durules 320 mg twice daily).

To assess the exchange of iron were performed laboratory blood tests: a general analysis (hemoglobin, erythrocytes), biochemical analysis (serum iron, TIBC, ferritin).

Asthenic state scales (ASC) and MFI-20 were used to detect and determine the degree of severity of AS. ASC was developed by L.D. Maykova and adapted by T.G. Chertova on the basis of clinical and psychological observations and the well-known questionnaire MMPI (Minnesota multidimensional personality list). The scale consists of 30 points-statements reflecting the characteristics of the asthenic state [16]. The MFI-20 asthenia scale (The Multidimensional Fatigue Inventory), which allows to obtain a subjective quantitative assessment of the overall severity of asthenia and its various aspects. This scale consists of 20 statements reflecting different

components of the asthenic disorder: general asthenia, physical asthenia, decreased activity, decreased motivation and mental asthenia [17, 18]. Quantitative analysis of the level of somatic health was carried out by the express system of G.L. Apanasenko. It consists of a series of simple indicators that are ranked and to each grade is assigned a corresponding score. The overall health score is determined by the sum of the scores and allows to distribute the subjects to 5 levels of health corresponding to a certain level of aerobic energy potential [19, 20]. The working capacity was determined with the help of a treadmill test according to the standard procedure [21]. The received data was processed using the «Microsoft2010» and «SPSS24» application software, to assess the significance of the differences in the relative values and the average values of the quantitative indicators were used the Student's t-test and the non-parametric test of Wilcoxon for dependent samples, the Spearman rank correlation coefficient - the differences were considered reliable at a probability level of 0.95 (p≤ 0.05).

3. Results

Analyzing the parameters of peripheral blood, it was revealed that the level of hemoglobin in the study group ranged from 71 to 110 g / l, total iron – from 1.3 to 34 mmol/l, total iron binding capacity (TIBC) – from 3.1 to 81.2 mmol/l, ferritin – from 1.4 to 42.7 ng / ml, which corresponds to the light and medium degrees of IDA. After 4 weeks of IP, there was an improvement in the parameters of iron metabolism, while the hemoglobin level increased 0.8 times, total iron - 0.8 times, ferritin - 0.9 times, TIBC decreased 0.9 times compared with baseline. Dynamics of indicators of «red» blood is presented in diagram 1.

Thus, it was established that substitution therapy had a positive effect on the iron metabolism of the study participants – all patients had an increase in the basic parameters of iron metabolism in varying degrees, depending on the severity of IDA expression. Normalization of the hemoglobin level was achieved in 67% of cases, total iron - in 53%, TIBC - in 83%, ferritin - in 47%.

When conducting a correlation analysis between the degree of anemia and AS, was

established an average direct dependence (Rx, y = 0.629). Consequently, in 95% of cases it can be argued that the level of hemoglobin in the blood affects the severity of the manifestations of AS - in other words, the lower the hemoglobin level, the more asthenia is explicated (Diagram 2).

According to the results of the questionnaire on ASC, it was established that in women with the surviving AS, the degree of its severity on the background of ferrotherapy significantly (p <0.05) regressed in all cases (Table 1).

At the same time, it was found that in 5 (41.6%) women, despite normalization of hemoglobin, remained complaints of weakness, decreased working capacity, drowsiness, lability of the nervous system.

The results of a survey of women on the subjective assessment scale of asthenia MFI-20 also confirm the maintenance of AS symptoms after a four-week course of ferrotherapy (Table 2): before treatment, AS was diagnosed in 100% of women, after - in 57.1%. It should be noted that among 14 women with surviving symptoms of AS more than half of patients (8), the hemoglobin level returned to normal after a 4-week course of treatment.

At the top of the list of complaints is a decrease in physical activity (22.2%). The decrease in motivation and activity was observed in 13.7% and 19% of cases, respectively. It was not possible to grade the signs of psychiatric asthenia in 2.2% of surveyed. There were no significant differences between the severity of activity decrease and mental asthenia evaluated in dynamics (p> 0.05).Thus, the normalization of the hemoglobin level achieved in the greater half of women (67%) leads to a decrease in the frequency of occurrence and a decrease in the severity of asthenia. So before the treatment course, the manifestations of AS were detected in all patients, after - preserved in 47% of cases (Table 2). Most of the patients before treatment had mild asthenia (63%), in some cases - medium (30%), strong only in 7%, after - a weak and moderate asthenia occur almost in equal shares (25.6% and 21.5%) (Table 1). Indeed, substitution therapy has contributed to reducing the frequency and severity of AS, but is not able to stop it in its entirety.

Analysis of the results of the ASC results and the scale of the subjective evaluation of asthenia MFI-20 showed that among the manifestations of AS, the decrease in physical activity and working capacity is the first priority. Analysis of working capacity in the dynamics showed an improvement in the functioning of the cardiorespiratory system after the IP course, was noted a decrease in the level of blood pressure and heart rate, a reduction of the time of stabilization of the heart rate after exercise, and were obtained statistical significant differences for all the studied parameters (Table 2).

To determine the effect of a chronic disease on the level of somatic health in the course of the research was conducted a comprehensive evaluation using the method of LG. Apanasenko. The obtained data in Table 3 showed improvement in all the studied parameters after a course of substitution treatment. Statistically significant differences before and after therapy are determined by indicators of vital index and recovery time of heart rate (p <0,05). It is noted that the level of somatic health is still «low» and corresponds to 2 points, with the initial - 0 points.

4. Discussions

The research showed that a 4-week course of substitution therapy contributed to a partial replenishment of the iron level in the blood. According to clinical recommendations, while use of an adequate dose of IP, the normalization of the hemoglobin level is noted after 3 - 4, in some cases the time is prolonged to 6 - 8 weeks from the beginning of treatment [16], therefore it is necessary to continue to take a maintenance dose of IP (half of the therapeutic dose) for 1 -1.5 months under the control of the GBA [19].

Has been established a moderate direct correlational dependence of AS explication on the severity of IDA - manifestations of AS are more expressed in patients with a second degree of IDA.

It was noted that, despite the rise in hemoglobin level, the symptoms of AS in the form of weakness, periodic headache, lability of the nervous system, decreased working capacity were preserved in 27% of the surveyed (according to ASC data). The results of MFI-20 also confirm the presence of signs of mild and moderate asthenia after treatment

in 57.1% of cases. In this case, the signs of mental asthenia have not been docked.

Despite the improvement of all parameters reflecting the level of somatic health, except VC and muscular strength, determined by the dynamometric method, it still remains "low" due to the long course of the disease, the lack of regular adequate physical activity.

The level of working capacity increased, primarily due to improved work of the cardiorespiratory system, which is associated with an increase in the level of iron in the blood and improvement of tissue trophism.

Similar data are given in the works of A.V. Strutynsky [22], V.N. Serov and co-author [23], V.A. Burlev and A.V. Malkoch [24], who showed that the use of the IP contributes to an increase in the level of hemoglobin, serum iron and ferritin, in more than 90% of women of different ages with IDA. Also in the work of Serov and co-author [23], were obtained the results about a decrease in the frequency and severity of such manifestations of AS as weakness, decreased working capacity, instability of the emotional background, sleep disturbance on the background of ferrotherapy. However, Michael Alleyne and co-author [1], Laura E. Murray-Kolb and John L. Beard Am J [9], was noted the positive effect of the IP on restoring cognitive function of the brain.

5. Conclusion

According to the data obtained, it is established that a short course of oral administration of the IP helps to partially eliminate iron deficiency. The increase in the studied parameters (hemoglobin, TIBC, ferritin) was observed in all surveyed, normalization – in more than half of patients. At the same time, the preservation of clinical manifestations of AS was detected both in individuals with normalized parameters of iron metabolism, and with reduced ones. Attention is drawn to the presence of mental asthenia, which indicates the neglect of the pathological process, due to chronic hypoxia of the brain, the need for a more detailed survey of these patients, the consultation of a neurologist, psychologist, psychiatrist. Almost all indicators of somatic health improved compared to the baseline, but its level as before the course of ferrotherapy is classified as low, due to the long course of the disease and tissue hypoxia. The decrease in heart rate, the level of blood pressure after exercise and the reduction in the recovery time of these parameters, reflect an increase in the level of working capacity after the course of IP, which also indicates a decrease in tissue hypoxia, in particular of the heart muscle.

Based on the data obtained from the research, it can be assumed that iron preparations that affect the replenishment of iron deficiency in the body can not fully influence to the degree of AS expression and the adaptive capabilities of the organism, which, perhaps, justifies the search for additional medicines for the correction of the aforementioned disorders.
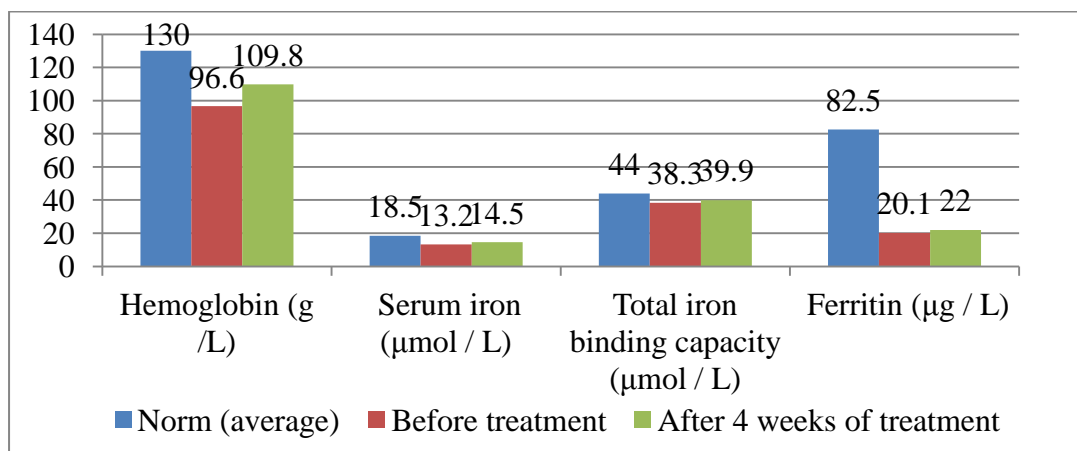

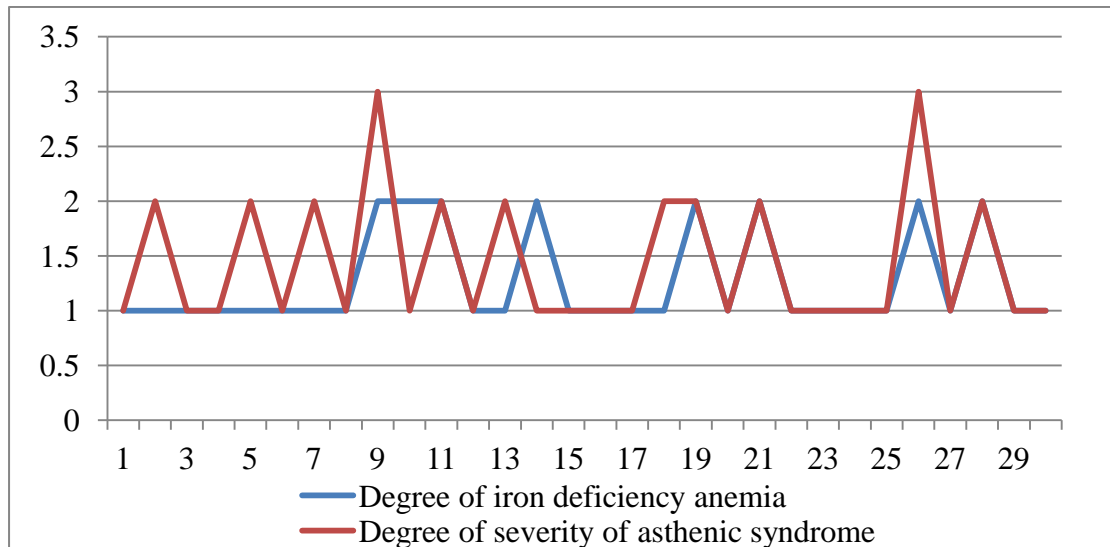**Diagram. 1.** Parameters of iron metabolism before and after a four-week course of taking iron preparations

Diagram. 2. Dependence of the severity of manifestations of asthenic syndrome on the degree of iron deficiency anemia

Table 1. The severity of asthenia before and after a four-week course of taking iron preparations (according to the results of the asthenic state scale)

	Iron deficiency anemia before treatment			Iron deficiency anemia after treatment			t- criterion	p-lewel
	N	p%	-/+ 95% CI	N	p%	-/+ 95% CI		
No asthenia	0	0	0,00; 0,00	18	52,8	33,75; 71,85	-5,79	0,000*
Low	19	63,3	45,26; 81,34	6	25,6	8,95; 42,25	3,18	0,003*
Middling	9	30	12,85; 47,15	6	21,5	5,82; 37,18	0,76	0,453
Severe	2	6,7	-2,66; 16,06	0	0	0,00; 0,00	1,47	0,149

* Statistically significant differences according to the criterion Z (standard normal distribution) p <0.05
CI- Confidence interval

Table 2. Indices of blood pressure in the group with iron deficiency anemia before and after a four-week course of iron preparations while performing a treadmill test

Indicators (Before / after treadmill)	Iron deficiency anemia (n = 30) before the course of iron preparations	Iron deficiency anemia (n = 30) after a course of iron preparations	p- lewel
Systolic blood pressure	112,3/168,1	117,8/135,5	0,000017*
Diastolic blood pressure	71,7/97,3	78,10/83,2	0,000103*
Heart rate	71,6/89,5	73,1/84,4	0,000125*
Recovery heart rate (seconds)	212,3	209,7	0,000039*

* Statistically significant differences in the nonparametric Wilcoxon test for dependent samples p <0.05

Table 3. Assessment of the health status of women with iron deficiency anemia before and after a four-week course of treatment.

Indicators	Iron deficiency anemia (n = 30) before the course of iron preparations	Iron deficiency anemia (n = 30) after a course of iron preparations
Body mass index	21,1	22,4
Points	0	0
Vital lung capacity (ml / kg)	48,0	50,4 *
Points	2	2
Hand dynamometry / body weight (%)	27,2	29,9
Points	0	1
Recovery heart rate (seconds)	212,3*	209,7*
Points	-2	-2
Score points	0	2
General health assessment	Low	Low

* Statistically significant differences in the nonparametric t-test of Student for dependent samples p <0.05

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