

Effectiveness of Treatment of Iron Deficiency Anemia in Pregnant Women at the Primary Health Care Level: A Comparative Evaluation of Ferric Carboxymaltose and Iron Sucrose

Djuraeva Gulnoza Tulkunovna

Tashkent State Medical University, Uzbekistan

Abstract. The purpose of the study: To compare the effectiveness of ferric carboxymaltose (FCM) and iron sucrose for treating iron-deficiency anemia (IDA) in pregnant women at the primary care level. **Materials and methods of the study:** A prospective study included 330 pregnant women with moderate IDA (Hb 70–99 g/L): 163 received FCM and 167 received iron sucrose. Thirty healthy pregnant women served as a control. Clinical, laboratory (hemoglobin, ferritin, TSAT, hepcidin, erythropoietin), and Doppler parameters were evaluated. **Results:** Baseline anemia severity was similar. After 4 weeks, the FCM group showed a higher Hb increase (+23.9 g/L vs +12.2 g/L; $p < 0.001$), normalized ferritin in 97.5% vs 85.0%, and fewer adverse reactions (8.6% vs 17.4%). Mean blood loss during delivery was lower with FCM (380 mL vs 470 mL; $p < 0.01$). **Conclusions:** FCM was more effective and better tolerated than iron sucrose, providing faster correction of IDA and improved obstetric outcomes.

Keywords: iron-deficiency anemia; pregnancy; ferric carboxymaltose; iron sucrose; intravenous iron therapy.

Relevance

Iron deficiency anemia in pregnant women is one of the most common medical problems in obstetric practice. According to WHO estimates, up to 40% of pregnant women worldwide suffer from anemia, and in most cases, the cause is iron deficiency.[1] TTA during gestation leads to chronic hypoxia, increasing the risk of complications for the mother (weakness, gestational hospitalization, anemic complications during childbirth) and the fetus (developmental delay, prematurity, hypotrophy).[7][8] Timely detection and correction of anemia is the most important task of antenatal observation at the level of primary health care, where the first contact of the pregnant woman with the healthcare system is carried out. However, routine screening based solely on hemoglobin determination has limited sensitivity.[3][4] The dissertation research showed that 37% of women with normal Hb (>110 g/l) already have latent iron deficiency (ferritin <15 mcg/l, LSD $<16\%$), which remains unrecognized.[2][8] Moreover, even moderate anemia can be accompanied by a disruption of uteroplacental blood flow: according to our data, with ferritin <15 mcg/l and TST $<10\%$, a decrease in the cerebroplacental ratio (CPR <1.1) and an increase in the uterine artery resistance index >0.75 are detected in 44.8% of pregnant women.[20] These dopplerometric changes are independent of hemoglobin levels and indicate the early development of fetoplacental hypoxia in iron deficiency. [7][20] Thus, for the prevention of perinatal complications, it is crucial not only to diagnose TTA but also to effectively compensate for iron deficiency in the shortest possible time.[5][8]

Therapy of TTA in pregnant women includes dietary measures and iron supplements. Oral iron-containing agents are widely used for the prevention and treatment of mild anemia, however, their effectiveness is limited in cases of severe deficiency and late gestational age.[8] In cases of moderate and severe anemia, especially if there is less than 8-10 weeks left until the expected delivery, parenteral iron therapy is recommended, which allows for faster replenishment of iron reserves.[3][4][5][18][16][19] At the PHC level, modern intravenous iron preparations with high dosage and safe profile are increasingly being used, which allows for treatment on an outpatient basis (in day hospitals). Among them, the sucrose hydroxide complex (three-valent iron-sucrose, JS) has become the "gold standard" for parenteral iron administration in recent decades, however, it requires multiple infusions (usually 5-6 injections of 200 mg to achieve a total dose of ~ 1 g).[4][6] A more recent formula - iron carboximaltozate (IFC, or carboximaltoza ferrite) - is distinguished by the possibility of administering a large dose (up to 1000 mg) per infusion, which is extremely convenient in outpatient practice.[6][11][12][13][15] A number of studies indicate that CMR provides a faster increase in hemoglobin and ferritin compared to iron-saccharose, with a comparable safety profile.[11][12][13][15][17][18] Nevertheless, data on the use of these drugs in pregnant women under PMCP conditions, taking into account dopplerometric indicators and distant obstetric outcomes, are insufficient.[8]

Research objective: to compare the effectiveness and tolerance of two parenteral therapy regimens for TTA in pregnant women (MST vs. TP) based on district women's consultations, analyzing clinical and laboratory indicators of anemia correction, uterine-fetal blood flow parameters, and immediate obstetric results.

Materials and methods.

Research design and participants: A prospective comparative study was conducted in 8 PHC institutions. Inclusion criteria: pregnant women 18-40 years old, gestational age 20-26 weeks, diagnosed with TTA II degree (Hb 70-99 g/l, ferritin <15 mcg/l), absence of other significant pathologies. Women with severe anemia (Hb <70 g/l) or urgent hospitalization, as well as chronic diseases affecting iron metabolism (hemoglobinopathies, hemolysis, etc.) A total of 330 patients with TTA were selected, who were divided into two comparable groups: the main group (n=163) received iron carboxymaltose treatment, and the comparison group (n=167) received iron-saccharose complex treatment. The distribution by groups was carried out taking into account the order of admission and informed consent to a particular drug (randomization was not carried out for ethical reasons, taking into account the preferences of patients and doctors). Additionally, a control group was formed consisting of 30 pregnant women without anemia (Hb >120 g/l, ferritin >30 mcg/l), comparable in age (average age ~27 years) and gestational age (II trimester).[2][3][4]

Therapy: In the main group, the domestic drug CMJ was used (1 ampoule of 500 mg of elemental iron); the dose was calculated based on iron deficiency and body weight, with an average of 1-2 infusions of 500 mg with an interval of 7-10 days (total ~1000 mg of iron per course). In the comparison group, iron (III) hydroxide sucrose was administered: 200 mg was administered intravenously drop by drop twice a week, a total of 5-6 infusions (total also ~1000 mg of iron). Both therapies were conducted in the day hospital of the polyclinic under the supervision of a doctor. All patients were provided with medical supervision during and after infusions (measuring blood pressure, pulse, observation of possible reactions for at least 30 minutes). Simultaneously with parenteral therapy, standard pregnancy management was carried out according to the national protocol.[11][12]

Evaluation of indicators: Before starting treatment, all participants underwent a detailed clinical blood test (Hb, hematocrit, erythrocytes, and RBC indices: MCV, MCH, MCHC), biochemical indicators of iron metabolism (serum iron, total iron-binding capacity, TNF, ferritin), as well as regulatory hormone levels (serum hepsidin and erythropoietin).[9][10] The listed laboratory tests were repeated after 2 weeks and after 4 weeks from the start of therapy. Additionally, on the 14th day, peripheral blood reticulocyte parameters were assessed as an early indicator of hematopoiesis. The clinical condition was monitored by questioning patients for the presence of anemia symptoms (weakness, dizziness, shortness of breath, tachycardia, paleness, taste disturbance, nail brittleness, etc.) - before treatment and after 4 weeks.[6]

To study the impact of anemia on the fetoplacental complex, all 330 women before treatment underwent dopplerometric examination (Mindray DC-70/40, transabdominal sensor 3.5-5 MHz). Uteroplacental blood flow indicators were assessed: pulsation index (PI) and resistance index (IR) in both uterine arteries, IR in the umbilical artery, as well as the cerebral-placental ratio (CPS = ratio of PI in the fetal middle cerebral artery to PI in the umbilical artery). Doppler was performed at 24-28 weeks,

and the results were compared with laboratory iron deficiency criteria. Repeated Doppler ultrasound after a course of therapy was performed selectively (upon indications, if fetoplacental insufficiency is suspected).[20]

Direct obstetric outcomes were observed in all participants before and after childbirth: the method of delivery, the volume of blood loss (measured in graduated containers, taking into account the weight of the diapers), the use of uterotonics, cases of postpartum anemia (Hb <110 g/l), and the need for repeated administration of iron supplements after childbirth were noted.[5]

Statistical analysis: Data processing was performed using the Statistica 13.0 package. The Shapiro-Wilk criterion was used to verify the normality of the distribution. Group quantitative indicators are represented as average \pm standard deviation with normal distribution or median (Me) and interquartile range with abnormal distribution. The comparison of mean values was performed using the *t*-Student criterion (for independent samples) or the paired *t*-criterion (for repeated measurements in the group). In the case of an abnormal distribution, the nonparametric Mann-Whitney criterion was used. Frequency indicators (percentages) were compared using the χ^2 test with a Yates correction. Differences were considered statistically significant at $p < 0.05$.

Results.

Participants' characteristics and initial data. The average age of the patients was 27.4 ± 3.1 years, 68% were multigravid (having had 1 or more births in their medical history). The CMJ and HS groups did not differ in terms of average age, parity, education level, and social status ($p > 0.1$). 21% of women had endocrine disorders (mainly obesity of I-II degree and subclinical hypothyroidism), ~16% had a history of gastrointestinal diseases (gastritis, duodenitis); ~25% had chronic inflammatory diseases of the reproductive system. The frequency of concomitant pathologies was the same in both groups. Thus, the distribution of aggravating factors is recognized as uniform. At the time of inclusion, all 330 patients were diagnosed with moderate anemia (TDA II degree: Hb in the range of 70-99 g/l).[3][4] The average hemoglobin level was 94.3 ± 3.9 g/l in the main (MS) and 95.1 ± 3.7 g/l in the comparison group (CL) ($p = 0.72$), which corresponds to moderate anemia; no differences were found between the groups. Hematocrit was ~29-30% in both groups (control: $36.8 \pm 1.2\%$). Average erythrocyte indices confirmed microcytic-hypochromic anemia characteristic of TTA: MCV ~75 fl, MCH ~25 pg, which is significantly lower than in healthy pregnant women (in the control group, MCV 85-90 fl, MCH ~30 pg; $p < 0.001$). The concentration of ferritin in the blood serum of patients with anemia averaged 9-10 mcg/l, NTJ - about 8%, indicating the depletion of iron reserves and low transport accessibility of iron.[2] In 52% of the examined individuals, ferritin was <10 mcg/l, meaning iron reserves were practically completely exhausted. At the same time, hepsidine levels were suppressed (<10 ng/ml in most patients), which is a compensatory reaction for increased iron absorption.[9][10] Erythropoietin increased against the background of anemia (average level ~55-60 mIU/ml, with a norm of ~20-30), however, the correlation between Hb and EPO was weak ($r \approx 0.1$, $p > 0.1$), indicating a regulatory imbalance with pronounced iron deficiency.

Dopplerometric examination (before the start of

therapy) in 123 pregnant women with TTA (included, by doctor's decision) revealed that some anemic patients already had signs of fetal blood circulation centralization. Thus, in 40% of women with ferritin <15 mcg/l, a decrease in CPS <1.1 (normal >1.1 in the second trimester) and a relative increase in vascular resistance in the uterine arteries (IR >0.75) were noted. These changes reflect the strain on compensatory mechanisms: even with a moderate decrease in Hb (average ~95 g/l), gestational anemia led to the redistribution of fetal blood flow in favor of the brain. In the control group, no similar deviations from Doppler were recorded. The data served as an additional argument for intensive care: the detection of blood flow disorders was considered an indication for the immediate transition from oral prevention to parenteral iron administration.[20]

Hemoglobin and red blood dynamics. The prescribed treatment led to a significant increase in hemoglobin levels in both groups, however, the growth rates differed. After 2 weeks of therapy, the average Hb level in the MS group increased from 94.3 to 104.1 g/l (increase +9.8±2.1 g/l), while in the MS group it increased from 95.1 to 100.8 g/l (increase +5.7±1.8 g/l, p<0.001 between groups). By the 4th week, the gap increased: in the MS group, Hb reached an average of 118.2±4.5 g/l (+23.9 g/l from the baseline), while in MS - 107.3±4.1 g/l (+12.2 g/l; p<0.001). Thus, only patients receiving carboxymaltose returned to normal hemoglobin values (>110 g/l) on average after a month of treatment. The proportion of women who achieved the target level of Hb ≥110 g/l was 84.7% in the MS group versus 52.1% in the MS group ($\chi^2=35.8$; p<0.001). By the end of the observation period (before childbirth), hemoglobin stabilized: none of the patients treated with MS had severe anemia; the Hb level in 96% remained ≥105 g/l. In the TS group, by the third trimester, a decrease in Hb <105 g/l (15.6% of cases) was observed again in some women, requiring repeated iron administration or erythromass transfusion during childbirth (2 cases, 1.2%). In the control group, the average Hb remained at ~124-128 g/l throughout pregnancy.[11][12][13][15]

Parallel to the increase in hemoglobin in both groups, the number of erythrocytes increased: from ~3.2-3.3×10¹²/l to ~3.8×10¹²/l after 4 weeks, however, a statistically significant intergroup effect was manifested only by the end of treatment (in the CMJ group, the average RBC was 3.95±0.21 versus 3.72±0.26 in the TS group; p<0.01). Hematocrits rose to ~34% (CMR) versus ~32% (CS) after 4 weeks (p<0.05). Erythrocyte indices also improved after therapy: MCV increased from ~75 to 82 fL (CMR) and to 79 fL (LC); MCH - from 25 to 28 pg (CMJ) and 27 pg (JS). This indicates partial correction of microcytosis after iron replenishment, with a more pronounced tendency towards normalization in MSG.[11][12]

The use of reticulocyte analysis allowed for early bone marrow response to therapy. As early as the 7th-10th day, a reticulocytic surge ("reticulocytic crisis") was observed in both groups: the absolute number of reticulocytes increased from ~0.03×10¹²/L (2.6‰ of the total number of erythrocytes) to ~0.10×10¹²/L (8.4‰). This increase was more than 3 times compared to the baseline (p<0.001) and preceded a significant increase in Hb, which confirms the validity of using reticulocytes as an early marker of TTA

treatment effectiveness. Although the differences between the groups in reticulocyte maximums did not reach statistical significance, in patients receiving MS, the peak of reticulocytosis occurred somewhat earlier (8-9 days versus ~11 days in MS), and its amplitude correlated with the subsequent increase in Hb ($r\approx 0.45$, p<0.01). This indicates more active and coordinated inclusion of erythropoiesis with rapid iron intake.[6][13]

Fire depot replenishment: Assessment of iron metabolism indicators demonstrated a clear advantage of the CMR scheme. The serum level of ferritin - a key indicator of iron reserves - increased by an average of +67.2 mcg/l after 2 weeks in patients of the main group, reaching ~77 mcg/l, while in the TS group - only by +32.5 mcg/l (up to ~42 mcg/l). By the 4th week, this difference became even more pronounced: the average ferritin in those receiving CSF was 112.4±8.5 mcg/l versus 65.2±7.1 mcg/l in TS therapy (p<0.001). Thus, the target values of ferritin ≥30 mcg/l (minimum required for the cessation of erythropoiesis by feedback mechanism) were achieved in 97.5% patients in the MS group, while in the TS group - in 85.0% ($\chi^2=14.0$; p<0.001). More than half of the women receiving CMR reached ferritin levels >70 mcg/l, indicating a complete saturation of the iron depot. In the comparison group, such a high reserve was formed only in 18%. At the same time, in 15% of patients, ferritin in the blood serum remained below 30 mcg/l even after a course of therapy, indicating incomplete compensation for the deficiency and the risk of anemia recurrence.[2][11][12][13][14][15]

Transferrin's iron saturation coefficient (TTS) - an indicator reflecting bone marrow iron availability - increased in both groups during treatment, but significantly higher when using CSF. Initially, in >85% of the examined individuals, TNF was <10%, indicating a pronounced transportable iron deficiency. After 4 weeks of therapy, the TSH increased by +25.8% in the SMH group versus +17.3% in the TS group (p<0.001). In absolute terms: the average STP reached ~32% (STP) vs ~23% (STP). In almost all women treated with carboxymaltose, TST exceeded the threshold of 20%, which is considered sufficient for effective erythropoiesis; on the contrary, in the iron-saccharose group, TST remained <20% in 22% of patients. The obtained results indicate that CMR not only saturates the depot faster but also provides better plasma iron availability for inclusion in hematopoiesis.[2][6]

Regulatory markers (hepsidin, erythropoietin). In response to iron replenishment, shifts occurred in hormonal regulation of metabolism. In the CMR group, an expected increase in the level of hepsidine was observed, reflecting the "closure" of railway lines during the depot filling. The start of hepsidine in most patients was <5-10 ng/ml; after 4 weeks, the median hepsidine level reached 21.5 ng/ml during CSF therapy versus 14.2 ng/ml during CSF (p<0.01). Normalization of hepsidine (≥20 ng/ml) was noted in 72.4% women of the main group and only in 51.5% - comparative (p=0.002). Insufficient growth of hepsidine against the background of iron-saccharose may indicate that in a significant proportion of patients in this group, depots are not fully replenished or active absorption of iron continues (i.e., the mechanism of negative feedback has not yet worked). At the same time, in the CMJ group, a pronounced increase in hepsidine confirms the achievement of "saturation" of the depot and the transition of the body to a regime to prevent overload with iron. This effect is important

for safety: a timely increase in hepsidine prevents excessive iron intake and potential complications of secondary hemochromatosis.[9][10]

Endogenous erythropoietin (EPO) after anemia correction demonstrated a decrease characteristic of tissue hypoxia reduction. Initially, the EPO level in many women exceeded the norm (>50-60 mIU/ml). At the 4th week of therapy, the average EPO decreased from ~57 to 43 mIU/ml (Δ -14.1), while at TS - from ~55 to 48 mIU/ml (Δ -7.4; $p < 0.01$). The distribution by thresholds is more indicative: 82.2% of patients receiving CSF had an EPO level of ≤ 45 mIU/ml (i.e., signal normalization) by the end of treatment, while in the SS group - only 58.1% ($p < 0.001$). EPO hyperproduction (>50 mIU/ml) persisted in every third woman with CH, indicating residual hypoxia and insufficient treatment effectiveness. In the main group, the vast majority reached an adequate physiological level of erythropoiesis regulation.[7][9]

Clinical effect and dopplerometry. Before the start of therapy, clinical manifestations of anemia were noted in most study participants: more than 78% of women in each group indicated at least three symptoms of TTA simultaneously (weakness, dizziness, shortness of breath, etc.). The frequency of the main complaints (general weakness ~72%, shortness of breath during exercise ~58%, dizziness ~50%, taste distortment ~25-30%, nail fragility ~35-40%) did not differ between the groups before treatment and significantly exceeded the control group (in pregnant women without anemia, similar complaints occurred only in 3-10% of cases, $p < 0.001$). This confirms that even with moderate anemia (grade II), pregnant women clinically develop a pronounced anemic syndrome with hypoxic and sideropenic symptoms. After 4 weeks of treatment, a distinct improvement in well-being was noted, especially in the CMJ group. The proportion of patients who retained ≥ 3 anemia symptoms decreased to 14% in the MS group versus 29% in the SS group ($p < 0.01$). Individual symptoms also significantly regressed when using CSF: weakness bothered only 11.6% of women (compared to 25.7% in HS), shortness of breath 8.6% (vs 21.6%), dizziness - 6.7% (vs 17.4%), taste disturbances - 2.5% (vs 6.6%). In all positions, the difference was statistically significant ($p < 0.01$). In more than 60% of patients treated with carboxymaltose, the clinical signs of anemia completely disappeared, while with iron-saccharose therapy, complete relief of symptoms was observed in approximately 45-50%, and residual complaints persisted in every fourth patient. Thus, in addition to laboratory criteria, CMS provided a faster functional effect, improving the quality of life of pregnant women in shorter periods.[6][11][13]

Doppler measurement indicators after a course of therapy did not significantly worsen in any patient; on the contrary, in most patients, stabilization of blood flow was noted against the background of an increase in Hb and ferritin. It was not possible to specifically compare the dopplerometric data between the MS and HS groups, as repeated ultrasound was performed not for everyone, but according to clinical indications. Nevertheless, it can be indirectly noted that among women receiving CSF, none of the cases of severe placental insufficiency developed (there were no cases of an increase in IR >0.8 or a critical decrease

in CPS <1.0 at later stages). In the HS group, 3 pregnant women required premature delivery at 37-38 weeks due to signs of deterioration of uterine-fetal blood flow against the background of persistent anemia (Hb <105 g/l). These observations indicate a potential correlation between the rate of anemia correction and the dynamics of Doppler indicators: more complete replenishment of iron (as in MS) contributes to the maintenance of fetoplacental blood flow compensation.[20]

Therapy tolerance and safety. Both studied drugs were generally well tolerated by pregnant women; no serious allergic reactions (anaphylaxis, Quincke's edema) were recorded. However, the frequency of undesirable phenomena was 2 times lower when using CSF: any side effects were noted in 8.6% of patients in the main group versus 17.4% in the comparison group ($p = 0.022$). Most undesirable phenomena were of a transient nature. In the CMJ group, transient skin reactions (itching at the injection site, short-term heat sensation) prevailed - 5 cases, as well as isolated episodes of headache after the procedure (2 cases). All symptoms were suppressed independently or with minimal measures (rest, plenty of drink). In the iron-saccharose group, similar effects were observed more frequently: skin itching - in 8 patients, fever - in 5, headache - in 6, dizziness - in 4, tachycardia - in 3. In addition, in 3 cases (1.8%), women refused to continue the course of ST after 3-4 infusions, motivated by fear of recurrence of unpleasant sensations. In the CMJ group, there were no interruptions in therapy, as the scheme provided for a maximum of 2 infusions, and no patient refused the second administration. Thus, the iron carboxymaltose tolerance profile proved to be more favorable, which is especially important in the context of outpatient use in emotionally labile pregnant women. A lower total dose of injections in SMEs reduces the risk of adverse reactions accumulating and increases adherence to treatment.[11][12][13][17]

Obstetric outcomes. Complete correction of anemia had a positive effect on the course of labor and the postpartum period. Analysis of obstetric indicators showed that there were no significant differences between the groups in the method of delivery: the proportion of spontaneous births through the natural birth canal was ~76% (CMC) and ~73% (CS), the frequency of cesarean section was 24% and 27%, respectively ($p > 0.5$). Surgical delivery was performed according to general indications (pelvic presentation, uterine scar, etc.) and was not associated with anemia. However, the volume of blood loss during childbirth differed significantly. In the MS group, the average blood loss was 380 ± 25 ml, while in the OS group 470 ± 30 ml ($p < 0.01$). In 9.2% of women who were treated for ST, blood loss exceeded 500 ml (pathological blood loss criterion), while among those treated for ST, such cases were 3.7% (difference insignificant, $p = 0.08$, but tendency is evident). No patients from the main group required hemotransfusion; in the comparison group, 2 women received an erythrocyte mass transfusion (after cesarean section against the background of Hb 92 and 95 g/l). The use of uterotonic drugs (oxytocin, carbetocin) for the prevention of hypotonic bleeding was required in 27% of women in the CHF group and only 18% in the CMF group ($p = 0.045$). Postpartum anemia (Hb <110 g/l on the first day after childbirth) was diagnosed in 19.2% of women who received iron-saccharose treatment, which is almost three times more frequently than in women

receiving CSF (6.7%; $p < 0.01$). Accordingly, the need to resume iron therapy in the postpartum period arose primarily in the TS group. These data indicate that iron carboxymaltolate provides a more stable clinical and hematological effect not only before childbirth but also maintains it in early puerperium, while with the use of iron sucrose, recurrence of deficiency occurs more frequently by the time of delivery.[5][7]

Unfavorable outcomes for the fetus (intrauterine developmental delay, newborn hypotrophy, neonatal anemia) in the treatment groups for TTA did not exceed the frequency of such outcomes in healthy mothers. The weight of newborns averaged 3220 ± 210 g (MS) and 3170 ± 240 g (HS), Apgar at the 1st minute was 7-8 points (without differences). There were no perinatal losses. Thus, the aggressive treatment tactics for anemia did not lead to negative consequences, but, on the contrary, likely contributed to the improvement of the newborn's condition by eliminating chronic hypoxia.[7]

Debate

The obtained results convincingly demonstrate the advantages of using iron carboxymaltolate for the treatment of iron deficiency anemia in pregnant women at the PHC level. Compared to traditional iron-saccharose therapy, CMR showed higher effectiveness in all main criteria: hemoglobin elevation rate, iron depot replenishment rate, normalization of regulatory indicators, and improvement of patients' clinical condition. After 2 weeks, a single CSF infusion ensured a nearly 2-fold increase in Hb compared to a series of CS infusions. By the 4th week, the difference reached >11 g/l, which is clinically extremely significant, especially considering gestational age. In most women who received MS, the anemia was fully corrected even before the beginning of the third trimester, while during MS therapy, a significant portion of patients continued to remain in a state of borderline anemia. Such an accelerated effect of SLE is of fundamental importance in conditions of late detection of TDA: it is known that anemia diagnosed after 20 weeks leaves little time for correction, and untreated anemia before childbirth is associated with a worsening of outcomes. This was confirmed in our work: women receiving TC had greater hemodynamic instability during childbirth and frequently required intensive therapy (transfusions, uterotonics), while treatment of MSG allowed the pregnant woman to deliver in a more stable condition.[3][4][5][6][11][12][15][16][17][18][19]

The key factor explaining the difference in effectiveness is the ability of CSF to quickly and fully saturate iron reserves. Due to the administration of a high dose (500-1000 mg) during 1-2 sessions, carboxymaltolate practically instantly eliminates depot deficiency, as evidenced by a sharp jump in ferritin in our patients (3-4 times the initial level after 2 weeks). Against the backdrop of depot saturation, hepsidine naturally increases, "closing the doors" for further iron absorption and thereby preventing overload. This physiological completion of the cycle restored iron metabolism balance in $>72\%$ of women who received CSF, whereas with the phased administration of iron-saccharose after 4 weeks, only $\sim 50\%$ achieved a similar homeostatic reaction. It can be assumed that the remaining $\sim 50\%$ of patients with HS were still in the compensation

phase, i.e., they continued to absorb iron (low hepsidine) and experience mild hypoxia (increased EPO). Indeed, the level of erythropoietin - a marker of tissue oxygenation - normalized significantly more often (82% vs. 58%) during MSG therapy. Thus, carboxymaltolate allowed for a more complete correction of tissue oxygen deficiency, while iron-saccharose, although it elevated hemoglobin, left a hidden deficit (incomplete functional effect) in a significant portion of patients. This conclusion is consistent with literature data: a major study by D. Breymann et al. (2017) showed that in pregnant women with TTA, the use of FCM leads to a more pronounced increase in ferritin and a decrease in EPO compared to iron-saccharose, which is interpreted as a sign of complete iron replacement and elimination of hypoxia. Our research confirms these observations and supplements them with data on regulatory markers (hepsidine).[6][9][10][14]

An important finding was a significant improvement in well-being and anemia symptoms against the background of MSG therapy. Although anemic syndrome is traditionally associated with low Hb levels, in pregnant women, changes in microcirculation and iron depletion play a significant role. It can be assumed that the rapid replenishment of iron reserves (reflected by the growth of ferritin and NTJ) led to accelerated restoration of tissue enzymatic processes, reduced sideropenic manifestations (such as appetite disturbance, skin changes), and improved functioning of the muscular and nervous systems (reduction of weakness, shortness of breath, dizziness). Indeed, in more than 60% of patients in the MS group, after 4 weeks, no symptoms of TTA remained, while in the TC group, complete suppression of symptoms was achieved only in 45%. Especially noticeable is the difference in symptoms such as fatigue and shortness of breath - they disturbed women twice less when treating MS than when treating MS. These data are practically important: improved well-being increases the pregnant woman's compliance, strengthens her confidence in the therapy, and, consequently, ensures a consistent observation. From the perspective of the PHC physician, choosing a scheme that brings relief to the patient faster can increase patient satisfaction with care and commitment to further recommendations.[6][7][8]

Safe and tolerance are key factors when choosing a pregnant woman's medication. In our study, iron carboxymaltolate demonstrated a favorable safety profile: the frequency of adverse reactions was low (8.6%) and, importantly, did not require discontinuation of treatment in any case. Iron-saccharosis was tolerated somewhat worse (17.4% of adverse events, including 1.8% refusal to continue infusions). Nevertheless, there were no serious complications in both groups, which confirms the overall safety of modern intravenous iron forms in pregnant women, as reported in other works. The advantage of CMR in terms of tolerance can be explained both by the smaller number of injections (less exposure to potential reactions) and, possibly, by the structure of the drug itself (stable carboxymaltose complex rarely causes the release of free iron, which triggers side effects). It is also necessary to note the psychological aspect: repeated visits and repeated infusions (in the case of ST) objectively increase the pregnant woman's anxiety, while a single administration of CMJ, successfully endured, forms confidence and relieves excess stress. In outpatient care, this plays a significant role, as monitoring resources are limited, and treatment regimens that

do not require frequent medical intervention are preferred. Our results generally coincide with studies where it has been shown that FCM (CMF) causes adverse phenomena less frequently, in particular, it causes transient hypotension and dyspepsia less than iron-saccharose.[11][12][13][17][18]

Special emphasis should be placed on consideration of economic efficiency of choosing one or another therapy in the PHC system. Despite the higher cost per unit of CMJ preparation, the total costs for the treatment course and subsequent management can be lower compared to MS due to a reduction in the number of infusions and the prevention of complications. Our data showed that the iron-saccharose regimen requires an average of 5-6 visits to the day hospital, while carboximaltozate requires 1-2 visits. This reduces the workload on the polyclinic (the time spent by medical personnel, the use of consumables), and increases the accessibility of the service for the patient (lower transportation and time costs). Moreover, reducing blood loss during childbirth in the MSG group (~90 ml relative to HS) has clinical and economic significance: every extra 100 ml of blood loss potentially increases the volume of infusion therapy, prolongs hospital stay, requires additional tests and medications. In our study, postpartum anemia occurred less frequently in women treated with MS, which allowed for a reduction in drug prescriptions in puerperium. All of the above indicates: investment in more effective anemia therapy pays off by reducing further costs. This is especially relevant for rural areas where resources are limited: preference should be given to schemes that ensure quick results with minimal visits. According to our data, iron carboximaltozate meets these requirements and can be considered a rational choice in PHC protocols for managing pregnancy with anemia.[11][12][5]

Research limitations: Note that our study was not randomized placebo-controlled (for ethical reasons, all patients received immediate care). There was no "blinding" between the treatment groups, which theoretically could introduce a small information shift (the doctor knew which drug the patient was receiving). However, objective quantitative indicators measured in the laboratory minimize this risk. Another limitation can be considered the lack of formal assessment of doppler after treatment in all women we focused only on clinical necessity. Further research with repeated Doppler control is planned to quantify whether rapid anemia correction improves fetal blood flow indicators. Finally, the comparative economic effectiveness of CMEs vs HS in our country requires further study, taking into account pharmacoeconomic calculations (preparation costs, logistics, management of complications). Nevertheless, it is now clear that the clinical effectiveness of MSG is transformed into an improvement in outcomes, and therefore, it also has an indirect economic effect.[18]

Conclusions: Parenteral therapy of iron deficiency anemia in pregnant women at the primary level using ferrite-carboximaltozate (CMZ) provides a faster, more potent, and more comprehensive effect compared to iron-saccharose. In a relatively short period (1 month), the normalization of hemoglobin in most patients, replenishment of iron depots, and restoration of physiological regulatory mechanisms (hepsidin-erythropoietin response) are achieved. This leads to improved well-being of pregnant women, reduced risk of

obstetric complications (pathological blood loss, postpartum anemia), and increased satisfaction with treatment. Factors of CSF success include the convenience of the scheme (minimum infusions), which is critical for outpatient practice, and a high safety profile. Taking into account the obtained data, it is recommended to more widely implement CMC in the practice of women's consultations for the therapy of TTA in the II-III trimesters, especially in cases of late detection of anemia or ineffectiveness of oral preparations. Simultaneously, it is necessary to increase the vigilance of PHC physicians regarding latent iron deficiency: along with hemoglobin monitoring, it is advisable to determine ferritin at least twice during pregnancy (in the 1st and 3rd trimesters), and if it decreases to <30 mcg/l, consider early parenteral iron administration without waiting for Hb to decrease. A comprehensive approach, including active screening, timely initiation of adequate therapy (including CSF), and monitoring of dopplerometric indicators for anemia, will reduce the frequency of gestational anemia and improve perinatal outcomes.[3][4][5]

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