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Correlation between body mass index and the results of the treatment of iron deficiency anemia in pregnant women

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Abstract

Background: Iron deficiency anemia (IDA) is a hematologic syndrome characterized by the deregulation of hemoglobin synthesis due to iron deficiency. During pregnancy, there is an increase of about six times of iron. A correlation between body mass index (BMI) and hemoglobin (Hb) in pregnant women with IDA during the treatment with "Sorbifer Durules" (SD) was evaluated.

Material and methods: A retrospective, cohort study. 40 medical cards of pregnant women diagnosed with IDA during the pregnancy and who were treated with SD: one tablet 2 times per day, were studied. The BMI and Hb levels were assessed in each trimester of pregnancy. The dynamic of Hb values was determined: ΔHb_{II-I} – the difference between Hb values of the 2nd and of the 1st trimesters, ΔHb_{III-II} – the difference between Hb values of the 3rd and of the 2nd trimesters. Statistics: Pearson's correlation coefficient.

Results: IDA was diagnosed in 15 out of 40 pregnant women in the 1st trimester of pregnancy (IDA1), in 19 – in the 2nd trimester (IDA2), in 6 – in the 3rd trimester (IDA3). 7 pregnant IDA1 with normal body weight (BMI = 18,5-25 kg/m^2) had ΔHb_{II-I}=14,28 g/l, 8 pregnant IDA1 with grade I obesity (BMI=30-35 kg/m^2) had ΔHb_{II-I}=26,12 g/l. Pearson correlation coefficient between BMI in the 1st trimester of pregnancy and ΔHb_{II-I} in pregnant IDA1: r=+0,617, p=0,014. The associations between BMI and ΔHb in pregnant IDA2 and IDA3 were negligible.

Conclusions: There is a substantial and significant association between BMI in pregnant women who developed IDA in the 1st trimester and Hb increase during the treatment with SD.

Key words: iron deficiency anemia, pregnancy, body mass index, hemoglobin.

Introduction

There are many diseases nowadays. For example, the International Classification of Diseases (ICD-10) developed by WHO in 1994, lists about 20 000 diseases. There are even more drugs in the world, and their number is increasing every year. It is very difficult for a modern doctor to keep track of innovations on the pharmaceutical market. He must know everything about the medicine: its belonging to a certain pharmacological group, its mechanism of action, take into account the indications and contraindications for its use, possible side effects. The doctor should know the form of release and dosage of this particular medicine.

Paracelsus said, "The dose makes the poison". The dosage is the key factor that determines the drug's effect on the body.

The study of the pharmacokinetic properties of the drugs allows us to determine the optimal route of their administration, which in the future contributes to a rational dosage for its use in medical practice. The information about the pharmacokinetic properties of drugs can clarify the indications and contraindications of their use. So, substances that easily penetrate the hematoplacental barrier should be used with caution during pregnancy. Antimicrobials that are actively excreted by the kidneys or accumulated in the liver are suitable for the treatment of urinary or biliary tract infections, respectively. The pharmacokinetics of drugs creates the basis for a rational search for new drugs with the desired patterns of distribution in the body, with higher activity or a wider spectrum of action [1].

The modification of the pharmacokinetics of drugs occurs due to important physiological changes in the mother's body during pregnancy. It is important to understand the dose-response relationship for optimizing the safe and effective use of drugs, especially in such a vulnerable population as pregnant women. The optimal dosage of drugs during pregnancy should provide maximal therapeutic efficacy, while minimizing the risk of maternal and fetal toxicity [2].

The study of rational pharmacotherapy during pregnancy is significant due to the limited possibilities of clinical research of drugs involving pregnant women, possible fetus complications, side effects of drugs on both the mother and the fetus. The need for drug support for a normal pregnancy is also a relevant issue [3].

According to various sources, 80% of women in Russia, 83% in Brazil, 62% in the USA, take at least one drug during pregnancy [4]. The average number of drugs per 1 pregnant woman is 11 ± 5.3.

The purpose of this study is to provide scientific evidence for the relationship between the pharmacokinetics of drugs and their dosage in pregnant women.

It is important for the practicing physician to know the particularities of dosage of drugs during pregnancy, depend-

ing on the principles of pharmacokinetics. The pharmacokinetics of the drug depends on many factors: genetics, coexisting diseases, physiological changes that the pregnant body undergoes. If these conditions are not taken into account, the risk of incorrect prescription of a drug dose is high. As a result, an insufficient pharmacological effect will occur in case of administering a small dose. Alternatively, in case of a larger dose, there is a danger of the effect of accumulation and an increased risk of side effects of the drug to appear. It is important to find the golden middle when setting the dose.

The features of the pharmacokinetics of drugs during pregnancy

Age, weight, body mass index, gender, race, ethnicity, renal and hepatic functions, genetic polymorphism, concomitant pathology, therapy, smoking, alcohol and nutrition – all these factors can contribute to the variability of the pharmacological response [5]. Pregnancy is also a physiological state of the body in which the pharmacokinetics of drugs changes (fig. 1).

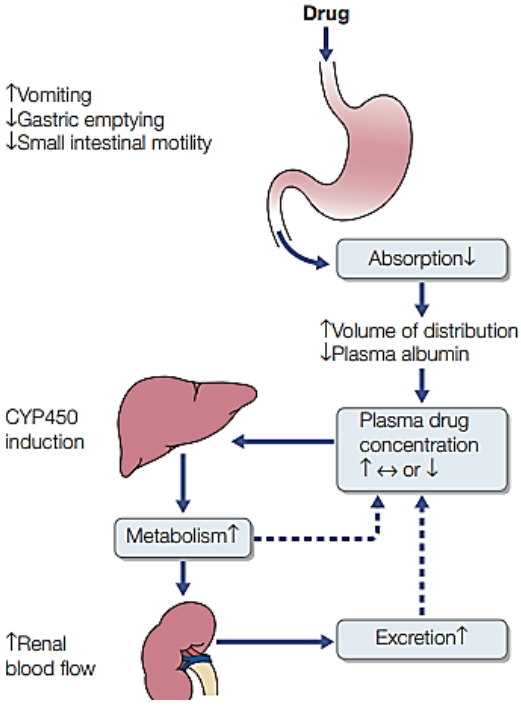

Fig. 1. Pharmacokinetic changes during pregnancy [6].

The absorption of drugs is influenced by many factors, such as: acidity of the stomach, transit time of food, metabolic and transport processes in the intestine. Nausea and vomiting, characteristic for the first trimester of pregnancy, can reduce the amount of drug available for absorption, so it is important to take the drug when nausea is minimal, for example, in the evening [2, 6]. During pregnancy, the production of gastric juice decreases and the secretion of mucus increases, as a result of which gastric pH increases to 5.6, with normal values of 1.5. Such changes can increase the ionization of weak acids (for example, acetylsalicylic acid) and reduce its absorption, but weak bases (for example, caffeine) will diffuse better, because they will not be ionized. Slowed intestinal motility and increased cardiac output improve blood circulation in the intestine and increase drug absorption [7] and accelerate its onset of action [6].

The pressure of increased in size uterus on the pelvic veins and the inferior vena cava prevents the outflow of blood from the rectum, which can interfere with absorption during the rectal route of administration. An increase in the body fat during pregnancy is a cause of deregulation of drug absorption in subcutaneous administration. In contrast, airway absorption may increase due to an increase of tidal volume characteristic for pregnancy [2].

The distribution of drugs was also changed. The plasma volume increases by 42%, reaching a total of 3.5 liters, and in parallel there is an increase in the volume of fluid in all parts of the body. Edema, which at least one third of women experience during pregnancy, can add up to 8 liters to the volume of extracellular fluid [6]. An expansion of the extracellular fluid volume will increase the distribution volume for hydrophilic drugs, but will decrease the plasma concentration of the drug. An expansion of the extracellular fluid volume will increase the distribution volume for hydrophilic drugs, but will decrease the plasma concentration of the drug. During pregnancy, the volume of the fat depot increases by about 4 kg, so the distribution volume for lipophilic drugs also increases.

It is known that the amount of plasma proteins changes both during normal pregnancy and in pathological conditions. With a normal pregnancy, albumin concentration decreases on average by about 10% after 20 weeks and by 13% after 32 weeks. The change of albumin's concentration is important in the prescription of drugs such as phenytoin, valproic acid, carbamazepine. Another plasma protein such as α-1-glycoprotein, which is involved in the binding of betamethasone, bupivacaine, lopinavir and lidocaine, is lower by 52% at the end of pregnancy (30–36 weeks of gestation) [8].

A complex biological barrier appears – the placental barrier. Lipophilic compounds pass through it (by diffusion). Ionized polar substances (e.g. Quaternary ammonium salts) cross the placenta poorly. The placenta also has a P-glycoprotein transporter [9]. Glycoprotein P is expressed on the maternal side of the placental membrane of syncytiotrophoblast. It removes xenobiotics and drugs from the circulatory system of the fetus into mother's circulatory system and also prevents the passage of several substrates through the blood-brain barrier to the fetus: calcium channel blockers, statins, macrolides, and some cytostatics [10]. For example, in antiretroviral therapy in a pregnant woman in order to prevent fetal HIV infection, it is extremely important to know that HIV protease inhibitors (for example, saquinavir), being a substrate of glycoprotein P, do not cross the placenta and thus do not protect the newborn [11].

The deposition of drugs during pregnancy in some tissues can lead to side effects. For example, tetracyclines bind to calcium and are deposited in bone tissue, contributing to impaired development of the skeleton of the fetus [12].

The metabolism of drugs by the liver during pregnancy is increased, mainly due to the induction of enzymes, possibly due to an increased level of hormones. Moreover, blood circulation in the liver does not change. This can lead to an increase in the excretion rate of these drugs (eg, theophylline) [6].

The activity of cytochrome P (CYP) isoforms such as CYP3A, CYP2D6, CYP2C9 increases, as a result of this the period of action of the non-metabolized form of the drug decreases and the daily dose of certain drugs should be increased: amlodipine, erythromycin [8]. However, each organism is individual. For example, in clinical practice, in connection with depression, pregnant women often take the antidepressant fluoxetine, which is metabolized by the CYP2D6 isoenzyme, the gene of which has a polymorphism. It was found that "slow CYP2D6 metabolizers" have adverse reactions during treatment with fluoxetine (sedation, cardiotoxicity, arrhythmias, etc.) more often, which is explained by high concentrations of the drug in the blood. Therefore, before prescribing antidepressants to pregnant women, it is necessary to conduct genotyping to identify the carriage of allelic variants of the CYP2D6 gene [11].

However, the activity of CYP1A2 and CYP2C19 decreases, therefore, the daily dose of drugs such as clozapine, theophylline, ondansetron, clopidogrel, omeprazole should be reviewed. It is known that progesterone and pregnanediol, the concentration of which increases during pregnancy, activate sulfation of a number of drugs, and vice versa they block the enzymes of UDP-glucuronyl transferase, which leads to a slowdown in glucuronidation in the second phase of metabolism for a number of drugs (for example, lamotrigine) [11].

Excretion of drugs by the kidney during pregnancy depends on filtration, secretion and reabsorption. During the first trimester, the glomerular filtration rate increases by 50% and continues to grow in the future. Little information about the effect of pregnancy on tubular secretion and drug reabsorption is available. An increase of tubular secretion during pregnancy for digoxin and amoxicillin has been reported. The renal clearance of ampicillin, cefuroxime, ceftazidime, cefradine, cefazolin increases in the second and third trimester, compared to non-pregnant women [2]. In this case, a dose adjustment of the drug is required.

During pregnancy, hepatic blood flow increases, which, in association with decreased binding of drugs to proteins, leads to an increase in clearance and lowered plasma concentrations of drugs [2].

Medicines and the fetus

The problem of evaluating the effect of drugs on the course and outcome of pregnancy is one of the most complex and least studied areas of clinical pharmacology. For most drugs, if they are not intended to treat complications of pregnancy and childbirth, for ethical reasons, special studies of their safety in pregnant women are not carried out. At the same time, most women use drugs of various pharmacological groups (antimicrobial, antianemic, painkillers, anti-inflammatory, psychotropic, multivitamins, etc.) during the gestational period, however, the benefit / risk ratio of their use during pregnancy has not been established.

The greatest danger poses the teratogenic effects of drugs, which are understood as anatomical malformations, impaired histogenesis with subsequent functional inferiority of the fetal organs and systems. In the early 60s of the twentieth century, more than 1000 children with phocomegaly were born in Europe (congenital absence of upper (proximal) parts of the limbs; in this case, the hands or feet, and sometimes both of them, are connected to the body by means of short stump). That is when the relationship of this developmental malformation with the use of the thalidomide tranquilizer during pregnancy was proven, i.e., the fact of drug teratogenesis was established. Preclinical studies of this drug, performed on several types of rodents, did not reveal its teratogenic properties. In this regard, in the absence of embryotoxic, embryoletal and teratogenic effects of the drug in the experiment still prefer not to recommend its use in humans during pregnancy until confirmation of the complete safety of such a drug after a statistical analysis of the results of controlled clinical trials of its use in pregnant women is performed [13].

Most countries use classifications of risk categories of drugs in pregnancy to indicate the potential risk of drugs to the fetus. The first of them was introduced in Sweden in 1978, and the next was the FDA (Food and Drug Administration) classification (1979), which was most widely used in the world. Based on FDA recommendations, the following categories of drugs are distinguished depending on teratogenicity:

- Category A: drugs in this group are harmless to the fetus throughout the whole pregnancy period (potassium chloride, iron preparations, multivitamins, triiodothyronine);
- Category B: experimental studies did not reveal teratogenic effects, or complications observed in animals were not found in children whose mothers were taking drugs included in this group (insulin, acyl salicylic acid, metronidazole);
- Category C: in animal studies, teratogenic or embryotoxic effects of the drug were detected, control tests were not carried out, or the effect of the drug was not studied (isoniazid, fluoroquinolones, gentamicin, antiparkinsonian drugs, antidepressants);
- Category D: the use of drugs carries a certain risk to the fetus, but the benefits of their use exceed the possible side effects (diazepam, doxycycline, kanamycin, diclofenac);
- Category X: the teratogenic effect of drugs of this group has been proven, their use is contraindicated before and during pregnancy (isotretinoin, carbamazepine, streptomycin) [14].

Material and methods

A retrospective cohort study of 40 cards of pregnant women, which were received at the University Hospital of Primary Care from 2017 to 2018, was conducted.

All women developed iron deficiency anemia (IDA) at a certain stage of pregnancy. IDA was confirmed by a hemoglobin blood test. Blood hemoglobin (Hb) values below 110 g/l. (trimesters I and II), in the trimester II – below 105 g/l and up to 90 g/l indicate IDA I degree, IDA degree II– hemoglobin – 70–89 g/l, IDA degree III – hemoglobin less than 70 g/l, according to WHO [15].

The incidence of pregnant with IDA depends on several factors: age, nationality, socioeconomic status, eating habits, diagnosis criteria [16, 17]. The study examined the following personal data of pregnant women: the age of the pregnant woman, gestational age at the time of registration, gestational age at the time of diagnosis IDA, the number of pregnancy, height, weight (in each trimester), hemoglobin (in each trimester). The study also looked at whether the pregnant woman suffered from co-existing diseases, such as liver, cardiovascular, respiratory, gastrointestinal, endocrine, gynecological, autoimmune diseases. In addition, the intake of medications for IDA was taken into account: the name, the dosage, the frequency of administration, before / after meals, and other medications.

The indicators of the first trimester corresponded to 11-12 weeks of pregnancy, the second – 23-24 weeks, the third - 32-33 weeks, in accordance with the antenatal visits of the pregnant woman to the clinic.

Additional calculations were performed to calculate the body mass index (BMI) of pregnant women in each trimester: BMI = weight (kg) /height $(m)^2$.

Women were divided into groups according to BMI:

<18.5 kg/m^2 – underweight.
18.5 – 25 kg/m^2 – normal weight.
25 – 30 kg/m^2 – overweight.
30 – 35 kg/m^2 – obesity class I.
35 – 40 kg/m^2 – obesity class II.
> 40 kg/m^2 – obesity class III.

Unfortunately, due to the lack of data, the gestational weight gain was not calculated since the weight prior to the pregnancy was not indicated in the medical cards.

The difference (increase) in hemoglobin between two trimesters was also calculated:

$$\Delta Hb_{m-n} = Hb_m - Hb_n$$

The difference in BMI between trimesters was calculated:

$$\Delta IMT_{m-n} = BMI_m - BMI_n$$

SPSS STATISTICS and MICROSOFT OFFICE EXCEL programs were used for calculations.

Results

The following results were revealed after processing the data.

Pregnant women were grouped into the following age groups (fig. 2).

The pregnancy number among all examined pregnant women is indicated in fig. 3. In the 1st place – women who are pregnant for the second time, in the 2nd place – pregnant women for the first time, in the 3rd place – women expecting a third child.

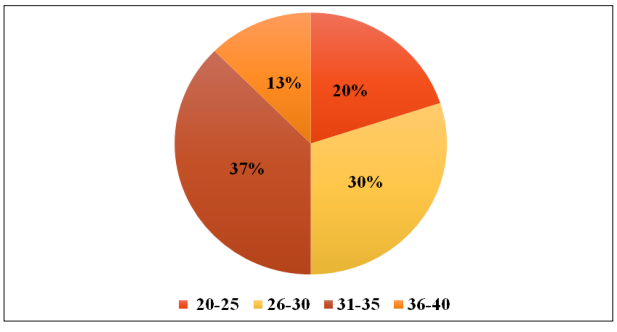

Fig. 2. The age groups of pregnant women.

Most pregnant women are between the ages of 31-35 years, a little fewer are between 26-30 years old, which may be explained by the achievement of a certain financial stability and favorable conditions for the birth of children by this period of life.

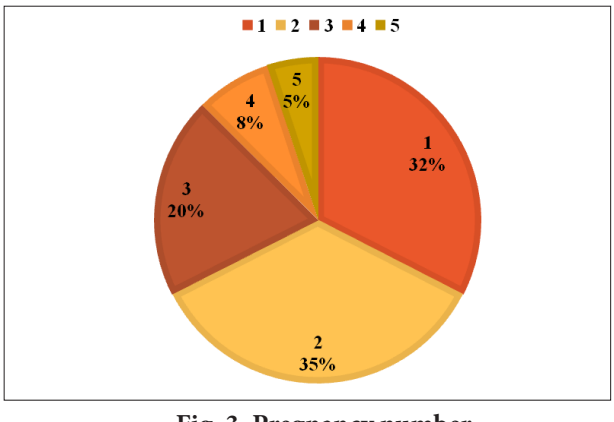

Fig. 3. Pregnancy number.

Two hundred and eighty-six women planning a pregnancy took part in a study conducted in Chisinau in 2010. The results of the study were summarized after childbirth. In conclusion, the author points out the following risk factors for the development of IDA in pregnant women: 1) meat consumption less than 1 time per week, 2) use of iron preparations less than 60 days during pregnancy, 3) low level of education, 4) three and more born children [18]. Note that 1/3 of the pregnant women in our study have already become mothers of many children. Why is IDA so common in pregnant women?

Iron deficiency (ID) is the most common malnutrition in the world [19] and the most common cause of anemia in pregnant women (up to 75%) [20]. According to the WHO, ID can be found in 3.6 billion people, among whom 2 billion people, that is, more than 30% of the world's population, suffer from anemia. The highest need for iron is observed in children in their first years of life (about 1 mg per day), which is associated with high rates of development; in the puberty, especially in girls in connection with the onset of menstruation (about 2 mg / day); in women of childbear-

ing age with monthly menstrual loss of iron (about 2.5 mg / day), in pregnant women (in the first trimester, 0.8 mg / day, in the second trimester – 4.0-5.0 mg / day, in the third trimester – up to 6.3 mg / day) due to active growth and fetal formation [21]. In general, uncomplicated pregnancy and childbirth are accompanied by a loss of 650 mg of iron [22]. It takes at least 2-3 years to restore the reserves of iron spent during pregnancy, childbirth and lactation [23]. Iron reserves do not have time to replenish with repeated pregnancy, in the presence of additional risk factors. ID in pregnant women is dangerous both for maternal health: decreased performance, general weakness, gestosis, premature detachment of a normally located placenta [24], and for the fetus: the risk of premature birth, the birth of a low birth weight child and even inhibition of the postnatal physical and neuropsychic development of the child are increased [25, 26].

It is important to understand that it is impossible to cure the patient IDA only with products rich in iron, since in them iron is mainly in the trivalent form (Fe^{3+}). But this does not mean that pregnant women should not be recommended to enrich their menu with food containing such an important trace element [27]. It is necessary to pay attention not so much to the amount of iron in the product as to the form in which it is presented. Iron is most effectively absorbed from products of animal origin, in which it is contained in the form of a heme, identical to that which is part of hemoglobin [28, 29]. The heme iron is absorbed by intestinal enterocytes unchanged. Gem is found in beef tongue, liver, rabbit, turkey, chicken, beef, fish [29]. Plant products: beans, pumpkin and sesame seeds, whole grains, thyme, parsley, field salad, contain non-heme iron, which is absorbed much worse, as it is presented in the form of Fe^{3+} and Fe^{2+}. Non-heme iron can be captured by cells of the intestinal mucosa only in the form of Fe^{2+} [28]. The intake of a large number of apples, pomegranates, carrots, beets, buckwheat, recommended earlier in the USSR, is not justified from the point of view of the limited absorption of iron from them [30].

It is impossible to eliminate IDA only by means of a diet, since the absorption of Fe from food is no more than 2.5 mg per day, while it is absorbed 15–20 times more from drugs [30].

Iron deficiency anemia (IDA) is a hematological syndrome characterized by impaired hemoglobin synthesis due to iron deficiency [31, 32] and, as a result, a decrease in the number of circulating red blood cells per unit blood volume is below normal for a given age and gender. IDA is hypochromic microcytic anemia, which is an independent nosological unit [33], but as a rule, IDA is associated with some disease or condition of the body that causes absolute iron deficiency. This gave some scientists reason to believe that IDA is always secondary, there is no idiopathic form of this disease [22].

Further in our study, concomitant diseases of pregnant women were identified (fig.4.). Gynecological pathology is a uterine fibroid, an ovarian cyst; autoimmune – vulgar psoriasis, autoimmune thyroiditis; endocrine – autoimmune thyroiditis, hyperthyroidism, hypothyroidism, type I diabetes mellitus; diseases of the respiratory system – bronchial asthma; cardiovascular diseases – varicose veins of the lower extremities, arterial hypertension of pregnant women, sinus tachycardia, WPW syndrome, hemorrhoids; liver disease – hepatitis B.

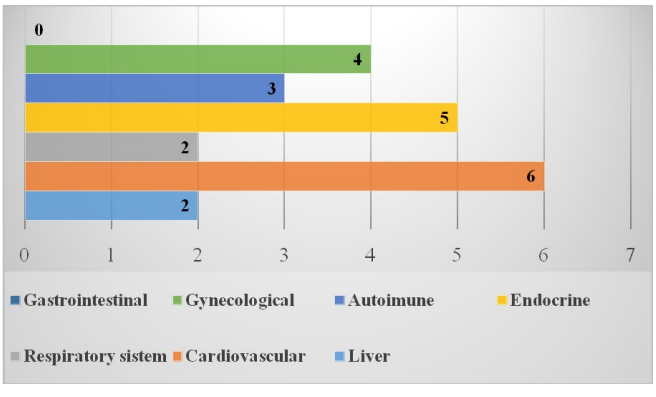

Fig. 4. Concomitant diseases during pregnancy.

As a result of counting, 19 out of 40 women suffered from concomitant pathology, which proves to us a high incidence of women of childbearing age with chronic diseases, which is probably one of the reasons for the development of IDA.

Pregnant women have been gaining weight for 9 months and BMI in each trimester has changed accordingly (fig. 5).

Fig. 5. BMI dynamics in three trimesters of pregnancy.

Thirty-two women out of 40 in the last trimester of pregnancy had a body weight greater than normal, but nevertheless if we compare the body weight parameters of pregnant women with the presence of IDA (fig. 6), we can draw interesting conclusions: during treatment with iron preparations, the best effect was observed in overweight women.

A prospective, cohort study of 100 pregnant women with different BMIs was conducted in Moscow, and doctors concluded that the higher the BMI, the less likely the development of anemia in the third trimester [34].

Iron absorption increases to 30-60% of the total amount in the diet in women with obesity during pregnancy, since the iron depot is exhausted and there is an increase in the

rate of erythropoiesis, as well as a slowdown of intestinal motility, which is characteristic of the second half of pregnancy, which lengthens the absorption period.

It is generally accepted that there are three possible causes that can lead to ID and anemia in obesity: 1) nutritional deficiency of iron, 2) an increase in the volume of circulating blood due to the intensive development of adipose tissue and, as a consequence, an increased need for iron, 3) the development of a chronic systemic inflammatory process in obesity [35]. The most likely cause of IDA in pregnant women is iron deficiency due to increased body need.

WHO (2016) recommends oral supplements with a content of 30-60 mg of elemental iron daily for pregnant women with normal hemoglobin levels to prevent IDA [15]. The equivalent of 60 mg of elemental iron is 300 mg of iron sulfate, 180 mg of iron fumarate or 500 mg of iron gluconate.

Pregnant women with IDA are prescribed 120 mg of iron per day until the hemoglobin reaches 105–110 g / l [36, 37]. After normalizing hemoglobin levels, the pregnant woman continues to take iron as usual (60 mg per day). Weekly supplements taken for at least 12 weeks increase the iron content in the body, as can be judged by the increase in hemoglobin and serum ferritin. The daily use of iron preparations should be continued until the end of pregnancy, as well as the first 6 months of breastfeeding [27].

Iron-containing drugs are recommended to be taken 30-40 minutes before meals, with 100 ml of water or juice. The medicine should not be washed down with tea, coffee, milk or taken with food, as they reduce the absorption of iron [27]. The tannin contained in tea negatively affects the absorption of iron from food [22].

It should be noted that iron medications in the intestinal lumen interact not only with food components, but also with drugs (oxalates, tannins, antacids, tetracyclines, chloramphenicol, penicillins), which complicates the absorption of iron [38, 39].

In the treatment of IDA, the study revealed:

1. Family doctors prescribed 100% of pregnant women an iron-containing drug according to WHO recommendations: Sulfate Fe^{2+} + Vitamin C in a proportion: 320 mg + 60 mg (Sorbifer Durules) 1 tablet 2 times per day; and issued free to insured pregnant women in accordance with the current Order No. 729/230A, issued on June 11, 2018 by the Ministry of Health, Labor and Social Protection of the Republic of Moldova and the National Health Insurance Company [40].

2. The reception of "Sorbifer Durules" was appointed before meals to all women, taken with a glass of water. However, after the appearance of nausea and discomfort in the epigastrium, the reception was postponed for after the meal to 11 pregnant women.

3. At the same time, other multivitamin and polymineral drugs were prescribed, such as Ojestan (folic acid, iodine, omega-3 fatty acids, vitamins E and D3), Prenatal (vitamins A, C, D3, E, B1, B2, B6, B12, B9, PP, iron, zinc, calcium).

Why was Sorbifer Durules preferred?

Firstly, the drug has an inherent delayed release, which is provided by the special Durules technology, when the active substance is contained in a biologically indifferent plastic matrix of a spongy structure. Iron is first released from the surface layer of the system, and then gradually from deeper layers. The empty carrier is destroyed and removed from the body. At the same time, the gastrointestinal mucosa is slightly irritated, due to the lower concentration of iron during its delayed release. The release of the active substance occurs regardless of the pH of the gastrointestinal tract [22].

Secondly, side effects when taking iron medication vary in degrees inherent in almost every drug and are manifested primarily by symptoms of gastrointestinal discomfort. These include a tendency to constipation or diarrhea, a change in the color of feces (black), nausea, heaviness in the epigastric region, and a metallic taste in the mouth [22, 41]. In retard forms of Fe^{2+} and Fe^{3+} medication, side effects are minimal.

Thirdly, in the work of P. A. Vorobyov [42] it is indicated that prices for iron-containing drugs can vary 10-15 times, and therefore patients and doctors are concerned about the ratio of cost and the resulting positive effect of the therapy. As an example, an analysis of several iron-containing drugs is carried out, on the basis of which the author concludes that the preparation "Sulfate Fe + Vitamin C" (Sorbifer Durules) has the lowest cost of ferrous iron, therefore, this medication is the most economically feasible in terms of "cost-efficiency".

The change in the number of pregnant women with IDA by trimester of pregnancy is indicated in fig. 6.

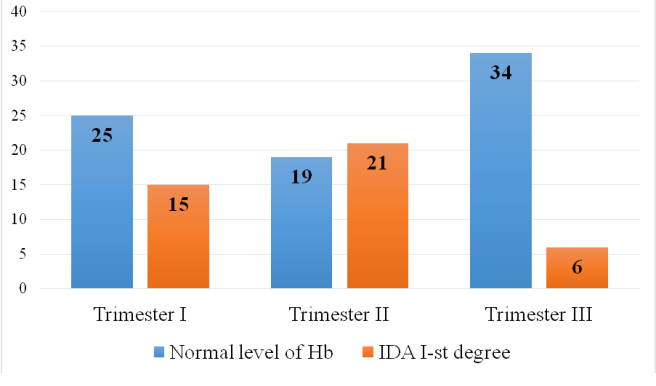

Fig. 6. The dynamics of IDA by trimester of pregnancy.

The largest number of pregnant IDA was observed in the second trimester, it includes women whose drug effect of Sorbifer Durules has not yet increased hemoglobin to normal levels in women with IDA detected in the first trimester, as well as newly discovered cases of IDA. In the second trimester, the stage of organ formation is very active in the growing fetus, as a result of which iron is used more intensively than in the first and hemoglobin decreases in direct proportion to the decrease in the mother's serum iron.

Table 1

Correlation of BMI_1 with ΔHb_{2-1} and ΔHb_{3-}

Parameter	Medium	Standard deviations	Pearson correlation (r)	Bilateral significance (p)	N
BMI_1	27.58	5.26			15
ΔHb_{2-1}	20.6	9.14	+0.617	0.014	15
ΔHb_{3-2}	3.86	7.53	+0.027	0.925	15

Note: we studied 15 cases of pregnant women who developed IDA in the first trimester and were prescribed treatment with iron-containing drugs.

Table 2

Correlation between ΔBMI_{2-1} and ΔHb_{2-1}

Parameter	Medium	Standard deviations	Pearson correlation (r)	Bilateral significance (p)	N
ΔBMI_{2-1}	1.59	0.66			15
ΔHb_{2-1}	20.6	9.14	-0.59	0.836	15

Table 3

Correlation between ΔBMI_{3-2} and ΔHb_{3-2}

Parameter	Medium	Standard deviations	Pearson correlation (r)	Bilateral significance (p)	N
ΔBMI_{3-2}	1.7	0.91			15
ΔHb_{3-2}	3.86	7.53	-0.318	0.247	15

Pearson correlation (r) is a two-dimensional measurement of the bond strength between two variables. If an increase in the values of one variable corresponds to an increase in the values of another variable, then the relationship is called direct (positive +); if an increase in the values of one variable corresponds to a decrease in the values of another variable, then the relationship is inverse (negative -). To assess the strength of the correlation the Cheddock table is used (tab. 4). The lower the probability (p-level value), the higher the statistical significance of the result. The result is considered statistically significant if the p-level does not exceed 0.05. That is, if $p < 0.05$, the correlation is significant, if $p > 0.05$, then the correlation is negligible.

We conclude that there is a positive (+), noticeable ($r = 0.617$) statistically significant relationship $p = 0.014$, $p < 0.05$ between BMI_1 and the increase in hemoglobin from the first to the second trimester of pregnancy (ΔHb_{2-1}) while taking the drug "Sorbifer Durules" (tab. 1).

Further attempts to find a connection between ΔIMT_{2-1} and ΔHb_{2-1}, between ΔIMT_{3-2} and ΔHb_{3-2} were unsuccessful, since the bilateral significance in the first case is $r = 0.836$, and in the second case $r = 0.247$ and both of them have $p > 0.05$, therefore, there is low significance (tab. 2, 3).

Moreover, among 15 women with IDA in the first trimester of pregnancy, in pregnant women with normal weight (n = 7), the increase in hemoglobin over 3 months of treatment with Sorbifer Durules averaged 14.28 g/l, and in pregnant women with class I of obesity (n = 8) – 26.12 g/l., that is, almost 2 times more.

These results are comparable with other sources. Women with normal and low BMI have a longer duration of anemia, even during treatment with Sorbifer Durules, as well as a slower increase in hemoglobin when taking iron supplements, compared with overweight women [43].

Women, especially those with normal and low BMI, can be recommended to increase the dosage of "Sorbifer Durules": 2 tablets – 2 times a day, which may contribute to an increase in Hb levels to the corresponding trimester of pregnancy values.

The absorption of iron medication can be accelerated by the simultaneous administration of succinic, ascorbic, pyruvic, citric acids, as well as fructose, sorbitol, methionine and cysteine. Calcium, vitamins C, B12, gastric acid, pepsin and copper contribute to the absorption of iron, especially if they come from animal sources [44].

Conclusions

1. The physiological changes that develop during pregnancy have a significant effect on the pharmacokinetics of drugs, which is reflected in the need to make appropriate amendments in the dosage regimen.

2. With obesity during pregnancy, iron absorption increases to 30-60% of the total amount in the diet, since the iron depot is exhausted and there is an increase in the rate of erythropoiesis, as well as a slowdown of intestinal motility, which lengthens the absorption period.

3. There is a positive, noticeable, statistically significant relationship between the BMI of pregnant women in whom IDA developed in the first trimester of pregnancy and the growth of hemoglobin during treatment with "Sorbifer Durules".

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