Anemia in Women of Reproductive Age

Alina V. Solovyova, Viola Gace, Kristina S. Ermolenko and Vadim A. Khorolskiy

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Abstract

Anemia is a common condition in women of childbearing age which is associated with wide spread hyperplastic processes in the uterus (leiomyomas, etc.) and abnormal and/or abundant uterine bleeding (AUB). Our study has considered the main causes of bleeding and the therapy aimed on limiting the amount of blood loss, as well as preoperative treatment of iron deficiency in women with uterine leiomyomas, planning for pregnancy.

The combination of anemia with other abnormalities in the woman’s health status is associated with complications during pregnancy such as premature births, the birth of small children and failure of the formation of neural tube in iron deficiency and hypoxia.

During the treatment of iron deficiency anemia (IDA) with saline iron, we noted severity and pain in the stomach in 11.9% of patients, nausea in 13.1%, constipation in 21.4%, and diarrhea in 7.1% of women. Such complications did not occur while treating with ferric iron. The use of drugs Iron III hydroxide polymaltose in women after the end of lactation resulted in normalization of the blood hemoglobin within 30 days and the number of erythrocytes and of serum ferritin by the 90th day.

Keywords: anemia, reproductive age, premature birth, uterine leiomyomas, abnormal uterine bleeding

1. Introduction

Anemia in women of reproductive age is the most common condition during pregnancy and post pregnancy days. Iron deficiency is associated with serious health problems such as impaired working capacity, weakness, malaise, headaches, cognitive impairment, decreased concentration or attention, etc. [1]. The lack of iron in the body can be due to inadequate intake, impaired absorption, increased needs and excessive losses. Inadequate intake of iron is often associated with a vegetarian (or vegan) diet, malnutrition or lack of iron in the...
diet. Same food with a predominant fat and sugar content, fast food, various diets used to maintain low body weight eventually lead to iron deficiency and/or anemia. In India, for example, about 30% of people are vegan; in Russia, this indicator is more modest—about 3–4%, as in most countries of Europe (Switzerland, Spain, Portugal, Poland, etc.). Impaired absorption of iron in the gastrointestinal tract (GIT) plays an important role in the development of iron deficiency and/or anemia. Diseases of the GIT are found in 20–24% of women of reproductive age [2]. Increased iron needs arise in children which is associated with their active growth. In adolescents, this is associated with an increase in the total mass of red blood cells and muscle mass. In young men, however, iron deficiency is less common than in girls, although their growth and growth rate are higher. In girls the high incidence of iron deficiency anemia is associated with the additional factor of blood losing during menstruation. Chronic blood loss and iron deficiency initiate in puberty if there is a disturbance of the development of menstrual function and they occur in a quarter of girls and adolescents [3]. Chronic repeated blood loss is the most common cause of iron deficiency anemia. The highest rates of iron deficiency are characteristic for women of childbirth age which is associated with monthly blood loss, pregnancy, parturition and lactation. A study conducted in 1998, by S. Kagamimori et al. has shown that 78% of Japanese schoolgirls have iron deficiency anemia (IDA) of varying severity 3 years after the onset of menstruation [4]. Women of childbearing age are at risk of developing IDA.

Many of them have chronic latent iron deficiency which remains undiagnosed for a long time as there are no expressed clinical symptoms and the body is well adapted to it. The content of iron and ferritin in the serum during pregnancy decreases as a result of an increase in the volume of plasma and an increase in total iron-binding capacity (TIBC), the percentage of transferrin is also reduced. Increased needs are only partially counter balanced by increased absorption in the intestine and mobilization of iron stores. If iron stores are partially or completely depleted at the beginning of pregnancy; which is observed with frequent and/or profuse menstruation, iron deficiency can be relative or absolute by the time of delivery. Up to 50–60% of women do not have enough iron reserves during pregnancy [5, 6] which is associated with adverse perinatal outcomes.

The data of Rosstat (2014) indicate that the number of women with abundant menstrual bleeding increased by 1.5 to 2 times in 10–15 years [26]. Women often do not consult a specialist for example, 59% of patients with heavy menstruation consider them normal and 41% are sure that they are not amenable to treatment [7]. Regular excessive loss of blood (more than 60–80 ml per cycle) disrupts the whole complex of physiological parameters, hemoglobin levels fall in erythrocytes and iron in plasma [8].

With physiological blood loss these changes are not observed. Adequate nutrition and a healthy lifestyle allow the body to independently restore the volume of blood and iron stores.

The consequence of monthly excessive menstrual blood loss with insufficient intake of iron is iron deficiency anemia which is confirmed by the following inferences [9]:

1. Patients with iron deficiency anemia lose a higher amount of menstrual blood in comparison with healthy women.
2. The users of hormonal contraceptives (even in the presence of a menstrual-like reaction), the iron content in the body is higher than in women who do not take estrogen-progestational agents and who have spontaneous menstruation.

With the purpose of revealing abundant menstrual flow (which causes IDA) the FIGO experts advice the gynecologist to ask their patients the following questions [10]:

1. How much bleeding is profuse?
   - Do you have to change the pads at night?
   - Do the protection pads completely soak in after 2 hours during the days of the most profuse bleeding?

2. Does menstrual blood loss affect the physical condition?
   - Do you observe the release of large clots of blood during menstruation?
   - Have you ever experienced any weakness or lack of air (symptoms of iron deficiency) during menstruation?

3. Does menstruation reduce the quality of life?
   - Does social life require correction in these days?
   - Are you worried about the unpleasant moments associated with bleeding?

2. Results of our studies

The duration of more than 7 days and the volume of blood loss over 80 ml as well as the presence of related physical, emotional and other problems are the characteristics of profuse menstruation. Normal menstruation is inherent in the duration of 2–7 days, the amount of blood lost is 50–80 ml and absence of pain that would disrupt the habitual life or require the intake of medication.

Detection of frequent and/or abundant uterine bleeding for more than 6 months should initiate a patient’s examination for hemoglobin and other indicators of red blood cells. The greatest need for iron occurs during pregnancy and lactation. Iron deficiency or IDA leads to many numerical obstetrical complications primarily associated with metabolic disorders in the placental tissue.

In cases of iron deficiency during the first trimester of pregnancy, development of “defective” endometrium is observed which is facilitated by the initiation of intensive peroxidation of lipids in its cells followed by a change in the excitability of cell membranes and a decrease in the functional activity of the tissue. This leads to an inadequate implantation of the fetal egg. There is lack of proper rearrangement of the spiral arteries. This process is high energy-intensive and in IDA the cells lack oxygen sufficient for energy metabolism. Without reorganization of the uterine arteries, adequate fetal blood supply is impossible and primary placental insufficiency develops.
In the 2nd trimester, IDA in pregnant women leads to hypoxic disorders [11]. Circulatory disorders in the placenta and a lack of oxygen cause a failure of the second wave of trophoblast invasion. Hypoxia provokes the release of stress hormone cortisol which negatively affects the growth of the fetus. With further progression of pregnancy in iron deficiency, oxygenation of the blood worsens and total pathological disturbances occur in the tissues which affects the fetoplacental complex, fetal growth, pregnancy and parturition. A systematic review of “Maternal anemia and pregnancy outcomes in low- and middle-income countries” according to the scientific data of world-wide publications in 2016 found that anemia during pregnancy is associated with significantly higher risks [12]:

- low birth weight (RR = 1.3);
- premature birth (RR = 1.6);
- perinatal mortality (RR = 1.5);
- neonatal mortality (RR = 2.7).

The course of pregnancy in women with IDA inevitably affects the physical and psychomotor development of her child. Iron deficiency has a significant limiting effect on the brain’s potential due to the negative impact on morphological structures.

The nervous system will reach its morphological maturity only then the brain will be ready for full work [13, 14].

All the basic structures of the nervous system are built up in the first trimester [11]. At the 3rd-4th weeks after fertilization a neural plate is formed. During 4–7 weeks neural tube is developed from which the brain and spinal cord are subsequently formed. By the end of the 8th week from the anterior part of the neural tube are formed five brain vesicles that give rise to all the parts of the brain such as the cerebral hemispheres, pons and cerebellum, middle and intermediate brain and medulla. In 5–10 weeks differentiation of some parts of the brain develops the cortex and subcortical structures.

In the second and third trimesters of pregnancy the structures of fetal nervous system are more complex. The neuronal precursor cells and the neuroglia begin to differentiate. From the 20th week nerve centers are formed which ensure the functioning of the main vital organs and begin the myelination processes. Disturbances of neurogenesis due to iron deficiency significantly limit the potential of the brain in the future.

In the third trimester cells differentiate into neurons and glial cells (astrocytes, oligodendrocytes, ependymocytes) grow axons and dendrites of neurons, synaptic contacts are formed and neural processes intensively myelinate. Obviously there should not be any iron deficiency for the prevention of defective morphological and functional development of the brain [11]. The slowdown of energy metabolism in the brain in iron deficiency occurs for two reasons; the activity of iron-requiring enzymes decreases and the amount of oxygen supplied to the cells decreases the expenditure during the intensive development processes increases by a factor of 2.
The results of numerous studies indicate the following facts:

1. Mental and psychological development is particularly affected by iron deficiency during intrauterine growth and/or in the early years of postnatal life.

2. The consequences of iron deficiency are expressed in adulthood, preventing the full realization of the inherent genetic potential [14–18].

Children who lacked iron in utero or infancy compared with peers who did not lack iron in the subsequent years of life especially during the age 19–28:

- lag behind in mental development;
- suffer from mental disorders;
- have delayed neuromotor development, difficult temperament (mettle);
- are depressed and apathetic, more anxious;
- suffer from attention deficit disorder combined with hyperactivity.

Analyzing the long-term studies (2012–2017) regarding the course of pregnancy in 321 women aged 19–45 years (continuous random sample) conducted at the Department of obstetrics and gynecology with the perinatology course of the Peoples Friendship University of Russia (Head of the Department, RAS Corresponding Member V.E. Radzinskiy) (Table 1) we found that there was no difference in the incidence of iron deficiency anemia among different age groups of women.

We also studied the frequency of iron deficiency anemia in women with preterm labor (PL). The subject of the study were 132 pregnant women who entered the maternity hospitals in Moscow to acquire medical assistance. Patients were divided into three groups: Group I - women with preterm labor at term of gestation from 22 to 27 weeks ± 6 days (n = 34); Group II - patients who gave birth prematurely at the gestation period of 28–37 weeks ± 6 days (n = 56) and Group III - women with term labor which constituted the control group (n = 42).

The greatest number of complications in all trimesters of pregnancy was observed in patients with PL including iron deficiency anemia (Figure 1). In the first trimester IDA was detected in 6 (17.6%) women with early PL and in 6 (10.7%) with PL at a period of 28–36/7 weeks in women who gave birth in time this complication was not observed. In the second trimester mild-to-moderate IDA was diagnosed in 9 (26.5%) of women who gave birth at the gestation age of 22–27/6 weeks, 15 (26.8%) gave birth within 28–36/7 weeks and 3 (7.1%) of women in the control group (p < 0.05). In the third trimester mild anemia was observed in group II in 15

| Age of women (years) | 19–24 | 25–29 | 30–34 | 35–39 | 40–45 |
|----------------------|-------|-------|-------|-------|-------|
| Number of women (n)  | 65    | 67    | 64    | 63    | 62    |
| Frequency of IDA n (%)| 14 (21.5%) | 15 (22.4%) | 14 (21.9%) | 14 (22.2%) | 14 (22.6%) |

p > 0.05 - the reliability of the differences is not revealed.

Table 1. Frequency of iron deficiency (IDA) anemia in pregnant women.
(26.8%) women and in 4 (9.5%) between those who gave birth in time. Anemia or iron deficiency is one of the factors of unfavorable perinatal outcomes.

After giving birth the frequency of IDA increased most significantly in women with PL and in women with early PR it was found in 11 (32.4%) of them in patients with preterm labor at a term of 28–36/7 with a frequency of 18 (32.1%). Anemia was found less often in women with term delivery - 5 (14.3%). One third of the women who had premature delivery suffered from IDA and this is not only because anemia developed during pregnancy but also because in women with PL significantly more often the delivery was an operative route (cesarean section). In the group with early PL in 5 (14.7%) in the group with PL in the period of 28–36/7 in 17 (30.3%) and the smallest number 3 (7.1%) of CS was performed in women with term delivery.

The results of the study confirmed the opinion of Professor Serov V.N. (2009) that premature birth is the delivery of a sick child from a sick woman. Anemia was more often diagnosed in women with premature labor.

All women with anemia with both preterm and term (n = 34) delivery were examined by the end of lactation (the average duration was 1.8 ± 0.4 years). In the postpartum period they received both bivalent and ferric iron. The number of erythrocytes, hemoglobin level and serum ferritin were measured. In 14 women there were no clinical and laboratory signs of anemia and iron suppression was based on the results of normalization of serum ferritin. Twenty patients were stopped taking iron supplements in the postpartum period on the basis of normalization of hemoglobin and revealed iron deficiency anemia of mild degree after lactation (Table 2). When determining the level of hemoglobin in the blood (Hb) it was found that the average level varied from 92 to 109 g/l (101.2 ± 1.3 g/l). Women were examined by a gastroenterologist.
and physician and treatment was prescribed by a physician. In the observed group there were no patients with blood diseases, inflammatory diseases and autoimmune diseases. Ten (50%) women were diagnosed with diseases of the gastrointestinal tract which was a risk factor for iron absorption and 3 (15%) patients were diagnosed with excessive menstrual bleeding (hormone therapy was prescribed). After 30 days the number of erythrocytes and hemoglobin reached to normal level. Serum ferritin reached normal values by day 90 (Table 2).

In the reproductive age anemia is the most common extragenital condition leading to health problems, adverse perinatal outcomes and often associated with organic diseases of the uterus. The International Federation of Gynecology and Obstetrics (FIGO) classification [19] identified the structural and non-structural causes of abnormal uterine bleeding. The results of the work of world-class experts [20] stated that in Russia about 50% of uterine bleeding is due to organic diseases of the uterus. In comparison, in the USA, Canada, Brazil, Korea and China this reason was found in 34–44% of women. Identification and recovery of women with uterine leiomyoma in the pre pregnancy period as in 20–50% of women leiomyoma is the cause of severe, irregular and prolonged uterine bleeding, iron deficiency anemia is a reserve for reducing complications of pregnancy and adverse perinatal outcomes.

A prospective study conducted from 2010 to 2015 included 292 women with uterine leiomyoma in female residents of the Krasnodar Territory. Inclusion criteria to the study were: reproductive age, uterine fibroids, pregnancy planning. Exclusion criteria: extragenital diseases leading to anemia; lack of reproductive plans; pregnancy.

The average age of women was 31.2 ± 1.5 years. Clinical characteristics and anamnesis (the medical history of a patient) of women are presented in Table 3. The inhabitants of the city were more than 160 (54.8%) compared to the residents of the village 132 (45.2%). More often women with fibroids had secondary specialized education - 161 (55.1%). Equally women were registered - 144 (49.3%) and unregistered - 135 (46.2%) marriages. 13 (4.5%) patients were unmarried but they planned a pregnancy.

The study of the reproductive anamnesis (Table 2) revealed that 179 (61.3%) of women had a history of delivery, i.e. they planned a second or third child. Practically all women 275 (94.2%) had an anamnesis for an official abortion. At the time of the examination none of the participants used any reliable means of contraception (COCs, IUDs). 183 (62.7%) of women reported using interrupted sexual intercourse and condoms the remaining 109 (37.3%) planned a pregnancy so they did not use contraception.

| Indicators            | Initial indicators | In 30 days      | In 60 days      | In 90 days      |
|-----------------------|--------------------|-----------------|-----------------|-----------------|
| Number of erythrocyte | 3.2 ± 0.3          | 3.9 ± 0.1’      | 4.1 ± 0.2’      | 4.2 ± 0.3’      |
| Hemoglobin content    | 101.2 ± 1.3        | 109.7 ± 1.1’    | 113.5 ± 1.2’    | 114 ± 0.9’      |
| Serum ferritin (fl)   | 23.2 ± 1.1         | 27.3 ± 1.3’     | 39.7 ± 1.2’     | 52.1 ± 0.2’     |

*p < 0.05 in comparison with initial indicators.

Table 2. Indicators of “red” blood smear in women with mild anemia (n = 20) treated with Iron III hydroxide polymaltozate.
The duration of uterine leiomyomas was 4.3 ± 0.2 (2–10 years). The main complaints of women planning pregnancy were bleeding in 201 (68.8%), pain syndrome in 161 (55.1%), disturbance of the function of neighboring organs in 135 (46.2%) and asthenic syndrome in 192 (45.5%).

The number of uterine fibroids per woman varied from 2 to 12 on average 5.4 ± 0.3 and the number differed depending on the localization of the node. Multiple uterine fibroids were found in 266 (91%) women. Subserous localization of leiomyomas was detected in 181 (62%) women, subserous-interstitial and interstitial - in 260 (89%) women. Submucous site localization was determined in 32 (11%) patients. The diameter of the largest fibroid node did not exceed 110 mm an average of 49.8 ± 18.4 mm (15–110 mm).

The average level of hemoglobin in the blood (Hb) varied from 82 to 145 g/l (116.2 ± 2.3 g/l). The lowest level of Hb was observed in women with a predominance of submucous localization of the nodes - 90.8 ± 1.6 g/l (82–99 g/l). Anemia was diagnosed in 158 (54.1%) women. Anemia of mild degree was detected in 79 (27.1%) women. Hemoglobin level in these women was in the range of 109–94 g/l (100.1 ± 0.7 g/l). Anemia of moderate severity was detected in 79 (27.1%) women, the hemoglobin level varied from 91 to 72 g/l (84.4 ± 1.1 g/l). All women experienced profuse menstrual and intermenstrual bleeding.

In 134 (45.9%) women anemia was not detected and the hemoglobin level was determined in the range of 120–145 g/l and averaged 127.5 ± 1.2 g/l. Outpatients with anemia were administered with divalent (84 - 28.8% women) and ferric iron (50 - 17.1% women). The comparative characteristics of the drugs revealed the following: in the treatment of IDA saline iron causes severity and pain in the stomach in 10 (11.9%), nausea in 11 (13.1%), constipation in 18 (21.4%) and diarrhea in 6 (7.1%) of women.

The average period of preparation for surgery after the administration of iron supplementation was 82.3 ± 0.1 days. In all women with mild anemia (79 - 27.1%) regardless of whether they received two or three-valent iron, normal level of red blood cell values were found. Normalization of the indices was achieved in 8 (2.7%) women with concomitant anemia of

| Parameter                             | Amount of women (n = 292) | Absolute number | Relative number, % |
|---------------------------------------|---------------------------|-----------------|--------------------|
| Social status                         |                           |                 |                    |
| Inhabitants of the city               | 160                       | 54.8            |                    |
| Inhabitants of the village            | 132                       | 45.2            |                    |
| Education                             | 125                       | 42.8            |                    |
| Secondary specialized education       | 161                       | 55.1            |                    |
| Registered marriage                   | 144                       | 49.3            |                    |
| Unregistered marriage                 | 135                       | 46.2            |                    |
| Unmarried                             | 13                        | 4.5             |                    |

Table 3. Clinical characteristics and anamnesis of women.

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medium degree. In 71 (24.3%) compensation indices were impossible due to excessive amount of bleeding. They had to undergo surgery with uncompensated indicators of red blood cells.

3. Discussion of the results

Uterine fibroids and polyps are an indication for surgical treatment and hysteroscopy. However, most abnormal and/or excessive amount of bleeding from the uterus requires medical therapy. The classification of FIGO [19] allows not only to determine the cause of abnormal and/or excessive amount of bleeding from the uterus but also to prescribe a therapy that helps to reduce blood loss:

1. Chronic abnormal uterine bleeding (AUB) is abnormal in terms of volume, regularity, and/or frequency of uterine bleeding during most cycles in the last 6 months. As a rule, this condition does not require immediate medical intervention.

2. Acute AUB is an episode of profuse bleeding in which the specialist has sufficient reason for urgent intervention in order to prevent further blood loss. It can occur against a background of chronic AUB or for the first time in life.

3. Intermenstrual AUB occurs between predictable periods of cyclic menstruation. FIGO experts recommend replacing the term intermenstrual abnormal uterine bleeding on the concept of metrorrhagia.

Classification of causes of AUB called PALM-COEIN relates the causes of uterine bleeding in women of reproductive age to one of the nine categories (Table 4). The first four, grouped in the PALM group can be identified visually (structural). The rest are not related to structural anomalies and objectification is not amenable (non-structural).

Diagnostic measures for abnormal uterine bleeding include not only establishing the cause of bleeding and examination but also for the presence of anemia (hemoglobin level, hematocrit, general blood test).

Treatment of IDA in abnormal uterine bleeding cannot include only iron drugs as repeated blood loss will not lead to normalization of blood parameters. In cases of structural changes (polyps, fibroids) surgery is required. Non-steroid anti-inflammatory drugs (NSAIDs) have a high efficiency (blood loss on the background of NSAID intake decreases by an average of 58%),

| PALM (structural)         | COEIN (non-structural)     |
|---------------------------|-----------------------------|
| Polyp                     | Coagulopathy                |
| Adenomyosis               | Ovulatory dysfunction       |
| Leiomyoma                 | Endometrial                 |
| Malignancy and hyperplasia| Iatrogenic                  |
|                           | Not yet classified          |

Table 4. Classification of causes of abnormal uterine bleeding (FIGO, 2011).
but it is not safe for the patient especially with prolonged use [8, 21]. The ability of NSAIDs to compensate uterine bleeding is due to inhibition of cyclooxygenase enzyme activity that leads to a decrease in the synthesis of prostacyclin that inhibits platelet aggregation. Tranexamic acid (synthetic lysine derivative) is an effective and a fairly safe drug which reduces blood loss by an average of 58%. The positive effect of tranexamic acid on the quality of life and sexual relations is reported [22, 23]. Contraindication to the administration of tranexamic acid is the presence of an episode of thrombosis. The mechanism of action of tranexamic acid is associated with reversible blocking of plasminogen and prevention of degradation of fibrin. Levonorgestrel-releasing intrauterine system (IUD-LNG) reduces menstrual blood loss by 74–97% [24]. During the first month with the use of IUD-LNG the duration of bleeding may increase. In adolescence IUD-LNG are not used since their mechanism of action is associated with endometrial atrophy.

Combined oral contraceptives (COCs) have a wide spread in reducing blood loss from the uterus. The effectiveness of COC is 43 - 88% [12]. Bleeding when using COC usually stops within 24 hours (the so-called hormonal hemostasis). The effect of COC is associated with the suppression of endometrial proliferation and the indirect reduction in the amount of blood loss.

The use of cyclic gestagens in the luteal phase are ineffective for the treatment of profuse menstruation, however they regulate the menstrual cycle [8]. Admission of medroxyprogesterone acetate (10 mg/day) or norethisterone acetate (2.5–5 mg/day) in a cyclic mode from the 16th to the 25th day provides a predictable bleeding profile.

Gonadotropin-releasing hormone agonists (GnRH agonists) are ineffective in the treatment of profuse menstruation. They are used only for certain indications as second line therapy [8]. These drugs completely block the function of the hypothalamic-pituitary-ovarian axis and cause amenorrhea in 89% of patients which is accompanied by severe side effects such as vaginal dryness, hot flashes, sweating, and with prolonged use (6 months or more) - osteopenia. The mechanism of action of GnRH agonists is associated with a decrease in the number of gonadotropin receptors in the pituitary gland with suppression of gonadotropin release and subsequent decrease in the level of estradiol to the state of hypogonadism.

For having a pregnancy with adequate iron reserves in the body it is extremely important that menstruating women of childbirth age do not experience a deficit in it. For the prevention of iron deficiency in this population in 2016 WHO (World Health Organization) updated the recommendations according to which iron drugs at a dosage of 60 mg/day should be taken to all menstruating women and adolescent girls for 3 months in the year and 3 months before conception. WHO experts recommend to use such preventive measures at the national level in countries where the incidence of anemia reaches 40%.

The optimal choice for women with iron deficiency (latent or already formed anemia), are oral drugs.

1. Bivalent iron drugs are ferrous sulfate, as well as fumarate, gluconate and glyceryl sulfate of iron.

2. Trivalent iron drugs are polymaltose complex of iron hydroxide, iron succinylate protein.

Preparations of two- and trivalent iron are comparatively effective but they have differences in tolerability and compliance.
In order to overcome the negative effects of salt iron and improve the tolerance an iron drug based on hydroxide of the polymaltose complex (HPC) was created which has advantages over iron salt drugs with high efficiency, safety, no risk of overdose, intoxication and poisonings and less dyspeptic complications. This allows us to recommend iron preparations based on the hydroxide of the polymaltose complex to women with IDA in their reproductive age [25]. Discontinuation of the treatment with iron drugs is indicated after the normalization of serum ferritin and replenishment of the iron storage.

4. Conclusion

Anemia in women of reproductive age is the most frequent extragenital disease. It impairs the quality of women life and in pregnancy, leads to complications of gestation (miscarriage, placental insufficiency, etc.) and adversely affects the growth and development of the fetus. Iron deficiency before conception will disrupt the formation of the nervous tissue (the brain), which is manifested by a decrease in intelligence, disturbances of psychomotor development and other abnormalities in the future. Often the cause of IDA or iron deficiency in women are the organic diseases of the uterus (polyps, fibroids) and functional disorders - abnormal and/or profuse uterine bleeding. Chronic iron deficiency as a rule remains undiagnosed for a long time as there are no expressed clinical symptoms and the body is well adapted to it. Therefore, role of the gynecologist in diagnosing anemia as well as revealing and treatment of gynecological diseases that led to IDA is important. All the iron drugs have the same efficacy but the fewest side effects (in gastrointestinal tract) have been in trivalent drugs which allows them to be recommended for the treatment of anemia in the reproductive age.

Author details

Alina V. Solovyova*, Viola Gace¹, Kristina S. Ermolenko¹ and Vadim A. Khorolskiy²

*Address all correspondence to: av_soloveva@mail.ru

1 Department of Obstetrics and Gynecology with the Course of Perinatology of the Peoples Friendship University of Russia (RUDN University), Moscow, Russian Federation

2 Obstetrics and Gynecology of the Perinatal Center of the Regional Clinical Hospital No. 2, Krasnodar, Russian Federation

References

[1] Pavlov AD, Morshchakova EF, Rumyantsev AG. Erythropoesis, Erythropoietin, Iron. Moscow: GEOTAR-Media; 2011. 304 p

[2] Radzinsky VE, editor. Guide to Outpatient Care in Obstetrics and Gynecology. 2nd ed., Revised, and additional. Moscow: GEOTAR-Media; 2014. 944 p
[3] A teenage girl as a patient. Endocrine gynecology of physiological pubertal: Optimal correction minimum. In: Kuznetsova IV, editor. Information Bulletin. Moscow: Editorial staff of the magazine Status Praesens; 2014. 20 p

[4] Kagamimori S, Fujita T, Naruse Y, Kurosawa Y, Watanabe M. A longitudinal study of serum ferritin concentration during the female adolescent growth spurt. Annals of Human Biology. 1998;15:413-419

[5] Ivanyan AN, Nikiforovich II, Litvinov AV. A modern view of anemia in pregnant women. The Russian Bulletin of the Obstetrician-Gynecologist. 2009;1:17-20

[6] Konovodova EN, Yakunina NA. Iron deficiency and pregnancy. RMZ. 2010;(19)

[7] Bitzer J, Serrani M, Lahav A. Women’s attitudes to heavy menstrual bleeding, and their impact on quality of life. Open Access Journal of Contraception. 2013;2013(4):21-28

[8] Heavy Menstrual Bleeding: Assessment and Management. URL: https://www.nice.org.uk/guidance/cg44/chapter/1-guidance

[9] Toxqui L, Pérez-Granados AM, Blanco-Rojo R, et al. A simple and feasible questionnaire to estimate menstrual blood loss: The relationship with hematological and gynecological parameters in young women. BMC Women’s Health. 2014;14(71). [PMID: 24886470]

[10] Bushnell DM, Martin ML, Moore KA, et al. Menorrhagia Impact Questionnaire: Assessing the influence of heavy menstrual bleeding on quality of life. Current Medical Research and Opinion. 2010;26(12):2745-2755. [PMID: 21043553]

[11] Mutovin GR, Zhilina SS, Umakhanova ZR. Neuroontogenesis and its disorders. Children’s Hospital. 2009;(2):36-50

[12] Rahman MM, Abe SK, Rahman MS, et al. Maternal anemia and risk of adverse events in the low- and middle-income countries: Systematic review and meta-analysis. Clinical Nutrition. 2016;103(2):495-504. [PMID: 26739036]

[13] Radlowski EC, Johnson RW. Perinatal iron deficiency and neurocognitive development. Frontiers in Human Neuroscience. 2013;7:585. [PMID: 24065908]

[14] Hare D, Ayton S, Bush A, Lei P. A delicate balance: Iron metabolism and diseases of the brain. Frontiers in Aging Neuroscience. 2013;5:34. [PMID: 23874300]

[15] Beard J. Iron deficiency alters brain development and functioning. The Journal of Nutrition. 2003;133(1):1468s-1472s. [PMID: 12730445]

[16] Milward E, Acikyol B, Bassett B, et al. Brain changes in iron loading disorders. In: Linert W, Kozlowski H, editors. Metal Ions in Neurological Systems. Wien: Springer-Verlag; 2012. pp. 17-25

[17] Sadrzadeh SMH, Saffari Y. Iron and brain disorders. American Journal of Clinical Pathology. 2004;121(1):s64-s70. [PMID: 15298151]
[18] Burke RM, Leon JS, Suchdev PS. Identification, prevention and treatment of iron deficiency during the first 1000 days. Nutrients. 2014;6(10):4093-4114. [PMID: 25310252]

[19] Munro MG, Critchley HO, Fraser IS. The FIGO classification of causes of abnormal uterine bleeding in the reproductive years. Fertility and Sterility. 2011;95(7):2204-2208. [PMID: 21496802]

[20] Andreeva EN, Hamoshina MB. Report: Abundant uterine bleeding. In: Educational Seminar “Innovations in Obstetrics and Gynecology from the Perspective of Evidence-based Medicine”; Ufa; 2016

[21] Lethaby A, Duckitt K, Farquhar C. Non-steroidal anti-inflammatory drugs for heavy menstrual bleeding. Cochrane Database of Systematic Reviews. 2013;1. Art. CD000400. [PMID: 23440779]

[22] Lethaby A, Farquhar C, Cooke I. Antifibrinolytics for heavy menstrual bleeding. Cochrane Database of Systematic Reviews. 2000;4. Art. CD000249. [PMID: 11034679]

[23] Wellington K, Wagstaff AJ. Tranexamic acid: A review of its use in the management of menorrhagia. Drugs. 2003;63(13):1417-1433. [PMID: 12825966]

[24] Jensen J, Mansour D, Lukkari-Lax E, et al. Bleeding patterns with the levonorgestrel-releasing intrauterine system when used for heavy menstrual bleeding in women without structural pelvic pathology: A pooled analysis of randomized controlled studies. Contraception. 2013;87(1):107-112. [PMID: 23040140]

[25] Chernov VM, Tarasova IS. Efficiency and safety of trivalent iron drugs in the treatment of iron deficiency anemia. The Attending Physician. 2013;(8). www.lvrach.ru

[26] Moscow: Rosstat. 2014
