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Research Article

A Strategy of "Resistance Blood Management" in Pregnant Women at Risk of Massive Obstetric Hemorrhage

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Abstract

The purpose of the study: To determine the effectiveness of treatment of anemia with intravenous iron (III) hydroxide sucrose complex (Sufer) in pregnant women with pathological placentation, as the first stage of "patient blood management" before delivery. Our studies have been limited to examining the effectiveness of an iron supplement for the treatment of anemia.

Methods: Among 86 pregnant women with placental pathology, 58 (70.7%) had anemia. Severe anemia with a hemoglobin level <70 g/l was in 13 (22.4%), and moderate anemia with a hemoglobin level <90 g/l - in 19 (32.8%). The first group included 18 (31.1%), pregnant women, with placenta previa with periodic blood loss during pregnancy. The second group consisted of 40 (68.9%) pregnant women with the invasive placenta. The gestation period in all women was 33 + 6 weeks. Anemia was treated by administering intravenous iron Sufer 3 times a week (5-7 injections).

Results: The main factor that led to pathological placentation was the scar on the uterus. In pregnant women of the second group with invasive placenta, the scar on the uterus was in 38 (95%) women. Severe anemia was present in 2 (11.1%) pregnant women with placenta previa and 2.4 times more often in pregnant women with invasive placenta -11 (27.5%). Moderate anemia was present in 4 (22.2%) women in the first group and in 15(37.5%) in the second group. In pregnant women with severe anemia, after 5-7 injections of the drug Sufer significantly increased the level of hemoglobin by 30 g/l, increased the number of erythrocytes to $2.8x10^{12}$/l, increased serum iron by 2 times, the level of ferritin increased to 19.6 μg/l and decreased transferrin content. For pregnant women with moderate anemia, 3-5 injections of the drug were sufficient to normalize the indicators. Normalization of blood parameters allowed to reduce the risk of bleeding, and the number of blood transfusions and improved treatment outcomes.

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Conclusion: Timely diagnosis of iron deficiency anemia in pregnant women with placental pathology is an important means of preventing massive blood loss and reducing the number of blood transfusions, as the first stage of the strategy "patient blood management". Intravenous iron (III) sucrose complex hydroxide (Sufer) has shown high clinical efficacy in the treatment of iron deficiency anemia in pregnant women with placental pathology and can be recommended for widespread use in practical medicine.

Keywords: Pregnancy; Placental pathology; Iron deficiency anemia; Patient blood management; Iron (III) sucrose hydroxide complex (Sufer).

Introduction

Major obstetric hemorrhage (MAH) is the leading cause of maternal mortality and major maternal morbidity, accounting for 27.1% of maternal deaths worldwide, ranging from 8% in developed areas to 32% in East Africa [1]. Critical and debilitating complications such as hemorrhagic shock, acute respiratory distress syndrome, disseminated intravascular coagulation, gastrointestinal deficiency, Fertility loss, hypophyseal necrosis (Sheehan's syndrome), and even maternal death can be caused by the delayed diagnosis of the disease in the mother and adequate medical care [2].

At present, patient blood management (PBM) is the timely application of evidence-based medical and surgical concepts aimed at maintaining hemoglobin levels, optimizing hemostasis, and minimizing blood loss to improve treatment outcomes [3,4].

Pregnant women who have an abnormal placenta, such as placenta previa or invasive placenta, are at risk for massive obstetric bleeding during pregnancy and childbirth. A significant percentage of such pregnant women have iron deficiency anemia. Treatment of anemia is of great importance in preparation for surgical delivery, which will reduce the need for blood transfusions and improve treatment outcomes [5-7]. Severe prenatal anemia is an important prognostic factor for adverse events that require intensive treatment during pregnancy.

The World Health Organization (WHO) reports that more than 40 percent of pregnant women worldwide suffer from anemia. Thus, 13 recent studies examining the relationship between prenatal anemia and the risk of massive obstetric bleeding have shown that severe prenatal anemia increases the risk of MAC (HS=3.54; 95% CI:1.20, 10.4, p-value=0.020) [8]. The WHO study found that severe maternal antenatal or postnatal anemia (of any type) was associated with an increased risk of maternal death (HI 2.36;95% CI 1.60-3.48) [9].

Iron deficiency is the most common cause of maternal anemia due to insufficient iron stores in early pregnancy, increased pregnancy-related iron requirements, and iron loss due to blood loss during childbirth. During pregnancy, serum ferritin concentration <30 μg/l means insufficient or empty iron stores and, therefore, an increased risk of developing iron-deficiency anemia. The value of ferritin in the serum <12 μg/l suggests an established iron deficiency with empty iron stores at all stages of pregnancy [10-12].

Three meta-analyses published in 2018-2019 assessed the benefits and risks of oral and intravenous iron based on randomized trials in pregnant or postpartum women with iron deficiency. These analyzes showed that iron

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supplements in any way (orally or intravenously) increase hemoglobin and ferritin; compared with oral iron, intravenous iron was associated with higher hemoglobin levels after therapy [11,12].

Intravenous iron is likely to be superior to oral iron in promoting rapid correction of anemia and iron deficiency, which may become more important as pregnancy progresses, and in ensuring iron deficiency in the developing fetus. None of the newborns was diagnosed with iron deficiency anemia in women receiving intravenous iron supplements. Studies have shown better efficacy in increasing hemoglobin and ferritin levels and a favorable safety profile with fewer side effects when using intravenous iron supplements [12,13]. Timely diagnosis and adequate treatment of iron deficiency anemia in pregnant women can prevent the development of a significant number of complications during pregnancy and childbirth, improve the well-being of pregnant women [11-13].

For patients with placenta previa and invasive placenta, qualified prenatal care and preoperative preparation include correction of iron deficiency anemia. Anemia is a controlled risk factor-timely examination and treatment of anemia in the antenatal period is a crucial means of preventing severe obstetric complications.

The aim of our study was to determine the effectiveness of treatment of anemia with intravenous iron (III) sucrose complex hydroxide (Sufer) in pregnant women with pathological placentation, as the first stage of "patient blood management", to prepare for surgical delivery.

Material and methods

Our clinical prospective study conducted at the regional peritoneal center included 86 pregnant women with placental pathology. Among them, 58(70.7%) had anemia. Severe anemia with a hemoglobin level <70 g/l was in 13(22.4%), moderate anemia with a hemoglobin level <90 g/l-in 19(32.8%), mild anemia with a hemoglobin level <105 g/l was in 26(44.8%) pregnant women. The first group consisted of 18(31.1%) pregnant women with placenta previa with recurrent blood loss during pregnancy. The second group consisted of 40(68.9%) pregnant women with invasive placenta. The gestation period in all women was 33+6 weeks. For pregnant women with severe and moderate anemia, intravenous iron (III) sucrose hydroxide (Sufer) was prescribed.

Sufer was developed to provide controlled digestible iron for iron transport and storage of proteins in the body (transferrin and ferritin, respectively). After intravenous administration, iron from the complex is absorbed mainly by the liver, spleen, and bone marrow. In the second stage, iron is used to synthesize hemoglobin, myoglobin, and other iron-containing enzymes, or stored in the liver as ferritin.

The average therapeutic dose was 150-200 mg depending on the level of hemoglobin, and the frequency of administration 3 times a week depending on the level of hemoglobin. The effectiveness of therapy was assessed weekly by subjective assessment of improvement in well-being and by laboratory parameters of peripheral blood.

The following parameters were determined in each patient before the start of Sufer and weekly during treatment: hemoglobin content, erythrocyte count, average

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hemoglobin content in the erythrocyte, serum iron, transferrin, ferritin.

Research results and discussion

The mean age of patients was 31 ± 2.3 years. 38 (65.5%) women were rural residents. More than 90% of women did not work. One in five women has a bad habit of smoking. Chronic alcoholism was in 2 pregnant women. There were only 6 primiparous women (10.3%). In addition to anemia, concomitant extragenital pathology was present in 28(48.3%) pregnant women of both groups. The following diseases were detected: congenital heart disease in 2(7.1%), hypertension in 5(17.8), chronic pyelonephritis in 3(10.5%), chronic glomerulonephritis in 1(3.5%), urinary tract 2(7.1%), pregestational diabetes 1(3.5%), epilepsy 1(3.5%), chronic pancreatitis 1(3.5%), chronic hepatitis 2 7.1%), cirrhosis of the liver in 1 (3.5%), bronchiectasis in 1(3.5%), chronic bronchitis in 3(10.7%), HIV infection in 5(17.8%) , varicose veins in 8(28.5%). There was no statistical difference between the groups. The combination of anemia with concomitant extragenital diseases is an important risk factor for complications of pregnancy and obstetric bleeding.

Obstetric history/pregnancy The first group	**The first group n=18 abs.h. (%)**	**Another group n=40 abs.h. (%)**
History of artificial abortions	2(11.1%)	4(10%)
More than 3	1(5.5%)	2(5%)
Spontaneous miscarriages	1(5.5%)	3(7.5%)
Infertility	2(11.1%)	2(5%)
IVF	2(11.1%)	1(2.5%)
Inflammatory diseases of the pelvic organs	4(22.2%)	4(10%)
Uterine fibroids	1(5.5%)	2(5%)
The threat of abortion:	2(11.1%)	5(12.5%)
in the first trimester		
in the second trimester	3(16.6%)	4(10%)
in the third trimester	3(16.6%)	6(15%)
Moderate preeclampsia	4(22.2%)	8(20%)
Preeclampsia is severe	-	1(2.5%)
Fetal growth retardation	4(22.2%)	12(30%)
Cesarean section in the anamnesis:		
1	2(11.1%)	8(20%)
2	2(11.1%)	15(37.5%)
3	-	10(25%)
4	-	2(5%)
5	1(5.5%)	1(2.5%)
Premature detachment of the placenta in the anamnesis	1(5.5%)	3(7.5%)
Myomectomy in the anamnesis	1(5.5%)	2(5%)

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Complicated postoperative period	2(11.1%)	4(10%)
History of blood transfusion	2(11.1%)	5(12.5%)
Stillbirth	2(11.1%)	3(7.5%)
Neonatal death	1(11.1%)	1(2.5%)

Table 1: Obstetric history and course of pregnancy.

According to our study, the main factor that led to pathological placentation was the scar on the uterus. In the first group of pregnant women with placenta previa, 7(38.8%) had a scar on the uterus. In pregnant women of the second group with invasive placenta, the scar on the uterus was 38(95%), which is 2.5 times more. The postoperative period was complicated in 11.1% of women in the first group and in 10% of women in the second group. Blood transfusion was performed in 12.5% of women in the second group. Only half of the women (bleeding and anemia) were able to explain the cause of the blood transfusion.

In the preoperative preparation for operative delivery, the treatment of anemia is important in order to reduce bleeding and indications for blood transfusion.

Among the examined pregnant women, 2(11.1%) pregnant women with placenta previa had severe anemia and 11(27.5%) pregnant women with invasive placenta were 2.4 times more likely. Moderate anemia was present in 4(22.2%) women in the first group and in 15(37.5%) women in the second group. In total, severe and moderate anemia was present in 6(33.3%) pregnant women of the first group and 26(65%) in the second group, who were treated with intravenous iron sufer 3 times a week, 5-7 times depending on the results treatment). Complaints in pregnant women in both groups did not differ. One in two pregnant women had a general weakness, one in a third of women with severe anemia, and one in four women with severe anemia and shortness of breath.

Indicators	Severe anemia		Moderate anemia	
	n=13		n=19	
	Before treatment	After treatment	Before treatment	After treatment
Hemoglobin g/l	65 ± 3.5	95 ± 5.2*	88 ± 3.8	110 ± 4.5*
Erythrocytes 10^{12}/l	1.8 ± 0.05	2.8 ± 0.2*	2.5 ± 0.1	3.2 ± 0.3*
Color indicator	0.8	0.9	0.9	1
Morphological changes of erythrocytes	Anisocytosis, poikilocytosis	No	Anisocytosis	No
Serum iron µmol/l	10.5 ± 0.2	20.6 ± 0.6*	12.5 ± 0.4	25.8 ± 0.8*
Ferritin mcg/l	11.5 ± 0.3	19.6 ± 0.8*	15.2 ± 0.5	28.5 ± 0.9*
Transferrin g/l	3.8 ± 0.02	3.2 ± 0.04	3.6 ± 0.01	3.1 ± 0.02

Table 2: Main laboratory indicators before and after treatment with Sufer. Note: *The probability of the difference is $p<0.05$.

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The results of treatment of iron deficiency anemia with intravenous Suffer were positive. There were no significant side effects of the drug. In pregnant women with severe anemia, after 5-7 injections of Sufer significantly increased hemoglobin by 30 g/l, increased the number of erythrocytes to 2.8x1012/l, increased serum iron by 2 times, ferritin increased to 19.6 μg/l and decreased transferrin content. In pregnant women with moderate anemia, 3-5 injections of the drug were sufficient to normalize the indicators. Prior to the operative delivery, all pregnant women had satisfactory results, which reduced the risk of bleeding, the number of blood transfusions, and improved treatment outcomes.

Conclusions

1. Pregnant women with placenta previa and invasive placenta are at risk for massive obstetric bleeding during pregnancy and childbirth.
2. Timely diagnosis of iron deficiency anemia in pregnant women with placental pathology is an important means of preventing massive blood loss and reducing the number of blood transfusions, as the first stage of the strategy "patient blood management".
3. Intravenous preparation of iron (III) sucrose hydroxide complex Sufer has shown high clinical efficacy in the treatment of iron deficiency anemia in pregnant women with placental pathology and can be recommended for widespread use in practical medicine

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