

EFFECTIVENESS OF THE RECOMBINANT ERYTHROPOIETIN USE IN ANEMIA OF PREGNANT WOMEN

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Summary. The article represents the data of the course of delivery and the state of newborns in 124 pregnant women with anemia; 63 of them – without pyelonephritis and 61 pregnant women – with chronic pyelonephritis. 30 pregnant women were – with a physiological course of pregnancy. It has been determined that the use of ferrotherapy in pregnant women with iron deficiency anemia is not always effective. As a result of the detection of the phenomenon of inadequate production of serum erythropoietin (sEP) in pregnant women with anemia, on this basis the inclusion of recombinant erythropoietin (rEP) into the treatment complex of anemia of pregnant women was offered for the first time. The influence of the applied treatment on the indicators of the state of newborns after the use of the traditional approach and inclusion into the therapeutic complex of rEP was noted.

Keywords: treatment of anemia of pregnant women, recombinant erythropoietin, iron.

Introduction

According to WHO, the incidence of iron deficiency anemia (IDA) in pregnant women varies from 21% to 80% in different countries taking into account the hemoglobin level, and varies from 49% to 90% for serum iron level. In underdeveloped countries, the frequency of IDA in pregnant women reaches 80%. In countries with a high standard of living and a lower birth rate, IDA is diagnosed in 8-20% of pregnant women [4, 13].

Iron deficiency anemia (IDA) in pregnant women is considered to be the one of the most common complications of gestational period [1]. The importance and topicality of this problem is explained by the fact that various complications of pregnancy, childbirth, which significantly affect the perinatal and maternal

morbidity and mortality rates, develop against the background of anemia [6, 7, 8].

A number of authors believe that in the early neonatal period, children born in mothers with latent iron deficiency or manifestation of IDA have an increased body weight loss, delayed prolapsed umbilical cord, prolonged course of physiological jaundice, impairment of the immune status and the process of formation of intestinal microbiocenosis. In future, such children are retarded in psychophysical development, despite the normalization of hematological parameters [2, 4]. The literature contains data indicating the association of anemia in children with the disorders of intellectual development, behavior, and disability [5]. Every third child born from anemic mother, is suffering from colds, anemia in 23.1%, and 20.6% have allergic

manifestations, most often in the form of exudative diathesis [9, 10]. Anemia in pregnant women, combined with placental insufficiency, causes a violation of fetal life as a result of violation of utero-placental circulation, the occurrence of degenerative processes in the placenta. This causes a slowdown in the growth of the fetus, the damage to its hematopoietic and nervous systems [3]. The deficiency of hemopoietic substances, as well as prolonged action of hemic hypoxia, leads to a decrease of non-specific immunity factors, which is especially pronounced in preterm infants. This is one of the reasons for the morbidity of the infants born from mothers with IDA purulent-septic infections [6, 12]. The objective of the study is to improve the effectiveness of treatment of anemia in pregnant women with the use of the traditional approach and inclusion into the treatment complex of recombinant erythropoietin on the basis of the assessment of the adequacy of serum erythropoietin production.

Materials and methods of the study

There were 124 pregnant women with anemia of moderate and severe degrees in the third trimester of gestation under our supervision, who were treated at the Departments of Obstetric Pathology and Extragenital Pathology of the Ivano-Frankivsk Regional Perinatal Center. All pregnant women with anemia of moderate to severe degrees were divided into two groups: pregnant women of the group I – without pyelonephritis (63 persons), pregnant women of the group II – with chronic pyelonephritis (61 persons). 30 pregnant women were included into a control group – with a physiological course of pregnancy.

Determination of the general blood count was performed using the hematological analyzer BC – 3000 plus / BC – 2800, automatic. (BC – 3000 plus / BC – 2800 Auto Hematology Analyzer), the firm “Mindray”, China.

Determination of the level of erythropoietin in human blood serum was performed using the immune enzyme method with the help of the “Vector-Best” test kit, Russia. The levels of sEP

in pregnant women with anemia of moderate to severe degrees were significantly various. For a detailed analysis of the level of sEP products, the method for assessing the adequacy of EP offered by Barosi G. [11] in pregnant women with anemia on the basis of studying the ratio of sEP and hematocrit, was for the first time used by us. The nomographic technique for interpreting the results of childbirthatory research using computer processing was used.

Statistical data processing was performed using the standard STATISTICA 7.0 program. The estimation of the probability of the difference in mean values was carried out using the Student’s twin t-criterion. Valid values were considered at $p < 0.05$.

Results of the study

All patients with anemia of moderate to severe degrees were prescribed iron replacement therapy (200 mg/day for elemental iron) during two weeks. After the course of iron replacement therapy with ferrum preparations, we found that not all pregnant women with anemia achieved a positive effect after the performed therapy. Thus, in 98 (79.0±3.7%) pregnant women, the positive effect of the offered therapy was noted, in 22 (17.7±3.4%) pregnant women no effect was observed ($p < 0.05$), and in 4 (3.2±1.6%) pregnant women there was a negative dynamics of hemoglobin level after the performed treatment ($p < 0.05$).

When comparing the sEP level of pregnant women with anemia with sEP level in pregnant women with a physiological course of pregnancy, it was determined that sufficient level of sEP occurred in 33 (26.6±3.9%) pregnant women with anemia. An inadequate level of sEP was diagnosed in 3 (2.4%±1.4%) pregnant women with anemia. In 88 (70.9±4.1%) pregnant women with anemia, the levels of sEP were significantly higher compared to the control group.

That is why the analysis of literature data and our research led to the study of the ratio of sEP and hematocrit. In this regard, using the method of Barosi G. [11], the phenomenon of

inappropriate EP products in gestational anemia was found.

As a result of the study it was determined, that in 98 (79.0±3.7%) pregnant women there was an adequate level of sEP of anemia, in 26 pregnant women (21.0±3.7%) an inadequate level of sEP of anemia was diagnosed. In this regard, based on the results of studying the levels of sEP and identifying the phenomenon of inadequacy of EP products, for the first time on this basis it was offered to include the recombinant erythropoietin into the treatment complex for pregnant women.

All pregnant women with adequate level of sEP were prescribed standard iron replacement therapy (200 mg/day for elemental iron),

10 pregnant women with inadequate level of sEP were prescribed standard iron replacement therapy, 16 pregnant women with inadequate level of sEP – standard iron replacement therapy in combination with rEP in the course dosage of 450 IU/kg of weight.

The effect of combined use of ferrotherapy with rEP on the positive dynamics of the course of childbirth in women, whose pregnancy was complicated by gestational anemia, was most pronounced as a result of complex treatment.

Characteristics of the course of childbirth in pregnant women with anemia after the performed treatment are represented in Table 1.

Table 1. Characteristics of the course of childbirth in gestational anemia after the treatment

Index	Control group, n=30	Pregnant women with adequate level of sEP (iron medicines), n=98	Pregnant women with inadequate level of sEP (iron medicines), n=10	Pregnant women with inadequate level of sEP (iron+rEP), n=16
	abs(P±m)	abs(P±m)	abs(P±m)	abs(P±m)
Physiological childbirth	28(93.3±4.6)	71(72.5±4.5)*	6(60.0±15.5)*	14(87.5±8.3)
Poor uterine contraction strength	6(20.0±7.3)	40(40.8±5.0)	5(50.0±15.8)	5(31.3±11.6)
Untimely discharge of amniotic fluid	3(10.0±5.5)	25(25.5±4.4)	3(30.0±14.5)	2(12.5±8.3)
Childbirth of postmature fetus	–	15(15.3±3.6)	2(20.0±12.7)	–
Caesarean section	2(6.7±4.6)	27(27.6±4.5)*	4(40.0±15.5)*	2(12.5±8.3)
Bleeding >200 ml	8(26.7±8.1)	46(46.9±5.0)	4(40.0±15.5)	3(18.8±9.8)

Note:

* - a significant difference of the indicators with the control group, p<0.05.

According to the results of Table 1, the number of physiological childbirths was higher in the group of pregnant women with inadequate level of sEP, who in addition to ferrum medicines, took rEP. In the same group, although not reliably, but less often the weakness of childbirth was noted, untimely discharge of amniotic fluid in the use of ferrotherapy and rEP. Against the background of the offered therapeutic complex, a decrease of the frequency of surgical interven-

tions in pregnant women was observed in the use of ferrotherapy and rEP. Our research showed that the frequency of bleedings in the group of pregnant women decreased against the background of the offered therapy, which was considered as a result of a positive effect on the hemostasis system.

The offered treatment complex positively influenced the condition of the fetus, which was further noted in newborns (Table 2).

Table 2. Influence of the applied treatment on the indicators of the newborns' state

Index	Control group, n=30	Pregnant women with adequate level of sEP (iron medicines), n=98	Pregnant women with inadequate level of sEP (iron medicines), n=10	Pregnant women with inadequate level of sEP (iron+rEP), n=16
	abs(P±m)	abs(P±m)	abs(P±m)	abs(P±m)
Prematurity	–	15(15.3±3.6)	3(30.0±14.5)	2(12.5±8.3)
Functional immaturity	–	25(25.5±4.4)	2(20.0±12.7)	1(6.3)
Hypotrophy	6(20.0±7.3)	20(20.4±4.1)	3(30.0±14.5)	2(12.5±8.3)
Traumatism	–	7(7.1±2.6)	1(10.0)	–
Pneumonias	–	14(14.3±3.5)	2(20.0±12.7)	1(6.3)
The syndrome of increased reflex excitability	4(13.3±6.2)	10(10.2±3.1)	2(20.0±12.7)	–
CNS depression syndrome	–	12(12.2±3.3)	1(10.0)	–
Loop of cord	6(20.0±7.3)	35(35.7±4.8)	4(40.0±15.5)	3(18.8±9.8)

As it is shown in the Table 2, in the group of pregnant women with inadequate level of sEP, who in addition to iron medicines, took rEP, the frequency of childbirth of preterm, functionally immature and hypotrophic children decreased. It should be noted that in this group of newborns

there were no cases of traumatism, a syndrome of increase or suppression of the central nervous system, and pneumonia occurred only in one newborn.

The influence of the offered therapy on the weight of newborns is described in Table 3.

Table 3. Influence of the offered therapy on a newborns' weight

Weight	Control group, n=30	Pregnant women with adequate level of sEP (iron medicines), n=98	Pregnant women with inadequate level of sEP (iron medicines), n=10	Pregnant women with inadequate level of sEP (iron+rEP), n=16
	abs(P±m)	abs(P±m)	abs(P±m)	abs(P±m)
Up to 2500 g	1(3.3)	22(22.5±4.2)*	3(30.0±14.5)*	2(12.5±8.3)
2500–3000 g	4(13.3±6.2)	30(30.6±4.7)	3(30.0±14.5)	2(12.5±8.3)
>3000 g	25(83.3±6.8)	46(46.9±5.0)*	4(40.0±15.5)*	12(75.0±10.8)

Note:

* - a significant difference of the indicators with the control group, $p < 0.05$.

According to the data from Table 3, there was a decrease in the percentage of birth of small infants in the group of pregnant women with inadequate level of sEP who received iron and rEP, with an increase of newborns weighing >3000 g. Low birth-weight babies were more likely to be born using the conventional therapy, indicating a lack of efficacy. There were no cases of perinatal death.

Discussion

Analyzing the results of treatment of pregnant women with IDA who have chronic pyelonephritis in the third trimester of gestation, it is possible to confidently note the positive effect of rEP on the course of pregnancy, the antenatal condition of the fetus, and later – the newborn's condition. Thus, in pregnant women, having received rEP in combination with ferrum medicines in terms of biophysical profile of the fetus, a satisfactory condition was noted in 75.0±10.8% of cases, no signs of severe hypoxia were observed. In this group of pregnant women, the percentage of physiological childbirths has significantly increased, the percentage of weakness of childbirth activity, the untimely discharge of amniotic fluid has decreased. Also,

the positive effect of the offered therapy was observed in newborns: the prevalence of premature childbirth, functionally immature and hypotrophic children reduced after the combined use of iron medicines and rEP. Number of newborns weighing >3000 g has increased.

Thus, the inclusion of rEP into the medical complex of anemia in pregnant women with chronic pyelonephritis is pathogenetically grounded, positively affects the course of pregnancy, childbirth, antenatal fetal condition. In this group of pregnant women, a favorable course of the postpartum and early neonatal period was noted.

Conclusions

1. Anemia in pregnant women leads to pronounced changes in the organism of the mother and the fetus, the development of complications in childbirth and postpartum period, adversely affects the further development of newborns.

2. Adequate treatment of anemia in pregnant women taking into account the inadequacy of EP products improves the clinical course of the disease, positively affects the course of pregnancy, childbirth and the state of newborns.

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