EDITORIAL

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Research Article

GESTATION OUTCOMES IN VARIOUS OPTIONS OF HELP FOR PREGNANT WOMEN WITH RH-IMMUNIZATION

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BACKGROUND: To date, several options for helping pregnant women with rhesus immunization are known: (a) "active tactics" in carrying out methods of efferent therapy in the form of basic operations (plasmapheresis, hemosorption) in combination with adjuvant methods (immunoglobulin, blood photomodification with ultraviolet, laser beams, ozone therapy) to pregnant women; (b) "wait-and-see active tactics" with observation of the pregnant woman, followed by intrauterine intravascular transfusions of washed donor red blood cells; (c) "mixed active tactics" with a sequential combination, alternation of these methods. In Russia, only option 2 with fetal transfusions of washed donor red blood cells is accepted as the basis and paid for. The objective of the study is to conduct a comparative analysis of pregnancy outcomes in women with rhesus immunization using different management options.

MATERIALS AND METHODS: A total of 392 women were followed up at seven different institutions in Russia and at the Donetsk Center for Maternal and Child Health (DNR), of whom 345 pregnant women (Group 1) received efferent therapy, 33 women (Group 2) had fetuses intrauterine bypass surgery, and 14 pregnant women (Group 3) had mixed efferent therapy and fetal PEEP bypass surgery.

RESULTS: The analysis showed that the most favorable results for the main clinical indicators (premature, operative delivery, fetal hypoxia at birth, etc.) were in Group 1 and 3 women, in which the perinatal mortality was 14.5/1000 and 0/1000, respectively, which was significantly lower than in Group 2 (176.5/1000). It was also found that in Groups 2 and 3 women, the mean intervals between repeated transfusions of washed donor red blood cells were 8.8 ± 0.2 and 21.4 ± 3.8 days ($p < 0.01$), which may be explained by the detoxifying effect of efferent therapy methods, preservation of fetal red blood cells and transfused donor red blood cells to the fetus with prolonged gestation and obtaining healthier and more viable progeny.

CONCLUSIONS: 1. Severe Rh conflict is a manifestation of a syndrome of systemic effects of aggressive metabolites of specific and nonspecific nature. 2. The etiopathogenetic measure in the prevention and treatment of HDF/HDN in rhesus conflict is efferent therapy methods for the mother, and transfusion of washed donor rhesus-negative red blood cells to the fetus is effective, but a temporary, palliative measure, as is the case in multiple organ failure. 3. In the treatment protocols, efferent therapy methods must be present to prevent fetal red cell destruction and, equally importantly, to prevent destruction of Rh-negative donor red cells transfused to the fetus.

Keywords: pregnancy; fetus; rhesus conflict; plasmapheresis; transfusion of donor red blood cells; perinatal losses.

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Научная статья

ИСХОДЫ ГЕСТАЦИИ ПРИ РАЗЛИЧНЫХ ВАРИАНТАХ ПОМОЩИ БЕРЕМЕННЫМ С РЕЗУС-ИММУНИЗАЦИЕЙ

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Актуальность. В России принята за основу выжидательно-активная тактика с наблюдением за беременными с последующим (по показаниям) переливанием донорских эритроцитов плоду.
Цель — провести сравнительный анализ исходов беременности при использовании разных вариантов терапии женщин с резус-иммунизацией.
Материалы и методы. В семи разных учреждениях России, а также в Донецком центре охраны материнства и детства (Донецкая Народная Республика) наблюдали 392 женщины, из которых 345 беременных (1-я группа) получали методы эфферентной терапии, у 33 женщин (2-я группа) плодам внутриутробно выполняли переливание отмытых донорских эритроцитов и 14 беременным (3-я группа) оказывали смешанную помощь с применением обоих методов.
Результаты. Анализ показал, что наиболее благоприятные результаты по основным клиническим показателям (преждевременные, оперативные роды, гипоксия плода при рождении и др.) были в 1-й и 3-й группах женщин, в которых перинатальная смертность составила 14,5/1000 и 0/1000 соответственно, что было существенно ниже, чем во 2-й группе (176,5/1000). Обнаружено, что во 2-й и 3-й группах женщин средние интервалы между повторными переливаниями отмытых донорских эритроцитов составили 8,8 ± 0,2 и 21,4 ± 3,8 дня ($p < 0,01$) соответственно, что можно объяснить детоксикационным эффектом методов эфферентной терапии, сохранением эритроцитов плода и перелитых донорских эритроцитов плоду с пролонгированием беременностей, получением более здорового и жизнеспособного потомства.
Выводы. 1. Тяжелый резус-конфликт есть проявление синдрома системных воздействий агрессивных метаболитов специфического и неспецифического характера. 2. Этиопатогенетической мерой в профилактике и лечении гемолитической болезни плода и новорожденного при резус-конфликте являются методы эфферентной терапии для матери, а переливание отмытых донорских резус-отрицательных эритроцитов плоду — эффективная, но временная, паллиативная мера, как и бывает при полиорганной недостаточности. 3. В лечебных протоколах обязательно должны присутствовать методы эфферентной терапии для профилактики разрушения эритроцитов плода и, что не менее важно, для профилактики разрушения резус-отрицательных донорских эритроцитов, перелитых плоду.

Ключевые слова: беременность; плод; резус-конфликт; плазмаферез; переливание донорских эритроцитов; перинатальные потери.

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BACKGROUND

Currently, two main approaches to the management of pregnant women with rhesus (Rh) immunization are employed to prevent perinatal losses in hemolytic disease of the fetus and the newborn (HDF/HDN). In the first approach (a "wait-and-see" technique prevalent in Russia), women are monitored, and in the presence of severe HDF, intrauterine intravascular transfusion of the washed donor red blood cells (RBCs) is performed on the fetus. In this case, perinatal mortality is 150–182/1000 [2, 6, 11, 14, 18, 21], which is not much different from the results of the last century (132–150/1000) when pregnant women received complex regimens of drug "desensitizing" therapy that has gone into the past [9, 10, 15].

HFD/HDN in Rh immunization causes fetal erythrocyte destruction: (a) intracellular (immune) hemolysis and (b) intravascular (toxic) hemolysis [8, 20].

A third, mixed, and therefore the most dangerous mechanism of hemolysis may be assumed [5]. The authors believe that detoxifying efferent therapy (RT) is the etiopathogenetic means of Rh immunization, which allows the removal of specific aggressive pathogens (Rh antibodies) and nonspecific toxic substances — autacoids (i.e., unoxidized metabolic products that accumulate on the membranes of RBCs in pregnant women and in fetal anemia) — from the mother–placenta–fetus (MPF) system.

Long ago, plasmapheresis was used reasonably in pregnant women with Rh immunization. However, plasma exfusions were performed aggressively, such as through repeated plasma exchange with removal per session of up to 2–2.5 L of plasma (up to 4% of body weight) and its replacement with fresh frozen plasma from different donors. Generally, up to 60 L of plasma were removed per pregnancy, leading to the development of new immunologic conflicts and disappointing results, i.e., plasmapheresis was discredited, and the vacant niche was occupied by fetal RBC transfusion (RBCT), which dominate the world and Russia today [26].

Currently, safe and effective regimens of plasma infusions with the introduction of human anti-Rho(D) immunoglobulin (IgG) are developed. Moreover, studies have reported the successful use of other basic ET techniques (such as hemosorption, cascade plasmafiltration, and immunosorption, in combination with complementary ET methods (such as ozone therapy and blood photomodification with laser and ultraviolet beams) for Rh immunization combined with preeclampsia, chronic placental insufficiency, intrauterine growth restriction, and antiphosphoslipid syndrome. In addition, the "active" use of ET from the beginning of pregnancy prolongs pregnancy until term delivery, frequently without the need for unsafe fetal RBCT and exchange blood transfusions for newborns [3, 19, 22–25, 27–30].

In 2008, Vetrov proposed a "mixed active technique" for the management of pregnant women with Rh immunization through early administration of medium-volume plasmapheresis in combination with blood photomodification (non-specific prevention of severe HDF) followed, if indicated, by fetal RBCT (treatment of HDF). This approach provided a classic sequence of care for women and their children, i.e., active prevention and treatment of HDF [5].

A similar technique was then proposed. However, repeated plasma exchange with albumin solution in the first stage was offered in combination with IgG administration to pregnant women until conditions for intravascular fetal RBCT were suitable at 22 weeks of gestation [31].

This study aimed to compare pregnancy outcomes in women with Rh immunization using active, "wait-and-see," and mixed active techniques.

MATERIALS AND METHODS

Gestational outcomes of 392 pregnant women with Rh incompatibility in seven obstetric facilities in different regions of Russia and Donetsk Center for Maternal and Child Health (Donetsk People's Republic) were analyzed.

In total, the mean age of the 392 pregnant women was 31.8 ± 0.2 years, and 76.0% and 56.0% of them had a history of somatic and gynecologic diseases, respectively.

All women were repeatedly pregnant with an average of 4.6 gestations each, 87.0% had repeated deliveries, and each fourth pregnancy resulted in a cesarean section. The prophylactic administration of IgG anti-D during invasive interventions and after previous pregnancies was performed in only 7.5% (29 of 392), i.e., specific prophylaxis for Rh immunization was practically never given to pregnant women before.

In every second patient (49.1%), the pregnancy was at risk of termination, and every third patient was diagnosed with anemia and urogenital infections.

The participants were divided into three groups. In group 1, 345 patients in early pregnancy with an Rh antibody titer of 1:32 or higher were treated with ET (average of 7.3 procedures each, i.e.,

"active technique"). The main surgery was medium-volume plasmapharesis performed on Russian equipment with plasma infusions of 25% of the volume of the circulating plasma (4% of the body weight) and plasma exchange with crystalloids. Occasionally, hemosorption, cascade plasma filtration, and immunosorption were used in concomitant obstetric pathologies, whereas 10% albumin solution and autoplasma treated on hemosorbent or by heparin cryoprecipitation were used in plasmapheresis if at risk of hypoproteinemia [12]. These techniques were combined with blood photomodification, ozone therapy, and IgG.

In group 2, 33 patients needed a "wait-and-see" technique with 1–4 fetal RBCT surgeries performed 7–12 days later (averaged 2.6 surgeries per person).

In group 3, 14 pregnant women were followed up using a "combined active technique" with sequential maternal ET and fetal RBCT. In 5 of 14 women with a history of fetal losses and concomitant somatic pathology (diabetes), the fetus received one additional session of plasmapheresis or hemosorption after each RBCT. In total, this group underwent an average of 5.1 major ET procedures, and fetuses underwent 1–4 surgeries (an average of 2.3 surgeries each).

All pregnant women underwent a comprehensive obstetric, clinical, and biochemical examination, and instrumental methods of fetal examination, such as ultrasonography, cardiotocography, and dopplerometry. In groups 2 and 3, amniocentesis and cordocentesis with fetal blood values were performed before RBCT.

Changes in the leukocyte intoxication index (LII) according to the formula of Kostyuchenko and Sokolov (2001) were calculated in all women to assess the degree of endotoxemia and the protective inflammatory response of the MPF system [12]:

$$\text{LII} = \frac{0{,}1 \cdot \text{Leukocytes (ths./cl)} \cdot \text{Neutrophils (\%)}}{100 - \text{Neutrophils (\%)}} \cdot$$

Quantitative results were statistically performed using Student's *t*-criterion and χ^2 in standard Statistica version 5.773. For all analyses, the level of statistical significance was set at $p < 0.05$.

RESULTS

The above mentioned somatic and gynecological diseases in the anamnesis and complications in the present pregnancy occurred more frequently but not significantly ($p > 0.05$) in groups 2 and 3. The incidence of fetal losses in the history of Rh incompatibility in group 1 was 7.3% ± 1.4%, which was significantly less frequent ($p < 0.05$) than those in groups 2 and 3, in which the rate was nearly identical (30.3% ± 8.0% and 28.5% ± 12.1%, respectively, $p > 0.05$).

In addition, some women with a history of fetal losses (group 1, $n = 12$; group 3, $n = 4$) received plasmapheresis during the pregravid preparation. The levels of Rh antibody titers in these women reached 1:1024–8196, decreased several orders of magnitude following plasmapheresis before the present pregnancy, and increased again during pregnancy.

Groups 1 and 3 were started on average significantly earlier than group 2 and had a later mean time to delivery and lower levels of Rh antibodies in the blood ($p < 0.05$–0.001; Table 1).

The analysis showed that complications in the second half of pregnancy (preeclampsia and chronic placental insufficiency) were more frequent in group 2 than in groups 1 ($p < 0.05$) and 3 ($p > 0.05$). This difference in the frequency of the above complications may be due to ET, with proven clinical properties including detoxification, Rh antibody titer reduction, hypotensive and anti-edema effects, improvement of blood microcirculation in vital organs, particularly in the placenta, and prolongation of pregnancy [4, 16].

The positive ET effect on homeostasis in pregnant women was evidenced by clinical and biochemical blood tests in groups 2 and 3. Before fetal RBCT, maternal ET was given only in 9 of 14 cases in group 3 (see above). However, this was reflected in the mean blood values, which were normal (except for LII, with a normal value up to 1.5 units) and differed significantly from the mean values in group 2 ($p < 0.05$). In the group without ET, tendencies toward anemia and hypercoagulability were observed, and bilirubin, alanine aminotransferase, and creatinine values approached the upper limit of normal, with a simultaneous increase in the mean LII and erythrocyte sedimentation rate (ESR). Such changes occur with the accumulation of toxic pathogenic autacoids in the MPF system and induction of a protective inflammatory response with concomitant stress on the function of natural detoxification systems (liver and kidneys) in the mother [5, 7]. Other authors refer these changes in homeostasis to "pregnant women norms," explaining that by "neuroendocrine influences of pregnancy" [4].

A high ESR characterizes the degree of loading of membrane receptors (glycocalyx) of erythrocytes with toxic metabolites, contributing to the degene-

Table 1 / Таблица 1

Clinical data of examined patients with Rh-conflict, *M* ± *m*, %
Клинические данные обследованных пациенток с резус-конфликтом, *M* ± *m*, %

Parameter / Показатель	Group 1 / 1-я группа (*n* = 345)	Group 2 / 2-я группа (*n* = 33)	Group 3 / 3-я группа (*n* = 14)
Mean onset of maternal efferent therapy and TWDRBC fetal, weeks / Средний срок начала эфферентной терапии матери и ПОДЭ плоду, нед.	14.0 ± 0.3	30.1 ± 0.4**	23.5 ± 0.5
Intervals between TWDRBC to fruits, days / Интервалы между ПОДЭ плодам, дней	–	8.8 ± 0.2**	21.4 ± 3.8
Preeclampsia / Преэклампсия	17 (4.9 ± 1.2)	7 (21.2 ± 7.3)*	1 (7.1 ± 6.2)
Chronic placental insufficiency and growth retardation syndrome / Хроническая плацентарная недостаточность и синдром задержки роста плода	12 (3.5 ± 1.0)	5 (15.2 ± 6.4)*	1 (7.1 ± 6.2)
The average titer of antibodies to childbirth, conv. units / Средний уровень титров резус-антител к родам, усл. ед.	641.9 ± 10.7	3430.2 ± 299.4**	1521.8 ± 339.4
Average term of delivery, weeks / Средний срок родоразрешения, нед.	36.5 ± 0.1	33.0 ± 0.3**	34.9 ± 0.4

*Difference in indices in patients of the 2nd group is significant ($p < 0.05$) in comparison with the data in the 1st group; **in comparison with the data in the 3rd groups. *Note*. TWDRBC — transfusions of washed donor red blood cells.
*Разница в показателях у пациенток 2-й группы достоверна ($p < 0,05$) в сравнении с данными в 1-й группе; **в сравнении с данным 3-й группы. *Примечание*. ПОДЭ — переливание отмытых донорских эритроцитов.

ration and destruction of membranes and cells with aggregation of red globules in the bloodstream and disruption of microcirculation and oxygen transport [13].

Consistent changes in homeostasis in the MPF system are evidenced by fetal blood tests. Ultrasonography detected toxic fetal edema in 69.7% ± 7.8% of cases in group 2 and 64.3% ± 12.8% in group 3 ($p > 0.05$). Mean fetal cord blood counts before the first RBCT were significantly worse in group 2 ($p < 0.05$) than in group 3 (Table 2).

The results of the maternal and fetal blood tests presented in Table 2 confirm that detoxification performed in group 3 contributed to the sanitation of the MPF system with the cessation of the protective inflammatory response (LII and ESR values), normalization of maternal liver and kidney function, lower fetal red cell destruction, and accumulation of toxic bilirubin in the blood compared with group 2 ($p < 0.05$).

Immediate and delayed complications are significant disadvantages of fetal RBCT [1]. Complications were noted in 14 of 47 patients in groups 2 and 3 (29.8% ± 6.6%), which was 10 times more frequent than that in group 1 during ET (one woman had rapidly relieved chills; 2.9% ± 0.9% [$p < 0.001$]). In 3 of 47 patients (6.3%, all from group 2) after RBCT, the circumstances necessitated an urgent surgical termination of pregnancy in the interests of the fetus. In total, fetal RBCT complications (needle exit from a vein and persistent fetal bradycardia) were 2.6 times more frequent in group 2 (36.4% ± 8.4%) than in group 3 (14.2% ± 9.3% [$p > 0.05$]). This may be associated with the contribution of maternal detoxification to the sanitation of the MPF system and increases in the resistance of this system (primarily of the fetus) to invasive and stressful procedures.

Notably, fetal RBCT is highly effective in the treatment of severe anemia. Thus, mean fetal hemoglobin increased by an average of 67.5% and 66.7% ($p > 0.05$) in groups 2 and 3, respectively, compared with baseline levels immediately after the intervention. However, the average toxic indirect bilirubin in the fetal blood decreased by only 3%–4% in both groups. Together with many other autacoid metabolites, conditions remain for the destruction of both fetal and donor Rh-negative erythrocytes transfused to the fetus. Group 2 needed repeated fetal RBCTs after an average of 8.8 ± 0.2 days, which was 2.4 times more frequent than that in group 3 (21.4 ± 3.8 days [$p < 0.01$]; Table 1).

The incidences of preterm and operative deliveries, fetal hypoxia at birth, and severe HDN requiring exchange blood transfusions were 2.6, 3.4, 6.3,

Table 2 / Таблица 2

Blood test values in fetuses and their mothers from groups 2 and 3 before the first fetal TWDRBC operation, *M* ± *m*, %
Показатели клинико-биохимических анализов крови у матерей и их плодов из 2-й и 3-й групп перед первой операцией переливания отмытых донорских эритроцитов плоду, *M* ± *m*, %

Parameter / Показатель	Group 2 / 2-я группа (n = 33)	Group 3 / 3-я группа (n = 14)
Mother / Мать		
Hemoglobin, g/l / Гемоглобин, г/л	107.2 ± 1.3*	112.2 ± 1.0
Fibrinogen, g/l / Фибриноген, г/л	4.7 ± 0.1*	4.1 ± 0.2
Bilirubin, μmol/l / Билирубин, мкмоль/л	19.2 ± 0.7*	14.2 ± 0.5
ALT, mmol/l/ Аланинаминотрансфераза, ммоль/л	32.3 ± 1.4*	8.8 ± 1.3
Creatinine, mmol/l / Креатинин, ммоль/л	0.9 ± 0.05*	0.6 ± 0.04
Leukocyte index of intoxication, c. u. / Лейкоцитарный индекс интоксикации, усл. ед.	2.4 ± 0.07*	1.7 ± 0.06
Erythrocyte sedimentation rate, mm/h / Скорость оседания эритроцитов, мм/ч	27.3 ± 0.7*	18.3 ± 0.4
Fetus / Плод		
The number of erythrocytes, million / Число эритроцитов, млн	1.6 ± 0.03*	1.8 ± 0.04
Hemoglobin, g/l / Гемоглобин, г/л	54.2 ± 3.0*	64.0 ± 3.7
Hematocrit, % / Гематокрит, %	19.2 ± 0.7*	22.5 ± 1.4
Bilirubin, μmol/l / Билирубин, мкмоль/л	45.6 ± 0.9*	33.1 ± 1.3

*The difference in indicators in the 2nd and 3rd groups is significant ($p < 0.05$). *Разница показателей во 2-й и в 3-й группах достоверна ($p < 0,05$).

and 3.2 times lower in group 1 that received ET, respectively, than in group 2 ($p < 0.001$). In groups 2 and 3, these clinical parameters were better in patients who received ET and fetal RBCT ($p < 0.05$ and $p > 0.05$, respectively; Table 3).

The mean fetal body weight in group 1 corresponded to that of full-term newborns. It was higher in group 2 (with a shorter gestational age) than in group 3, apparently due to toxic edema of tissues.

Perinatal losses in group 1 were 5 premature infants (345 women delivered 348 fetuses, including 3 twins), which was 14.5/1000. Two fetuses died antenatally, and three died in the first days after delivery (in one case due to birth trauma). Of these, four fetuses died of similar reasons, i.e., plasmapheresis was started late (at 26–28 weeks of gestation), and when the antibody titers dropped and cardiotocography, Doppler parameters, and ultrasound findings showed normal values, the women were discharged home. Subsequently, increased plasma antibody levels were observed, which required repeated ET; however, women were still monitored as outpatients without assistance.

In group 2, 6 premature newborns of 34 children (1 twin) died from severe HDF/HDN (5 children antenatally and 1 child postnatally). In group 3, no deaths occurred.

Overall, in group 2 women who received a "wait-and-see" techniques (only fetal RBCT), the perinatal mortality rate of 176.5/1000 was consistent with the literature [2, 8, 13, 19, 22] and was 12.2 times higher than that in group 1 (active techniques with early maternal ET, 14.5/1000 [$p < 0.005$]). In group 3 (mixed active techniques with sequential maternal

Table 3 / Таблица 3

Clinical data on childbirth and the course of the neonatal period in children, *M* ± *m*, %
Клинические данные о родах у матерей и течении периода новорожденности у их детей, *M* ± *m*, %

Parameter / Показатель	Group 1 / 1-я группа (*n* = 345)	Group 2 / 2-я группа (*n* = 33)	Group 3 / 3-я группа (*n* = 14)
Preterm birth / Преждевременные роды	128 (37.1 ± 2.6)*	32 (97.0 ± 3.0)	13 (92.9 ± 6.7)
C-section / Кесарево сечение	87 (25.2 ± 2.4)*	28 (84.9 ± 6.2)	11 (78.6 ± 10.9)
The average body weight of the fetus, g / Средняя масса тела плода, г	2936.0 ± 28.3*	2318.8 ± 80.6	2212.6 ± 64.2
Apgar <7 points in live births, *n* (%) / Апгар <7 баллов у родившихся живыми, *n* (%)	49 out of 346 (14.2 ± 1.9)*	22 out of 28 (89.3 ± 5.9)	5 out of 14 (35.7 ± 12.8)**
Need for replacement blood transfusion for a child, *n* (%) / Потребность в заменных переливаниях крови ребенку, *n* (%)	97 out of 346 (28.0 ± 2.4)*	25 out of 28 (89.3 ± 5.9)	5 out of 14 (35.7 ± 12.8)**
Perinatal mortality, per 1000 / Перинатальная смертность, на 1000	5 out of 348, 14.5	6 out of 34, 176.5	0

*Разница в показателях у пациенток 1-й и 2-й групп достоверна ($p < 0,05$); **разница показателя во 3-й достоверна с данными во 2-й группе ($p < 0,05$). *The difference in indicators in patients of the 1st and 2nd groups is significant ($p < 0.05$); **The difference in the indicator in the 3rd group is significant with the data in the 2nd group ($p < 0.05$).

ET and fetal RBCT or combined procedure), no fetal deaths occurred.

DISCUSSION

Clinical material analysis showed that pregnancy is a powerful sensitizing factor to the Rh antigen, with increased isoimmunization largely determining the degree of fetal erythrocyte destruction. Simultaneously, pregnant women have latent endotoxemia by childbirth caused by the accumulation of aggressive metabolites with toxic properties following inherent changes in the MPF system (conquest of the "placental foothold," development of the fetal egg, hormonal restructuring, "diabetization of the body" of the woman, bile extraction disorders, urodynamics, and tendency to constipation) [16, 17]. Clinically, this is expressed by changes in homeostasis with a shift from average laboratory values to "pregnant women's norms" or worse. This is what was found in women who did not receive ET.

In addition to immune and intracellular hemolyzes of fetal erythrocytes in Rh incompatibility, intravascular toxic and mixed variants of blood cell destruction may occur, which result from a combination of Rh immunization with diseases of natural detoxification systems and pregnancy complications in the mother, when fetal anemia develops following the accumulation of non-oxidized toxic metabolites [4]. This postulate is confirmed by a significant increase in the intervals between fetal RBCT and ET in pregnant women [7].

CONCLUSIONS

1. Severe Rh incompatibility is a manifestation of a syndrome of systemic effects of aggressive metabolites of specific and non-specific nature.

2. The etiopathogenetic measure in the prevention and treatment of HDF/HDN in Rh incompatibility is the ET method for the mother, whereas the transfusion of donor Rh-negative RBCs to the fetus is an effective, but temporary and palliative measure as occurs in multiple organ failure.

3. During treatment, ET must be present to prevent fetal red blood cell destruction and, no less importantly, the destruction of transfused donor RBCs.

ADDITIONAL INFORMATION

Authors' contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

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