WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979, Volume 3, Issue 8, Aug., 2022

CHANGES IN CYTOKINE PROFILE AND INTERFERONS IN WOMEN AT HIGH RISK FOR POSTPARTUM BLEEDING

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To identify the effect of dipyridamole on cytokine and interferon levels in 32 pregnant women with anemia, a study was conducted. Pregnant patients with anemia received basic therapy and for the purpose of immunocorrective therapy, dipyridamole was prescribed at a dose of 75 mg / day for three weeks. Three weeks after treatment, the examined women taking dipyridamole showed a significantly significant decrease in the levels of proinflammatory (IL-1β, IL-2, IL-8, TNF-α) cytokines and interferon (IFN-γ) compared with patients receiving only basic therapy. Along with this, the concentration of anti-inflammatory (IL-10) cytokine in women with anemia with a combination of basic therapy and dipyridamole was significantly higher than similar indicators in pregnant women using only basic therapy.

Keywords: cytokines, humoral factor, anemia, coagulation hemostasis, IL-1α, IL-1β, IL-8, TNFa, fibrinolysis, obstetric bleeding.

Relevance

The hemostasis system, interacting with all the body's defense systems, is responsible for maintaining the circulating blood in the vascular bed in a liquid state, and also prevents the development of bleeding in various vascular injuries (1,2,3). In obstetric practice over the past decades, among antiplatelet agents, dipyridamole (curantyl) has been successfully used, which is available in the form of dragees or tablets, the latter is distinguished by a more complete and rapid release of the active substance, since a lower content of hydrophilic substances in the tablet shell accelerates its dissolution. There is evidence that, along with antiplatelet action, it has been established that dipyridamole potentiates the vasodilating effect of the endothelial relaxing factor, inhibits erythrocyte aggregation, and to a lesser extent has a fibrinolytic effect as a result of the release of plasminogen from the vascular wall [8,9]. Curantyl does not

increase the tone of the uterus, reduces peripheral resistance, does not have an embryotoxic effect, improves uteroplacental and fetoplacental blood flow [4,5,6]. A number of scientific studies substantiate that an important advantage of dipyridamole in comparison with other antiplatelet agents is its immunocorrective effect. The drug is an interferon inducer and thereby increases nonspecific anti-inflammatory resistance [8,9]. Thus, it can be determined. that dipyridamole causes stabilization of cell membranes, including lysosomal ones, reduces the production of prostaglandins, helps restore normal capillary permeability, inhibits the aggregation of polymorphonuclear leukocytes, blocks complement activation, potentiates the vascular effects of pressor amines, reduces the lack of energy supply of the body, prevents the accumulation of lactate, inhibits apoptosis, thus inhibits the development and progression of DIC by reducing the flow of tissue thromboplastin and inhibition of platelet adhesion. All the above effects of dipyridamole are able to level the development of physiological dysfunction of many systems, including the immune system, as well as pathological symptoms. Currently, the subject of many scientific studies is the ability of dipyridamole to inhibit the appearance and synthesis of pro-inflammatory cytokines (IL-1β, IL-6), as well as TNF-α (7,8).

The effect of dipyridamole on other parts of the immune system has not been fully studied, and this determined us to conduct a study to study the immunocorrective effect in pregnant women. Therefore, the objective of our study was to study the effect of dipyridamole on the course of pregnancy, cytokine profile and blood interferons, as well as on hemostasis.

Purpose of the study. To this end, we studied the effects of dipyridamole (curantyl N) on the cytokine profile and blood interferons in women with gestational anemia and the threat of postpartum hemorrhage.

Table 1. Blood cytokines and interferons in examined women before and after dipyridamole therapy, M±m

Показатели	Groups			
	Pregnant women with anemia who received basic, n=19		Pregnant women with anemia who received basic, + dipyridamole, n=32	
	Before therapy	After therapy	Before therapy	After therapy
IL-1β,пг/ml	8,92 ± 2,4	7,64 ± 2,21**	8,92 ± 2,42	4,94 ± 2,42**
IL-2, пг/ml	11,5±1,54	10,5±2,4**	12,81±1,83	7,5±1,5**
IL-6, пг/ml	3,15±0,4	3,02±0,15*	3,41±0,16	2,18±0,15*
IL-8, пг/ml	12,89±0,14	11,47±0,25***	13,32±0,18	10,49±0,14***
IL-10, пг/ml	6,24±0,52	6,48±0,26	5,19±0,15	8,12±0,32***
TNFα, пг/мл	6,49±0,14	5,94± 0,34	6,63± 0,25	4,04± 0,22
IFN-γ	68,13±2,47	72,70±2,41	152,90±2,49*	72,70±2,41

Note. ***-p<0.001; ** - p<0.01; * - p<0.05 - compared with the indicators of pregnant women without anemia.

Research results identify the effect of dipyridamole on the levels of cytokines and interferons in 32 pregnant women with anemia, a study was conducted. Pregnant patients with anemia received basic therapy (hormonal support, antispasmodics, vitamins), and for the purpose of immunocorrective therapy, dipyridamole was prescribed at a dose of 75 mg/day for three weeks. Three weeks after treatment, the examined women who took dipyridamole showed a significantly significant decrease in the levels of pro-inflammatory (IL-1β, IL-2, IL-8, TNF-α) cytokines and interferon (IFN-γ) compared with patients who received only basic therapy. Along with this, the concentration of anti-inflammatory (IL-10) cytokine in women with anemia with a combination of basic therapy and dipyridamole was significantly higher than similar indicators in pregnant women using only basic therapy (Table 1).

When assessing the effect of dipyridamole on indicators of vascular-platelet hemostasis, a significantly significant decrease in the levels of induced platelet aggregation (with ADP, collagen, adrenaline) was found in women with anemia and who received complex therapy with dipyridamole compared with the control group and with patients before treatment, as well as compared with patients who received only basic therapy. We also found a significant decrease in the levels of fibrinogen and soluble fibrin-monomer complexes in patients who received complex basic therapy for anemia in combination with dipyridamole compared with patients before treatment and women who received only basic therapy. According to research data, it can be noted that IL-2 plays an extremely important role in the differentiation and proliferation of T-lymphocytes, and IL-8 belongs to chemokines and is a powerful chemotactic and activating factor for neutrophils. An increase in the level of these cytokines indicates the participation of an immunological component in the pathogenesis of anemia [7,8].

It should be noted that in the 2nd group of pregnant women, despite a significant decrease in the level of IL-6 - by 33.3% in the first trimester, in the second and third trimesters there was a tendency to increase it. At the same time, the level of this cytokine in the third trimester almost reached the values of pregnant women without anemia. Most likely, this is due to the preparation of the body for childbirth and increased synthesis of other pro-inflammatory cytokines that induce the synthesis and release of IL-6 [4, 9]. With repeated pregnancy, a decrease in the concentration of IL-10 was also observed in relation to the comparison group: in the first trimester by 19.8%, in the second trimester by 37.3%, and in the third trimester by 54.1%.

Discussions and Conclusions

Excessive production of pro-inflammatory and a decrease in the level of anti-inflammatory cytokines in anemia of pregnancy indicates the progression of systemic inflammation and a decrease in defense mechanisms. An increase in the level of pro-inflammatory cytokines negatively affects erythropoietin-producing cells, inhibits post-receptor signal transduction pathways in erythroid cells. The results of the study indicate that in women with anemia after complex treatment, including dipyridamole, there is a decrease in the level of pro-inflammatory cytokines, an increase in the content of anti-inflammatory cytokines, as well as positive dynamics in clinical symptoms.

Thus, the results of our study using dipyridamole, which has not only an antiaggregatory effect, but also immunomodulatory properties, showed good results in correcting the cytokine profile and blood interferons in women with gestational anemia and the threat of postpartum hemorrhage. Accordingly, the use of dipyridamole in the complex therapy of pregnant women with anemia made it possible to improve hemostasis and normalize the immunological status.

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