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The Phenomenon of Self-Regulation of the Osmotic Resistance of Human Erythrocytes and the Participation of Oxytocin in it

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Abstract

Relevance and Purpose: Previously, we proposed a method for assessing the osmotic resistance of erythrocytes (ORE), based on determining the number of hemolyzed erythrocytes during their strictly fixed exposure in distilled water containing 2.5 mM CaCl2. This method has shown that as the duration of exposure increases (30, 45, 60, 90 and 120 s), the percentage of hemolyzed erythrocytes increases. It has previously been shown that erythrocyte resistance to the hypoosmotic environment depends on gender: the osmotic resistance of erythrocytes in non-pregnant women is much lower than in men; during an uncomplicated pregnancy the osmotic resistance of erythrocytes increases. The purpose of this work was to assess the osmotic resistance of erythrocytes (ORE) of pregnant women using the method of V. Tsirkin et al. (Patent 2419792. Russian Federation: IPC G01N33 / 48. 07.12.2009. Publ. 27.05.2011. Bull. No. 15). To determine the percentage of hemolyzed erythrocytes, four exposure times of erythrocytes in distilled water were used, including 15 s, 45 s, 120 s and 300 s. To prove the possibility of using the technique to assess the effect of biologically active substances on the osmotic resistance of erythrocytes a 45-second exposure of erythrocytes in distilled water (DW) was used. The choice of oxytocin as a biologically active substance made it possible to explain the phenomenon of self-regulation of the osmotic resistance of erythrocytes, which was revealed in the study of the intensity of hemolysis of erythrocytes in distilled water, depending on the duration of exposure.

Methodology: A study of heparinized venous blood of 12 women in different stages of uncomplicated pregnancy (from 12 to 31 weeks) was carried out. It was received in a volume of up to 6 ml, with the personal consent of the women, in an antenatal clinic in vacuum tubes with Na-heparin. The osmotic resistance of erythrocytes (ORE) was assessed by the method of V. Tsirkin et al. (2011) by determining the percentage of hemolyzed erythrocytes (PHE) after their strictly limited duration of exposure in distilled water (DW) containing 2.5 mM CaCl2. The cessation of exposure in DW was achieved by adding a 6% NaCl solution to the suspension of erythrocytes in a ratio of 1:1, after which the level of hemolysis of erythrocytes was assessed during their 15-, 45-, 120-, and 300-second exposure in DW, as well as the effect of oxytocin (in concentrations of 10-7, 10-6, 10-5, 10-4 and 10-3 IU / ml of Krebs solution) on the ORE under the conditions of a 45-second exposure of erythrocytes in DW. In all cases, the percentage of hemolyzed erythrocytes was determined by the percentage of the hemoglobin content in the supernatant (Hbs) to the hemoglobin content in the suspension (Hbtotal). The supernatant was obtained after 10 min centrifugation of the erythrocyte suspension at 1000 rpm. The hemoglobin level in the test blood, in the suspension, and in the supernatant was determined by the standard hemoglobin cyanide method using a hemoglobin calibration solution and a transforming solution (Drabkin's reagent), which converts hemoglobin into cyanmethemoglobin (Agat-med LLC, Moscow). The color intensity of Drabkin's reagent, i.e., the hemoglobin content, was assessed by the extinction index on Photocolorimeter (KFK-2 uhl-4.2) using a green light filter (wavelength 540 nm) and a 10-mm-thick cuvette.

Results and Conclusions: When using the method for assessing the osmotic resistance of erythrocytes (ORE), based on determining the percentage of hemolyzed erythrocytes (PHE) with their strictly fixed time exposure in distilled water (DW) containing 2.5 mM CaCl2, it was shown that with an increase in the duration of exposure of erythrocytes in the DR from 15 up to 120 s, the PHE increases. However, with a longer exposure, i.e. at 300 s, the PHE decreases. Oxytocin in concentrations of 10-8-10-4 IU / ml increases the osmotic resistance of erythrocytes (ORE) exposed to a 45-second exposure in the DW, which allows us to consider oxytocin as an inhibitor of aquaporin AQP1 and recommend its use to reduce tissue edema. The idea of the existence of a self-regulation mechanism of the ORE is formulated, which most likely is realized due to the paracrine effect of oxytocin released from the erythrocyte under the influence of hypotension of the environment. The concept of erythrocytes as a source of oxytocin is substantiated, thanks to which the fetus and newborns receive oxytocin for brain development, and adults - for the regulation of physiological processes. The degree of ORE, determined under conditions of hypotension, indirectly reflects the content of oxytocin in the erythrocyte. A low content of oxytocin in the erythrocytes of pregnant women can be the cause of preeclampsia, premature birth, and probably other obstetric complications.

The study is devoted to assessing the stability of red blood cells of women with uncomplicated pregnancy during exposure to red blood cells over a wide time range (15 s, 45 s, 120 s and 300 s) and studying the effect of oxytocin (10-8 - 10-4 IU/ml) on osmotic resistance of erythrocytes (under conditions of their 45-second exposure in distilled water) In all experiments, the percentage of hemolysed erythrocytes was calculated by the ratio of the hemoglobin content in the supraventricular fluid to its initial content, and hemoglobin was determined by the standard hemoglobin cyanide method using Drabkin reagent. It is shown that with an increase in the duration of exposure of erythrocytes in distilled water from 15 to 120 c, the percentage of hemolysed erythrocytes increases, but with a longer exposure, i.e., at 300 c, the percentage of hemolysed erythrocytes decreases. This suggests the presence of a mechanism of self-regulation of osmotic resistance of erythrocytes, which is most likely realized due to the paracrine effect of oxytocin exiting the erythrocyte under the influence of hypotension of the environment, since it has been found that oxytocin even in low concentrations (10-8 IU/ml) increases osmotic resistance of erythrocytes. The idea of erythrocytes as a source of oxytocin is substantiated, thanks to which the fetus receives oxytocin for brain development. The authors believe that oxytocin acts as a blocker of water transport to erythrocytes and other cells, which can be used to combat the hydration of the body's cells, and the low content of oxytocin in the erythrocyte may be the cause of the formation of a number of obstetric complications.

Keywords: Hypoosmotic resistance of erythrocytes; Oxytocin; Self-regulation of water transport; Fetus; Brain; Obstetric complications

Abbreviations: ORE: Osmotic Resistance of Erythrocytes; DW: Distilled Water; PHE: Percentage of Hemolyzed Erythrocytes; ESR: Erythrocyte Sedimentation Rate

Introduction

As is known, to date there is no single, generally accepted method for assessing the osmotic resistance of erythrocytes (ORE). Previously, we proposed a method for assessing the ORE based on determining the number of hemolyzed erythrocytes during their strictly fixed time exposure in distilled water (DW) containing 2.5 mM $CaCl_2$ [1-3]. This method shows that as the duration of exposure increases (30 s, 45 s, 60 s, 90 s and 120 s), the percentage of hemolyzed erythrocytes (PHE) increases. For example, for male erythrocytes, this indicator was 17%, 26%, 38%, 50% and 66%, respectively, and the $T_{50\ indicator}$, i.e. the duration at which 50% of erythrocytes are hemolyzed is 88 s [1]. It has been shown that the resistance of erythrocytes to a hypoosmotic medium depends on gender. So, in women in the follicular phase of the cycle, PHE was 25%, 39%, 55%, 78% and 88%, respectively, and the values of $T_{50\text{-}55}$ s. This means that the ORE for non-pregnant women is significantly lower than for men.

In uncomplicated pregnancy, ORE increases. For example, in the second trimester, the PHE values were 12%, 25%, 38%, 51%, and 61%, respectively, and the $T_{50\ index}$ was 77 s [1]. In connection with these data, we recommended to use a 45-second exposure of erythrocytes in the DV to assess the effect of various biologically active substances on the ORE [1-3]. The main methodological difficulty in this technique was the need to count erythrocytes that were not subjected to hemolysis. For these purposes, the classic count of erythrocytes in the Burger chamber was used. But even against the background of the availability of hemocytometers, this circumstance prevented the wide application of the technique. Therefore, we proposed to evaluate the PHE by the percentage of hemoglobin content in the supernatant (Hb_s) to the total hemoglobin content in the erythrocyte suspension (Hb_{total}), determining hemoglobin by the standard hemoglobin cyanide method [4], which uses a hemoglobin calibration solution and a transforming solution (Drabkin reagent), which converts hemoglobin to cyanmethemoglobin.

The purpose of this work was to assess the osmotic resistance of erythrocytes (ORE) of pregnant women according to the method of V.I. Tsirkin et al. (Patent 2419792. Russian Federation: IPC G01N33/48. 07.12.2009. Published on 05.27.2011. Bull. No. 15) under the conditions for determining the percentage of hemolyzed erythrocytes according to the above method, i.e. by defining PHE as a percentage of $Hb_{precipitation}$ / Hb_{total}, using four types of erythrocyte exposure to DV, including 15 s, 45 s, 120 s and 300 s. In addition, the aim of the work was to prove the possibility of using the technique to assess the effect of biologically active substances on the ORE when using a 45-second exposure of erythrocytes to the DV. As such a substance, we chose oxytocin, which, as is known [5-7], is considered as an inducer of labor activity. Previously, using the method proposed by us, we studied the effect of adrenaline [2,3] and showed that adrenaline has little effect on the ORE. The choice of oxytocin turned out to be much more successful and, most importantly, it allowed us to explain the phenomenon of self-regulation of the ORE, revealed in the study of the intensity of erythrocyte hemolysis in DV, depending on the duration of exposure.

Materials and Research Methodology

We studied venous heparinized blood of 12 women with different terms (from 12 to 31 weeks) of uncomplicated pregnancy. It was received in a volume of up to 6 ml with the personal consent of the women in the conditions of the antenatal clinic in vacuum tubes with Na -heparin (“ Ningbo Greetmed Medical instruments Co., Ltd., China), in connection with which the authors express their gratitude to the medical staff and the head of the antenatal clinic, obstetrician-gynecologist T.V. Cherepanova. ORE was assessed by the method of V.I. Tsirkin et al. [3], i.e. by determining the PHE after their exposure is strictly limited in duration in DV containing 2.5 mm Cal_2. Termination of exposure to the DV was achieved by adding a 6% NaCl solution to the erythrocyte suspension in a ratio of 1:1, after which the level of hemolysis of erythrocytes during their 15-, 45-, 120-, and 300-s exposure to the DV, as well as the effect of oxytocin (in concentrations of 10^{-7} , 10^{-6} , 10^{-5} , 10^{-4} and 10^{-3} IU / ml of Krebs solution) on ORE under conditions of 45-second exposure of erythrocytes to DV. In all cases, the percentage of hemolyzed erythrocytes was determined by the percentage of hemoglobin in the supernatant (Hb_s) to the hemoglobin content in suspension (Hb_{total}). The supernatant was obtained after centrifugation of the erythrocyte suspension at 1000 rpm for 10 minutes. The level of hemoglobin in the test blood, in the suspension, and in the supernatant was determined by the standard hemoglobin cyanide method [4], using a hemoglobin calibration solution and a transforming solution (Drabkin’s reagent), which converts hemoglobin into cyanmethemoglobin (OOO Agat-med, Moscow). The color intensity of the Drabkin reagent, i.e. hemoglobin content was estimated by the extinction index on a KFK-2 uhl-4.2 photocolorimeter using a green light filter (wavelength 540 nm) and a cuvette 10 mm thick.

The study design was as follows. Initially, the content of hemoglobin in the studied venous blood was determined. For this, 0.02 ml of whole blood was added to 5 ml of Drabkin’s reagent. Then the percentage of hemolyzed erythrocytes was determined during their 15-, 45-, 120-, and 300-s exposure to Krebs solution, i.e. under isotonic conditions (1st control, or K-1). To do this, 0.1 ml of whole blood was added to 0.5 ml of Krebs solution; the suspension was kept at room temperature for 15 s, 45 s, 120 s and 300 s, respectively; stopped spontaneous hemolysis of erythrocytes. After that, 0.02 ml of this suspension was added to 5 ml of Drabkin’s reagent, i.e. the hemoglobin content in the suspension was determined (Hb_{total}). Then the suspension was subjected to 10 minutes centrifugation at 1000 rpm and 0.02 ml of the supernatant was added to 5 ml of Drabkin’s reagent, and thereby the level of hemoglobin in the supernatant (Hb_s) was determined. After that, the percentage of hemolyzed erythrocytes

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was calculated as a percentage of Hb_s / Hb_{total}. By analogy with the 1st control (C-1), the 2nd control (C-2) was performed, in which DV containing 2.5 mM $CaCl_2$. Otherwise, the 2nd control was carried out according to the above scheme, i.e. 0.1 ml of whole blood was added to 0.5 ml of DV and after 15 s, 45 s, 120 s and 300 s, respectively, 0.5 ml of 6% NaCl solution was added to it, after which the hemoglobin content in the suspension was estimated (Hb_{total}) and in the supernatant (Hb_s).

Then, by analogy with C-2, the effect of oxytocin on the ORE was evaluated with a 45-second exposure of erythrocytes to the DV together with oxytocin (experiment). To do this, 0.1 ml of whole blood was added to the test tube, 0.01 ml of Krebs solution containing oxytocin in a known concentration (for example, 10^{-7} IU /ml) was added to it. This mixture was kept for 5 minutes at room temperature, and then 0.5 ml of DW with 2.5 mm $CaCl_2$ was added to it, i.e. caused hemolysis. Strictly after 45 s, 0.5 ml of a 6% NaCl solution was added to the suspension, after which the hemoglobin content in the suspension (Hbtotal), in the supernatant (Hb_s) was estimated, and the percentage of hemolyzed erythrocytes was calculated. Similarly, the experiment was carried out with other concentrations of oxytocin.

The results were expressed as the median of the 25th and 75th percentiles, and the differences between the experience with C-1 and C-2 were assessed using the Wilcoxon test, considering them statistically significant at $p < 0.05$ [8]. Oxytocin from Gedeon Richter (Hungary) was used in the experiments. It was previously diluted in Krebs solution at concentrations of 10^{-7}, 10^{-6}, 10^{-5}, 10^{-4} and 10^{-3} IU/ml. When added to DW (at a ratio of 1:10), the actual concentration of oxytocin decreased 10 times. The Krebs solution used in the work contained (in mM): NaCl, 136; KCl - 4.7; $CaCl_2$ - 2.52; $MgCl_2$ - 1.2; KH_2PO_4 - 0.6; $NaHCO_3$ - 4.7; glucose -11 (pH - 7.4).

Research Results

Using the classic hemoglobin cyanide method for determining hemoglobin, which, in terms of labor intensity and time, is much simpler than the method of counting erythrocytes using a microscope, we found that the median, as well as the 25th and 75th percentiles of the hemoglobin content in whole blood of pregnant women were 134.4 (130; 152) g/l, which corresponds to known standards. When erythrocytes were exposed to Krebs solution at room temperature for 15 s, 45 s, 120 s, and 300 s, the PHE turned out to be close to zero; spontaneous hemolysis of erythrocytes during their exposure to the Krebs solution was practically absent. This also confirms the classical principles of the physiology of erythrocytes and indicates the possibility of applying the proposed modification of the method for assessing the ORE. It was established that at 15-, 45-, 120-, and 300-second exposures of erythrocytes to DW containing 2.5 mM $CaCl_2$, PHE was 17.2 (14; 26) %, 19.1 (16; 33) %, 23.6 (18; 30) % and 14.1 (7; 20) % of the initial content of erythrocytes (Figure 1). These results indicate that in the range from 15 to 120 seconds, with an increase in the duration of erythrocyte exposure, the percentage of hemolyzed erythrocytes also increases. This is consistent with the data obtained earlier in the visual count of non-hemolyzed erythrocytes in the Burger chamber, although in the cited studies, PHE values were higher [1]. For example, in the study of capillary blood of pregnant women (II trimester), it was found that with 30-, 45-, 60-, 90- and 120-second exposure of erythrocytes to the DW, the PHE values were respectively 12%, 25%, 38%, 51% and 64%. However, as our experiments showed (Figure 2), with a 300-second exposure, PHE became statistically significantly lower than with a 120-second exposure (14.1% vs. 23.6%, $p<0.05$). In the work cited above, A.I. Krysova et al. [1] did not study such exposure duration.

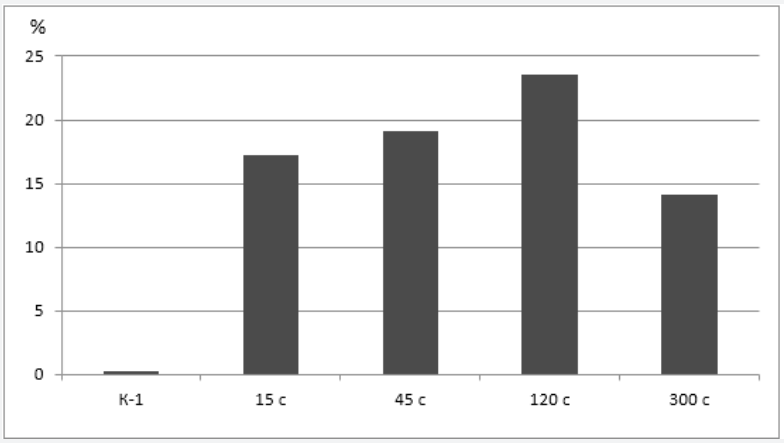

Figure 1: Percentage of hemolyzed erythrocytes of venous blood of pregnant women at 15-, 45-, 120- and 300-second exposures in distilled water containing 2.5 mM CaCl2. K-1 - the same indicator during exposure of erythrocytes in Krebs solution.

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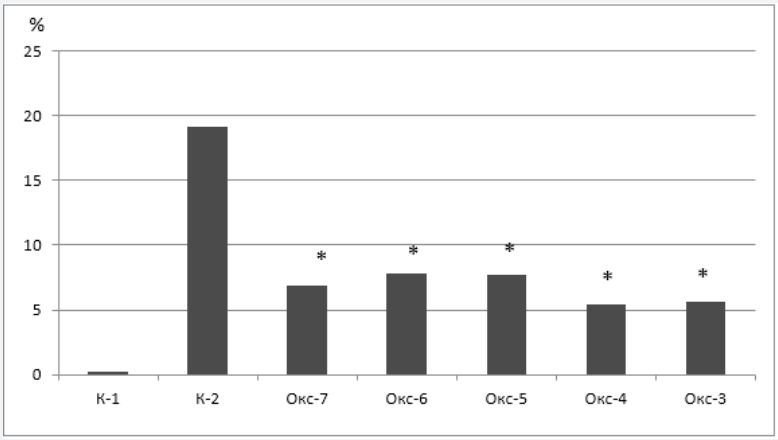

Figure 2: The percentage of hemolyzed erythrocytes in the 1st control sample, i.e. at 45-second exposure in Krebs solution (K-1), in the 2nd control sample, i.e. with a 45-second exposure in distilled water (K-2), and with a 45-second exposure in distilled water against the background of oxytocin at concentrations of 10^{-7}, 10^{-6}, 10^{-5}, 10^{-4} and 10^{-3} IU / ml (respectively, Ox-7, ... Ox-3); * - differences with K-1 and K-2 are statistically significant ($p < 0.05$) according to Wilcoxon's test.

We regard the decrease in PHE at a 300-s exposure as a reflection of the mechanism of self-regulation of the osmotic resistance of erythrocytes, which is discussed in more detail when discussing the results of the study. It is possible that oxytocin is involved in this phenomenon. This assumption follows from the results of studying the effect of oxytocin on PHE under conditions of their 45-s exposure to DV. Indeed, experiments with the addition of oxytocin to the DV showed that oxytocin, even at low concentrations (for example, 10^{-7} IU / ml) with a 45-second exposure of pregnant women's erythrocytes to the DV, statistically significantly ($p<0.05$) reduced PHE from 19 ,1 (16; 33)% in control (K-2) to 6.9 (5; 8)%, and with the addition of oxytocin at concentrations of 10^{-6}, 10^{-5}, 10^{-4} and 10^{-3} IU / ml this figure 1 was 7.8 (5; 10)%, respectively; 7.7 (5; 10)%; 5.4 (5; 7)% and 5.6 (5; 12)%. Differences between the effects of different concentrations of oxytocin were not statistically significant, although they showed a trend according to which, with an increase in the concentration of oxytocin, the resistance of erythrocytes to a hypotonic environment increase ($p > 0.05$).

Discussion of the Results of the Study

In itself, the ability of oxytocin to increase the ORE is, in our opinion, of great practical interest since it indicates the ability of oxytocin to reduce the entry of water into the cell. We explain this by the fact that oxytocin, like mercury salts [2,9-13], blocks the main water channel of erythrocytes, aquaporin 1 (AQP 1), and thereby reduces the entry of water into the erythrocyte. Note that the presence of AQP 1 (either the 28 kDa protein or the CHIP 28 protein) in erythrocytes has been established by many authors [11-19]. It has been shown that each erythrocyte contains up to 120-160 thousand AQP1 molecules [14]. This protein plays a leading role not only in water transport in erythrocytes, but also in CO_2 transport [19]. Tyrosine phosphorylation of AQP1 is known to change the activity of the channel [18]; obtained during the implantation period, oxytocin can suppress the expression of AQP1 mRNA [20]. All these data indicate the ability of oxytocin to reduce the entry of water into the cell, and therefore it can be argued that it is advisable to use oxytocin as an inhibitor of the entry of water into the cell, which can be important for relieving tissue edema, including cerebral edema. As is known so far, the number of drugs capable of reducing the entry of water into cells by inhibiting aquaporins is extremely small [11,13]. Among them are mercury salts, which, however, are highly toxic [2,9-13], and the drug dimethyl sulfoxide, blocking AQP 1 [11].

It should be noted that the blocking effect of 0.05 mM $HgCl_2$ on the entry of water into the erythrocyte was also noted in our laboratory [2] when assessing the ORE according to the method of Tsirkin V.I. et al. In this work, it was confirmed that, against the background of mercury salts, erythrocytes can stay in the DV for a long time without undergoing hemolysis. Obviously, oxytocin can be considered as one of the safe inhibitors of aquaporin AQP 1, which can be used to combat tissue swelling, including in pre-eclampsia and eclampsia. One of the evidence for the ability of oxytocin to reduce the entry of water into the erythrocyte is the data of our laboratory on a decrease in the erythrocyte sedimentation rate (ESR) of pregnant women under the influence of oxytocin, especially its low (10^{-7}, 10^{-6} IU/ml) concentrations [21,22]. It is possible that the ability of oxytocin to reduce the entry of water into the erythrocyte increases under the influence of the non-genomic action of estradiol, since estradiol enhances the effect of oxytocin on ESR [22].

Returning to the explanation of the phenomenon of the decrease in the percentage of hemolyzed erythrocytes during

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their 300-second exposure, we will make one more assumption. It is based on literature data [6,23], according to which the oxytocin gene controls prohormone synthesis, i.e. neurophysin and oxytocin. It is possible that during pregnancy, in view of the need of the fetus for oxytocin as a factor regulating the maturation of brain neurons [24-26], during erythropoiesis at the stage preceding the removal of the nucleus, the oxytocin gene is expressed. As a result, granules (similar to the vesicles of Hering's bodies of the neurohypophysis) containing neurophysin and oxytocin are formed in the erythrocyte. In the lacunae of the placenta, the erythrocyte releases oxytocin, which is transferred to the fetus and thereby contributes to the formation of neocortical neurons. Returning to the results of our study, we note that in a hyposmotic environment, oxytocin is released from erythrocytes. After leaving the erythrocyte, oxytocin paracrine activates oxytocin receptors and thereby blocks AQP1, which increases the resistance of the erythrocyte to a hypotonic environment.

We do not exclude that the increase in the resistance of women's erythrocytes to the hypoosmotic environment noted in [1] during pregnancy may be associated with an increase in the content of oxytocin in erythrocytes during this period. Thus, future studies should prove that, indeed, preprohormone is stored in the erythrocytes of pregnant women, i.e. oxytocin + neurophysin. If our hypothesis is correct, then we can assume that anemia of pregnancy is dangerous for the fetus, not only from the point of view of reducing oxygen transport (hypoxia), but also from the point of view of the formation of oxytocin deficiency during pregnancy, which, as is known [25-27], has important for the development of the brain of the fetus and newborn. Therefore, the administration of non-peptide oxytocin receptor agonists to the mother, which can stay in the environment for a long time without being destroyed by oxytocinase or excreted by the kidneys, may be one of the ways to prevent fetal brain development disorders in anemia.

The hypothesis of the existence of a mechanism of self-regulation of the ORE allows us to take a fresh look at the pathogenesis of preeclampsia and the threat of preterm birth (TPB). According to Krysova A.I. et al. [1], ORE in women with preeclampsia is reduced. For example, their T_{50} index is reduced to 47 s (instead of 77-85 s in the absence of pregnancy complications). Indirectly, this means that in such women, the content of oxytocin inside the red blood cells is reduced, which reduces the delivery of oxytocin to the fetus. And perhaps the answer to this situation is the formation of pre-eclampsia. With TPB, the $T_{50\ indicator}$ is also reduced to 45 s [1]. This may be due to a compensatory decrease in the production of oxytocin by hypothalamic neurons to block preterm labor. Under these conditions, it is obvious that the fetus also receives less oxytocin, which affects its development. The hypothesis about the existence of a mechanism of self-regulation of the ORE allows us to explain the gender differences in the ORE to the hypoosmotic environment, in particular, the higher ORE in men compared to non-pregnant women, which was previously established in our laboratory [1,2]. We do not exclude that in men the content of oxytocin in erythrocytes is increased. This is probably necessary for the regulation of sexual behavior, erection, spermatogenesis, and ejaculation, which, as is known [5-7,28-30], is realized with the participation of oxytocin.

The concept of the existence of a mechanism of self-regulation of erythrocyte resistance to a hypoosmotic environment explains, to a certain extent, the possibility of erythrocytes passing without damage through a hypotonic environment in portal vessels. Indeed, Y. Chu et al. [18] showed that a human intake of water in a volume of 500 ml leads to the creation of a hypotonic medium in the portal vessels; however, despite this, water does not enter erythrocytes and does not destroy them. According to the authors [18], this is due to the inactivation of aquaporin AQP 1 due to its tyrosine phosphorylation, which reduces the activity of the channel and thus prevents excessive water ingress into the erythrocyte. We do not rule out that oxytocin is also involved in this regulation, leaving the erythrocyte to its surface, due to which aquaporin AQP 1 is inhibited. The insufficiency of this compensatory mechanism can probably lead to increased hemolysis of erythrocytes. We are aware that many assumptions have been made in our article, each of which requires detailed proof and, above all, proof of the presence of oxytocin inside the erythrocyte, the mechanism of transport of oxytocin into the erythrocyte, the mechanism of exocytosis, the presence of a mechanism of self-regulation of the ORE in men and non-pregnant women, and others. moments.

Conclusions

a) Using the method for assessing the osmotic resistance of erythrocytes, based on determining the percentage of hemolyzed erythrocytes (PHE) during their exposure strictly fixed in time in distilled water (DW) containing 2.5 mm $CaCl_2$, it was found that with an increase in the duration of exposure of erythrocytes in DW from 15 to 120 s, PHE increases, but with a longer exposure, i.e. at 300 s PHE decreases.

b) The same method showed that oxytocin at concentrations of 10^{-8}-10^{-4} IU/ml increases the osmotic resistance of erythrocytes (ORE) subjected to a 45-second exposure to DV, which allows us to consider oxytocin as an inhibitor of aquaporin AQP1 and recommend it used to reduce tissue swelling.

c) An idea was formulated about the presence of a mechanism of self-regulation of the ORE, which, most likely, is realized due to the paracrine effect of oxytocin, which is released from the erythrocyte under the influence of hypoosmotonic environmental .

d) The idea of erythrocytes as a source of oxytocin is substantiated, thanks to which the fetus and newborns receive oxytocin for brain development, and adults for the regulation of physiological processes.

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e) The degree of ORE, determined under conditions of hypoosmotonic, indirectly reflects the content of oxytocin in the erythrocyte. Low levels of oxytocin in red blood cells can cause pre-eclampsia, threatened preterm labor, and possibly other obstetric complications.

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