

# **Ozonotherapy as the Main Component of the Complex Treatment of Threatened Abortion**

Guennadi O. Gretchkanev

Department of Obstetrics and Gynecology, Medical Academy of Nizhny Novgorod,  
Pl. Minina 10/1, 603005 Nizhny Novgorod, Russia

## **Abstract**

80 pregnant women with threatened abortion of infectious (40) and endocrine (40) genesis were treated with medical ozone. We established the following laboratory changes:

- The study of lipid peroxidation processes on the background of ozonotherapy showed a decrease in the primary and secondary molecular products. The average 22,1% increase in the total antioxidative plasma activity was established.
- The patients treated with ozone showed an average week's increase in progesterone concentration 3,3 times higher, in placental lactogen 2,4-3,6 times higher as compared with the conventional treatment.
- After using ozonotherapy, we established a credible decrease (by 20-50%) in circulating immune complexes. That correlated with intensification of the phagocytic activity. The level of IgM had a tendency to normalize.

Thus, owing to its varied positive effects on pregnant women ozonotherapy has proved to be an effective method of treatment and prophylaxis of threatened abortion.

## **Introduction**

The problem of threatened abortion being of great medical as well as social importance remains one of the most topical in obstetrics and gynecology. In reference to Russian authors, frequency of this pathology is 10-25% (4,5). There are 40-80% of premature neonates in the structure of perinatal mortality (1), among them there are 50% of deadborn, 60-70% cases of neonatal mortality and 67-75% cases of infant mortality (2). In reference to the above data, there is an urgent need for new, probably not-traditional therapeutical approaches to this medical problem.

The use of ozone in the medicine has been known for over 100 years, in that period the most important aspects of action of this gas on human body were established – its disinfection activity, its ability to stimulate the circulation, to stabilize the state of cell membranes and so on. Medical ozone has been widely used in surgery, various specialities of internal medicine, intensive care, dermatology und other medical fields, but till now there have been only isolated reports about ozone applications in the treatment of gynecological pathologies.

The aim of the present investigation was to establish and to demonstrate a great therapeutical potential of ozone for such a complex pathology as threatened abortion.

## **Materials and Methods**

130 patients with threatened abortion were observed, 90 of them received medical ozone as a part of complex treatment, and 40 got only conventional treatment. Depending on the pregnancy term when threat of abortion arose, all patients were divided into 2 groups:

I group – patients with threatened abortion in I trimester (70 women);

II group – patients with threatened abortion in II trimester (60 women).

The function of placental complex and reproductive system of women inside the test and control groupes was evaluated according to estriol, estradiol, progesterone, placental lactogen, prolactin levels of peripheral blood. For that purpose we used a radioimmunological method with assistance of the following sets: CTEPOH-E3-125, PИO-IIИ-125 and enzyme immunoassay (device of system AMERLIT).

The immunological investigation included determination of an absolute quantity of leukocytes and lymphocytes in blood, a relative quantity of T- and B-lymphocytes with subpopulations of T-helpers and T-suppressors, concentrations of serum immunoglobulins (IgA, IgM, IgG), the phagocytic activity of neutrophiles, the level of circulating immune complexes (CIC). The T-lymphocytes were determined by means of rosette-formating reaction with sheep erythrocytes, the subpopulations of T-helpers and T-suppressors were investigated by means of rosette test and test for theophylline sensitivity. The B-lymphocytes were determined by means of rosette-formating reaction with sheep erythrocytes, the phagocytic activity of neutrophiles was evaluated with assistance of standard latex particles. The quantity of immunoglobulins of A, M, G groups in blood serum was determined by means of radial immunodiffusion, CIC – after V. Gashkova.

The thorough analysis of patients' clinical data made it obvious that most of them had a combination of several factors of threatened abortion (infectious-inflammatory, dyshormonal, immunological and so on) that made it difficult to divide the patients into the groups according to disease etiology. That was why the groups of patients were formed in accordance with the pregnancy term when threat of abortion arose. Depending on the method of treatment each group was further divided into the test (with ozonotherapy) and the control (with conventional treatment) subgroups. The test subgroup inside I group consisted of 50 patients, the control – of 20, inside II group – 40 and 20 patients, respectively. The subgroups to be compared were quite equal in patients' age, etiology of threatened abortion and other parameters.

Ozonotherapy was carried out in the form of intravenous drop-by-drop infusions of ozonated physiological saline solution which was produced by conveying an ozone-oxygen gas mixture with ozone concentration 400 mcg/L through a bottle with 400 ml of sterile physiological 0,9% sodium chlorid solution for 10-15 minutes at flow rate 1 L/min. The ozonated solution was administered in the form of drip into the elbow vein at flow rate 8-10 ml/min that lasted 40-50 minutes (duration of one procedure).

Along with ozonotherapy the patients of test subgroups received spasmolytic or tocolytic preparations (depending on the pregnancy term), glucocorticoids for hyperandrogenemia, in

isolated cases – treatment with antibiotics for infectious-inflammatory diseases, in case of isthmio-cervical insufficiency there was a need for its surgical correction.

The patients of control subgroups, which were treated without ozonotherapy, received spasmolytic preparations, glucocorticoids and antibiotics (according to the indication) as well as metabolic therapy including the use of synergists – Krebs' cycle substrates and cofactors: thiaminpyrophosphate, riboflavin, mononucleotide, calciumpantothenat, lipoic acid,  $\alpha$ -tocopherol acetate; metabolic preparations: cyanocobalamine, pyridoxal phosphate, phytin, folic acid, potassium orotate, and infusion-transfusion therapy.

## Results and Measurements

In laboratory conditions we conducted a preliminary experiment in order to select the doses of ozone depending on its action on blood samples taken from the patients with threatened abortion. As a criterium for safety and efficiency of the given doses of ozone it was considered a decrease in the molecular products of lipid peroxidation (LP) as well as intensification of the total antioxidative activity (AOA) of blood serum. The choice was based on the objectivity and informativity of the above indices as well as their importance for prognosis of obstetric pathologies including threatened abortion (3).

As a result of the conducted experiment in vitro it was established that the manner of action of ozone on LP and AOA levels of blood depended on its dosage. Ozone concentration 400 mcg/L of an ozone-oxygen mixture delivered from ozone generator was considered the optimal one for saturation of physiological saline solution and its further administration into the blood for the given concentration caused a considerable increase in AOA and a tendency towards a decrease in the molecular products of LP. Higher ozone concentrations (800 mcg/L and 1200 mcg/L) led to reverse processes. Based on the above results, we have accepted the saturation ozone concentration 400 mcg/L as the optimal one for using in clinical conditions owing to its positive effect on LP and AOA levels of blood plasma in patients with threatened abortion.

Our investigation conducted in clinical conditions convincingly demonstrated that as from the 2<sup>nd</sup>-3<sup>d</sup> day of ozone treatment the patients with threatened abortion showed a credible decrease in the molecular products of LP and a simultaneous increase in AOA. The optimal correlation between the above indices was achieved on the 5<sup>th</sup> day of treatment that defined the number of procedures (five).

The investigation into the immediate effect of ozonotherapy on clinical aspects of threatened abortion convincingly demonstrated an improvement in patients' state. There was evidence of much faster easing of pain as compared with the control that allowed to reduce the use of spasmolytic remedies, to decrease general nervous excitability in an absolute majority (90%) of patients, to improve their sleep and appetite. The appearances of early toxicosis decreased or disappeared in 90% of patients. Owing to the use of medical ozone we did not observe any side effects or adverse reactions or complications.

We established quite favourable influence of ozonotherapy on the efficiency of treatment of threatened abortion. So, owing to complex therapeutic procedures with ozone the pregnancy was preserved and prolonged to the physiological terms of labour in 86% of patients inside I

group and in 85% of patients inside II group. In the control subgroups of I and II groups it was possible to preserve the pregnancy in 65% and 60% of cases, respectively.

Having compared the course of pregnancy among the patients of I group, we established that the most frequent complication was repeated threat of miscarriage. But among the patients treated with ozonotherapy it was observed 1,9 times more rarely than among the patients treated without ozonotherapy (16,3% and 30,8%, respectively). Late gestosis - the second frequent complication of pregnancy - was observed among the patients of test subgroup 2,1 times more rarely than in the control (11,6% and 23,1%, respectively). Inside I group 93% of test subgroup patients and 92% of control subgroup patients which preserved the pregnancy had easy delivery (7% and 8%, respectively, had Cesarean delivery). The analysis of a delivery course showed that among the patients treated with ozone in I trimester weakness of delivery activity was observed 2,3 times more rarely than in the control (2,3% and 2%, respectively). Otherwise, the course of delivery and early postnatal period among the patients of test and control subgroups had no differences. There was one more fact taken into consideration that the state of newborn babies was better if their mothers had received ozonotherapy in I trimester of pregnancy as compared with the control. So, inside the test subgroup 80% of newborn babies received 7-10 points according to Apgar's score, in the control - 60%.

The analysis of a further (following the time of threatened abortion) course of pregnancy inside II group made it obvious that the most frequent complication was late gestosis which was observed among the patients treated with ozone only 1,3 times more rarely than in the control (26,3% and 33,3% of cases, respectively). The second frequent complication - repeated threat of abortion - was observed among the women of test subgroup 1,9 times more rarely than in case of conventional treatment (17,6% and 33,3% of cases, respectively).

The frequency of Cesarean delivery inside the test and control subgroups was the same (10% in each). During the analysis of a delivery course it was established that among the patients treated with ozone in I trimester of pregnancy weakness of delivery activity was developed 1,8 times more rarely than in the control. The state of newborn babies was also better in case their mothers had received ozonotherapy: the maximal value according to Apgar's score (7-10 points) was given to 80% of babies, while in the control - only to 58,3%.

The thorough laboratory monitoring of the state of pregnant women treated with ozonotherapy allowed us to get objective data of clinical observations. In particular, it was established that medical ozone used in case of threatened abortion stimulated the hormonogenic function of fetoplacental complex (FPC) more intensively than the conventional treatment. So, ozonotherapy used in I trimester of pregnancy led to an average week's increase in estradiol 3,6 times higher ( $p<0,05$ ), in progesterone 3,3 times higher ( $p<0,05$ ), in placental lactogeron 3,6 times higher ( $p<0,05$ ), in prolactin 2 times higher ( $p<0,05$ ) than the conventional treatment. Medical ozone used in II trimester of pregnancy caused a credible increase in estriol, and an average week's increase in placental lactogen was 2,4 times higher ( $p<0,05$ ) than in the control.

Ozonotherapy had a favourable effect on the immunity of patients by inducing a decrease in the circulating immune complexes (CIC) in patients with threatened abortion by 30-39,5% (Table I), a decrease in group and anti-Rh antibodies by 2-8 times that reduced a risk of damage caused by the above factors.

Table I: The influence of ozonotherapy and conventional treatment on circulating immune complexes (CIC) in patients with threatened abortion

	I trimester		II trimester	
	The test group	The control group	The test group	The control group
CIC before treatment, U/ml	105,4 ± 17,9	53,6 ± 13,7	95,6 ± 15,8	50,6 ± 15,4
CIC after treatment, U/ml	74,8 ± 12,1 p < 0,05	52,1 ± 12,1 p > 0,05	57,9 ± 9,9 p < 0,05	78,2 ± 26,0 p > 0,05
CIC in health, U/ml	20 - 130			

Note: p – credibility of difference between the values after and before treatment

Medical ozone used in the complex treatment of threatened abortion produced a more expressed positive effect on the lipid peroxidation processes and the antioxidative defense system as compared with the control.

So, owing to ozonotherapy the level of primary molecular lipid peroxidation products – diene conjugates – decreased by 25-51% (Table II), the level of the end ones – Schiff's bases – decreased by 34-48% (Table III), the total antioxidative plasma activity increased by 21-37% (Table IV) that improved a prognosis of the disease.

Table II: The influence of ozonotherapy and conventional treatment on diene conjugates (DC) in patients with threatened abortion

	I trimester		II trimester	
	The test group	The control group	The test group	The control group
DC before treatment, nmol/mg of total lipides	5,78 ± 0,97	4,5 ± 1,0	6,95 ± 1,45	3,22 ± 0,73
DC after treatment, nmol/mg of total lipides	3,73 ± 0,77 p < 0,01	5,4 ± 1,0 p > 0,05	3,43 ± 0,87 p < 0,01	3,42 ± 0,35 p > 0,05
DC in health, nmol/mg of total lipides	2,78 ± 0,74			

Note: p – credibility of difference between the values after and before treatment

Table III: The influence of ozonotherapy and conventional treatment on Schiff's bases (SB) in patients with threatened abortion

	I trimester		II trimester	
	The test group	The control group	The test group	The control group
SB before treatment, rel.U/mg of total lipides	363,2 ± 68,0	251,1 ± 65,0	535,6 ± 181,0	166,6 ± 22,7
SB after treatment, rel.U/mg of total lipides	202,4 ± 32,9 p < 0,01	454,7 ± 136,5 p > 0,05	259,8 ± 72,7 p < 0,05	216,0 ± 20,7 p > 0,05
SB in health, rel.U/mg of total lipides	241,8 ± 35,5			

Note: p – credibility of difference between the values after and before treatment

Table IV: The influence of ozonotherapy and conventional treatment on the total antioxidative activity (AOA) of blood serum in patients with threatened abortion

	I trimester		II trimester	
	The test group	The control group	The test group	The control group
AOA before treatment, rel.U	0,083 ± 0,005	0,1 ± 0,005	0,085 ± 0,004	0,11 ± 0,005
AOA after treatment, rel.U	0,11 ± 0,0007 p < 0,01	0,082 ± 0,004 p > 0,05	0,109 ± 0,002 p < 0,01	0,1 ± 0,002 p > 0,05
AOA in health, rel.U	0,12 ± 0,02			

Note: p – credibility of difference between the values after and before treatment

## Discussion

The received results indicate that ozonotherapy used in the complex treatment produces not only the direct positive effect on clinical aspects of threatened abortion. The prolongation of pregnancy to the physiological terms of delivery was achieved in much more patients than in the control, it was decreased a risk of such gestational complications as repeated threatened abortion and late gestosis, it was reduced a possibility of weakness of delivery activity.

The established ability of ozone to produce a positive effect on LP level in case of threatened abortion by decreasing concentrations of diene conjugates and Schiff's bases and by simultaneously increasing the AOA of blood plasma is considered an objective precondition of the well-known membrane stabilizing effects of ozonotherapy. The importance of the last for restoration of the function of fetoplacental system is difficult to overestimate (3). The decrease in free-radical reactions, lessening of their disturbing effect evidently provides a basis for the stimulating effects of ozonotherapy on the hormonogenic function of placenta. In comparison with the control, a credibly higher increase in estradiol, progesterone, placental

lactogen, estriol established in the course of an investigation is not only of great importance, but also improves a prognosis of the disease.

The immunomodulating effects of medical ozone on patients with threatened abortion appeared to be quite selective. Most of changes took place in the humoral link of immunity, in particular, at the level of circulating immune complexes (CIC) which considerably decreased. There is no need to speak about the possible disturbing effects of CIC on placenta cell membranes, there is a high possibility of their adhesion to the last ones. The intensified elimination of CIC as well as of group and anti-Rh antibodies liquidates one of the most essential factors of the pathogenesis of threatened abortion.

### Conclusion

Thus, thanks to its numerous therapeutical effects ozonotherapy increases the efficiency of treatment and allows therefore to avoid the use of many medicines traditionally applied for treatment of threatened abortion. The selected approach to ozone application in the complex treatment of obstetric complications has proved to be effective against gestosis and pregnancy anemia as well (6,7). The lessening of drug load on the women's and fetus' organisms is considered an additional motivation for widely including medical ozone into the complex treatment of threatened abortion and other gestational complications.

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