

Publication date: 1.03.2021

DOI: 10.51871/2588-0500\_2021\_05\_01\_4

**UDC 618.3-06:615. 835.3**

## **PREVENTION MEASURES OF PLACENTAL INSUFFICIENCY DURING HIGH-RISK PREGNANCY**

L.V. Tsallagova<sup>1,2</sup>, L.V. Majsuradze<sup>1,2</sup>, S.V. Sagkaeva<sup>1</sup>

<sup>1</sup>FSBEI of HE "North Ossetian State Medical Academy" of the Ministry of Health of the Russian Federation, Vladikavkaz, Russia

<sup>2</sup>Institute of Biomedical Research of Vladikavkaz Scientific Center of the Russian Academy of Sciences, Vladikavkaz, Russia

**Key words:** feto-placental insufficiency, ozone therapy, limontar, high-risk pregnancy, preventive measures, perinatal outcomes.

**Annotation.** The purpose of the study is to optimize prevention care of placental insufficiency during high-risk pregnancy by inclusion ozone therapy and limontar antihypoxic drug in the programs according to the features of pregnancy termination, state of the early born, frequency of perinatal complications. There has been conducted research study in maternity welfare center of Out-patient clinic №1 in Vladikavkaz. The study included 75 pregnant women with diagnosed placental insufficiency (the average age was  $28.6 \pm 2.14$  years old). Three groups were formed by random sampling. In the main group the patients received prevention treatment by using ozone therapy and limontar; in the group of comparison they were prescribed only limontar; the pregnant women of the control group did not receive any prophylaxis. The clinical effect of the use of the preventive care of placental insufficiency with pregnant women was assessed by the features of the outcome of pregnancy, the state of the early born, frequency of perinatal complications. After the carried out preventive measures the women who received comprehensive prevention treatment of placental insufficiency had a significant decrease in the incidence of complications of gestation period and perinatal morbidity by 3.5 ( $p < 0.01$ ) times in relation to the indicators in the group of comparison and 4.7 ( $p < 0.01$ ) times in relation to the data in the control group. In the main group there was no progression of placental insufficiency, while in the group of comparison the progression was in 31.8% of cases, in the control group – in 56%. Application of medicamentous- and ozone therapy in complex of preventive measures of placental insufficiency in case of high-risk pregnancy contributes to the improvement of perinatal outcomes.

**Introduction.** One of the urgent problems of modern obstetrics is fetoplacental insufficiency (FPI), the frequency of which varies widely (34-45%) [1, 2].

It should be considered that the initial importance in the prevention of FPI belongs to the correction of violations of the fetoplacental perfusion (FPP) [6]. The conducted literary research showed that inclusion of physical factors in treatment programs for patients with various chronic diseases provides a significant increase in the effectiveness of therapeutic measures [3, 4, 5]. A number of works indicates the improvement of uterine-placental perfusion (UPP), normalization of endometrial morphological structure, process recovery under the influence of ozone therapy (OT) [7, 8, 9, 10]. The positive effect of limontar antihypoxic drug on adaptation processes of a pregnant woman are also well-known. according to the research of A.A. Dzhumagaziev and L.R. Rakhimova (2015) on the use of limontar in combination with glycine for the rehabilitation of newborns with perinatal hypoxic-ischemic injury to the central nervous system stated that against the background of the metabolites reception by the 10th day there is a rapid normalization of neurological status with reduction of the main clinical symptoms [11].

The purpose of the study is to optimize preventive treatment of placental insufficiency during high-risk pregnancy by inclusion ozone therapy and limontar antihypoxic drug in the programs according to the features of pregnancy outcome, the state of an early born, frequency of perinatal complications.

**Methods and organization.** There has been conducted a research study in a maternity welfare center of Out-patient clinic №1 in Vladikavkaz. The study included 75 pregnant women with diagnosed placental insufficiency (the average age was  $28.6 \pm 2.14$  years old) who agreed to take part in the research and practice work.

Three groups were formed by the method of blind sampling. The control group (CG) consisted of 25 patients. They did not receive PI prevention care. The group of comparison (GC) included 22 patients, they received only medicamentous therapy with limontar. In the main group (MG) 28 patients underwent PI prevention care: medicamentous therapy with limontar antihypoxic drug for one pill a day (previously powdered and dissolved in 200.0 ml of water), 30 minutes before meals during 10 days and OT in the form of intravenous drop infusions of ozonised physiological solution (saline bubbling was carried out by passing an ozonic-oxygenous gas mixture through a sterile saline vial, ozone concentration 1500  $\mu\text{g/L}$ ) with capacity of 200.0 ml every second day for a course of 5 procedures.

The clinical effect of the use of PI preventive treatment with pregnant women was assessed by the features of outcome during pregnancy, the state of a newly born according to Apgar scale in the first minute and 5 minutes after birth, the frequency of perinatal complications. Uterine blood flow dopplerometry and ultrasound of placental structure were performed on Toshiba SSA-340A ultrasound device

(Japan). Fetal monitoring (FM) was performed on Partecust Cardiomonitor (Germany). Statistical processing of the material was carried out using common methods of parametric and non-parametric statistics based on the standard package of applied statistical analysis "STATGRAFICS FOR WINDOWS," the domestic software product "STADIA" and the package "EXCEL."

**Results and discussion.** The conducted preventive measures provided significant restoration of placental thickness with pregnant women of the MG and the GC: in 72.7% ( $p < 0.01$ ) cases up to normative values ( $32.6 \pm 2.25$  mm) and in 47.4% ( $p < 0.01$ ) cases (up to  $35.6 \pm 2.48$  mm), which indicated an improvement in compensatory mechanisms. In the CG, placental thickness indicators remained the same after 14 days ( $42.3 \pm 2.55$  mm), which indicated the development of secondary FPI in this group.

The use of oxygen-ozone mixture and pharmacotherapy provided a significant improvement in FPI with the pregnant of the MG. Thus, with the echography of the placenta in 80% ( $p < 0.01$ ) of cases, the number of cysts and cystic inclusions decreased, in 81.3% ( $p < 0.01$ ) there was a decrease in frequency of polyhydramnios or hypamnion, in 81.8% ( $p < 0.01$ ) there was premature placenta aging, which was significantly better in relation to the dynamics of the corresponding indicators in the GC and CG. It should be noted that at the end of the course of preventive care there was a more significant dynamics ( $p < 0.05$ ) in the GC when using limontar than in the CG.

The practicability of FPI preventing with an oxygen-ozone mixture and limontar was evidenced by the dynamics of doppler analysis indicators. In the main group by the end of the prevention course there was a significant decrease in vascular resistance indices to normative values: in 74% of cases the average values of systolic-diastolic ratio decreased by 8.8%; resistance index – by 19.7% ( $p < 0.05$ ); pulsation index – by 14.3%. In the GC under the influence of limontar there was only a tendency to improve dopplerometric indicators. In the CG these indices remained the same and were a prognostic sign of persisting FPI.

Table 1

Dopplerometric blood flow rates in uterine arteries

Indices	Preventive period	Indices of healthy women (n=25)	Control group (n=25)	Group of Comparison (n=22)	Main group (n=28)
Systolodiastolic ratio	before	1,90±0,18	2,35±0,34	2,32±0,29	2,15±0,34
	after		2,58±0,29	2,24±0,17	1,96±0,22
Pulsation index	before	0,55±0,07	0,78±0,07	0,75±0,09	0,76±0,06
	after		0,75±0,08	0,69±0,09	0,61±0,05*
Resistance index	before	0,32±0,04	0,44±0,05	0,41±0,02	0,42±0,06
	after		0,43±0,02	0,38±0,04	0,36±0,02

Note: \* -  $p < 0.05$ ; \*\* -  $p < 0.001$  - reliability of differences compared to indicators before prevention; " -  $p < 0.05$  - reliability of differences with respect to indicators in the CG.

Intrauterine fetal condition was assessed during the pregnancy in the II and III trimesters by Cardiocotography. After carrying out preventive measures, the patients of the MG had an improvement of the frequency of fetal movement during 30 minutes by 33.7% ( $p < 0.01$ ), in the GC – by 24.7% ( $p < 0.05$ ), heart oscillation rate improved by 42.6% ( $p < 0.01$ ) and 34.3% ( $p < 0.01$ ), a change in heart rate during fetal movement was by 34.6% ( $p < 0.05$ ) and 21.9 ( $p < 0.05$ ) respectively. It should be noted that the dynamics in these both groups was significantly more pronounced with respect to the similar data in the CG.

The conducted analysis of the morbidity of the second half of pregnancy with the observed women showed that the incidence of threatened miscarriage in the MG decreased significantly, amounting to 17.9 versus 36.4% in the GC and 40% in the CG. FPI progression was in 0%, 31.8% and 56% of cases, intrauterine fetal hypoxia was in 10.7%, 36.4% and 48% cases respectively (Table 2). It confirmed the expediency of carrying out preventive care by limontar and OT in case of placental insufficiency with pregnant women at high-risk groups.

Table 2

Frequency of pregnancy complications with the examined pregnant women

Complications during pregnancy	CG (n=25)		GC (n=22)		MG (n=28)	
	abs.	%	abs.	%	abs.	%
Threatened miscarriage	10	40	8	36,4	5	17,9*
Moderate pre-eclamsia	11	44	7	31,8	3	10,7*
Progression of PI	14	56	7	31,8*	0	0
Fetal hypoxia	12	48	8	36,4	3	10,7*

Note: \* –  $p < 0,05$  – validity of differences relative to control and comparison groups.

The analysis of pregnancy outcomes revealed a high incidence of premature birth during 29-30 weeks with the pregnant women (40%) who did not undergo preventive care. Six of these patients (24%) had birth delivery with the help of caesarean section. In the GC the incidence of premature delivery within 33-34 weeks was observed in 18.2% of cases, while 2 (9.10%) of them had a delivery by caesarean section.

The women who received a preventive course of pharmaco-ozone therapy, had premature delivery within 36-37 weeks of pregnancy in only 10.7% of cases and only 1 patient (3.60%) had a delivery by caesarean section.

In the CG 24.0 % of parturient women had a long latency period (more than 10 hours), 40.0 % of patents had anomalies of birth activity in the postpartum and early postpartum periods, 16.0% had pathological blood loss – in 16.0%, 40.0% of

the women had hystercervicorrhesis of I-II stage. It should be noted that 28.0% of them underwent episiotomy and perineotomy. The patients of the GC who received only pharmacotherapy with limontar, had anomaly of birth activity in 27.2% of cases, long latency period in 18.2%, pathological blood loss in 13.6%. Only 9.12% had hystercervicorrhesis, and 27.3% of women in labor underwent episiotomy and perineotomy. The patients of the MG against the background of complex PI prevention, 17.9% of the patients suffered from anomaly of birth forces, 10.7% had a long latency period, 10.7% had pathological blood loss. Hystercervicorrhesis was observed with only 7.12% and 21.4% of women in labor underwent episiotomy and perineotomy.

Thus, there is a clear correlation between the decrease in the incidence of childbirth complications and the postpartum period in the MG (1.55 times more in relation to the GC and 2.59 times – CG), which confirms a high clinical effectiveness of the use of limontar and OT for the prevention of PI with pregnant women of high risk group. This is explained by immunocorrecting, antioxidant action of OT, as well as the correction of microcirculatory and rheological disorders under its influence as well as metabolic effects of limontar [6, 8].

**Infant health screening.** Nowadays, there is no doubt that one of the manifestations of PI is the development of chronic prenatal fetal hypoxia. That is why early diagnosis and adequate therapy of FPI becomes of particular importance [1].

Neonatal status was assessed in the first minute and 5 minutes after the birth. The women who underwent comprehensive preventive treatment of PI (MG) gave birth to babies with a good assessment of the body's functional abilities according to Apgar scale (8-10 points). Their number was 2.3 ( $p < 0.01$ ) times more than in the CG and 2.0 ( $p < 0.05$ ) times more compared to the data in the GC. 14.3% of newborns had a satisfactory rating according to Apgar scale in the MG, while in the GC – with 36.4%, and in the CG – with 32% of children. Unsatisfactory condition of newborns in the MG was observed in 3.60% of cases, in the GC – in 13.6%, and in the CG – in 28% of cases.

A study of the physical development of children at birth revealed that 82.1% of newly born children were born with normal weight indicators; the average mass of newborns was  $3300 \pm 226.0$  g. 17.9% had a hypotrophy of the 1st stage; the average mass of newborns was  $2550 \pm 186.0$  g. The results were obtained with the same reliability when analyzing growth indicators. Comparative analysis showed that statural-weight values of newborns from the parturient women of the MG who underwent PI prophylaxis in combination with complex medicamentous-ozone therapy were better by 1.5 ( $p < 0.05$ ) times compared to the data in the GC where only pharmacotherapy was used and 1.8 ( $p < 0.01$ ) times as related to the data in the CG

where there was no PI prophylaxis. 7 newborns of the total number of the babies were transferred to Children's Republican Clinical Hospital in Vladikavkaz for further treatment.

### **Conclusion.**

1. Complex medicamentous-ozone therapy ensured an improvement of uterine-placental perfusion (UPP) by 17.5% ( $p<0.05$ ), which leads to the reduction in the incidence of antenatal fetal hypoxia.

2. The use of limontar tissue metabolism regulator and ozone therapy in a complex of preventive measures of placental insufficiency during high-risk pregnancy contributes to the improvement of perinatal outcomes: the number of babies with a good assessment of body's functional abilities according to Apgar scale was 2.3 ( $p<0.01$ ) times more in relation to the control group and 2.0 ( $p<0.05$ ) times more in relation to the data in the comparison group.

3. There has been determined high clinical effectiveness of complex pharmaco-ozone therapy in the prevention of FPI with pregnant women of the risk group, which was manifested by the absence of progression of placental insufficiency, while in the group of comparison where the patients underwent only pharmacotherapy with limontar, the progression was noted in 31.8% of cases, in the control group where no prevention was carried out – in 56%.

**Conflict of interest.** The authors declare no conflict of interest.

### **References**

1. Savel'eva G.M. Obstetrics: A National Guide / G.M. Savel'eva, G.T. Suhih, V.N. Serov, V.E. Radzinskij // M.: GEOTAR-Media. – 2019. – 2 ed., revis. and ext. – 1080 p.

2. Strizhakov A.N. The relationship of placental insufficiency with the manifestation of various clinical variants in preeclampsia / A.N. Strizhakov, Yu.V. Tevikov, I.S. Lipatov, D.V. Pechkurov // Obstetrics, Gynecology and Reproduction. – 2018. – Vol. 12. – № 3. – P. 17-28.

3. Kajsanova A.S. The system of medical technologies of sanatorium-resort rehabilitation of patients with erosive and ulcerative esophagoduodenal diseases: Dissertation. / A.S. Kajsanova // Pyatigorsk. – 2013. – 255 p.

4. Oranskij I.E. Physiobalneotherapy in maintaining the health of the working population of the Urals / I.E. Oranskij, E.I. Lihacheva, N.A. Roslaya, L.A. Konevskih, G.N. Hasanova, A.A. Fedorov, O.A Chudinova // Physiotherapy, Balneology, Rehabilitation – 2006. – № 5. – P. 48-55.

5. Fedorov A.A. Experience in implementing technologies of restorative

medicine in the system of improving the working population of the middle Urals / A.A. Fedorov, I.E. Oranskij, O.A. Chudinova, N.O. Milovankina // Resort Medicine. – 2014. – № 4. – P. 73-76.

6. Stadnikova E.N. Medical ozone in the treatment of chronic placental insufficiency in pregnant women with a burdened obstetric history / E.N. Stadnikova, S.N. Hachak, M.D. Andreeva, I.V. Zelenskaya, N.V. Sokolova // National Health. – 2018. – № 3. – P. 85-88.

7. Manelis E.S. Non-drug methods of treatment of intrauterine fetal hypoxia / E.S. Manelis // Reflexology. – 2015. – № 2. – P. 36-39.

8. Ovsepyan N.R. Magnetic-IR-light-laser and ozone therapy in the prevention of complications after spontaneous miscarriage: dissertation / N.R. Ovsepyan // M. – 2020. – 23 p.

9. Tyunina A.V. Prevention of post-abortion endometritis using ozone and bacteriophage therapy: Dissertation / A.V. Tyunina // Ivanovo. – 2017. – 24 p.

10. Fedorov A.A. Ozone therapy for gastroduodenal pathology associated with helicobacter pylori / A.A. Fedorov, A.S. Gromov, S.V. Sapronenok., V.Yu. Kurochkin, Z.M. Zhernakova // Issues of Balneology, Physiotherapy and Exercise Therapy. – 2006. – № 6. – P. 34-37.

11. Dzhumagaziev A.A. The use of metabolic drugs for the rehabilitation of newborns with cerebral ischemia / A.A. Dzhumagaziev, L.R. Rahimova // Doctor.ru. – 2015. – № 5-6 (106-107). – P. 63-66.

### **Spisok literatury**

1. Savel'eva G.M. Akusherstvo: Natsional'noe rukovodstvo / G.M. Savel'eva, G.T. Suhij, V.N. Serov, V.E. Radzinskij // M.: GEOTAR-Media. – 2019. – 2-e isd., pererab. i dop. – 1080 s.

2. Strizhakov A.N. Svyaz' platsentarnoj nedostatochnosti s manifestatsiej razlichnyh klinicheskikh variantov pri preeklampsii / A.N. Strizhakov, Yu.V. Tevikov, I.S. Lipatov, D.V. Pechkurov // Obstetrics // Akusherstvo, ginekologiya i reproduktsiya. – 2018. – T. 12. – № 3. – S. 17-28.

3. Kajsanova A.S. Sistema meditsinskih tekhnologij sanatorno-kurortnoj reabilitatsii bol'nyh s erozivno-yazvennymi ezofagogastroduodenal'nymi zabolevaniyami: Dis. doktora med. nauk/ A.S. Kajsanova // Pyatigorsk. – 2013. – 255 s.

4. Oranskij I.E. Fiziobal'neoterapiya v sohranении zdorov'ya rabotayushchego naseleniya Urala / I.E. Oranskij, E.I. Lihacheva, N.A. Roslaya, L.A. Konevskih, G.N. Hasanova, A.A. Fedorov, O.A. Chudinova // Fizioterapiya, bal'neologiya, reabilitatsiya – 2006. – № 5. – S. 48-55.

5. Fedorov A.A. Opyt realizatsii tekhnologij vosstanovitel'noj meditsiny v

sisteme ozdorovleniya rabotayushchego naseleniya srednego Urala / A.A. Fedorov, I.E. Oranskij, O.A. Chudinova, N.O. Milovankina // Kurortnaya meditsina. – 2014. – № 4. – S. 73-76.

6. Stadnikova E.N. Meditsinskij ozon v terapii hronicheskoy placentarnoj nedostatochnosti u beremennyh s otyagoshchennym akusherskim anamnezom // E.N. Stadnikova, S.N. Hachak, M.D. Andreeva, I.V. Zelenskaya, N.V. Sokolova // Natsional'noe zdorov'e– 2018. – № 3. – S. 85-88.

7. Manelis E.S. Nemedikamentoznye metody lecheniya vnutriutrobnoj gipoksii ploda / E.S. Manelis // Refleksologiya. – 2015. – № 2. – S. 36-39.

8. Ovsepyan N.R. Magnito-IK-sveto-lazernaya i ozonoterapiya v profilaktike oslozhnenij posle samoproizvol'nogo vykidysya. / N.R. Ovsepyan // M. –2020. – 23 s.

9. Tyunina A.V. Profilaktika posleabortnogo endometrita s ispol'zovaniem ozono- i bakteriofagoterapii: Avtoref. dis. kand. med. nauk. / A.V. Tyunina // Ivanovo. – 2017. – 24 s.

10. Fedorov A.A. Ozonoterapiya pri gastroduodenal'noj patologii, assotsirovannoj s helicobacter pylori / A.A. Fedorov, A.S. Gromov, S.V. Sapronenok., V.Yu. Kurochkin, Z.M. Zhernakova // Voprosy kurortologii, fizioterapii i lechebnoi fizicheskoi kultury. – 2006. – № 6. – S. 34-37.

22. Dzhumagaziev A.A. Primenenie metabolicheskikh preparatov dlya reabilitatsii novorozhdennyh s cerebral'noj ishemiej / A.A. Dzhumagaziev, L.R. Rahimova // Doktor.ru. – 2015. – № 5-6 (106-107). – S. 63-66.

**Information about the authors: Larisa Vladimirovna Tsallagova** – Doctor of Medical Sciences, Professor, the Head of the Department of Obstetrics and Gynaecology №1 of FSBEI HE NOGMA MH of the Russian Federation; director of IBMI VSC RAS, Vladikavkaz, e-mail: [akusherstvo\\_1@mail.ru](mailto:akusherstvo_1@mail.ru); **Liana Vasilievna Majsuradze** – Doctor of Medical Sciences, Chair Professor of Obstetrics and Gynaecology department №1 of FSBEI HE NOGMA MH of the Russian Federation; senior researcher of IBMI VSC RAS, Vladikavkaz, e-mail: [akusherstvo\\_1@mail.ru](mailto:akusherstvo_1@mail.ru); **Svetlana Vladimirovna Sagkaeva** – graduate student of the Department of Obstetrics and Gynaecology №1 of FSBEI HE NOGMA of the Ministry of Healthcare of Russia, Vladikavkaz, e-mail: [akusherstvo\\_1@mail.ru](mailto:akusherstvo_1@mail.ru).