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The Pharma Innovation

ISSN: 2277- 7695
TPI 2015; 4(7): 82-84

www.thepharmajournal.com
Received: 26-07-2015
Accepted: 27-07-2015

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Haemodynamic changes in utero-placental-fetal complex on the background of the complex therapy of preeclampsia in combination with hypothyroidism

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Abstract
On the basis of the performed studies it was determined a greater efficiency of developed and implemented therapeutic and preventive measures in comparison with traditional ones in the conduct of pregnant women with preeclampsia in combination with hypothyroidism.

Keywords: pregnancy, preeclampsia, hypothyroidism.

1. Introduction
Today it is known that the endothelial dysfunction has a leading role in the pathogenesis of preeclampsia, in particular, "gestational endotheliopathy" [1, 8]. The consequence of which is the violated kidney function, increasing of hypertensive syndrome and the risk of edema, cerebral edema particularly [2]. It is believed that the basis of the pathogenesis of endothelial dysfunction is a violation of tsytotrofoblast invasion in endometrial wall segments of the spiral arteries (SA). The gestational transformation of SA is delayed when the invasion of tsytotrofoblast is disabled and as a manifestation is an increase vascular resistance [4]. The above mentioned morpho-functional changes in the SA do not help to reduce vascular resistance, which has negative affects on the fetal life support [5, 7, 8].
There is no doubt the fact that timely diagnostic of disorders of becoming utero-placental-fetal circulation and selecting of the appropriate correction have fundamental diagnostic importance in the case of reduction of perinatal loss in women with preeclampsia in combination with hypothyroidism.

2. The Aim of Research: the aim of this study is to explore the main indicators of blood flow in the functional biosystem mother-placenta-fetus, fetal biophysical activity and the consequences of delivery in women with preeclampsia in combination with hypothyroidism depending on the impact of corrective therapy.

2.1. Material and Methods: We conducted the comparative analysis of the effectiveness of therapy in the two representative groups of pregnant women with preeclampsia in combination with hypothyroidism. The first group consisted of 50 pregnant women who conducted our developed and proposed treatment and preventive measures. The second group included 50 patients who received traditional therapy according to the recommendations of the clinical protocol [3]. The control group consisted of 50 somatic healthy pregnant women with physiological pregnancy. Ultrasound examination was performed on the apparatus «Toshiba» - Model SLA-38AS (Japan).
The obligatory volume of fetometry included: determination of the biparietal size of the head, length of the femur and the average diameter of the abdomen. At the extended fetometry the fronto-occipital size and the perimeter of the head were determined. The volume of the abdomen of the fetus was calculated using the formula: (APAS + TAS) x 1,57,
Where APAS – antero-posterior abdominal size;
TAS – transverse abdominal size.
The evaluation of blood flow velocity curves (BFVC) in utero-placental-fetal complex was conducted by determination of systolic-diastolic ratio (S/D), resistance index (RI) and pulsation index (PI).
The conclusion about fetal biophysical activity was based on the results of ultrasound examination of the fetal breathing movements (FBM) and the number of generalized fetal

movements (GFM) for 30 minutes of examination. The assessment of muscular tonus was conducted on the basis of the ability of the fetus to return to a state of flexion after physical activity.

With the help of fetal monitor Sonicaid Team Care the dynamic control for variability of frequency of warm reductions of the fetus and index STV - an indicator of acidemia, were performed [6].

The determination of the hormones: estriol, progesterone, placental lactogen (PL), human chorionic gonadotropin (hCG), cortisole were examined with the help of enzyme immunoassay (ELISA) of the kits BAH (Kharkiv).

A combined preparation was used in the basic therapy to eliminate iodine deficiency. Its formula included: organic potassium iodide (50 - 60 mg), vitamin A and vitamin D2 and polyunsaturated omega-3 fatty acids.

Small doses of aspirin (75 mg/day) were included in the therapy when hemostasis was violated. We used actovegin (200 mg 2 times / day inside for 4 - 6 weeks) to activate angiogenesis, metabolic processes and to improve microcirculation.

The treatment of hypothyroidism was carried out by assigning of L-thyroxine (100 μg/day) controlled by the levels of thyroid-stimulating hormone (TSH) and thyroxine (fT4).

Statistic processing of the study results was performed using modern methods of variation statistics with the help of standard statistical analysis software Microsoft Excel 5.0.

3. Results

There was a significant difference of vascular resistance in the spiral arteries (SA) of the uterus relative to the control indicators in patients with a traditional therapy (group II): systolic-diastolic ratio (S/D) (2.45±0.15 and 1.98±0.06, $p<0.05$), resistance index (RI) - (0.78 ± 0.03 and 0.69 ± 0.04, $p<0.05$), pulsation index (PI) - (1.51±0,02 and 1.39±0.02, $p<0.05$, it indicated a lack of cytotrophoblast invasion in endometrial wall of the SA.

The indicators of vascular resistance in SA in pregnant women on the background of developed therapeutic and preventive measures (group I), respectively, were: C/D – 2.12±0.08, RI – 0.71±0.03, PI – 1.34±0.02 and did not significantly differ from that of the control group, but still remained higher than at similar rates of physiological pregnancy (C/D – 1.98±0.06, RI – 0.69±0.04, PI – 1.39±0.02, $p>0.05$). This confirms the positive influence of developed therapeutic and preventive measures on the formation of low-resistant blood flow in the basin of the uterine vessels.

A high diastolic component in the I group of 8 (20.0%), in the II group - in 26 (65.0%), according to Doppler (CWC). This indicates a delay of gestational transformation with the formation of low-resistant blood flow in the utero-placental vessels.

The study of hemodynamics in umbilical artery on the background of traditional therapy showed that the indicators of vascular resistance were significantly higher than in the control group.

Thus, the index of C/D was (2.51±0.15, $p<0.05$), RI - (0.71±0.02, $p<0.05$), PI - (1.15±0, 04, $p<0.05$), indicated the delay of fetalis of placenta. These indicators did not significantly differ between the control group on the background of developed therapeutic and preventive measures, at the same time ($p<0.05$). The proposed treatment and preventive measures helped to increase the adaptive capacity of the fetus to prenatal existence, the indicators of biophysical activity of the fetus CTG, FBM, GFM and rate adaptation STV indicated it [6].

Thus, basal heart rate (BCSS) amounted to (146.2±7.1 beats/min), the instantaneous amplitude of oscillations (11.8±0.3 beats/min), the instantaneous frequency of oscillations (8.1±0.9 beats/min), the amplitude of sporadic accelerate (21.3±1.7 beats/min), length accelerate (20.1±1.6 beats/min), the number of sporadic decelerate (5.9±0.7) for 20 min did not significantly differ relative to the control group ($p>0.05$).

STV index was> 4 ms, indicating the absence of signs of fetal acidemia. At the same time in group II this figure ranged from 3.5 to 4 ms, which showed a delayed recovery of fetal reserve capacity on a background of traditional therapy. There were short episodes of FBM (1,6±0,2) for 30 minutes of inhale-exhale type.

There were also observed double, triple and palpebrate movements that differed by brief returns to the inspiratory phase during the expiratory phase.

Generalized fetal movements for the 30 minutes period were on average 1.8±0.5.

The fetus was in a state of flexion for a long time after generalized movements.

It was noted an increased frequency of premature aging of the placenta (group I-10.0% and group II-30.0%) . This indicates the development of placental insufficiency, especially in women of group II on the background of traditional therapy.

When evaluated the clinical efficacy of the developed and proposed preventive measures, noted the improvement of hormonal function of the placenta, in particular, a significant increasing of placental lactogen in group I by 1.4 times relative to the group II. The levels of estriol in the I group were not significantly different from the control group and amounted to 54.1±2.4 nmol/l ($p>0.05$). Human chorionic gonadotropin in group I amounted to 328.4±11.7 nmol/l, in group II – 324.9±12.1 nmol/l, which was significantly higher than in the control group (respectively 363.5±13.8 nmol/l, $p<0.05$). The level of cortisol in pregnant women was by 1.1 times higher on a background of traditional therapy that pointed to chronic stress in the fetus. There was statistically significant reduction of progesterone in pregnant women of the second group relative to the control group ($p<0.05$).

There was a positive trend to reduce the frequency of intrauterine growth retardation of the fetus that developed on the background of therapeutic and preventive measures. The asymmetrical form of intrauterine growth retardation of the fetus in the I group was 38.0%, 20.0% less than in the group II (58.0%), respectively. Chronic fetal hypoxia in group I was 56.0%, in group II – 84.0%.

Apgar scale of 8 - 9 points in the first minute in group I was 85.0%, in group II - 70.0%. According to the 6 - 7 points this figure was 15.0% in group I, in group II - 17.5% and 10.0% in the control group.

The average Apgar scale at 5 minutes respectively were: in group I – 8.63± 0.12 points, in group II – 7.89±0.15 points, in the control group – 8.74±0.16 points.

We noted a reduced hypoxic encephalopathy in 1.3 times, hemorrhagic syndrome in 1, 2 times, vegetative dysfunction in 1.4 times in children of group I.

Early neonatal mortality was 2.5% in group II. Neonatal mortality in group I and in the control group was not observed.

4. Conclusions

1. An important factor in the etiopathogenesis of preeclampsia in combination with hypothyroidism is epithelial dysfunction, which occurs on a background of delays gestational transformation of SA in utero-placental vessels.
2. The disorders of gestational transformation of the spiral arteries into utero-placental blood vessels are ones of the leading causes of diffusion-perfusion failure in utero-placental blood flow and the development of fetal distress.
3. Timely diagnostics and an adequate correction of disorders of gestational transformation in utero-placental blood flow on the basis of our introduced therapeutic and preventive measures has ensured the improving of the consequences of delivery and reduction of hypoxic encephalopathy in 1.3 times, hemorrhagic syndrome in 1.2 times, vegetative dysfunction in 1.4 times.

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