

New Approaches to the Study of Elementosis in Obstetrics

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Received: 17-05-2019, **Revised:** 13-06-2019, **Accepted:** 15-07-2019, **Published online:** 23-08-2019

How to cite this article: Tatyana V. Pavlova, Natalia B. Pilkevich, Vasilii A. Petrukhin, Elena S. Malyutina, Arkady V. Nesterov, Vera A. Markovskaya, Anton N. Kaplin and Lyudmila O. Zemlianskaia (2019) New Approaches to the Study of Elementosis in Obstetrics, Journal of International Pharmaceutical Research 46(4): 276-280

Abstract

Objective: to study macro- and micronutrients in the tissues of the placenta, umbilical cord, and uterus, as well as the erythrocytes of the mother-placenta-fetus system during pregnancy against the background of thyroid gland (TG) pathology of various origins, diabetes I, and gestational diabetes mellitus (DM) (diabetes mellitus DM).

Methods: the study used clinical material from 184 pregnant women, 154 of them are women with thyroid disease and 30 are a control group. The thyroid gland (TG) was studied using the Alokka-5500 ultrasound apparatus, as well as triiodothyronine and total thyroxine, free thyroxine, thyroid hormone, and thyroglobulin antibodies were determined. Elemental analysis of oxygen, carbon, phosphorus, calcium, magnesium, iron, nitrogen, aluminum, sodium, and sulfur was carried out using an X-ray spectrum detector (EPAX), integrated with Quanta 600 FEG scanning electron microscope.

Results: The study of the main vital elements in the erythrocytes of the umbilical arteries found that significant changes in the macro element composition are due to oxygen. Its content in group 1 was $30.41 \pm 2.10\%$, in group 2 - $30.71 \pm 1.34\%$, group 3 - $35.92 \pm 2.31\%$, group 4 - $30.92 \pm 2.31\%$, group 5 - $32.93 \pm 2.20\%$ ($43.92 \pm 2.15\%$ - control group). The content of sodium, potassium in the groups with hypothyroidism, diffuse toxic goiter (DTG) and DM I increased. The content of magnesium, phosphorus in the umbilical arteries decreased in the following order: euthyroidism, gestational diabetes, hypothyroidism, diabetes mellitus, DTG. The oxygen content in umbilical veins decreased greater than in the arteries.

The amount of sodium and calcium increased with a further decrease in magnesium, phosphorus, and potassium. The macro- and microelement analysis near the vascular wall of the umbilical cord in the pathology of the mother's thyroid gland found that the content of oxygen, magnesium, phosphorus, and calcium is significantly reduced in endocrinopathies.

Summary: as a result of the study, it was established that women with the diseases of the thyroid gland and diabetes have uteroplacental ischemia observed against the background of tissue-vascular lesions, changes in the anatomical and functional states of erythrocytes, macro- and microelement composition, resulting in the developing destruction of tissue in the mother-placenta-fetus system, which contributes to the further progression of tissue and circulatory hypoxia.

Keywords: Pregnancy, Trace Elements, Thyroid Gland, Diabetes Mellitus.

Introduction

The stability of the chemical composition is one of the most important and essential conditions for the normal functioning of the body. The kinetics, distribution, and deposition of metal ions are subject to the biochemical regulation of the macro organism.

The change in the concentration of each of the trace elements is interrelated. Both a deficit of macro- and micronutrients and their increased concentration can lead to adverse consequences for human [1-3]. The urgency of this problem growth along with an extraordinary load on the female body during pregnancy [4-14]. The study of elementosis in the mother-placenta-fetus system is one of the understudied issues. Among the abnormal conditions

in pregnant women, endocrinopathies should be noted, which leaders are both thyroid disease (TG) and pancreatic disease, primarily diabetes mellitus (DM) [1, 5, 6, 15, 16]. Therefore, the objective of the research was to study macro- and micronutrients in the tissues of the placenta, umbilical cord, and uterus, as well as the erythrocytes of the mother-placenta-fetus system during pregnancy against the background of thyroid gland pathology of various origins, diabetes I, and gestational diabetes mellitus.

Materials and Methods

The study used clinical material from patients whose deliveries proceeded in the perinatal center of St. Joasaph Belgorod Regional Clinical Hospital.

The women with thyroid pathologies were grouped as follows:

- Group 1 - pregnant women with euthyroid condition against thyroid pathology - thyroid hypertrophy 1–2 degree, mixed goiter (36 cases);
- Group 2 - women with hypothyroidism — postoperative hypothyroidism, autoimmune thyroiditis, congenital hypothyroidism (56);
- Group 3 - women with diffuse toxic goiter - DTG (35).
- Women with DM were grouped as follows:
 - Group 4 - pregnant with DM I (15);
 - Group 5 - women with gestational DM (12).

The control group (6) consisted of 30 randomly selected pregnant women without endocrinopathy and any severe somatic and obstetric pathology.

Obstetric history, concomitant extragenital pathology, the course of pregnancy and delivery were studied. Along with the clinical methods of examination generally accepted in obstetrics, a number of special research methods were included.

Thus, the study of the thyroid gland was carried with ultrasound using the Alokka-5500 apparatus, as well as additional laboratory research methods (determination of triiodothyronine and total thyroxine, free thyroxine, thyroid hormone, and thyroglobulin antibodies). The level of glucose in the blood plasma was determined, including under load. A standard clinical trial of newborns was also carried out.

A macroscopic and histological examination of placentas, umbilical cords, and uterus specimens was carried out.

To determine macro- and trace elements pointwise, fragments of the placenta and uterus were obtained during a cesarean section, 0.25±0.10 cm in size (5 samples each), which were examined in FEI Quanta 200 3D scanning electron microscopes and FEI Quanta 600 FEG without additional material processing after 45±15 minutes post surgery.

Elemental analysis of oxygen, carbon, phosphorus, calcium, magnesium, iron, nitrogen, aluminum, sodium, and sulfur was carried out using an X-ray spectrum detector (EPAX), integrated with Quanta 600 FEG scanning electron microscope. It was based on the generation of continuous fluorescent radiation during the bombardment of the test samples with a beam of primary x-rays.

The sensitivity of the method was 0.1–0.3%, depending on the type of atoms. During the statistical analysis of the material, both intensive and extensive indicators of averages were calculated, the reliability of differences between averages and relative values was determined using Student's t-test.

Results and Discussion

The ultrasound study diagnosed decompensate fetoplacental insufficiency (FPN), accompanied by fetal growth retardation syndrome, in group 1 in 21.6%, 2 - 29.6%, 3 - 32.1%, 4 - 30.5%, 5 - 23.4% (8.3% - control group).

A study of uteroplacental and fetal blood flow revealed unsuccessful data in patients with congenital hypothyroidism, polyglandular syndrome, and DM I.

The study of the PBF (placental blood flow) values up to 32 weeks of gestation often revealed increased resistance in umbilical cord arteries in pregnant women with DM I as well as hypothyroidism, polyglandular syndrome, and congenital hypothyroidism.

The study of the complications of pregnancy found that the risk of abortion and pre-eclampsia was more typical of pregnant women with autoimmune thyroiditis (AIT) and DM I.

The course of delivery, complicated by labor abnormalities, fetal hypoxia, rupture of the uterus and vagina, was more often observed in patients with insufficient hypothyroidism, DM I and gestational DM compensation.

The study of the main vital nutrients in the red blood cells of the umbilical arteries found that significant changes in the macro element composition occur due to oxygen (Table 1, Fig. 1).

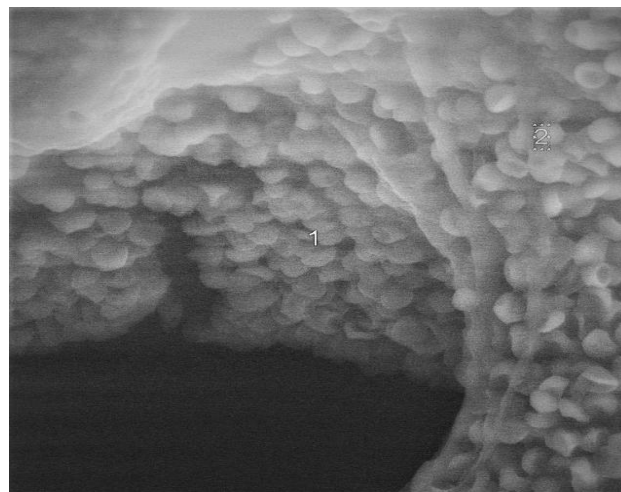


Figure -1: Fragment of the umbilical cord of a woman with diffuse toxic goiter

Impaired folding of the endothelium. Plethora, stasis and sludge of red blood cells, both in the lumen of the vessel and behind it. The shape of a part of the cells is changed.

The numerals "1" and "2" designate the places for the determination of macro- and trace elements. SEM (x2000).

Table -1: Peculiarities of macro- and microelement analysis in red blood cells of umbilical arteries in case of maternal thyroid and diabetes pathology in the mother (as a percentage comparison)

Peculiarities of macro and microelement analysis in erythrocytes	Control	DTZ	Hypothyroidism	Euthyroid state	Diabetes I	Gestational Diabetes
C	49.40±3.21	61.19±2.85*	62.35±3.01*	57.04±3.32*	63.14±3.32*	60.06±3.52*
N	3.00±0.11	3.10±0.05	4.01±0.01*	2.40±0.02	3.02±0.03	2.43±0.03
O	43.92±2.15	30.71±1.34*	30.41±2.10*	35.92±2.31*	30.92±2.31*	32.93±2.20*
Na	0.28±0.01	0.63±0.01*	0.60±0.01*	0.27±0.02	0.68±0.02	0.28±0.01
Mg	0.18±0.02	0.10±0.02*	0.09±0.01*	0.15±0.02*	0.05±0.02*	0.10±0.02*
P	0.38±0.02	0.29±0.02*	0.26±0.01*	0.36±0.01	0.267±0.02	0.35±0.01
S	0.81±0.03	0.21±0.03	0.88±0.01	0.83±0.11	0.88±0.11	0.83±0.11
K	0.25±0.02	0.74±0.10*	0.40±0.12*	0.25±0.04	0.55±0.04	0.26±0.03
Ca	1.00±0.01	0.55±0.02	0.31±0.13	2.00±0.03	1.00±0.03	2.01±0.02
Si	0.28±0.01	0.13±0.02	0.05±0.02	0.29±0.02	0.20±0.02	0.29±0.01
Cl	0.49±0.02	0.67±0.12*	0.40±0.04	0.48±0.02	0.47±0.02	0.45±0.01
Fe	0	0.83±0.01*	0.24±0.02*	0	0.84±0.02*	0

*p<0.05 with respect to the control group

The content of sodium, potassium in the groups with hypothyroidism, diffuse toxic goiter (DTG) and DM I increased. The content of magnesium, phosphorus in the umbilical arteries decreased in the following order: euthyroidism, gestational diabetes, hypothyroidism, DM I, DTG. The oxygen content in umbilical veins decreased greater than in the arteries.

The amount of sodium and calcium increased with a further decrease in magnesium, phosphorus, and potassium. The macro- and microelement analysis near the vascular wall of the umbilical cord in the pathology of the mother's thyroid gland found that the content of oxygen significantly reduced along with magnesium, phosphorus, and calcium in endocrinopathies. Changes in the composition of sodium and potassium are statistically insignificant. The study of macro- and trace elements in the villous chorion (Table 2, Fig. 2, 3) showed that the oxygen content decreased significantly in the following order: control group (23.29±1.41%), euthyroid state (19.35±1.03%), gestational DM (17.65±1.05%), DTG (16.86±1.05), DM I (15.81±1.03), hypothyroidism (14.88±1.01). The content of sodium, magnesium, phosphorus, calcium, and potassium also decreased in a similar sequence.

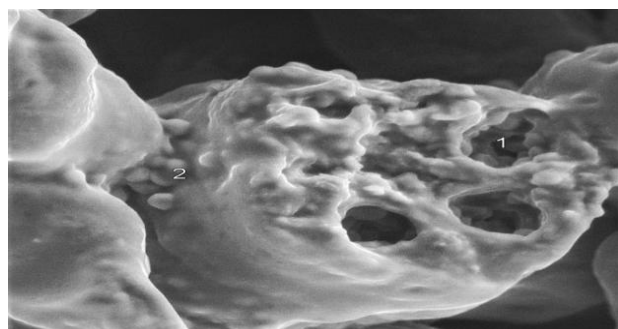


Figure -2: A fragment of the placenta of a woman with hypothyroidism (autoimmune thyroiditis).

The shape of the vessels changed. Red blood cell count reduced.

The number "1" denotes the place where the macro and trace elements are defined inside the villi, "2" - in the intervillous space. SEM (3000).

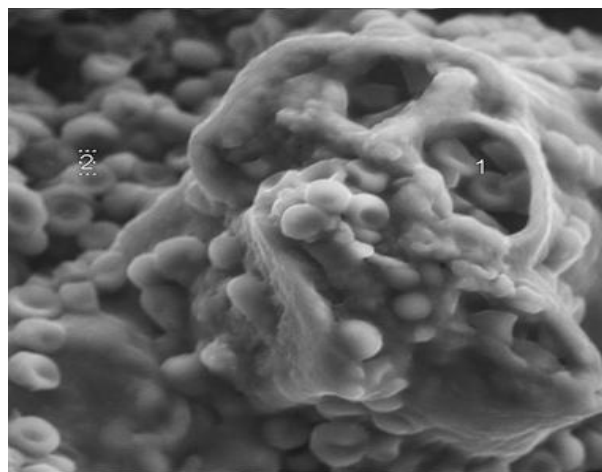


Figure -3: Fragment of the villous tree of a woman's placenta with diffuse toxic goiter.

The shape of the vessels changed. Plethora, stasis and sludge both inside the villi and in the intervillous space.

The number "1" denotes the place for studying macro- and trace elements inside the villi. "2" - in the intervillous space. SEM (4000).

The study of macro and micronutrients in erythrocytes inside the villi vessels found a significant reduction in the oxygen content during DTG in the mother (23.01±2.65%) and DM I compared to the control group (45.12±2.31%). There was a tendency to a decrease in magnesium, potassium, phosphorus, and sodium.

Table -2: The content of micro and macronutrients in erythrocytes inside the vessels of the villi in the pathology of the thyroid and diabetes in the mother (as a percentage)

Peculiarities of macro and microelement analysis in erythrocytes	Control	DTZ	Hypothyroidism	Euthyroid state	Diabetes I	Gestational Diabetes
C	43.50±2.05	51.10±3.54*	44.02±3.45	48.50±2.86	52.00±2.86	50.20±2.36
N	8.50±1.05	9.30±1.50	8.70±0.47	7.04±1.06	7.34±1.06	7.52±1.05
O	45.12±2.31	33.01±2.65*	40.82±2.03	42.13±2.06	37.73±2.06	40.03±2.06
Na	0.18±0.04	0.92±0.06*	0.54±0.02*	0.19±0.02	0.59±0.02	0.18±0.02
Mg	0.10±0.01	0.15±0.01	0.31±0.01	0	0	0
P	0.51±0.08	0.51±0.02	0.43±0.02	0.50±0.03	0.40±0.03	0.51±0.03
S	0.60±0.02	0.91±0.05	0.51±0.03	0.60±0.03	0.61±0.03	0.61±0.03
K	0.26±0.03	1.18±0.10*	0.86±0.11*	0.24±0.02	0.23±0.02	0.22±0.01
Ca	0.21±0.01	0.35±0.02	0.91±0.12*	0.23±0.01	0.24±0.01	0.24±0.01
Si	0.05±0.02	0	0.15±0.03	0.05±0.05	0.05±0.03	0.05±0.03
Cl	0.30±0.05	1.27±0.03*	0.73±0.02	0.33±0.03	0.32±0.02	0.34±0.03
Fe	0.21±0.01	0.71±0.02*	0.96±0.13*	0.19±0.03	0.29±0.01	0.19±0.04
Cu	0	0.56±0.02*	1.06±0.01*	0	0	0

*p<0.05 with respect to the control group

The study of elementosis in the intervillous space of the placenta showed a significant decrease in the oxygen content in the presence of both thyroid pathology: DTG (22.43±1.34%), hypothyroid conditions (37.91±2.10%), and DM I (23.32±1.34%), gestational DM (36.35±2.28%) compared with the control group (45.67±2.15%). There was a tendency to an increase in the content of sodium and potassium in these groups. All groups with endocrinopathy showed a tendency to a decrease in the content of phosphorus and magnesium.

Uteroplacental ischemia diagnosed in the presence of the thyroid abnormalities and DM in the mother leads to persistent hypoxia of the fetus. During the analysis of the neonatal complications, we revealed an increase in complications, including asphyxia, respiratory distress syndrome (SDR), hypoxic-ischemic central nervous system damage, developmental abnormalities, and fetal growth retardation syndrome (FGRS). The most significant number of complications is typical of newborns from mothers with DM I, polyglandular syndrome, and congenital hypothyroidism. The study of other vital elements showed that the content of potassium, which contributes to the normalization of blood pressure and improves the supply of oxygen to the brain of the fetus, decreased significantly, both in the vessels of the terminal villi of the placenta and umbilical cord, which also adversely affects the development of the fetus and newborn.

Participation of sodium along with potassium in the maintenance of acid-base balance through buffer systems ensures the water balance of the body. In addition, about the third part of this macronutrient falls on the skeleton, which is important for intrauterine formation. We have revealed its significant increase in the vessels of the umbilical cord and in the placenta, including terminal villi. The revealed hypernatremia promotes hyperosmolarity of the blood and leads to hypohydration of cells and their possible destruction. The result may be the

development of edema and alkalosis. The disruption of membrane structure in the umbilical and placental erythrocytes due to the loss of a number of the studied macronutrients (potassium, phosphates, magnesium) by cells, overhydration of erythroid cells, their swelling, loss of discoid form, their rounding (spherocytosis) may be a result of an increase in sodium content.

The main regulators that maintain a constant blood level of calcium and phosphorus are calcitonin and parathyroid hormone, which are the product of the thyroid (C-stand) and parathyroid glands. Dysregulation of calcium-phosphorus metabolism leads to hypocalcemia observed in the hypothyroidism of the parathyroid glands, which is often detected in the thyroid pathology. Lack of calcium in the extracellular water and blood leads to an increase in the permeability of the biological membrane to ions, nervous system stimulation and muscle contraction, which can cause miscarriages and premature labor, which is typical of women with thyroid pathology. We found hypocalcemia in all components of the umbilical cord.

Phosphorus metabolism is closely related to calcium metabolism, which maintains pH balance and regulates the activity of the central nervous system. We have shown its significant decrease in the umbilical cord and, as a result of this condition, in the placenta in the following sequence: gestational DM, euthyroid condition, hypothyroidism, DTG, DM I. At the same time, hypo-phosphatemia leads to inhibition of the formation of macroergic compounds (adenosine triphosphate, creatine phosphate), impaired formation of ribonucleic acid (RNA) and deoxyribonucleic acid (DNA), delayed bone mineralization, development of rickets, osteomalacia, and osteoporosis.

Magnesium is a cofactor of about three hundred cellular enzymes, including those involved in the DNA and RNA synthesis; it also improves the metabolism in the vascular wall. Magnesium

promotes the absorption of calcium, phosphorus, potassium, vitamins B, C, E. We have shown an absolute deficiency of magnesium in all studied components of the umbilical cord and placenta, until its complete disappearance. Among the consequences occurring in the mother-placenta-fetus system in the presence of hypomagnesemia, destructive disorders associated with impaired carbohydrate and protein metabolism, as well as tissue calcification should be noted.

Summary

Thus, women with the diseases of the thyroid gland and diabetes have uteroplacental ischemia observed against the background of tissue-vascular lesions, changes in the anatomical and functional states of erythrocytes, macro- and microelement composition, resulting in the developing destruction of tissue in the mother-placenta-fetus system, which contributes to the further progression of tissue and circulatory hypoxia. The oxygen content in erythrocytes decreases in the following sequence: euthyroid condition, gestational DM, hypothyroidism, DM I, DTG, and leads to persistent fetal hypoxia and then to an unfavorable variant of its development. Elevated levels of potassium, sodium, and calcium, along with magnesium and phosphorus deficiency, as well as their imbalance are a factor in the development of hyperosmolarity and hypohydration, which contributes to the formation of alternative damage, and as a result, causes the development of the critical condition of the fetus and progressive uteroplacental insufficiency.

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