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THE LEVEL OF CARDIAC PEPTIDE NT-PROBNP INCREASES DURING PRE-ECLAMPSIA OF PREGNANT WOMEN

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Summary

The cardiac peptide NT-proBNP, produced and secreted mainly by the left ventricular myocardium, is one of the most important biochemical markers of heart disease. It is known that the concentration of this peptide increases significantly in the blood of patients with heart failure and cases of transplant rejection. However, NT-proBNP levels have not yet been studied in the course of the development of pathological conditions associated with pregnancy, in particular, in pre-eclampsia.

The aim of the research. *To study the level of cardiac peptide NT-proBNP of pregnant women with pre-eclampsia.*

The materials and methods. *The total number of women examined was 90. 60 (main group) women in their 32-36 weeks of pregnancy complicated by moderate pre-eclampsia were examined. The control group consisted of 30 women of the same gestational age whose pregnancies were uncomplicated. The study was conducted at the Chernivtsi Regional Perinatal Center and Medical Center for Infertility Treatment (Chernivtsi, Ukraine). The MAGLUMI BNP test system (manufacturer: Shēnzhèn New Industries Biomedical Engineering, Shenzhen, China) was used to study NT-proBNP levels; venous blood was collected once from pregnant women on an empty stomach at 8 am. The examinations were conducted at the «Educational and Scientific Laboratory» of the Bukovina State Medical University, which is certified. The study adhered to biomedical ethics guidelines. Statistical processing was performed using the MedCalc software package produced by MedCalc Inc (Ostend, Belgium), and Student's t-test for unequal samples was used.*

Results of the research. *It was revealed that the average level of NT-proBNP in the group of women with pre-eclampsia was likely higher than in the control group (79,5±37,4 pg/mL and 32,0±12,0 pg/mL in the control group, p<0,001). It is reasonable to assume that variations in NT-proBNP levels, specifically an increase in its concentration in blood plasma in pre-eclamptic pregnant women relative to healthy pregnant women, are a highly significant biochemical marker that serves as an indicator of both the condition of cardiomyocytes and the stress on the body's compensatory systems resulting from pre-eclampsia.*

Conclusions. *The level of the cardiac peptide NT-proBNP significantly increases in the blood of women whose pregnancy was complicated by pre-eclampsia. This may, in our opinion, indicate pathological changes in the myocardium caused by an increased load on the heart in the development of hypertension caused by pre-eclampsia in pregnancy.*

Key words: *Pregnancy; Pre-Eclampsia; Heart Failure; NT-proBNP.*

Introduction

Peptide NT-proBNP (N-terminal fragment of brain sodium-uretic peptide type B) is an important biomarker for diagnosing and predicting cardiovascular diseases, particularly heart failure. Its usage is fairly widespread in medical practice due to its high sensitivity and specificity.

Biochemical properties and physiological role of NT-proBNP: this peptide is an inactive fragment formed by the breaking of proBNP into active BNP and inactive NT-proBNP. It is synthesized by cardiomyocytes in response to increased ventricular filling pressure and myocardial biochemical stress [1]. NT-proBNP has a long half-life, which makes it convenient for laboratory diagnostics.

Diagnostic value of NT-proBNP: first, this peptide is a gold standard for confirming the diagnosis of acute and chronic heart failure [2]. Thresholds may vary depending on the age and renal function of patients. NT-proBNP also has diagnostic value in acute coronary syndrome, and its elevated level correlates with the severity of myocardial ischemia and the risk of negative consequences manifesting as heart failure with a decrease in left ventricular ejection fraction [3]. Other conditions: NT-proBNP is also used to estimate the prognosis in pulmonary hypertension, valvular heart disease, sepsis, and chronic renal failure [4].

The factors influencing the level of NT-proBNP are divided into physiological and pathological. Physiological factors include age, sex, and weight. Pathological factors comprise renal failure, left ventricular hypertrophy, anemia, etc. Angiotensin-converting enzyme inhibitors, beta-blockers, and diuretics can change the level of NT-proBNP [5].

NT-proBNP has advantages over other biomarkers, such as BNP, due to its greater stability in serum and lower sensitivity to changes in the short-term perspective [5]. Therefore, this peptide shows promise as a diagnostic marker for myocardial conditions. Regular monitoring of NT-proBNP levels allows for the assessment of the effectiveness of heart failure therapy and the prediction of the risk of re-hospitalization and death [5]. At the same time, there is very little information in the current scientific literature on changes in the concentration of NT-proBNP in women's blood plasma during pregnancy and in pregnancy-related pathological conditions, in particular, pre-eclampsia.

Pre-eclampsia is one of the most serious gestational pathologies, characterized by hypertension and proteinuria after the 20th week of pregnancy [6]. It significantly affects women's cardiovascular health over the long run in addition to how their pregnancy goes. The effects of pre-eclampsia on the cardiovascular systems of pregnant women, laboring women, postpartum women, and women giving birth have long been the subject of scientific investigation. The influence of pre-eclampsia on cardiac function is currently understood to be caused by a number of pathways, with endothelial abnormalities being a major one. In addition to decreased endothelial synthesis of nitric oxide NO, thromboxane, prostacyclin, and other vasoactive substances required for the physiological functioning of the fetoplacental unit during pregnancy, pre-eclampsia is linked to endothelial dysfunction,

which results in decreased vasodilation, increased vascular resistance, and hypertension. [7]. In addition, some patients may develop left ventricular hypertrophy, especially in the setting of pre-existing hypertension. Increased stress on the heart causes structural changes, in particular concentric left ventricular hypertrophy, which reduces its systolic and diastolic function [8].

Preeclampsia is associated with the impairment of the function of the endothelium, which leads to the reduction of vasodilation, an increase in vessels' resistance and hypertension, and the decrease of endothelial synthesis of nitric oxide NO, thromboxane, prostacyclin, and other vasoactive substances essential for physiological functioning of the fetoplacental unit during pregnancy. [7]. Moreover, some patients may develop left ventricular hypertrophy against the background of hypertension existing before the pregnancy. An increased load on the heart causes structural changes including concentric left ventricular hypertrophy, which decreases its systolic and diastolic function. [8].

The activation of anti-inflammatory cytokines and the accumulation of free radicals happens during pre-eclampsia as well. These processes facilitate myocardial remodeling and the development of fibrosis. [9].

Clinical consequences of myocardial remodeling during pre-eclampsia include acute heart failure and long-term cardiovascular risks. Women with pre-eclampsia have an increased risk of developing heart failure during pregnancy and in the early postpartum period; in addition, pre-eclampsia is an independent risk factor for the development of hypertension, coronary heart disease, and heart failure later in life [10]. At the end of pregnancy, even after normalization of blood pressure, diastolic dysfunction of the heart may be observed, indicating long-term changes in the structure of the heart muscle [10].

Cardiac function tests in pre-eclampsia include echocardiography, which is used to assess systolic and diastolic function, detect left ventricular hypertrophy and other structural changes, magnetic resonance imaging, which allows a detailed assessment of myocardial remodeling and fibrosis, and the study of biomarker levels. In addition to NT-proBNP, troponins and some other indicators are also used to assess the degree of heart damage.

Thus, pre-eclampsia has a substantial impact on the function of the heart in both short and long-term perspectives. It requires meticulous cardiological monitoring of women who experience pre-eclampsia even after the end of their pregnancy.

The aim of the research. To study the level of cardiac peptide NT-proBNP in women, whose pregnancy was complicated by pre-eclampsia.

Material and methods of the research. 60 women at their 32-36 weeks of pregnancy complicated by moderate pre-eclampsia were examined. The diagnosis was made according to the criteria, provided in the decree of Ministry of Health of Ukraine № 151 from 24.01.2022. The control group was composed of 30 women of the same gestational age but without any complications during their pregnancies.

The research was conducted on the basis of the non-profit community hospital «Chernivtsi regional perinatal center» and the Medical Center of infertility treatment (Chernivtsi, Ukraine). Test-system MAGLUMI BNP (manufacturer: Shēnzhèn New Industries Biomedical Engineering, Shenzhen, China) was used to study the levels of NT-proBNP; the venous blood of these pregnant women was taken twice at 8 AM on an empty stomach. The taken blood was placed in tubes with EDTA to obtain plasma and centrifugated at 15000 rpm for 15 minutes at room temperature (18-22°C). Blood plasm was received after the centrifugation. The blood specimens without the signs of hemolysis were chosen for the study. 500 μL of plasma was collected in disposable tubes and placed in an automatic chemiluminescent immune analyzer MAGLUMI 1000 (after calibration of the reagent and measurement of control solutions) and the results were obtained after 40 minutes. Statistical processing was performed using the MedCalc software package manufactured by MedCalc Inc (Ostend, Belgium), and a Student's t-test for unequal samples was used.

The study was conducted with the informed consent of the patients. The research was approved by the Biomedical Ethics Commission of the Bukovina State Medical University in accordance with the rules for conducting medical-scientific research (Protocol No. 9 dated 20.06.2024).

The results and discussion

It was established that the average level of peptide NT-proBNP in the group of women with pre-eclampsia was likely higher in comparison with the control group (79,5±37,4 pg/mL and 32,0±12,0 pg/mL in the control group, $p<0,001$), as picture 1 shows. Therefore, the level of NT-proBNP in the blood of pregnant women with preeclampsia was 2,48 times higher than in healthy women.

The received results are indicative of the following: the women with pre-eclampsia have increased synthesis of cardiomyocytes of the studied peptide NT-proBNP. This, as we believe, happens due to some factors. Firstly, more sympathetic-adrenal activation of the myocardium causes the heart's stroke volume to increase in pre-eclampsia [11,12]. Secondly, this disease increases peripheral vascular resistance, which raises the post-load on a pregnant woman's heart muscle. Pregnant women with pre-eclampsia have increased vasoconstriction as a result of these pathological changes, which in turn causes a secondary increase in the synthesis of NT-proBNP by cardiomyocytes. This is evident if we consider the changes in renal function characteristic of pre-eclampsia, specifically an increase in the synthesis of angiotensin II against the backdrop of activation of the renin-angiotensin-aldosterone system. [13-15].

Pre-eclampsia is also associated with endothelial dysfunction which influences the balance of vasodilators and vasoconstrictors. Particularly, the increase of the level of soluble fms-like tyrosine kinase 1 (sFlt-1), which is the antagonist of vascular endothelial growth factor (VEGF), is observed. This leads to the decrease of bioavailability of VEGF, which negatively affects the endothelial function and can facilitate the development of glomerular endotheliosis – typical kidney damage in preeclampsia [16-18]. This pathophysiological mechanism also promotes systemic vasoconstriction increasing the myocardial post-load, causing an increase of blood pressure in the left ventricle and, consequently, cardiomyocytes NT-proBNP [19, 20].

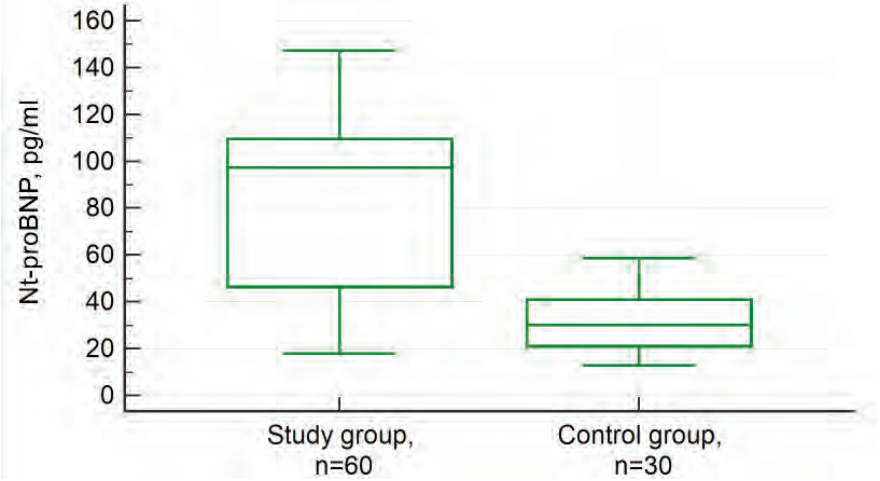

Figure 1. NT-proBNP, pg/ml

Consequently, it is reasonable to assume that variations in NT-proBNP levels, specifically an increase in its concentration in blood plasma in pre-eclamptic pregnant women relative to healthy pregnant women, are a highly significant biochemical marker that serves as an indicator of both the condition of cardiomyocytes and the stress on the body's compensatory systems resulting from pre-eclampsia.

Conclusions. The level of the cardiac peptide NT-proBNP increases in the blood of women whose pregnancy was complicated by pre-eclampsia. The increase is statistically significant: according to our data, this indicator increases by 2.48 times compared to healthy pregnant women. This may, in our opinion, indicate pathological changes in the myocardium caused by an increase in the load on the heart during the development of hypertension, which is caused by pre-eclampsia in pregnant women.

The prospects in further research.

Conflict of interests. The authors declare no conflict of interests

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РІВЕНЬ СЕРЦЕВОГО ПЕПТИДУ NT-PROBNP ПІДВИЩУЄТЬСЯ ПРИ ПРЕЕКЛАМПСІЇ ВАГІТНИХ

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Резюме.

Серцевий пептид NT-proBNP, що продукується і виділяється здебільшого міокардом лівого шлуночка, є одним з найбільш важливих біохімічних маркерів серцевих захворювань. Відомо, що концентрації даного пептиду вірогідно зростають в крові хворих на серцеву недостатність, а також при відторгненні трансплантованого серця. Однак, дотепер не проводилось вивчення рівнів NT-proBNP при розвитку патологічних станів, пов'язаних з вагітністю, зокрема, при прееклампсії вагітних.

Мета дослідження. Вивчити рівень серцевого пептиду NT-proBNP у вагітних з прееклампсією.

Матеріали та методи. Обстежено 60 жінок в терміні вагітності 32-36 тижнів, при цьому їхня вагітність була ускладнена помірною прееклампсією. Контрольну групу склали 30 жінок в тому ж терміні гестації, у яких вагітність перебігала без ускладнень. Дослідження проводилось на базі КНП «Чернівецький обласний перинатальний центр» та Медичного центру лікування безпліддя (м. Чернівці, Україна). Для вивчення рівнів NT-proBNP використовувалась тест-система MAGLUMI BNP (виробник: Shēnzhèn New Industries Biomedical Engineering, Шеньчжень, Китай); венозна кров у вагітних жінок забиралась однократно натще о 8-й годині ранку. Дослідження проведено із дотриманням положень про права людини та біомедицину. Статистичну обробку виконали за допомогою програмного пакету MedCalc виробництва MedCalc Inc (Остенде, Бельгія), використовувався t-критерій Стьюдента для неоднакових вибірок.

Результати дослідження. Було встановлено, що середній рівень NT-proBNP у групі жінок з прееклампсією був вірогідно вищим, порівняно з контролем (79,5±37,4 пг/мл, в контрольній групі 32,0±12,0 пг/мл, $p<0,001$). Можна обґрунтовано припустити, що зміна рівня NT-proBNP, а саме, підвищення його концентрації в плазмі крові у вагітних жінок з прееклампсією, порівняно зі здоровими вагітними жінками, є надзвичайно важливим біохімічним маркером – індикатором не тільки стану кардіоміоцитів, але і напруження компенсаторних систем всього організму вагітної, що викликано прееклампсією.

Висновки. Рівень серцевого пептиду NT-proBNP вірогідно зростає в крові жінок, чия вагітність ускладнилася прееклампсією. Це може, на нашу думку, свідчити про патологічні зміни в міокарді, зумовлені збільшенням навантаження на серце при розвитку гіпертензії, причиною якої є прееклампсія вагітних.

Ключові слова: вагітність; прееклампсія; NT-proBNP; серцева недостатність.

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