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LEVELS OF N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE AND ELECTROCARDIOGRAPHIC AND ECHOCARDIOGRAPHIC PARAMETERS OF THE HEART IN EARLY-ONSET PREECLAMPSIA DURING PREGNANCY

Summary.

N-terminal pro-brain natriuretic peptide (NT-proBNP) is a cardiac peptide primarily synthesized and secreted by left ventricular myocytes. It is recognized as one of the principal biochemical markers of cardiovascular disorders. Elevation of its concentration has been consistently observed in patients with heart failure. However, investigations into the association between NT-proBNP levels and electrocardiographic or echocardiographic findings in pregnancy-related pathological conditions, particularly preeclampsia, remain limited.

The aim of the research. *To evaluate the association between NT-proBNP concentrations and electrocardiographic and echocardiographic parameters of the heart in early-onset preeclampsia.*

Material and methods. *A total of 90 pregnant women were enrolled in the study. All participants underwent examination between 32 and 36 weeks of gestation. The main group comprised 60 patients with pregnancies complicated by early-onset moderate preeclampsia. The control group included 30 women with uncomplicated pregnancies.*

NT-proBNP levels were measured using the MAGLUMI NT-proBNP assay (Shenzhen New Industries Biomedical Engineering Co., Ltd., Shenzhen, China). Venous blood samples were collected once at 08:00 after an overnight fast. Electrocardiography was performed using a Heaco ECG600G six/twelve-channel electrocardiograph. Echocardiography was conducted with a GE Voluson E8 Expert ultrasound system (serial number 3143/1144/0178; GE Healthcare, Austria).

The study was approved by the Bioethics Committee of Bukovinian State Medical University (Protocol No. 2 dated 9 February 2015). Numerical data were analysed using statistical methods. The investigation was performed as part of a research project at the Department of Obstetrics and Gynecology, Bukovinian State Medical University (Chernivtsi, Ukraine).

Statistical analysis was carried out on a personal computer using Statistica software (Microsoft Excel 2010, Microsoft Office 2010, and MedCalc version 16.1), with application of Student's t-test for independent samples.

This study was conducted as part of the research project entitled «Preservation and Restoration of Reproductive Health in Women and Girls with Obstetric and Gynecological Pathologies» at the Department of Obstetrics and Gynecology, Bukovinian State Medical University; state registration number 0121U110020 (2021-2025).

Results. *Mean NT-proBNP levels were found to be substantially higher in women with preeclampsia than in the control group (79.5 ± 37.4 pg/mL versus 32.0 ± 12.0 pg/mL; $p < 0.001$). In patients of main group with early-onset preeclampsia, increased thickness of the left ventricular posterior wall was observed both in diastole (1.10 ± 0.05 cm versus to 0.82 ± 0.05 cm in the CG, $p < 0.0001$), and in systole (1.30 ± 0.04 cm versus 1.10 ± 0.05 cm, $p < 0.0001$). Comparable changes were noted for the interventricular septum thickness: 1.30 ± 0.05 cm in systole versus 1.10 ± 0.06 cm ($p < 0.0001$) and 1.09 ± 0.05 cm in diastole versus 0.80 ± 0.04 cm ($p < 0.0001$). Alterations in electrocardiographic parameters were identified in the MG compared with women with uncomplicated pregnancies. The duration of the P wave was increased (129.4 ± 9.0 ms versus 98.3 ± 11.4 ms; $p < 0.0001$), as was the QRS complex (107.9 ± 9.6 ms versus 88.8 ± 10.2 ms; $p < 0.0001$). Prolongation of the T wave was also observed (261.5 ± 9.2 ms versus 180.2 ± 10.6 ms; $p < 0.0001$). An increase in the QT/QTc interval was noted (461.7 ± 10.0 ms versus 402.8 ± 10.2 ms; $p < 0.0001$)*

Correlations between the parameters examined were established as follows: in women with preeclampsia, a weak positive correlation was observed between plasma NT-proBNP levels and interventricular septum thickness in diastole ($r = 0.291$; $p = 0.0093$), together with a weak negative correlation with the QT/QTc interval ($r = –0.21$; $p = 0.001$). In the CG, NT-proBNP levels exhibited a moderate positive correlation with left ventricular posterior wall thickness in diastole ($r = 0.312$; $p = 0.0089$) and a weak negative correlation with the QT/QTc interval ($r = –0.205$; $p = 0.02$).

Conclusions. *1. Plasma levels of the cardiac peptide NT-proBNP are markedly elevated in women with pregnancies complicated by preeclampsia. 2. Electrocardiographic and echocardiographic parameters obtained in women with early-onset moderate preeclampsia are consistent with early manifestations of left ventricular hypertrophy. 3. Increased thickness of the ventricular walls and interventricular septum represents a morphological marker of myocardial remodelling in response to haemodynamic overload. 4. Electrocardiographic findings – prolongation of the PR, QRS, and QT intervals together with increased duration of the P and T waves – indicate delayed impulse conduction in the myocardium as well as potential alterations in repolarisation processes in the context of moderate preeclampsia.*

Keywords: *Echocardiography; NT-proBNP; Preeclampsia; Pregnancy.*

Introduction

Cardiac natriuretic peptides, particularly the N-terminal fragment of brain natriuretic peptide (NT-proBNP), serve as key biomarkers that reflect the state of the cardiovascular system. Changes in NT-proBNP concentration occur in response to various cardiac pathologies, rendering it a valuable tool for diagnosis and prognosis [1].

Fluctuations in the levels of this peptide have been extensively investigated in diverse cardiovascular diseases. For example, in the presence of coronary heart disease, NT-

proBNP concentration indicates the extent of myocardial ischaemia and the risk of developing heart failure: higher peptide levels are associated with a greater likelihood of persistent cardiac dysfunction [2]. In patients with arterial hypertension, elevated NT-proBNP levels signify pressure overload and the development of left ventricular hypertrophy, thereby increasing the risk of heart failure and associated complications [1].

Consequently, monitoring of NT-proBNP levels is essential for the timely detection of pathological changes and adjustment of treatment in various cardiovascular disorders. At the same time, certain physiological conditions can alter this parameter in the absence of overt pathology. Pregnancy represents one such condition. Specific complications unique to pregnancy may induce sustained changes in plasma NT-proBNP concentrations, with preeclampsia being one such complication. However, the association between NT-proBNP concentrations and electrocardiographic or echocardiographic findings in pregnancy-associated pathological conditions, particularly preeclampsia, has not yet been investigated.

Preeclampsia (PE) is one of the most serious complications of pregnancy [3-5]. It is characterised by elevated blood pressure and proteinuria after 20 weeks of gestation [6] and affects not only the course of pregnancy [7, 8] but also the long-term cardiovascular health of the woman [9].

Research indicates that the primary mechanism underlying the effects of PE involves endothelial dysfunction. This leads to reduced vascular relaxation, increased vascular resistance, the development of hypertension, and diminished synthesis of vasoactive substances (nitric oxide, thromboxane, prostacyclin) essential for normal function of the fetoplacental complex [11-16].

PE is accompanied by activation of proinflammatory cytokines and free radicals, which promote myocardial remodelling and the development of fibrosis [15-17].

In some women with a history of preeclampsia, residual left ventricular hypertrophy persists, particularly in those with pre-existing arterial hypertension, resulting in impaired systolic and diastolic cardiac function [17]. Even after normalisation of blood pressure, diastolic function may remain compromised, suggesting persistent structural changes in the myocardium [19].

From a clinical perspective, this increases the risk of heart failure and other cardiovascular diseases in the future. Women with a history of preeclampsia have a higher risk of developing acute heart failure both during pregnancy and in the early postpartum period, as well as an elevated risk of hypertension, coronary heart disease, and chronic heart failure later in life [20-24].

Thus, PE exerts a substantial influence on the cardiovascular system in both the short and long term, necessitating careful cardiological monitoring of women following delivery [25].

Echocardiography, magnetic resonance imaging, and biomarker analysis – including NT-proBNP, troponins, and other markers – are employed to evaluate cardiac status [26]. The integration of electrocardiography and echocardiography allows for a comprehensive assessment of the electrical and structural-functional activity of the heart during pregnancy and the postpartum period. Regular cardiological examinations facilitate the timely identification of pathological changes, optimisation of management, and reduction of risks to the mother and fetus [27, 28].

Biochemically, NT-proBNP is generated through the cleavage of proBNP into active B-type natriuretic peptide (BNP) and the inactive NT-proBNP fragment. It is released by cardiomyocytes in response to increased ventricular filling pressure and wall stress [29, 30]. Owing to its longer half-life in circulation, NT-proBNP serves as a reliable marker for laboratory monitoring.

However, the association between NT-proBNP concentrations and electrocardiographic or echocardiographic findings in pregnancy-associated pathological conditions, particularly preeclampsia, has not yet been investigated.

The aim of the research: to investigate the association between concentrations of N-terminal pro-B-type natriuretic peptide (NT-proBNP) and electrocardiographic and echocardiographic parameters of the heart in early-onset preeclampsia.

Material and methods. A total of 90 women were enrolled in the study. All pregnant women underwent examination between 32 and 36 weeks of gestation. The main group (MG) comprised 60 patients with pregnancies complicated by early-onset moderate preeclampsia. The control group (CG) consisted of 30 women with uncomplicated pregnancies of comparable gestational age. Patients were included in the study groups after providing informed consent.

Patients were recruited at the delivery unit of the Chernivtsi Regional Perinatal Center (municipal non-profit enterprise, Chernivtsi, Ukraine). Laboratory analyses were performed at the certified Educational and Research Laboratory of Bukovinian State Medical University.

NT-proBNP levels were determined using the MAGLUMI NT-proBNP assay (Shenzhen New Industries Biomedical Engineering Co., Ltd., Shenzhen, China). Venous blood samples were obtained once at 08:00 after an overnight fast. For analysis, 500 μL of plasma was placed in disposable tubes and loaded into the MAGLUMI 1000 automatic chemiluminescent immunoassay analyser.

Electrocardiography was performed using a Heaco ECG600G six/twelve-channel electrocardiograph. Echocardiography was conducted with a GE Voluson E8 Expert ultrasound system (serial number 3143/1144/0178; GE Healthcare, Austria).

The study was approved by the Bioethics Committee of Bukovinian State Medical University (Protocol No. 2 dated 9 February 2015). The investigation complied with ethical principles set forth in the Declaration of Helsinki (1964-2013), the Council of Europe Convention on Human Rights and Biomedicine (1997), the World Medical Association Declaration of Helsinki, and Order No. 690 of the Ministry of Health of Ukraine (dated 23 September 2009).

Statistical analysis was carried out on a personal computer using Statistica software (Microsoft Excel 2010, Microsoft Office 2010, and MedCalc version 16.1), with application of Student's t-test for independent samples.

This study was conducted as part of the research project entitled «Preservation and Restoration of Reproductive Health in Women and Girls with Obstetric and Gynecological Pathologies» at the Department of Obstetrics and Gynecology, Bukovinian State Medical University; state registration number 0121U110020 (2021-2025).

Results and discussion

Mean plasma NT-proBNP levels were found to be significantly higher in women with pregnancies complicated by PE than in those with uncomplicated pregnancies (79.5 ± 37.4 pg/mL versus 32.0 ± 12.0 pg/mL; $p < 0.001$). Thus, NT-proBNP concentrations in pregnant women with PE were approximately twice those observed in women with uncomplicated pregnancies.

Differences in echocardiographic parameters of the left ventricle and electrocardiographic characteristics between the main and control groups were established in the present study.

Table 1 presents a comparison of electrocardiographic parameters in women with early-onset moderate PE and in women with uncomplicated pregnancies.

As shown in Table 1, significant prolongation of all measured electrocardiographic intervals was observed in women with early-onset moderate PE.

Table 2 presents the results of echocardiographic examination in pregnant women with moderate PE.

Table 1

Electrocardiographic parameters in women with early moderate PE

Parameter	The experimental group (n=60)	The control group (n=30)	p
ECG – PR interval/ms	208,0 ± 9,1	161,3 ± 8,4	<0,0001
ECG – P wave/ms	129,4 ± 9,0	98,3 ± 11,4	<0,005
ECG – QRS complex/ms	107,9 ± 9,6	88,8 ± 10,2	<0,005
ECG – T wave/ms	261,5 ± 9,2	180,2 ± 10,6	<0,005
ECG – QT/QTc/ms	461,7 ± 10,0	402,8 ± 10,2	<0,0001

Note: the data are presented as a mean ± standard deviation.

Table 2

Echocardiography parameters in women with early moderate PE

Parameter	The experimental group (n=60)	The control group (n=30)	P
LVPW diastole	1,10 ± 0,05	0,82 ± 0,05	<0,0001
LVPW systole	1,30 ± 0,04	1,10 ± 0,05	<0,005
IVS systole	1,30 ± 0,05	1,10 ± 0,06	<0,005
IVS diastole	1,09 ± 0,05	0,80 ± 0,04	<0,0001

Note: the data are presented as a mean ± standard deviation.

Table 2 presents the results of echocardiographic examination in pregnant women with moderate PE. . As evident from Table 2, patients with early-onset moderate preeclampsia exhibited a significant increase in the thickness of the left ventricular posterior wall (LVPW) and interventricular septum in both systole (IVS systole) and diastole (IVS diastole) compared with the control group. These findings may indicate remodelling of the left ventricular walls, characteristic of early (mild) myocardial hypertrophy.

Analysis of associations between the parameters investigated revealed the following: in women with PE, plasma NT-proBNP concentrations demonstrated a weak positive correlation with interventricular septum thickness in diastole ($r = 0.291$; $p = 0.0093$; Figure 1).

Additionally, a weak negative correlation was identified between NT-proBNP concentrations and the QT/QTc interval in the main group ($r = –0.21$; $p = 0.001$; Figure 2).

In the control group, NT-proBNP levels showed a moderate positive correlation with left ventricular posterior wall thickness in diastole ($r = 0.312$; $p = 0.0089$; Figure 3) and a weak negative correlation with the QT/QTc interval ($r = –0.205$; $p = 0.02$; Figure 4).

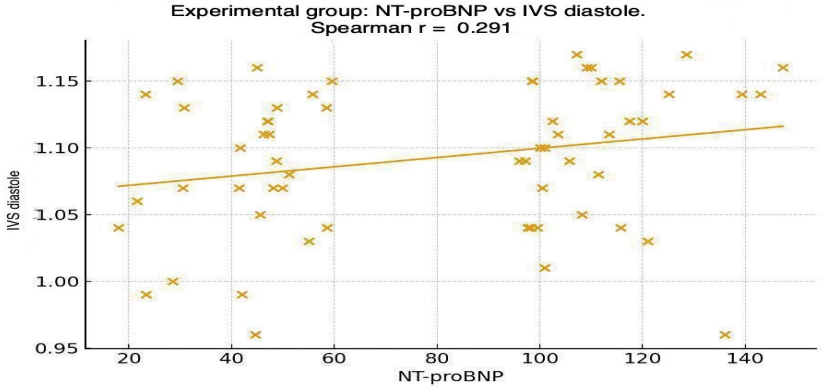

Fig. 1. Data distribution and correlation graph between NT-proBNP and the thickness of interventricular septum in a group of women with PE.

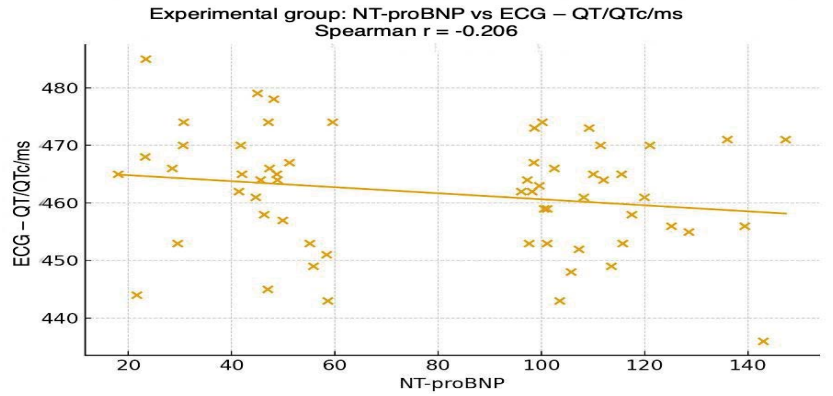

Fig. 2. Data distribution and correlation graph between NT-proBNP and QT/QTc interval in a group of women with PE.

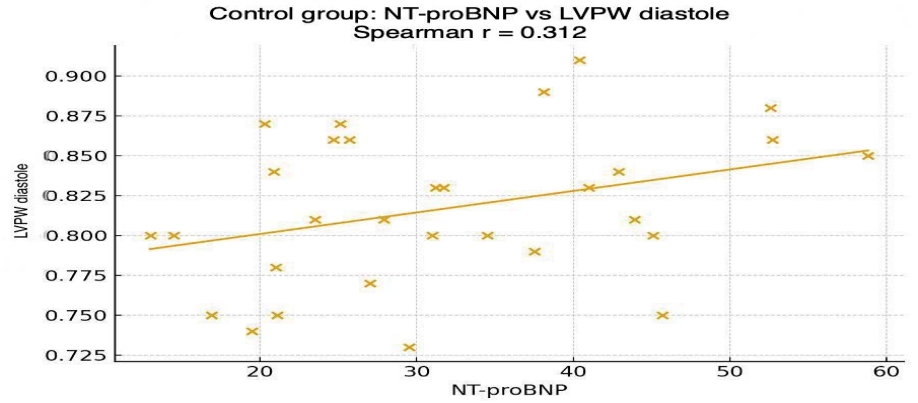

Fig. 3. Data distribution and correlation graph between NT-proBNP and left ventricular posterior wall thickness in diastole in a with uncomplicated pregnancy.

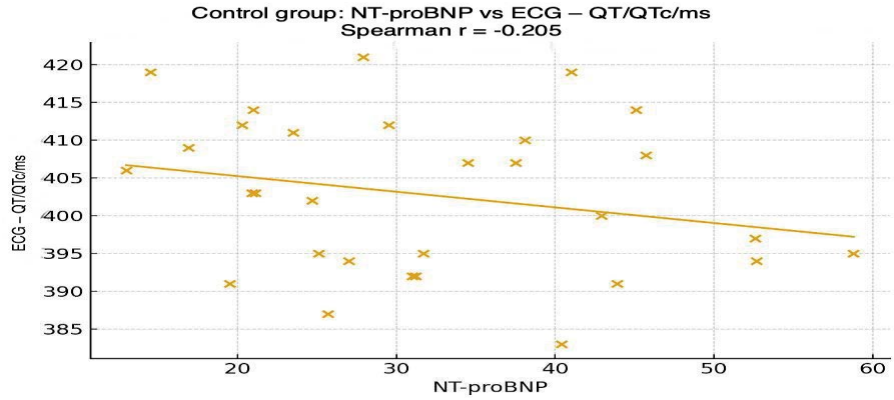

Fig. 4. Data distribution and correlation graph between NT-proBNP and QT/QTc interval in a group of women with uncomplicated pregnancy.

As previously noted, the N-terminal fragment of brain natriuretic peptide (NT-proBNP) serves as a biomarker that reflects the state of the cardiovascular system and myocardial function [28]. During pregnancy, its concentration may vary in response to both physiological and pathological processes.

It should be emphasised that the data obtained regarding changes in myocardial functional status in pregnant women with early-onset moderate PE are consistent with typical manifestations of incipient left ventricular hypertrophy. Increased thickness of the ventricular walls and interventricular septum represents a morphological marker of myocardial remodelling resulting from chronic haemodynamic overload [29]. Electrocardiographic findings – prolongation of the PR, QRS, and QT intervals together with increased duration of the P and T waves – indicate delayed impulse conduction in the myocardium as well as potential alterations in repolarisation processes, which aligns with existing literature on the pathogenesis of PE in pregnant women [30].

The results of the present study confirm the diagnostic value of a comprehensive evaluation of echocardiographic and electrocardiographic parameters for the early detection and monitoring of left ventricular hypertrophy, even in its incipient stages, as a consequence of PE during pregnancy.

This assessment plays a crucial role in the long-term health of women following delivery, particularly with respect to the risk of developing chronic hypertension. Monitoring of this key parameter, NT-proBNP, will enable clinicians to identify women at risk of chronic hypertension and to initiate appropriate management in a timely manner.

Conclusions

Plasma levels of the cardiac peptide NT-proBNP are markedly elevated in women with pregnancies complicated by PE.

Electrocardiographic and echocardiographic parameters obtained in women with early-onset moderate preeclampsia are consistent with typical manifestations of incipient left ventricular hypertrophy.

Increased thickness of the ventricular walls and interventricular septum serves as a morphological marker of myocardial remodelling in response to haemodynamic overload.

Electrocardiographic signs – prolongation of the PR, QRS, and QT intervals together with increased duration of the P and T waves – reflect delayed impulse conduction in the myocardium as well as possible alterations in repolarisation processes in the context of moderate PE.

The prospects for further research. Development of predictive models to identify pregnant women with preeclampsia who are at increased risk of cardiovascular complications.

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

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РІВНІ СЕРЦЕВОГО ПЕПТИДУ NT- PROBNP ТА ПОКАЗНИКИ ЕЛЕКТРОКАРДІОГРАФІЧНОГО ТА УЛЬТРАЗВУКОВОГО ДОСЛІДЖЕННЯ СЕРЦЯ ПРИ РАННІЙ ПРЕЕКЛАМПСІЇ ВАГІТНИХ

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Резюме.

N-кінцевий промозковий натрійуретичний пептид NT-proBNP – серцевий пептид, який переважно синтезується та секретується міокардом лівого шлуночка. Він вважається одним із ключових біохімічних маркерів серцевих захворювань. Відомо, що його рівень у крові достовірно підвищується у пацієнтів із серцевою недостатністю. Втім, досі не проводилися дослідження взаємозв'язків між концентрацією NT-proBNP та показниками ЕКГ, та ультразвукового дослідження серця при патологічних станах, пов'язаних із вагітністю, зокрема при прееклампсії.

Мета дослідження. Вивчити зв'язок між концентраціями в сироватці крові серцевого пептиду NT-proBNP та показниками ЕКГ і ультразвукового дослідження серця при ранній прееклампсії вагітних.

Матеріал і методи. Загальна кількість жінок, включених до дослідження, склала 90 осіб. Всі вагітні були обстежені в терміні вагітності 32-36 тижнів. До основної групи увійшли 60 вагітних із ранньою помірною прееклампсією. Контрольну групу склали 30 жінок із фізіологічним перебігом вагітності. Рівень NT-proBNP визначали за допомогою тест-системи MAGLUMI BNP (виробник: Shēnzhèn New Industries Biomedical Engineering, Шеньчжень, Китай); забір венозної крові у вагітних проводили одноразово натще о 8:00 ранку. ЕКГ серця проводилось на апараті Heaco ECG600G, 6/12-канальний кардіограф медичний апарат ЕКГ. УЗД серця проводилось із використанням системи ультразвукового апарату GE Voluson E8 Expert 3ав. 3143/1144/0178 Виробник: General Electric, Австрія. Схвалення Комісії з питань біоетики Буковинського державного медичного університету (Протокол № 2 від 09.02.2015 р.). Статистична обробка результатів здійснювалася на персональному комп'ютері із використанням пакету програмного забезпечення «Statistica» (StatSoft Inc., Version 13, США), Microsoft Excel (2010), Microsoft Office (2010) та MedCalc Software (Version 16.1). Порівняння кількісних показників здійснювалося із використанням t-критерію Стьюдента для незалежних вибірок. Дослідження проводили у межах комплексної науково-дослідної роботи кафедри акушерства і гінекології БДМУ на тему: «Збереження та відновлення репродуктивного здоров'я жінок та дівчат при акушерській і гінекологічній патології»; державний реєстраційний номер: 0121U110020; термін виконання 01.2021-12.2025 рр.

Результати. У вагітних із ранньою ПЕ діагностовано вірогідно вищий середній рівень NT-proBNP, порівняно з контролем (79,5±37,4 пг/мл і 32,0±12,0 пг/мл, p<0,001). У пацієнток основної групи спостерігалося вірогідне збільшення товщини задньої стінки, у порівнянні з КГ як у фазі діастоли (1,10 ± 0,05 см проти 0,82 ± 0,05 см, p < 0,0001), так і під час систоли (1,30 ± 0,04 см

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проти 1,10 ± 0,05 см, p < 0,0001). Подібні зміни відмічалися і для міжшлуночкової перетинки: у систолу її товщина досягала 1,30 ± 0,05 см проти 1,10 ± 0,06 см (p < 0,0001), а в діастолу – 1,09 ± 0,05 см проти 0,80 ± 0,04 см (p < 0,0001). У дослідній групі також виявлено зміни електрокардіографічних показників, порівняно зі здоровими вагітними. Середній інтервал PR у жінок з прееклампсією був подовжений до 208,0 ± 9,1 мс порівняно з 161,3 ± 8,4 мс у контрольній групі (p < 0,0001). Тривалість зубця P збільшилася до 129,4 ± 9,0 мс проти 98,3 ± 11,4 мс (p < 0,0001), а комплекс QRS – до 107,9 ± 9,6 мс проти 88,8 ± 10,2 мс (p < 0,0001). Зубець T подовжувався до 261,5 ± 9,2 мс порівняно з 180,2 ± 10,6 мс (p < 0,0001). Також відмічено збільшення інтервалу QT/QTc до 461,7 ± 10,0 мс проти 402,8 ± 10,2 мс (p < 0,0001). Нами встановлено наступні кореляційні зв'язки між показниками, що вивчалися: у жінок з прееклампсією значення NT-proBNP в плазмі крові слабко корелювало з товщиною міжшлуночкової перетинки в діастолу (r = 0,291, p = 0,0093), а також демонструвало слабку негативну кореляцію з інтервалом QT/QTc (r = –0,21, p=0,001). У контрольній групі рівень NT-proBNP також демонстрував помірну кореляцію з товщиною задньої стінки лівого шлуночка в діастолу (r = 0,312, p = 0,0089) та слабку негативну – з інтервалом QT/QTc (r= – 0,205, p=0,02).

Висновки. 1. Рівень серцевого пептиду NT-proBNP вірогідно зростає в крові жінок, чия вагітність ускладнилася прееклампсією. 2. Отримані в групі жінок з ранньою помірною прееклампсією показники ЕКГ та УЗД серця відповідають типовим проявам початкової гіпертрофії лівого шлуночка. 3.Збільшення товщини стінок і міжшлуночкової перетинки є морфологічним маркером ремоделювання міокарду під впливом гемодинамічного перевантаження. 4. Електрокардіографічні ознаки – подовження інтервалів PR, QRS, QT та збільшення тривалості зубця P і T – відображають як уповільнення проведення імпульсу в міокарді, так і можливі зміни реполяризаційних процесів на тлі помірної прееклампсії.

Ключові слова: NT-proBNP; прееклампсія; вагітні жінки; ЕКГ, ехокардіографія.

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