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LEADING ARTICLE

Pregnancy as the risk factor of arrhythmias

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Summary

Objective

To investigate the features of arrhythmias and define possible etiological factors of their development in pregnant women.

Materials and methods

133 patients (average age 27,1±5,7 years) during II-III trimesters of pregnancy were investigated, 113 of them had complex arrhythmias, 20 women had normal sinus rhythm. Depending on presence or absence of arrhythmia and cardiovascular pathology all patients were divided into three groups. Group I (n=62) included women with arrhythmias and organic lesions of cardiovascular system: congenial or acquired heart disease, cardiomyopathies, post-myocarditis cardiosclerosis. Group II (n=51) included patients with idiopathic arrhythmias, control group (n=20) included almost healthy women with normal sinus rhythm.

Results

According with 24hour ECG monitoring, arrhythmias of III-IV classes (classification of Lown B. и Wolff N., 1971) were registered with the same frequency in both groups of patients. At the same time maximal number of ventricular extrasystoles was detected in the group of "idiopathic" heart rhythm lesions and the biggest number of supraventricular extrasystoles was found in the Group I of patients. Pregnant women with mitral valve prolapse had significantly lower frequency of supraventricular extrasystoles, but at the same time the occurrence of ventricular extrasystoles was comparable with main observation groups.

Conclusion

Complex arrhythmias arise both in pregnant women with concomitant cardiovascular pathology and in women without organic lesions of organs and metabolic processes. It requires precise dynamic observation of these patients.

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Key words
Arrythmias, pregnancy, cardiovascular disease, idiopathic arrythmia.

Introduction

Currently there is no official statistical information about arrhythmia frequency in pregnancy, but existing data demonstrate that in 1976-1978 cardiac rhythm and conductivity abnormalities were registered in 5,0% of pregnant women, and in the next decades this number increased up to 11,3% [1], and in 1990 arrhythmias occurred in 7-15,7% of pregnant women [2]. Documented maternal mortality from primary arrhythmias hasn't been registered yet, at the same time experts say that arrhythmias can be letal, and British Confidential Study of cardiac mortality identified 9% of these cases as "sudden adult cardiac death" syndrome [3].

At the same time there are some evidences about arrhythmia development in patients with hemodynamic lesions and significant anatomic changes in cardiovascular system (CVS) [4, 5]. Pregnancy with its hemodynamic, hormonal, vegetative and metabolic changes can become a proarrythmogenic factor especially considering the fact that "female heart" is basically predisposed to arrhythmias. first of all it is related to gender features of electrophysiological processes in heart. In 1920 Bazett H.C. noticed that females have higher heart rate (HR) than males on electrocardiogram (ECG), that they have longer QT interval on electrocardiogram, that remains relatively long after HR correction comparing with males [6]. Villareal R.P. with coauthors demonstrated that 10-20 seconds more long QT interval, and these differences become more significant during menstruation [7]. Apart of these, women have smaller QRS complex duration and voltage, P wave and PR interval duration shortening [8,9]. Non specific changes of repolarization occur more often in women [10]. At first instance, these differences can be explained with initially smaller dimensions of heart in women, but they persist even after correction of heart mass and body weight. These results can be explained with the influence of female sex hormones on potassium and calcium channels. In particular, it was found that estrogens lead to QT duration increase by influencing fast and slow sodium channels current and sodium-calcium exchanges [9]. This exploration was lately proved with other studies that demonstrated how vegetative nervous system takes part in cardiac rhythm regulation [11-12]. Gender features can be related not only to electrophysiological processes, but also to arrhythmia's character. Several epidemiological studies found out that supraventricular tachycardia with narrow QRS complex that develops according with re-entry mechanism in atrioventricular node, is twice more frequent in women than in men [13, 14], and in contrary, supraventricular tachicharia that appears due to re-entry mechanism in atrioventricular node with the presence of additional conductive path is twice more frequent in men [15]. Unfortunately specific studies that would investigate cardiac rhythm abnormalities and define possible etiological factors of their development have not been made still. This problem was chosen as the aim of this work.

Materials and methods

133 women in II and III trimester of pregnancy (average age 27,1±5,7 years) were included in this study after signing the informed consent. All patients were admitted to cardiological department of Moscow City Hospital №63. Apart of routine examination and laboratory diagnostics that included blood tests for electrolytes (sodium, potassium) and thyroid gland hormones (triiodothyronine(T3), thyroxin (T4), thyrotropic hormone (TTH)) patients underwent two-dimensional and Doppler echocardiography (EchoCG) in M-, B-, and continuous wave modes with "Logic-400" machine, 24-hours Holter ECG monitoring, using "Medilog Prima" and "Schiller MT-200".

Statistical analysis was performed using "Biostatistics. Version 4.03" software. We used standard approaches of variation statistics and Student's test for estimation of paired comparisons. Differences were considered significant if p-value was < 0.05.

Results

113 of 133 patients were diagnosed with complex abnormalities of cardiac rhythm (main group) and 20 women had normal cardiac rhythm (control group). According with patients' history, 84 (63,2%) women didn't have bad habits, 49 (36,8%) women used to smoke in past or continued to smoke during pregnancy, and the amount of cigarettes smoked for day varied from 2 to 30, average pack-year number was 5,3±1,8. Almost one half of patients had burdened family history of cardiovascular diseases and metabolic abnormalities: arterial hypertension of one or two parents occurred in 55,6% of cases, myocardial infarction or stroke of one or two parents appeared in

8,2% of cases, obesity – in 33,1% of cases, diabetes mellitus – in 4,5% of cases.

Women didn't complain of palpitations, intermittence before the beginning of current pregnancy. Starting from the middle of the I trimester or initial part of the II trimester patients with arrhythmias started to feel intermittence, "sinking heart", palpitation, sometimes paroxysmal, weakness, increased fatigability, and manifestation of these symptoms led to additional examination. Patients were divided into three groups according with the presence or absence of arrhythmia or other cardiovascular pathology. The group I (n=62) included women with cardiac rhythm abnormalities and organic changes of CVS. The group II included 51 patients with arrhythmias and without observed organic changes of CVS, endocrine system, gastrointestinal tract, thus their arrhythmia was classified as "idiopathic". The third (III) group (n=20) was considered as a control, it included almost healthy women with normal sinus rhythm and the same duration of gestation as the patients of first two groups.

According with the results of clinical and instrumental examination, in the I group such organic changes of CVS were present: hypertrophic cardiomyopathy without left ventricle efferent tract obstruction (n=3), open oval foramen (n=3), dilatation cardiomyopathy without the signs of cardiac insufficiency (n=4), mitral valve insufficiency of rheumatic etiology (n=4), ventricular septal defect that was not treated surgically (n=6), corrected Fallot's tetrad (n=1) and postmyocarditis cardiosclerosis (n=10). Mitral valve prolapse (MVP) was present in many patients (n=30), and I grade mitral regurgitation was found in 9 cases and II grade mitral regurgitation was found in 21 case.

Analysis of the results of 24-hours Holter ECG monitoring included several parameters: main pacemaker, average heart rate (HR) (day/night/24 hours), number of supraventricular extrasystoles (SVES, during hour and during 24 hours), number of ventricular extrasystoles (VES, during hour and during 24 hours), and VES class according with Lown B. and Wolff N. classification in Ryan-McKenn modification. According with these results, the number of extrasystoles during 24 hours varied from 8 thousands to 50 thousands in pregnant women with arrhythmia, couplets (13-80 during 24 hours) and triplets (3-150 during 24 hours) were registered in some women (n=6 and 4 respectively), 5 women had runs of ventricular tachycardia (1-5 during 24 hours) with HR varying from 156 to 229 beats per minute. These cardiac rhythm abnormalities resembled to II-IV class of Lown B.-Wolff N. classification. There were no statistically significant differences in VES gradation between the groups of pregnant women with arrhythmia, but the difference of VES and NVES number was considered statistically significant. The biggest amount of VES was registered in the group of "idiopathic" arrhythmias, and the biggest number of NVES was found in the group of organic cardiac pathology. Group of healthy patients was characterized with normal sinus rhytm and single NVES (Table 1).

Table 1. **Cardiac rhythm abnormalities according with 24-hours Holter ECG monitoring in the groups of patients (M±SD)**

Characteristic	Group I (n=62)	Group II (n=51)	Group III (n=20)
VES class, Lown B. and Wolff N classification	2,9±1,6	2,1±1,8	2,4±1,3
VES number/24 hours.	4300±300	6200±530 [1), 3)]	500±40 [1), 2)]
SVES number/ 24 hours	3800±300	2000±150[1), 3)]	600±50 [1), 2)]

Comment: [1)] — p<0,05 in comparison with Group1; [2)] — p<0,05 in comparison with Group II; [3)] — p<0,05 in comparison with group III.

Taking into account high number of patients with MVP and its high occurrence in population in general, it was particularly interesting to check the character of arrhythmias in this category of pregnant women. We distinguished this group of patients from the group of women with arrhythmias and background cardiovascular pathology (Table 2).

Pregnant women with MVP had SVES significantly less frequently than patients of other groups; practically, there was just one patient who had 1000 SVES during 24 hours. But the number of VES was comparable with the results of the group of "idiopathic" arrhythmias.

Table 2. **SVES/VES ratio in groups of pregnant women with different pathologies (M±SD)**

Extrasystole character	Average number during 24 hours	Organic cardiac pathology (except MVP) (n=32)	MVP (n=30)	«Idiopathic» arrhythmias (n=51)
SVES	1870±290 (max. 17 200)	3900±380 (max. 13 000)	70±11 [1), 2)] (max. 1000)	1800±220 [1)] (max. 17 200)
VES	5160±320 (max. 15 750)	3200±240 (max. 8000)	5300±430 [1)] (max. 15 000)	6200±540 [1)] (max. 15 750)

Comment: [1)] — p<0,05 in comparison with organic cardiac pathology; [2)] — p<0,05 in comparison with «idiopathic» arrhythmias.

Discussion

Rich experience of modern clinical cardiology demonstrates that the reasons of cardiac rhythm abnormalities are very different and still poorly studied. Patients with changed hemodynamics, hormonal status, general and water-salt metabolism and increased load of CVS have high risk of arrhythmia development, and all these predisposing factors are present in pregnant women. Gestation period is characterized with physiologically increased activity of renin-angiotensin-aldosterone system, that raises up circulating blood volume mostly increasing plasma volume up to 40%. The most significant hemodynamic characteristic during pregnancy is increased stroke volume (SV), that increases up to 30-45% in rest state comparing with its values before pregnancy. SV growth increases cardiac output (CO), that reaches maximum during 26-32 week of pregnancy being increased up to 33-50% comparing with initial levels. Physiological tachycardia that develops during pregnancy raises up HR by 15-20 beats per minute by the end of pregnancy comparing with initial levels. 12-34% decrease of peripheral vascular resistance occurs during pregnancy [16]. Our study demonstrated that these hemodynamic factors can lead to arrhythmias in patients with organic lesions of CVS. More than that, important factor of CVS adaptation to pregnancy is systemic vasodilation caused not only by increased nitrogen oxide (NO) and other vasodilating factors secretion, but also by increased levels of estrogens and progesterone, that increase adrenoreceptors' sensitivity to hormones of sympathoadrenal system. Starting from the beginning of pregnancy and up to delivery time reactivity of ß-receptors increases and reactivity of α-receptors decreases, that is necessary to reduce contractive activity of myometrium and provide the carrying of pregnancy [17]. ß-receptor density in myometrium increases due to progesterone action. ß-receptor activation can lead to arrhythmia development, as it was shown in previous studies [18, 19]. Probably so-called "idiopathic arrhythmias" are mostly caused by proarrhythmogenic effect of sympathoadrenal system, functional condition of which increases being influenced by female sexual hormones.

Increased ectopic activity is also related to vegetative dysfunction in patients with MVP, that traditionally is considered as a normal and not requiring therapy especially without hemodynamically significant mitral regurgitation. It is known that MVP is characterized with genetically determined defect of collagen synthesis and lowered levels of intratissular magnesium concentration. In case of magnesium deficiency fibroblasts produce defective collagen of mitral valve cusps. Clinically MVP often manifests with abnormal vegetative regulation of cardiac rhythm that is registered with more than 70% frequency [21]. During pregnancy even almost healthy women can develop the symptoms of such vegetative dysfunction like hypersympathicotonia [22], and patients with MVP can have more prominent symptoms which can lead to lowering the quality of life and, from the point of view of the authors, influence intracardiac hemodynamics, and in case of other risk factors presence they can also provoke resistant ventricular tachiarrythmias.

Thus, the results of the study indicate that complex cardiac rhythm abnormalities in pregnant women develop as the consequence of cardiovascular pathology that includes congenital and acquired valvular disease, postmyocarditis cardiosclerosis, MVP with moderate regurgitation, or they appear in women without organic changes of internal organs and metabolic processes, that requires precise dynamic observation of these patients, and in case of hemodynamic instability or developing life-threatening arrhythmias it is necessary to start well-timed adequate therapy.

Conflict of interest: None declared.

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