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Результати добового моніторингу електрокардіограми залежно від стану жовчного міхура

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Хвороби жовчного міхура (ЖМ) асоціюються із структурними та функціональними змінами серця. Біліарна автономна вісцеро-вісцеральна кардіонейропатія (БАВВКНП) та постбіліарна автономна кардіонейропатія (ПБАКНП) характеризуються розладами ритму та провідності, депресією сегмента ST та ознаками гіпертрофії лівого шлуночка у пацієнтів з різними патологічними станами ЖМ. Метою цього дослідження було порівняти результати добового моніторингу електрокардіограми (ЕКГ) у пацієнтів з БАВВКНП, ПБАКНП та нормальним ЖМ. У 138 амбулаторних пацієнтів з серцево-судинними та позасерцевими захворюваннями було проведено 24-годинний моніторинг ЕКГ. Учасників було поділено на три групи: незмінений ЖМ (n = 54); БАВВКНП (n = 72); ПБАКНП (n = 12). Пацієнти з ПБАКНП характеризувалися відсутністю депресії сегменту ST, вкорочення інтервалу PR, пароксизмальної надшлуночкової тахікардії, симпатоадреналового овердрайву у ранковий час, міграції водія ритму та дисфункції синусового вузла. БАВВКНП характеризувалася розвитком активних ектопічних вогнищ у міокарді, збільшенням серцевого викиду, потовщенням стінки ЖМ та підвищенням загального рівня білірубіну. Пацієнти з ПБАКНП відрізнялися від осіб без кардіонейропатії більшою частотою серцевих скорочень у нічний час, відсутністю епізодів депресії сегмента ST, меншою тривалістю комплексу QRS, а також меншою кількістю моноцитів крові.

Ключові слова: жовчний міхур, серце, добовий моніторинг електрокардіограми.

Results of 24-hour Electrocardiogram Monitoring Depending on Gallbladder Condition

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Gallbladder (GB) diseases are associated with structural and functional cardiac abnormalities. Biliary autonomous viscero-visceral cardioneuropathy (BAVVCNP) and post-biliary autonomous cardioneuropathy (PBACNP) are characterized by rhythm and conduction disorders, ST-segment depression, and signs of left ventricular hypertrophy in patients with various GB disorders. The aim of this study was to compare results of 24-hour electrocardiogram (ECG) monitoring in patients with BAVVCNP, PBACNP, and normal GB. 138 outpatients with cardiovascular and extracardiac disorders underwent 24-hour ECG monitoring. They were divided into three groups: intact GB (n=54); BAVVCNP (n=72); PBACNP (n=12). PBACNP patients were characterized by the absence of ST-segment depressions, PR interval shortenings, paroxysmal supraventricular tachycardia, sympathoadrenal overdrive in the mornings, pacemaker migration, or sinus node dysfunction. BAVVCNP was characterized by the development of active ectopic foci in the myocardium, increased cardiac output, GB wall thickening, and elevated total bilirubin level. Patients with PBACNP differed from those without cardioneuropathy by faster nocturnal heart rate, absence of episodes of ST-segment depression, shorter QRS duration, and lower blood monocyte count.

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Keywords: Gallbladder, heart, 24-hour electrocardiogram monitoring.

Introduction. Nowadays there is a growing body of evidence about complex associations between gallbladder (GB) diseases and both structural and functional cardiac abnormalities. The association between GB diseases and electrocardiographic (ECG) changes was first described in 1878 [1]. Nonspecific ST-segment and T-wave abnormalities or arrhythmias are frequently observed in patients with acute cholecystitis. Kumar et al. (2020) described reflex bradycardia in patients with GB disorders, and a complete heart block secondary to acute cholecystitis [2]. Franzen et al. (2009) published a clinical case, where an otherwise healthy patient developed complete atrioventricular block without an escape rhythm during exacerbation of chronic cholecystitis that resolved after laparoscopic cholecystectomy [3]. A case report by Lau et al. (2015) described a sinus arrest and bradycardia in a patient with acalculous cholecystitis that resolved after cholecystectomy [4]. Other authors have demonstrated ST-segment elevation alone or in combination with the right bundle bunch block in patients with acute acalculous cholecystitis that disappeared after antibiotic therapy [5, 6].

Our previous study pointed to the possibility of biliary autonomous viscero-visceral cardioneuropathy (BAVVCNP) and post-biliary autonomous cardioneuropathy (PBACNP) characterized by rhythm and conduction disorders, ST-segment depression, and signs of left ventricular hypertrophy in patients with various

GB disorders [7]. These changes may result from cardio-biliary reflex mediated by the vagus nerve [2, 8]. Animal models demonstrated that GB distension might promote reflex coronary vasoconstriction and contribute to the increase of plasma renin activity [9].

Methods. After signing of written informed consents, 138 outpatients (66 [47.8%] men and 72 [52.2%] women; median age 51.5 [33.0; 61.0]; 34.78% with essential or symptomatic arterial hypertension; 33.33% with chronic forms of coronary artery disease; 25.36% with metabolic cardiomyopathy, 18.84% with cardioneurosis, and 21.74% with extracardiac disorders) underwent 24-hour ECG monitoring. The latter was performed using the Holter ECG Workstation BS6930-12 system (Poland). Participants were divided into three groups: group 1 — no cardiopathy, intact GB (n=54); group 2 — BAVVCNP with GB disorders determined by ultrasonographic evidence of biliary sludge, cholesterosis, polyps, deformations, cholecystitis, or cholelithiasis (n=72); group 3 — PBACNP after prior cholecystectomy due to cholelithiasis (n=12).

Statistical analysis was performed using Statistica for Windows 12.0 (Statsoft, USA). Non-parametric tests were employed since the *majority of parameters were non-normally distributed.* Data were presented as median [lower; upper quartile] or percentages; inter-group differences were compared using the Mann-Whitney test. Associations were analyzed using the Kendall rank correlation coefficient (τ). P values less than 0.05 were considered statistically significant.

Results and discussion. Analyzed parameters of 24-hour ECG monitoring in group 3 significantly differed from the other two groups (i.e., absence of ST-segment depressions, PR interval shortenings, paroxysmal supraventricular tachycardia, sympathoadrenal overdrive in the mornings, pacemaker migration, or sinus node dysfunction — Table 1). The highest percentage of women in group 3 points to a possible role of the female gender as a risk factor of cholelithiasis.

Table 1

Parameters of 24-hour ECG monitoring in patients with intact gallbladder (group 1), gallbladder abnormalities (group 2), and after cholecystectomy (group 3)

Parameter	Group 1 (n=54)	Group 2 (n=72)	Group 3 (n=12)
Heart rate, bpm	75.0 [71.0; 87.5]	77.5 [68.0; 83.0]	83.5 [80.5; 85.0]
Nocturnal heart rate (22:00-07.00), bpm	56.0 [49.0; 62.0] p_{1-3}=0.01	55.5 [49.5; 63.5] p_{2-3}=0.04	66.0 [64.5; 67.0] p_{2-3}=0.04; p_{1-3}=0.01
Maximal heart rate, bpm	128.0 [116.5;147.5]	122.0 [111.0;137.0]	130.0 [125.0;132.0]
Minimal heart rate, bpm	50.0 [45.0; 55.0]	53.0 [44.0; 57.0]	52.0 [50.0; 57.0]
Mean heart rate, bpm	75.0 [66.0; 79.0]	71.5 [67.0; 80.0]	74.5 [70.0; 82.0]
Number of premature beats per day, n	7.0 [0.0; 92.0] p_{1-2}=0.009	48.0 [5.0; 342.0] p_{1-2}=0.009	24.0 [3.0; 288.0]
Incidence of ST interval depression, %	12.96±4.58 p_{1-3}<0.05	22.22±4.90 p_{2-3}<0.05	0±0 p_{1-3}<0.05; p_{2-3}<0.05
Incidence of premature beats, %	70.37±6.21	79.17±4.78	75.00±12.50
Incidence of parasystoles, %	50.00±6.80	48.61±5.89	66.67±13.60
Incidence of supraventricular tachycardia, %	75.93±5.82	65.28±5.60	66.67±13.60
Incidence of supraventricular bradycardia, %	14.81±4.83	12.50±3.90	8.33±7.96
Incidence of atrioventricular blockade, %	9.26±3.99	4.17±2.36	8.33±7.96
Incidence of shortened PR interval, %	5.56±3.10	2.78±1.94	0±0
Incidence of supraventricular paroxysmal tachycardia, %	5.56±3.10	1.38±1.38	0±0
Incidence of sympathoadrenal overdrive in the mornings, %	3.70±2.57	4.17±2.36	0±0
Incidence of paroxysmal atrial fibrillation, %	1.85±1.81	4.17±2.36	16.67±11.39
Incidence of pacemaker migration, %	1.85±1.81	5.56±2.69	0±0
Incidence of sinus node dysfunction, %	11.85±1.81 p_{1-2}<0.05; p_{1-3}<0.05	2.78±1.94 p_{1-2}<0.05	0±0 p_{1-3}<0.05

Patients with BAVVCNP had a significantly higher number of premature beats (p=0.009), less common sinus node dysfunction (p<0.05), higher cardiac output (p=0.02), thicker GB wall (p=0.02) compared to those with intact GB, presumably due to the persistent inflammation and high total bilirubin (p=0.07) which is a known indicator of endogenous intoxication. Thus, BAVVCNP is characterized by the signs of GB wall inflammation along with the development of active ectopic foci in the myocardium and increased cardiac output due to autonomic system imbalance.

In contrast to BAVVCNP, patients with PBACNP and removed GB demonstrated some improvement in cardiac function characterized by fewer episodes of ST depression (p<0.05), lower values of cardiac output (p=0.033), and shorter QRS duration (p=0.014). These changes occurred in the background of the diminished pathophysiological influence of the vagus nerve. The latter is proven by a significantly faster heart rate at night-time (p=0.04). Despite that, GB removal was associated with a considerably higher total cholesterol level (p=0.023) that requires the special attention of physicians. Compared with group 1, patients with PBACNP had significantly faster nocturnal heart rate (p=0.011), absence of episodes of ST-segment depression or sinus node dysfunction (both p<0.05), and shorter duration of QRS complexes (p=0.016). These changes were associated with lower monocyte count (p=0.011), which is of utmost importance since the role of monocytes in the destabilization of atherosclerotic plaques and formation of their necrotic cores is well established [10].

To sum up, our study demonstrated that BAVVCNP was characterized by the development of active ectopic foci in the myocardium, increased cardiac output, GB wall thickening, and elevated total bilirubin level. Along with higher nocturnal heart rate and lower cardiac output, patients after cholecystectomy had better intraventricular conduction and no episodes of ST-segment depression, but higher serum cholesterol level. Patients with PBACNP differed from those without cardioneuropathy by faster nocturnal heart rate, absence of episodes of ST-segment depression, shorter QRS duration, and lower blood monocyte count.

Limitations of the study include a small number of participants, no group adjustment according to age, sex, diagnosis, etc., and lack of comparison of clinical data before and after cholecystectomy. Nevertheless, we hope that this study can draw the attention of researchers and clinicians to the viscero-visceral reflex interplay between GB and heart.

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