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PULSE PRESSURE CLASSES AND DOSAGE OF THE MAIN GROUPS OF CARDIAC MEDICATIONS IN PATIENTS AT THE ANNUAL FOLLOW-UP PERIOD AFTER PACING

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Dose factor of the main groups of cardiac medications in five pulse pressure (PP) classes was studied in 220 patients (110 men and 110 women) at the annual stage after pacing, the average age 70 ± 9 years. Patients with the IV and V class of PP require the administration of higher doses of antiarrhythmics, diuretics, calcium channel blockers and ACE inhibitors.

KEY WORDS: pulse pressure, cardiac pacing, cardiac medications

КЛАСИ ПУЛЬСОВОГО АРТЕРІАЛЬНОГО ТИСКУ І ДОЗУВАННЯ ОСНОВНИХ ГРУП КАРДІОЛОГІЧНИХ ПРЕПАРАТІВ У ПАЦІЄНТІВ НА РІЧНОМУ ПЕРІОДІ ПІСЛЯ ПОСТІЙНОЇ ЕЛЕКТРОКАРДІОСТИМУЛЯЦІЇ

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Вивчено коефіцієнт дози кардіологічних препаратів в п'яти класах пульсового артеріального тиску (ПАТ) на річному періоді спостереження після імплантації електрокардіостимуляторів (ЕКС) у 220 пацієнтів (110 чоловіків і 110 жінок) у віці 70 ± 9 років. Пацієнти з імплантованими ЕКС в IV і V класах ПАТ вимагають призначення антиаритмічних препаратів, діуретиків, антагоністів кальцію та інгібіторів ангіотензіперетворюючого ферменту в більш високих дозах.

КЛЮЧОВІ СЛОВА: пульсовий артеріальний тиск, постійна електрокардіостимуляція, кардіологічні

КЛАССЫ ПУЛЬСОВОГО АРТЕРИАЛЬНОГО ДАВЛЕНИЯ И ДОЗИРОВКА ОСНОВНЫХ ГРУПП КАРДИОЛОГИЧЕСКИХ ПРЕПАРАТОВ У ПАЦИЕНТОВ НА ГОДОВОМ ПЕРИОДЕ ПОСЛЕ ПОСТОЯННОЙ ЭЛЕКТРОКАРДИОСТИМУЛЯЦИИ

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Изучен коэффициент дозы кардиологических препаратов в пяти классах пульсового артериального давления (ПАД) на годовом периоде наблюдения после имплантации электрокардиостимуляторов (ЭКС) у 220 пациентов (110 мужчин и 110 женщин) в возрасте 70 ± 9 лет. Пациенты с имплантированными ЭКС в IV и V классах ПАД требуют назначения антиаритмических препаратов, диуретиков, антагонистов кальция и ингибиторов ангиотензипревращающего фермента в более высоких дозах.

КЛЮЧЕВЫЕ СЛОВА: пульсовое артериальное давление, постоянная электрокардиостимуляция, кардиологические препараты

INTRODUCTION

Pulse pressure (PP) is an important component in blood pressure control and outcomes predicting, especially in patients with chronic heart failure (CHF), ischemic heart disease, atrial fibrillation (AF) [1–2]. Pacemaker implantation, changing the

pumping function of the heart, influences the PP, which should be taken into account in the pharmacological support of patients [3–4]. However, changes in the major groups of cardiac medication doses depending on the PBP class in patients at the annual follow-up period after pacemaker implantation has not yet been studied.

OBJECTIVE

The goal of our work was to evaluate the changes in the doses of medications in different classes of PBP in patients at the annual follow-up period after pacemaker implantation.

MATERIALS AND METHODS

220 patients (110 men and 110 women) aged 70 ± 9 years before and after pacemaker implantation and cardiac resynchronization therapy (CRT) were examined: DDD (R) regimen – 132 patients, VVI (R) - 69, CRT (P / D) – 19. Indications for pacing were atrioventricular (AV) block – 125 patients, bundle branches block – 55 patients, sick sinus syndrome (SSS) – 51 patients, permanent atrial fibrillation (AF) – 70 patients, dilated cardiomyopathy (DCM) – 16 patients.

Exclusion criteria were: age less than 40 years, the presence of concomitant angina pectoris of IV functional class (FC), chronic heart failure (CHF) of IV FC, stimulation of the right and / or left ventricle (RV/LV) less than 50 % for the entire observation period.

Before and after pacing, drug therapy was represented by next medications, with average therapeutic doses:

- B01AA anticoagulants – warfarin 5 mg, including new anticoagulants B01AE – direct thrombin inhibitors – dabigatran etexilate (pradaxa 300 mg) and B01AF – direct Xa factor inhibitors – rivaroxaban (xarelto 20 mg);
- B01AC antiplatelet agents – clopidogrel and acetylsalicylic acid 75 mg;
- C01BD antiarrhythmic drugs - amiodarone 200 mg;
- C03 diuretics – hydrochlorothiazide 12.5 mg, furosemide 40 mg, torasemide 5 mg, indapamide 2.5 mg, spironolactone 50 mg;
- C07A β - blockers – metoprolol 100 mg, bisoprolol 5 mg, nebivolol 5 mg, carvedilol 6,25 mg, betaxolol 5 mg, atenolol 50 mg;
- C08 Ca-channel blockers – C08CA dihydropyridine derivatives – amlodipine 10 mg, nifedipine 90 mg and C08DA phenylalkylamine derivatives – verapamil 80 mg;
- C09A angiotensin converting enzyme (ACE) inhibitors – enalapril 10 mg, lisinopril 10 mg, ramipril 5 mg, fosinopril 10 mg;
- C09C angiotensin II receptor blockers (ARB) – losartan 50 mg, candesartan 8 mg;

– C10AA inhibitors of hydroxylmethylglutaryl (HMG) coenzyme A (CoA) reductase – simvastatin 20 mg, atorvastatin 20 mg, rosuvastatin 10 mg.

For each group of drugs, the dose factor was calculated as the average therapeutic dose for the drug taken as 1,0.

Patients were classified into five classes of PP: I – very low PP - less than 20 mm Hg, II – low PP – more than 20 but less than 40 mm Hg, III – normal PP – 40 – 60 mm Hg , IV – high PP – more than 60 but less than 80 mm Hg, V – very high PP – more than 80 mm Hg.

The dose factor was defined in each class of PP for drugs, mentioned above, prior to pacing, in the early period (3–5 days), 6 months and 1 year after pacemaker implantation.

Statistical analysis was performed using Microsoft Excel (for parametric data M – mean value, sd - standard deviation). The significance of differences between groups was determined by a nonparametric Mann-Whitney U-test. The expected result was defined confidence level $p < 0.05$.

RESULTS AND DISCUSSION

In the table the dose factor of the major groups of cardiac drugs in the PP classes in patients in a year after pacing is presented.

Initially, the dose factor of anticoagulants, antiaggregants, ARBs and HMG CoA reductase inhibitors was at the average therapeutic level in all PP classes and did not change at the follow-up stages after pacing.

The dose factor of antiarrhythmic drugs (amiodarone) was equally smaller in II and III classes and greater in the V class of PP. In the early postoperative period, the dose factor was increased in all classes - the higher the PP class, the greater the dose factor - and it subsequently decreased to the initial values in IV, V and, to a greater degree, in II, III PP classes.

Initially, the dose factor of diuretics was equally smaller in II, III and greater in the V classes of PP. It increased in all classes of PAD and, to a greater extent, in IV and V at all stages of follow-up after pacing.

The dose factor of β -blockers was smaller in II and equally greater in IV, V classes of PP. In the early postoperative period, it increased to an equal degree in the IV, V classes and to a lesser degree in the III and II classes of the PP, respectively, and did not change after.

Initially the dose factor of Ca-channels blockers did not change in the early

postoperative period in all PP classes. Six months after pacing it decreased in IV, V classes to the average therapeutic level and, to a greater degree, in class III of PP and remained at the same level. In the II class of PP, Ca-channels blockers were not used throughout the observation period.

Initially, the lowest dose factor of ACE inhibitors was observed in II PP class and the

largest in IV and V classes of PP. The dose factor did not change in all classes in the early postoperative period but decreased in 6 months and a year after pacing – to a greater degree in II and III PP classes and to a lesser degree - in IV and V classes of PP.

Table

The dose factor of the main groups of cardiac medications in PP classes in patients in a first year after pacing (M ± sd)

Meds	Classes of PP															
	II				III				IV				V			
	Before pacing	After 3-5 days	After 6 months	After 1 year	Before pacing	After 3-5 days	After 6 months	After 1 year	Before pacing	After 3-5 days	After 6 months	After 1 year	Before pacing	After 3-5 days	After 6 months	After 1 year
anticoagulants	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0
antiplatelets	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0
antiarrhythmics	1.2 ± 0.3	1.5 ± 0.5	1.3 ± 0.2	1.1 ± 0.4	1.2 ± 0.3	1.5 ± 0.5	1.3 ± 0.2	1.1 ± 0.4	1.6 ± 1.4	1.8 ± 1.2	1.7 ± 1.3	1.6 ± 1.2	1.8 ± 0.2	2 ± 0.2	1.9 ± 0.1 ^{x#}	1.8 ± 0.2
diuretics	1 ± 0.2	1.1 ± 0.2	1.1 ± 0.4	1.1 ± 0.4	1 ± 0.2	1.1 ± 0.3	1.1 ± 0.5	1.1 ± 0.4	1.3 ± 0.5	1.4 ± 0.6	1.5 ± 0.4	1.6 ± 0.2	1.5 ± 0.5	1.6 ± 0.3	1.7 ± 0.2	1.8 ± 0.4
β-blockers	0.6 ± 0.1	0.7 ± 0.2	0.7 ± 0.2	0.7 ± 0.3	0.8 ± 0.4	0.9 ± 0.4	0.9 ± 0.3	0.9 ± 0.4	0.9 ± 0.4	1.0 ± 0.4	1.0 ± 0.3	1.0 ± 0.3	0.9 ± 0.5	1.0 ± 0.5	1 ± 0.2	1 ± 0.4
Ca-channel blockers	-	-	-	-	1 ± 0	1 ± 0	0.9 ± 0.1	0.9 ± 0.1	1.2 ± 0.2	1.2 ± 0.2	1 ± 0	1 ± 0	1.3 ± 0.2	1.3 ± 0.2	1 ± 0	1 ± 0
ACE inhibitors	0.9 ± 0.2	0.9 ± 0.2	0.8 ± 0.3	0.7 ± 0.3	1 ± 0.3	1 ± 0.3	0.9 ± 0.2	0.8 ± 0.2	1.2 ± 0.2	1.2 ± 0.2	1.1 ± 0.4	1 ± 0.3	1.3 ± 0.2	1.3 ± 0.2	1.2 ± 0.3	1.1 ± 0.2
ARBs	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0
Statins	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0

Note: **p* < 0.05 - between values in III and II, IV, V PP classes, ^x*p* < 0.05 - between values in II and IV, V PP classes, [^]*p* < 0.05 - between values in IV and V PP classes, [#] *p* < 0.05 - between values in the same PP class before and after pacing.

The change of the dose factor in groups of cardiac medications in patients at the annual follow-up period after pacing has been studied previously in regard to the duration of the QTc interval, the QRS complex and the functional class of chronic heart failure [5–7].

However, there appears to be no data on dose factor changes dependently on the PP class.

In our work, the increase in dose of diuretics and β-blockers with an increase in the PP class in patients at the annual follow-up period after pacing was shown. Our data is indirectly confirmed by the results of other

authors [8], showed the direct relations between the PP level and the prescribed dose of medications in patients without pacing.

The increase in the dose factor of antiarrhythmic drugs in the early period after pacing with subsequent reduction of their dose, as well as the dose of Ca-channels blockers and ACE inhibitors, indirectly correlates with the data presented in the literature [6–8].

The absence of changes in the dose factor of anticoagulants, antiplatelets, ARBs and HMG CoA reductase inhibitors in all PP classes after pacing is indirectly confirmed by data of some authors [5, 8].

Our study has showed that the dose factor of antiarrhythmic drugs, diuretics, Ca-channels blockers and ACE inhibitors in patients at different follow-up periods after pacing increases with the PP class, which confirms the great importance of assessing the PP class when choosing the doses of cardiac medications.

CONCLUSIONS

1. In patients after pacing, the dose factor of the main groups of cardiac medications correlates with the PP classes and, the greater the PP class, the greater the dose rate of the medications.

2. After pacing an increase of the dose factor of antiarrhythmic drugs (amiodarone) in the early period and diuretics and β -blockers throughout the observation period with an increase in the PP class is required.

3. The long term period of pacing contribute to reduction of the dose factor of antiarrhythmic drugs (amiodarone), Ca-channel blockers and ACE inhibitors in all classes of PP, to a greater extent - in II and III classes.

4. The dose factor of anticoagulants, antiplatelet agents, ARBs and HMG CoA reductase inhibitors does not depend on the PP class and does not change over the entire observation period.

5. Patients after pacing with IV and V classes of PP require the higher doses of antiarrhythmics, diuretics, Ca-channel blockers and ACE inhibitors.

PROSPECTS FOR FUTURE STUDIES

It seems rational to study the optimization of drug therapy in patients after pacing in various classes of PP in a period of more than one year with correction of the frequency of administration and the doses of various medications.

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