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CHANGING OF THE DOSE COEFFICIENT OF THE MAJOR GROUPS OF DRUGS FOR PATIENTS WITH IMPLANTED PACEMAKERS, DEPENDING ON THE STAGE OF HYPERTENSION

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We observed 131 patients (70 men and 61 women) aged 69,5 ± 11,6 at the annual stage of drug therapy after implantation of pacemakers in the DDD / DDDR modes, VVI / VVIR and CRT-P / CRT-D. Patients were divided into 2 groups – I and II stage of AH. . In each group, the dose rate was defined in major groups of cardiac drugs at every stage of research. The results showed that the dose coefficient of the major groups of cardiac drugs in patients with pacemaker and AH was determined by the stage of AH, what is more AH stage III required higher doses of diuretics and anti-arrhythmic drugs than AH stage II during the hole period of observation. Patients with implanted pacemaker and AH require more careful titration of the major groups of cardiac drugs, taking into account the stage of AH.

KEY WORDS: pacing, the stage of hypertension, the dose rate

ЗМІНА КОЕФІЦІЄНТА ДОЗИ ОСНОВНИХ ГРУП МЕДИЧНИХ ПРЕПАРАТІВ У ПАЦІЄНТІВ З ІМПЛАНТОВАННИМИ ЕЛЕКТРОКАРДІОСТИМУЛЯТОРАМИ В ЗАЛЕЖНОСТІ ВІД СТАДІЇ АРТЕРІАЛЬНОЇ ГІПЕРТЕНЗІЇ

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Спостерігали 131 пацієнта (70 чоловіків і 61 жінку) у віці 69,5 ± 11,6 на річному етапі підтримуючої медикаментозної терапії після імплантації електрокардіостимуляторів (ЕКС) в режимах DDD / DDDR, VVI / VVIR і CRT-P / CRT-D. Пацієнти були розділені на 2 групи – I та II стадії АГ. У кожній групі визначався коефіцієнт дози основних груп кардіологічних препаратів на кожному з етапів дослідження. Результати показали, що коефіцієнт дози основних груп кардіологічних препаратів у пацієнтів з ЕКС і АГ визначався стадією АГ, причому на всьому періоді спостереження АГ III стадії вимагала більш високих доз призначення діуретиків та анти аритмічних препаратів, ніж АГ II стадії. Пацієнти з імплантованими ЕКС і АГ вимагають більш ретельного титрування основних груп кардіологічних препаратів з урахуванням стадії АГ.

КЛЮЧОВІ СЛОВА: електрокардіостимуляція, стадія артеріальної гіпертензії, коефіцієнт дози

ИЗМЕНЕНИЕ КОЭФФИЦИЕНТА ДОЗЫ ОСНОВНЫХ ГРУПП МЕДИКАМЕНТОЗНЫХ ПРЕПАРАТОВ У ПАЦИЕНТОВ С ИМПЛАНТИРОВАННЫМИ ЭЛЕКТРОКАРДИОСТИМУЛЯТОРАМИ В ЗАВИСИМОСТИ ОТ СТАДИИ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИИ

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Наблюдали 131 пациента (70 мужчин и 61 женщину) в возрасте 69,5 ± 11,6 на годовом этапе поддерживающей медикаментозной терапии после имплантации электрокардиостимуляторов (ЭКС) в режимах DDD/DDDR, VVI/VVIR и CRT-P/CRT-D. Пациенты были разделены на 2 группы – I и II стадии АГ. В каждой группе определялся коэффициент дозы основных групп кардиологических

препаратов на каждом из этапов исследования. Результаты показали, что коэффициент дозы основных групп кардиологических препаратов у пациентов с ЭКС и АГ определялся стадией АГ, причем на всем периоде наблюдения АГ III стадии требовала более высоких доз назначения диуретиков и антиаритмических препаратов, чем АГ II стадии. Пациенты с имплантированными ЭКС и АГ требуют более тщательного титрования основных групп кардиологических препаратов с учетом стадии АГ.

КЛЮЧЕВЫЕ СЛОВА: электрокардиостимуляция, стадия артериальной гипертензии, коэффициент дозы

INTRODUCTION

Permanent cardiac pacemaker is the leading method for treatment patients with significant bradyarrhythmias, improving survival and quality of life [1–2], however, always requires the modification of concomitant drug therapy [3]. Despite this, the change in the dose of the main groups of cardiac drugs in patients with pacemakers, depending on the stage of arterial hypertension (AH), has not been studied.

OBJECTIVE

The aim of the study was to evaluate the change in the dose of the main groups of cardiac drugs in patients with cardiac pacemaker at the annual stage of observation, depending on the stage of AH.

MATERIALS AND METHODS

131 patients (70 men and 61 women) aged 69,5 ± 11,6 years who underwent permanent pacing were examined in the department of ultrasound and clinical instrumental diagnosis and minimally invasive interventions SI «V. T. Zaytsev Institute of General and Emergency Surgery NAMS of Ukraine». The II stage of AH was diagnosed in 92 patients, 39 – had the III stage of AH according to the recommendations of the Association of Cardiologists of Ukraine [4]. The indications for pacemaker implantation were atrio-ventricular block(AV) – 87 people(62 %), permanent atrial fibrillation(AF) – 19 people (14 %) and sick sinus node syndrome(SSS) – 34 people (24 %) with pacing modes DDD/DDDR and VVI /VVIR and dilated cardiomyopathy (DCM) – 2 people (2 %) with cardiac resynchronization therapy (CRT-P and CRT-D).

Patients aged less than 40 years, presence of concomitant stable angina IV functional class (FC), chronic heart failure (CHF) IV FC and/or stage III, the stimulation of the right ventricle (RV) and/or left ventricular (LV) less than 50 % were excluded from the study.

Drug therapy before the implantation, in the early postimplantation period (3–5 days), after 6 months and 1 year after depending on the stage of AH was represented by the following groups of drugs: C03 diuretics (furosemide, torasemide, hydrochlorothiazide); C07A betaadrenergetic blockers (carvedilol, metoprolol, bisoprolol, nebivolol); C08C A calcium channel antagonists (dihydropyridine derivatives – amlodipine, nifedipine and fenilalkilamin derivatives – verapamil); C09A angiotensin converting enzyme (ACE) inhibitors (enalapril, lisinopril, ramipril); C09C angiotensin II receptor blockers (ARBs) (losartan, candesartan). Apart from this were used: B01A A anticoagulants (warfarin); B01A C antiplatelet therapy (aspirin, clopidogrel); B01A E direct thrombin inhibitors (dabigatran etexilate), and V01A F direct factor Xa inhibitors (rivaroxaban) (new anticoagulants); C01B D01 amiodarone; C01A A hydroxymethylglutaryl inhibitors (HMG) coenzyme A (CoA) (statins) (atorvastatin, simvastatin).

Dose coefficient for each group of drugs has been calculated as the average value among the ratios of each drug dose group versus middle therapeutically for this drug, taken as 1.0. It corresponds to the group of anticoagulants warfarin 5 mg; antiplatelet agents – 75 mg of aspirin and 75 mg clopidogrel; 75 mg of dabigatran etexilate and 5 mg rivaroxaban; 200 mg amiodarone; 10 mg ivabradine; in the group of diuretics – 40 mg furosemide, 5 mg torasemide, 12.5 mg hydrochlorothiazide, 2.5 mg indapamide; in the group of beta-adrenergic blockers – 5 mg bisoprolol, 100 mg metoprolol, 12,5 mg carvedilol, 5 mg nebivolol, 5 mg betaxolol, 50 mg atenolol; in the group of calcium channel antagonists – amlodipine 10 mg, nifedipine 90 mg, verapamil 80 mg; in the group of ACE inhibitors – 10 mg enalapril, 10 mg of lisinopril, 5 mg ramipril, 10 mg fosinopril; group ARBs – 50 mg losartan, 8 mg candesartan; in the group of statins – 20 mg

atorvastatin, 20 mg simvastatin, 10 mg rosuvastatin.

Patients were divided into 2 groups – II and III stage AH. In each group, the dose coefficient for each group of drugs was determined at each stage of the study.

The results obtained are processed after forming the database. Statistical evaluation was performed using Microsoft Excel (for parametric data: M – mean value, sd – standard deviation; for nonparametric data: absolute (n, the number) and relative (p, %) of the unit). The probability of differences between groups was determined using a nonparametric U – Mann-Whitney test. The expected result was determined by level of reliability $p < 0,05$ and $p < 0,01$.

RESULTS AND DISCUSSION

The results of the study of the dose coefficient of prescribing antihypertensive drugs in patients with cardiac pacemaker at the annual stage of observation, depending on the stage of AH are presented in tab. 1.

Table 1

The dose coefficient of prescribing antihypertensive drugs in patients at the annual stage of observation after implantation of cardiac pacemaker, depending on the stage of AH (M ± sd, %)

Drug	Stage of AH							
	II stage				III stage			
	Before implantation	3-5 after	6 month.	1 year	Before implantation	3-5 after	6 month.	1 year
C 03A Diuretics	0,9 ± 0,1	1,1 ± 0,3	1 ± 0,2	1 ± 0,2	1,1 ± 0,8	1,3 ± 0,8	1,2 ± 0,8	1,2 ± 0,8
C07A BAB	0,8 ± 0,4*	0,9 ± 0,3^	0,8 ± 0,3	0,8 ± 0,3	0,9 ± 0,2*	0,9 ± 0,2^	0,9 ± 0,3	0,8 ± 0,4
C08 CA Ca-channel antagonists	0,9 ± 0,1	0,8 ± 0,1	0,9 ± 0,2	0,9 ± 0,2**	1 ±	0,9 ± 0,1	0,9 ± 0,2	0,8 ± 0,2**
C 09A ACE-inhibitor	1 ± 0,1	0,9 ± 0,2^	0,8 ± 0,2	0,8 ± ,2	1 ± 0,2	0,9 ± 0,1^	0,8 ± 0,2	0,8 ± 0,2
C09 C ARBs II	1 ± 0	1 ± 0	1 ± 0	1 ± 0	0	0	1 ± 0	1 ± 0

*Note: * p < 0.05 - between values in the group of AH before the implantation of pacemaker; ^p < 0.05 – between values in the group of AH in the acute period after the implantation of pacemaker; ** P < 0.05 – between values in the group of AH in 1 year after the implantation of pacemaker.*

Initially, the dose coefficient of diuretics was determined by the stage of AH and was higher in the stage III of AH. With the implantation of pacemaker in the early postoperative period, it increased further subsequently decreased in both groups, however, exceeding the initial level.

Before the implantation of pacemaker, the dose coefficient of β-blockers was higher in the group of AH stage III. After the implantation of pacemaker in the early postoperative period, the dosage increased in the II stage of AH, at an annual stage it decreased in both groups.

Initially, the dose coefficient of Ca antagonists was higher in the group stage III of AH. With the implantation of pacemaker in the early postoperative period, the dosage was reduced in both groups, however, by the annual period in the group stage II of AH, it returned to the initial doses. In stage III of AH, the dosage was reduced at all stages of the observation.

Initially the same dose coefficient of ACE inhibitors with implantation of cardiac pacemaker consistently decreased at all stages of observation in both groups.

Before the implantation of cardiac pacemaker, the dose coefficient of ARBs II was higher in the group stage II of AH and remained an average therapeutic at all stages of observation. With stage III of AH, the dosage was increased by the annual stage of observation.

The results of the study of the dose coefficient of prescribing main groups of cardiac drugs in patients with cardiac pacemaker at the annual stage of observation, depending on the stage of AH are presented in tab. 2.

Table 2

The dose coefficient of prescribing main groups of cardiac drugs in patients at the annual stage of observation after implantation of cardiac pacemaker, depending on the stage of AH (M ± sd, %)

Drug	Stage of AH							
	II stage				III stage			
	Before the implantation	3-5 after	6 month.	1 year	Before the implantation	3-5 after	6 month.	1 year
B 01A A Anticoagulant	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0
B 01A C Antiplatelet	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0
C 01B Antiarrhythmic	1,5 ± 0,5	1,6 ± 0,5	1,3 ± 0,9*	1,1 ± 0,9**	1,6 ± 0,7	1,8 ± 0,8	1,2 ± 0,7*	1,2 ± 0,7**
C01A A Statins	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0

*Note: *p < 0.05 - between values in the group of AH in 6 months after implantation of the pacemaker; ** P < 0.05 - between values in the group of AH in 1 year after implantation of the pacemaker.*

Initially, the dose coefficient of antiplatelet agents, anticoagulants and statins was the same in both groups and did not change at all stages of the observation.

Before the implantation of cardiac pacemaker, the dose coefficient of antiarrhythmic drugs was higher in the group stage III of AH. With the implantation of pacemaker, the dosage increased in the early postoperative period and then gradually decreased by the annual period in both groups.

This study showed that implantation of cardiac pacemaker in patients with AH requires an increase in the dose of diuretics, β-blockers and antiarrhythmic drugs in the early postoperative period, which corresponds to the data [5–7].

The dose coefficient of the main groups of cardiac drugs in patients with ECS and AH was determined by the stage of AH, besides, at the annual stage of follow-up AH III stage required higher doses of diuretics and antiarrhythmic drugs than in the group stage II of AH, the data are new and have not been confirmed in the literature.

CONCLUSIONS

1. The dose coefficient of the major groups of cardiac drugs in patients with pacemaker and AH was determined by the stage of AH, what is more AH stage III required higher doses of diuretics and anti-arrhythmic drugs than AH stage II during the hole period of observation.

2. Patients with implanted pacemaker and AH require more careful titration of the major groups of cardiac drugs, taking into account the stage of AH.

PROSPECTS FOR FUTURE STUDIES

It seems appropriate to study drug optimization in patients with AH and cardiac pacing in a period of more than one year with correction of the frequency and doses of the main groups of cardiac drugs.

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