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## FREQUENCY OF DETACHED CARDIAC DRUGS PRESCRIBING IN PATIENTS OF DIFFERENT CLASSES QRS COMPLEX DURATION ON THE PERMANENT PACING BACKGROUND

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The frequency of beta-blockers, amiodarone, antiplatelet agents (acetylsalicylic acid), anticoagulants (warfarin), statins, angiotensin-converting enzyme inhibitors, diuretics and angiotensin II receptor antagonists prescribing was determined in 114 patients (56 – women, 58 – men) with permanent pacemakers in VVI/VVIR (40 patients), DDD/DDDR (26 patient), cardiac resynchronization therapy (14 patients) and separate group was made up of 34 patients with sinus sick syndrome in DDD/DDDR pacing mode in 3 QRS complex duration classes: 1 – under 119 ms (normal), 2 – 120-149 ms (elongate) and more than 150 ms (significantly elongate). The patients' average age was  $69 \pm 7$  years. The results showed that the same groups of drugs are being prescribed as in patients with pacemakers as in patients without them. More frequent prescribing of beta-blockers was associated with prevention of the development of possible device-induced arrhythmias and chronic heart failure. More rare appointment acetylsalicylic acid and statins was associated with the lack of attention to therapeutic support. Frequency of prescribing most of used drugs in patients with implanted pacemaker increases with QRS complex duration class.

**KEY WORDS:** permanent pacing, QRS complex duration, cardiac drugs

## ЧАСТОТА ПРИЗНАЧЕННЯ ОКРЕМИХ ГРУП КАРДІОЛОГІЧНИХ ПРЕПАРАТІВ У ПАЦІЄНТІВ У РІЗНИХ КЛАСАХ ТРИВАЛОСТІ QRS КОМПЛЕКСУ ПРИ ПОСТІЙНІЙ ЕЛЕКТРОКАРДІОСТИМУЛЯЦІЇ

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Вивчена частота призначення бета-блокаторів, аміодарону, антиагрегантів (ацетилсаліцилової кислоти), антикоагулянтів (варфарину), статинів, інгібіторів ангіотензин-перетворюючого ферменту, антагоністів рецепторів ангиотензину II і діуретиків у 114 пацієнтів (56 – жінок, 58 – чоловіків) віком  $69 \pm 7$  років з імплантованими електрокардіостимуляторами в режимах стимуляції VVI/VVIR (40 пацієнтів), DDD/DDDR (26 пацієнт) і окремо з синдромом слабкості синусового вузла (34 пацієнт), кардиоресинхронізуючою терапією (14 пацієнтів) в 3 виділені класи тривалості QRS комплексу: 1 – до 119 мс (нормальний), 2 – 120-149 мс (подовжений) і 3 – більше 150 мс (значно подовжений). У пацієнтів з імплантованими електрокардіостимуляторами у терапевтичному супроводі використовуються ті ж групи лікарських препаратів, що і у пацієнтів поза електрокардіостимуляції. Більш часте призначення бета-блокаторів у них пов'язано з необхідністю профілактики розвитку можливих ЕКС-індукованих аритмій, і більш рідкісне призначення ацетилсаліцилової кислоти і статинів – у зв'язку з недостатньою увагою до їх терапевтичного супроводу. Частота призначення більшості використовуваних лікарських препаратів у пацієнтів з імплантованими електрокардіостимуляторами наростає із збільшенням класу тривалості QRS комплексу.

**КЛЮЧОВІ СЛОВА:** постійна електрокардіостимуляція, тривалість QRS комплексу, кардіологічні препарати

**ЧАСТОТА НАЗНАЧЕНИЯ ОТДЕЛЬНЫХ ГРУПП КАРДИОЛОГИЧЕСКИХ  
ПРЕПАРАТОВ У ПАЦИЕНТОВ В РАЗНЫХ КЛАССАХ  
ПРОДОЛЖИТЕЛЬНОСТИ QRS КОМПЛЕКСА ПРИ ПОСТОЯННОЙ  
ЭЛЕКТРОДИОСТИМУЛЯЦИИ**

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Изучена частота назначения бета-блокаторов, амиодарона, антиагрегантов (ацетилсалициловой кислоты), антикоагулянтов (варфарина), статинов, ингибиторов ангиотензин превращающего фермента, антагонистов рецепторов ангиотензина II и диуретиков у 114 пациентов (56 – женщин, 58 – мужчин) в возрасте  $69 \pm 7$  лет с имплантированными электрокардиостимуляторами в режимах стимуляции VVI/VVIR (40 пациентов), DDD/DDDR (26 пациент) с АВ-блокадой и отдельно с синдромом слабости синусового узла (34 пациент), кардиоресинхронизирующей терапией (14 пациентов) в 3 выделенных классах продолжительности QRS комплекса: 1 – до 119 мс (нормальный), 2 – 120-149 мс (удлиненный) и более 150 мс (значительно удлиненный). Результаты показали, что у пациентов с имплантированными ЭКС в терапевтическом сопровождении используются те же группы лекарственных препаратов, что и у пациентов вне ЭКС. Более частое назначение бета-блокаторов у них связано с необходимостью профилактики развития возможных ЭКС-индуцированных аритмий и хронической сердечной недостаточностью, и более редкое ацетилсалициловой кислоты и статинов – в связи с недостаточным вниманием к их терапевтическому сопровождению. Частота назначения большинства используемых лекарственных препаратов нарастает с увеличением класса продолжительности QRS комплекса.

**КЛЮЧЕВЫЕ СЛОВА:** постоянная электрокардиостимуляция, продолжительность QRS комплекса, кардиологические препараты

## INTRODUCTION

QRS complex as electrocardiograph phenomenon is a measure of the duration of one of the most critical periods of systole, namely isovolumetric contraction [1]. The increase of QRS complex duration is considered as independent predictor of increased mortality and rehospitalization in patients with chronic heart failure (CHF) with reduced ejection fraction (EF) and coronary heart disease (CHD) [2-4], including with implanted pacemakers [5].

The drugs which are used in patients with pacemaker affect not only the work of the device, but QRS complex duration also. That is why the influence of these drugs cannot be ignored [6]. Studies which investigate drugs effects on different QRS complex duration are limited [7-9], concerning patients with pacemaker are united [10], and taking into account QRS complex duration were not conducted.

## OBJECTIVE

The purpose of this study is to evaluate the frequency of prescribing different groups of cardiac drugs in patients with permanent pacemaker in QRS complex duration classes.

## MATERIALS AND METHODS

114 patients (56 – women, 58 – men) who underwent permanent pacemaker therapy were examined in the department of ultrasound, clinical and instrumental diagnosis and minimally invasive technologies SI «Zaitsev V.T. Institute of General and Emergency Surgery NAMS of Ukraine» in pacing modes VVI/VVIR (40 patients), DDD/DDDR (26 patients) with atrio-ventricular block (AV-block) and separately with sick sinus syndrome (SSS) (34 patients), cardiac resynchronization therapy (CRT) (14 patients) in 3 selected QRS complex duration classes: 1 – under 119 ms (normal) , 2 – 120-149 ms (extended) and more than 150 ms (significantly extended). Patients' average age was  $69 \pm 7$  years.

QRS complex duration was measured as the average of three consecutive ECG complexes in leads II, V5, V6 on the computer electrocardiograph Cardiolab+2000 in the early postoperative period (third - fifth day after pacemaker implantation).

Frequency of beta-blockers, amiodarone, antiplatelet agents (acetylsalicylic acid), anti-coagulants (warfarin), statins, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor antagonists II (ARA II) and diuretics was determined.

Frequency of different groups cardiac drugs prescribing was calculated in the relative units (p, %) in Microsoft Excel, and the average error percentage (sp) was determined too. The significance of differences between the values in QRS complex duration classes was estimated using the non-parametric U-

Mann–Whitney test. The differences were considered as reliable if  $p < 0.05$ .

## RESULTS AND DISCUSSION

Frequency of different groups of cardiac drugs prescribing in patients with implanted pacemaker is presented in table.

Table

**Frequency of different groups of cardiac drugs prescribing in QRS complex duration classes, (% ± sp)**

Drugs	Total patients, n	Frequency of prescribing			
		Total	QRS complex duration classes. (ms)		
			< 119	120-149	> 150
Beta-blockers	68	60 ± 5	30 ± 15	41 ± 6**	86 ± 5***
Amiodarone	17	15 ± 3	10 ± 9	13 ± 5	18 ± 5
Antiplatelet agents (acetylsalicylic acid)	34	30 ± 4	30 ± 15	22 ± 6	38 ± 7
Anticoagulants (warfarin)	12	11 ± 3	10 ± 9	9 ± 4	12 ± 5
Statins	29	25 ± 4	20 ± 13	19 ± 5**	34 ± 7
ACE inhibitors	70	61 ± 5	40 ± 15	43 ± 7**	94 ± 3***
ARA II	32	28 ± 4	10 ± 9	17 ± 5	24 ± 6
Diuretics	26	23 ± 4	20 ± 13	17 ± 5	30 ± 6

Legend: n – the absolute value; sp – average error rate;

\*  $p < 0.05$  – reliable level of differences in QRS complex duration classes 1 and 2;

\*\*  $p < 0.05$  – reliable level of differences in QRS complex duration classes 2 and 3;

\*\*\*  $p < 0.05$  – reliable level of differences in QRS complex duration classes 1 and 3.

Beta-blockers and ACE inhibitors were prescribed more frequently in the studied groups of drugs. The frequency of their prescribing was the same, what corresponds to the data [11, 12]. The frequency of their prescribing was increased from one to another QRS complex duration classes, as well as increased functional classes of CHF in patients with extended and significantly extended QRS complex. The frequency of beta-blockers prescribing in patients with implanted pacemaker was higher than in patients without pacemaker, what was associated with the possible development of pacemaker-induced arrhythmias [13].

The next most frequently prescribed drugs were antiplatelet agents (ASA) and ARA II, it was identified no significant differences in their prescription between QRS complex duration classes. We did not found the literature data on the frequency of ASA and

ARA II prescription in patients with implanted pacemaker. The frequency of ASA prescription in our group of patients was significantly lower than in patients without implanted pacemaker [14], and the frequency of ARA II prescription corresponded to that in patients without pacemaker [15].

Despite the fact that statins are shown a greater extent in patients with permanent pacemaker vs. patients without pacemaker, due to their pleiotropic anti-fibrotic and antiarrhythmic effects regarding the possible development of atrial fibrillation (AF) [16, 17], they were prescribed only in 25 % of our patients, what was significantly lower frequency than in patients with coronary atherosclerosis without pacemaker, which was more than 53 % according to a study EUROASPIRE II [18]. Increased frequency of statin use in class 3 against classes 1 and 2

QRS complex duration was explained by more severe condition of this class of patients.

Diuretics and amiodarone were more rarely prescribed, and it was identified no significant differences in the frequency of prescribing between QRS complex duration classes. It is known that diuretics prescribing and as a result hypokalemia is associated with QRS complex duration prolongation [19].

Warfarin was the least administered drug. It was prescribed in patients with atrial fibrillation mainly. Strategy of continuous warfarin therapy is associated with reduced risk of thromboembolic complications in these patients with a background on permanent pacing [20].

The frequency of calcium channel blockers, ivabradine, digoxin, direct peroral anticoagulants did not taken into account in our study because of their infrequent use.

In accordance with the results obtained in patients with permanent pacemaker the same groups of cardiac drugs are used as in patient without pacing, however, the frequency of assignment between the drugs can be substantially different. Significantly more frequent use of beta-blockers in patients with permanent pacemaker was explained by arrhythmogenic effects of pacing therapy [13]. Less frequent use of drugs of other groups may be exists due to insufficient attention to their

therapeutic support. The frequency of cardiac drug prescribing in patients with permanent pacemaker is significantly affected by the QRS complex duration class.

## CONCLUSIONS

1. The same groups of drugs are used as in patients with permanent pacemakers as in patients without pacing. More frequent prescribing of beta-blockers was associated with prevention of development of possible pacemaker-induced arrhythmias. More rare appointment of acetylsalicylic acid and statins are linked to the lack of attention to their therapeutic support.

2. Prescribing frequency of most used in patients with pacemakers drugs increases with QRS complex duration class, what probably reflects more severe clinical situation and a worse prognosis in these patients.

3. Patients with pacemakers in QRS complex duration classes 120-149 ms and > 150 ms are need more intensive drug therapy.

## PROSPECTS FOR FUTURE STUDIES

It seems appropriate to explore the possibilities of optimization of medical support patients with implanted pacemaker taking into account QRS complex duration class.

## REFERENCES

1. Su Y. Relationships between paced QRS duration and left cardiac structures and function / Y.Su, W.Pan, X.Gong [et al.] // *Acta Cardiologica*. – 2009. – Vol. 64(2). – P. 231–238.
2. Tavazzi L. Multicenter prospective observational study on acute and chronic heart failure: one-year follow-up results of IN-HF (Italian Network on Heart Failure) outcome registry / L. Tavazzi, M.Senni, M. Metra [et al.] // *Circ Heart Fail*. – 2013. – Vol. 6(3). – P. 473–481.
3. Lin Y. J. Incremental changes in QRS duration predict mortality in patients with atrial fibrillation / Y. J. Lin, Y. B. Liu, C. C. Chu [et al.] // *Pacing Clinical Electrophysiology*. – 2009. – Vol. 32. – P. 88–94.
4. Chen S. Paced QRS duration as a predictor for clinical heart failure events during right ventricular apical pacing in patients with idiopathic complete atrioventricular block: results from an observational cohort study (PREDICT-HF) / S. Chen, Y. Yin, X.Lan [et al.] // *European Journal of Heart Failure*. – 2013. – Vol. – 15(3). – P. 352–359.
5. Sumiyoshi M. Clinical significance of QRS duration during ventricular pacing / M. Sumiyoshi, Y. Nakata, T. Tokano [et al.] // *Pacing Clinical Electrophysiology*. – 1992. – Vol. 15. – P. 1053–1064.
6. Fonarow G.C. Association between performance measures and clinical outcomes for patients hospitalized with heart failure / G.C. Fonarow, W.T. Abraham, N.M. Albert [et al.] // *JAMA*. – 2007. – Vol. 297. – P. 61–70.
7. Greenspon A.J. The effects of antiarrhythmic drugs on the signal-averaged electrocardiogram in patients with malignant ventricular arrhythmias / A.J. Greenspon, G.A. Kidwell, M. DeCaro [et al.] // *Progress of Cardiovascular Diseases*. – 1993. – Vol. 35. – P. 399–406.
8. Starr J. M. Hypertensive Old People in Edinburgh (HOPE) Study: electrocardiographic changes after captopril or bendrofluazide treatment / J. M. Starr, L. J. Whalley // *Age Ageing*. – 1993. – Vol. 22 (5). – P. 343–348.

9. Bashir Y. Comparative electrophysiological effects of captopril or hydralazine combined with nitrate in patients with left ventricular dysfunction and inducible ventricular tachycardia / Y. Bashir, J. F. Sneddon, S. O. Nunain [et al.] // *British Heart Journal*. – 1992. – Vol. 67. – P. 355–360.
10. Takemoto Y. Beta-blocker therapy induces ventricular resynchronization in dilated cardiomyopathy with narrow QRS complex / Y. Takemoto, T. Hozumi, K. Sugioka [et al.] // *Journal of American College of Cardiology*. – 2007. – Vol. 49. – P. 778–783.
11. Wang N. C. EVEREST Investigators. Clinical Implications of QRS Duration in Patients Hospitalized With Worsening Heart Failure and Reduced Left Ventricular Ejection Fraction / N. C. Wang, A. P. Maggioni, M. A Konstam [et al.] // *JAMA*. – 2008. – Vol. 299. – P. 2656–2666.
12. Patti G. Randomized trial of atorvastatin for reduction of postoperative atrial fibrillation in patients undergoing cardiac surgery: results of the ARMYDA-3 (Atorvastatin for Reduction of MYocardial Dysrhythmia After cardiac surgery) study / G. Patti, M. Chello, D. Candura [et al.] // *Circulation*. – 2006. – Vol. 114. – P. 1455–1461.
13. Григоров С.С. Электрокардиограмма при искусственном водителе ритма сердца / С.С. Григоров, Ф.В. Вогчал, О.В. Костылева // *Медицина*. – 1990. – С. 103–106.
14. Silva M.V. Platelet antiaggregants in primary and secondary prevention of atherothrombotic events / M.V. Silva, L.M. Dusse, L.M. Vieira [et al.] // *Arquivos Brasileiros De Cardiologia*. – 2013. – Vol. 100(6). – P. 78–84.
15. Долженко М.Н. Возможности применения блокаторов рецепторов ангиотензина II в лечении пациентов с ишемической болезнью сердца / М.Н. Долженко, Ю.А. Лучинская // *Ліки України*. – 2012. – №3–4 (2). – С. 65–70.
16. Gillis A.M. Beneficial effects of statin therapy for prevention of atrial fibrillation following DDDR pacemaker implantation / A.M. Gillis, M. Morck, D.V. Exner [et al.] // *European Heart Journal*. – 2008. – Vol. 29. – P. 1873–1880.
17. Tsai C.T. Atorvastatin prevents atrial fibrillation in patients with bradyarrhythmias and implantation of an atrial-based or dual-chamber pacemaker: a prospective randomized trial / C.T. Tsai, L.P. Lai, J.J. Hwang [et al.] // *American Heart Journal*. – 2008. – Vol. 156. – P. 65–70.
18. Clinical reality of coronary prevention guidelines: a comparison of EUROASPIRE I and II in nine countries. EUROASPIRE I and II Group. European Action on Secondary Prevention by Intervention to Reduce Events // *Lancet*. – 2001. – Vol. 357(9261). – P. 995–1001.
19. Мальцев В. И. Гомеостаз натрия и калия в организме, его нарушения / В.И. Мальцев, В.К. Казимирко // *Здоровье Украины*. – 2004. – № 89. – С. 15–18.
20. Ghanbari H. Meta-analysis of safety and efficacy of uninterrupted warfarin compared to heparin-based bridging therapy during implantation of cardiac rhythm devices / H. Ghanbari, W.S. Phard, H. Al-Ameri [et al.] // *American Journal of Cardiology*. – 2012. – Vol. 110. – P. 1482–1488.