Effects of Cardiac Drugs on Pacemaker Therapy: A Review Article

Edafe EA1,2*, Okoro TEO1, Akpa MR2 and Stanley CN3

1Department of Internal Medicine, Niger Delta University, Amassoma, Nigeria.
2University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria.
3Department of Pharmaceutical Microbiology, University of Port Harcourt, Nigeria.

*Correspondence:
Edafe EA, Department of Internal Medicine, Niger Delta University, Amassoma, Nigeria.

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ABSTRACT

A pacemaker patient who takes cardiac medication must be informed of the possible drug interaction. Medication effect on pacemaker function could lead to increase or decrease threshold. The pacemaker output should be programmed to allow an adequate pacing margin of safety. The objective of this review article was to discuss the effects of cardiac medications on pacemaker threshold.

Keyword
Pacemaker, Cardiac drugs, Effects of cardiac drugs.

Introduction

Drug effect on pacemaker function could lead to increase or decrease threshold. Some cardiac drugs have been shown to cause alteration in pacemaker activities [1-3].

This alteration could present in decrease or increase threshold. Some of these drugs that persistently result in pacemaker alterations are classified as (1) medications that increase pacemaker threshold (2) medications that lower the pacemaker threshold.

Medications That Increase Pacemaker Threshold

Class I anti-arrhythmic drugs

Class IA drugs eg quinidine and procainamide may increase pacing thresholds [1-3]. Procainamide may lead to failure in capturing at toxic level [4]. It increases in threshold of pacemaker activity in humans. Quinidine may increase threshold of pace maker activity.

Class IB drugs (lidocaine and mexilitine) are not thought to have a clinically significant effect on pacing thresholds [1-3]. Individual studies describing an effect of each of these agents in humans and/or animals, the use of these drugs in paced patients is safe.

Class IC drugs eg flecainide, encaidine, and propafenone increase pacing threshold. These drugs should be avoided in patients with pacemaker-dependent [5-8].

Medications That Lower the Pacemaker Threshold

Class IC drugs must be used cautiously in pacemaker patients, especially in those who are pacemaker-dependent. The possibility of a rise in threshold should always be considered in pacemaker-dependent patients. Pacemaker output should be programmed to allow an adequate pacing margin of safety.

Class II medications

Beta blockers: Sympathetic stimulation lowers pacing threshold. So beta-blockers would raise pacing threshold. But studies have been inconsistent. In clinical practice, these class of drugs do not show a significant rise in pacemaker threshold [1-3].

Calcium channel blockers have not been reported to have any significant effect on chronic pacing thresholds in humans [1-3].

Class III medications

Amiodarone has been shown to affect defibrillation thresholds, but there is no convincing evidence that it significantly affects pacing thresholds.

Medications That Lower the Pacemaker Threshold

Corticosteroids lower pacemaker threshold. Steroid-eluting lead prevents the usual rise in pacing threshold after pacemaker implantation [9]. Sympathomimetic agents, such as epinephrine, ephedrine, and isoproterenol, also have been reported to decrease pacing threshold [10].

Sensing thresholds are much less commonly recognized to
be affected by cardioactive drugs. Significant clinical sensing problems have not been found with any of the drugs discussed in relation to pacing threshold.

<table>
<thead>
<tr>
<th>Vaughan Williams Classification</th>
<th>Anti-arrhythmic Drugs</th>
<th>Effect for pacing threshold</th>
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<tbody>
<tr>
<td>1A</td>
<td>Quinidine ↑</td>
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<tr>
<td></td>
<td>procainamide ↑↑</td>
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<td></td>
<td>ajimaline ↑</td>
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<td></td>
<td>disopyramide ↑</td>
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<td></td>
<td>cibenzoline ↑↑</td>
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<td></td>
<td>pirmeno ↑</td>
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<td>1B</td>
<td>Aprindine ↑</td>
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<td></td>
<td>lidocaine →</td>
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<td>phenytoin →</td>
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<td>mexiletine ↑</td>
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<td>IC</td>
<td>Propafenone ↑↑↑</td>
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<td></td>
<td>pilosicainide ↑↑↑</td>
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<td>flecainide ↑↑↑</td>
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<tr>
<td>1A</td>
<td>Propranolol →</td>
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<tr>
<td>1B</td>
<td>Amiodarone →</td>
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<td>sotalol →</td>
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<td>1C</td>
<td>Verapamil →</td>
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<td>Digoxin → or ↑</td>
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Table 1: Effects of anti-arrhythmic drugs for pacing threshold.
Key: ↓: decrease; →: no change; ↑: increase.

Antihypertensive in pacemaker patients
Data on the effect of many drugs (calcium channel blockers, ACE inhibitors, angiotensin II receptor antagonists, and others.) used for the treatment of patients with cardiovascular disease with implanted pacemaker are scars. In the medical support of patients with hypertension and an implanted pacemaker is used angiotensinconverting enzyme (ACE) inhibitors, angiotensin II receptor antagonists (ARA, sartans), beta-blockers (BAB), diuretics, calcium channel blockers. For the treatment of comorbid cardiovascular diseases is used ivabradine, digoxin, statins, warfarin, dabigatran, rivaroxaban, apixaban, aspirin, amiodarone, which may influence the course of hypertension [11,12].

Angiotensin Converting Enzyme (ACE) inhibitors
ACE inhibitors are among the common drugs used in the treatment of hypertension, left ventricular hypertrophy and heart failure. They have protective effects on target organs [13,14]. They provide cardio-vascular and renoprotective effect and the reduction in the incidence of cardiovascular complications and increases life expectancy of patients with their long-term use [13,15].

ACEIs have demonstrated it ability to cause LVH regression [16]. Several randomized studies CONSENSUS and SOLVD have shown, that treatment with ACE inhibitors led to reduction in mortality (relative risk reduction (RR) of 27% in CONSENSUS and 16% in SOLVD).

The PROGRESS study involved 1923 patients. It showed that perindopril significantly (by 28%) reduced the risk of a recurrent stroke in patients with cerebrovascular diseases on the background of AH.it also significantly reduced the risk of cardiovascular disease (26%) and the risk of myocardial infarction (38%) [3,16]. The HOPE trial also showed that ramipril compared with placebo significantly caused regression of LVH [17].

ACE inhibitors in patients with pacemaker have been noted to cause lengthening of QTc intervals in 31% of patients with cardiac pacers [18,19]. The use of ACE inhibitors in patients with a pacemaker and cardiac resynchronization therapy may lead to increase in left ventricular ejection fraction [20]. There are no data on the effect of ACE inhibitors in patients with AH and pacemaker.

Angiotensin II Receptor Antagonists (ARA)
They are used in the treatment of hypertension and heart failure. They differ from ACEIs in that they do not produce dry cough and angioneurotic edema [21]. ARB could reduce systolic and diastolic BP by 50–70% within 24 hours [22-24]. LIFE trial showed a 13% reduction in major cardiovascular events and greater regression of LVH in the losartan group [25-27].

ARB have shown to lengthen QTc interval by 8-13% in patients with pacemaker [19]. There are no trials on the effect of ARB in patients with arterial hypertension and a pacemaker.

Non-Dihydropyridine Derivatives (Diltiazem and Verapamil)
They are used for treatment of ischemic disease and hypertension [28,29]. There is no clinical trials on the effects of diltiazem on ischemic heart disease, pacemaker and hypertension.

The effect of verapamil in patients with cardiac pacing has been shown to increase percentage of stimulation [28]. Cardiac pacing had no effect on the frequency and dosage of the prescription of calcium channel blockers [19]. However, there are no data on the effect of calcium channel blockers in patients with AH and pacemaker.

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References
5. Hellestrander KJ, Burnett PJ, Milne JR. Effect of the antiarrhythmic agent flecainide acetate on acute and chronic


