Introduction

Anti-arrhythmic drugs are often prescribed for pacemaker and implantable cardioverter-defibrillator (ICD) patients for a number of reasons. However, we must be aware that anti-arrhythmic drugs may influence pacing threshold and defibrillation threshold. Sometimes awareness on the part of the physician is critical for patients with an implanted pacemaker or an ICD.

I. Effects of anti-arrhythmic drugs on pacing threshold

Patients with implanted pacemakers often have tachyarrhythmias, such as atrial fibrillation. Anti-arrhythmic drugs usually have bradycardiac effects.\textsuperscript{1–8} Pacemaker implantation allows the use of anti-arrhythmic drugs for patients with bradycardia. However, pacing threshold is sometimes increased by the anti-arrhythmic drugs.

Factors affecting pacing threshold are posture, exercise, diet, sleep, minerals, pH, hormones, autonomic tones, and underlying diseases.\textsuperscript{2} Type of pacing leads\textsuperscript{9} and anti-arrhythmic drugs\textsuperscript{1–8} also have great impacts on the pacing threshold.

Effects of anti-arrhythmic drugs for pacing threshold are shown in Figure 1. Effects of anti-arrhythmic drugs for pacing threshold are summarized as follows:

1. Vaughan Williams class Ia anti-arrhythmic drugs may increase pacing threshold. However the effects are usually minimallittle.
2. Class Ib anti-arrhythmic drugs have little influence on pacing threshold.
3. Class Ic anti-arrhythmic drugs have the strongest effects on increasing pacing threshold. It may increase the pacing threshold up to five-fold.
4. Class II, III, IV anti-arrhythmic drugs have little influence on pacing threshold.

A significant positive correlation between prolongation of QRS and increase of pacing threshold under the use of propafenone has been reported\textsuperscript{8} and class Ic anti-arrhythmic drugs have the strongest effects for increasing pacing threshold. Therefore, increasing effects of pacing threshold may be related to suppression of Vmax in phase 0 of the cardiac muscle action potential. Pacing threshold is decreased by increasing sympathetic nervous tones and is increased by increasing parasympathetic nervous tones. Adverse effects of class Ia anti-arrhythmic drugs on pacing threshold may be suppressed by anticholinergic effect of class Ia anti-arrhythmic drugs. Influences of anti-arrhythmic drugs are different patient to patient although the reasons are not clear. Pacing threshold is dramatically increased by anti-arrhythmic drugs in a particular patient; how-

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<table>
<thead>
<tr>
<th>Vaughan Williams classification</th>
<th>Anti-arrhythmic drugs</th>
<th>Effect for pacing threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>quinidine, procainamide, ajimaline, disopyramide, cibenzoline, pirmenol</td>
<td>↑↑↑↑↑↑ (?)</td>
</tr>
<tr>
<td>Ib</td>
<td>lidocaine, phenytoin, mexiletine</td>
<td>↑</td>
</tr>
<tr>
<td>Ic</td>
<td>propafenone, pilsicainide, flecaïnide</td>
<td>↑↑↑↑↑ ↑↑↑↑↑</td>
</tr>
<tr>
<td>II</td>
<td>propranolol</td>
<td>→</td>
</tr>
<tr>
<td>III</td>
<td>amiodarone, sotalol</td>
<td>→</td>
</tr>
<tr>
<td>IV</td>
<td>verapamil</td>
<td>→</td>
</tr>
<tr>
<td>V</td>
<td>digitalis</td>
<td>→↓</td>
</tr>
</tbody>
</table>

\(\downarrow\): decrease, \(\rightarrow\): no change, \(↑\): increase
ever, pacing threshold is not changed by anti-arrhythmic drugs in other patients. As the pacing output is usually set at more than twice the safety margin, there is no problem if the increase of pacing threshold is less than that level. However, when the increase of pacing threshold is greater than twice, pacing failure may occur.

Steroid-eluting electrodes suppress the increase of pacing threshold after pacemaker implantation. One report shows that steroid-eluting electrodes may suppress the adverse effect of anti-arrhythmic drugs on the pacing threshold. However, these effects still remain unclear.

II. Effects of anti-arrhythmic drugs on defibrillation threshold (DFT)

ICD is highly effective for lethal arrhythmia in terms of improvements of survival rates. However, ICD does not have suppressive effects on the incidence of ventricular tachycardia (VT) or ventricular fibrillation. Inappropriate shock is also a big problem. Atrial fibrillation is one of the most common reasons of inappropriate shock. Anti-arrhythmic drugs are used for the suppression of atrial fibrillation. DC shock is very painful for patients and both appropriate and inappropriate DC shock may be suppressed by the use of anti-arrhythmic drugs. Anti-arrhythmic drugs, especially amiodarone, are often prescribed in ICD patients for this reason. Intervals of VT are sometimes prolonged by anti-arrhythmic drugs. Slowing the VT rates sometimes makes detection of VT difficult. Moreover, anti-arrhythmic drugs may have influences for DFT. Cardioversion may fail if DFT increases over the energy of DC setting.

Effects of anti-arrhythmic drugs on the defibrillation threshold (DFT) are shown in Table 1. As DFT measurements may be difficult, results are not same in each report. Generally, Ikr blockers may improve DFT, and Iks blockers may increase DFT. Many anti-arrhythmic drugs such as amiodarone (chronic phase), atropine, diltiazem, verapamil, and flecainide may increase DFT. Disopyramide, procaainamide, and propafenone do not change DFT. However, opinions differ regarding this matter.

We should pay attention to amiodarone. Although amiodarone can improve DFT in the acute phase (Ikr blocking effects are dominant), amiodarone increases DFT in the chronic phase (Iks blocking effects are dominant). Fortunately, the OPTIC study showed that there is little clinical impact on the deteriorated effects for DFT of amiodarone. Although amiodarone increased DFT, the effect with modern ICD systems is very small. Therefore, DFT reassessment after the institution of antiarrhythmic drug therapy with amiodarone may not be required routinely.

Table 1 Effects of anti-arrhythmic drugs for defibrillation threshold

<table>
<thead>
<tr>
<th>Drug</th>
<th>Increase</th>
<th>No Change</th>
<th>Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone (chronic)</td>
<td>β blocker</td>
<td>Amiodarone (acute)</td>
<td></td>
</tr>
<tr>
<td>Atropine</td>
<td>Disopyramide</td>
<td></td>
<td></td>
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<tr>
<td>Diltiazem</td>
<td>Procaainamide</td>
<td></td>
<td></td>
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<tr>
<td>Verapamil</td>
<td>Propafenone</td>
<td></td>
<td></td>
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<tr>
<td>Flecainide</td>
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</table>

References

5) Huang SK, Hedberg PS, Marcus FI: Effects of anti-arrhythmic drugs on the chronic pacing threshold and the endocardial R wave amplitude in the conscious dog. PACE 1986; 9: 660–669