Basic Cardiac Electrophysiology and Common Drug-induced Arrhythmias

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KEYWORDS

- Drug-induced • Arrhythmias • Electrocardiography • Automaticity
- Triggered activity • Re-entry • Proarrhythmic

KEY POINTS

- Cardiac function is dependent on normal electrical and mechanical activity.
- Many drugs administered to alleviate symptoms also have the negative side effect of altering cardiac function.
- At the cellular level, drugs often block or interact with ion channel functioning and most commonly impact cardiac repolarization.
- Triggered activity, automaticity, and re-entry are 3 typical mechanisms for drug-induced arrhythmia.
- Understanding cell activity and action potentials helps in understanding how drugs can interact and cause arrhythmias.

INTRODUCTION

Drugs can be a double-edged sword, providing the benefit of symptom alleviation and disease modification, but potentially causing harm from adverse cardiac arrhythmic events. Drug-induced arrhythmias are defined as the production of de novo arrhythmias or aggravation of existing arrhythmias as a result of previous or concomitant pharmacologic treatment.[1] Drug-induced arrhythmia episodes were first described in patients receiving quinidine,[2] an antiarrhythmic, and within the last few years a variety of cardiovascular and noncardiovascular drugs have been shown to possess proarrhythmic properties. These properties arise from several electrophysiologically distinct and identifiable mechanisms,[3] the most common of which impairs cardiac

repolarization.[4] The purpose of this review is to summarize normal cardiac cell and tissue function, to look at the actions of common drugs that affect cardiac repolarization, and to examine the adverse effects of commonly administered antiarrhythmics.

CARDIAC ACTION POTENTIAL

At an organ level, normal electrical activation of the heart begins in the sinus node, initiating an ongoing activation of atrial muscle cells and continuing to the atrioventricular (AV) node. The AV node delays the activation toward the ventricles, optimizing the time for filling of the ventricles by the atrial contraction. In the ventricles, the AV node is connected to the His-Purkinje system. The His-Purkinje system acts as a fast "highway" distributing the electrical activation in the ventricles toward the ventricular myocardial cells. The specialized cells forming this conduction system are known as pacemaker cells (sinus nodal, AV nodal, and His-Purkinje cells), and the contractile units within the heart are known as myocardial cells (atrial and ventricular).

All myocardial cells possess 2 inherent characteristics that can contribute to arrhythmias: conductivity (the ability to transmit an electrical impulse) and excitability (the ability to respond to an electrical impulse). Pacemaker cells also possess an extra characteristic that can cause arrhythmias, automaticity: the ability to spontaneously generate electrical impulses. Central to the ability to perform any of these functions is the cells action potential (AP) (Fig. 1). The AP is an elegant interplay of multiple types of ions moving over the myocardial cell membrane. Regulating most ion movements are special types of transmembrane proteins called voltage-gated ion channels. These ion channels span across the cell membrane and provide a mechanism, much like a doorway, for the movement of ions into and outside the cell. Review of cellular cardiac depolarization and repolarization illustrates the function of these ion channels.

When a stimulus reaches a resting myocardial cell, alterations in the membrane's potential triggers specific voltage-gated sodium channels to open. Opening these channels allows sodium to rush into the cell, resulting in cardiac depolarization, and is considered phase 0 of the AP. In phase 1 of the AP, the increase in membrane potential peaks, triggering the closure of the sodium voltage-gated channels and the
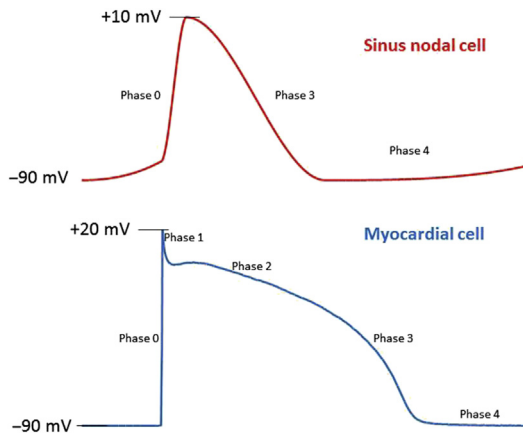

Fig. 1. Myocardial and pacemaker APs. The pacemaker cells do not express phases 1 and 2 of the typical AP of myocardial cells and never truly reach a "resting state." (*Courtesy of Peter van Dam, PhD, PEACS BV, Arnhem, Netherlands.*)