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Propafenone Toxicity After Amiodarone Initiation: A Case Report

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Abstract

Introduction: Propafenone is a class 1c antiarrhythmic that is used for the treatment of ventricular and supraventricular arrhythmias. Propafenone acts to block fast inward sodium channels in a rate dependent manner to prolong the QRS interval. The effect of acute propafenone toxicity mainly involve cardiovascular symptoms including hypotension, bradycardia, ventricular dysrhythmias, widening QRS, and heart block.

Case Presentation: A 67-year-old female presented to the ICU status post aortic valve replacement, ascending aorta replacement, and left atrial appendage clip. The patient was initiated on an amiodarone infusion for atrial fibrillation prophylaxis. She was restarted on home propafenone on post-operative day 2. On post-operative day 9 an EKG illustrated a wide complex tachycardia. Propafenone was immediately discontinued. On post-operative day 11 the patient converted to narrow complex atrial fibrillation with slowing of her heart rate consistent with the use-dependent nature of 1c antiarrhythmics.

Conclusion: Cytochrome P450 inhibition caused by post-operative amiodarone administration was the likely cause of propafenone toxicity in this patient. This case demonstrates the importance of understanding the pharmacokinetics and pharmacodynamics of specific medications.

Keywords: Propafenone toxicity, Amiodarone, Cytochrome P450

Introduction

Propafenone is a class 1c antiarrhythmic that is used for the treatment of ventricular and supraventricular arrhythmias. As a class 1c antiarrhythmic, propafenone acts to block fast inward sodium channels in a rate dependent manner to prolong the QRS interval [1]. Propafenone also exhibits B-adrenoreceptor antagonist and weak calcium antagonist activity [2]. Propafenone is available in oral and intravenous formulations. It is hepatically metabolized via cytochrome p450 into two active metabolites, 5-hydroxypropafenone and 5-depropylpropafenone. Half-life ranges from 2-10 hours in patients with normal cytochrome p450 activity and 12 to 32 hours in slow metabolizers, which comprises approximately 7% of the population [2, 3].

We report a case of propafenone toxicity in a patient upon resumption of her home regimen after having no prior side effects.

Case presentation

A 67-year-old female with a history of hypertension, diastolic heart failure, paroxysmal atrial fibrillation, bicuspid aortic valve, and chronic kidney disease presented to the operating room for aortic valve replacement, ascending aorta replacement, and left atrial appendage clip. Home medications included propafenone 300 mg three times daily to control her atrial fibrillation.

Surgery and subsequent intensive care unit (ICU) admission were unremarkable. A baseline EKG was obtained on post-operative day 1 (Fig. 1). The patient was initiated on a low dose amiodarone infusion at 0.5mg/kg for atrial fibrillation prophylaxis. She was restarted on home propafenone on post-operative day 2 and was transferred to a telemetry floor on post-operative day 5. On post-operative day 9 an EKG was performed for concern of ventricular tachycardia on bedside telemetry; this illustrated a wide complex tachycardia (Fig. 2). The patient was asymptomatic, hemodynamically stable, and subsequently transferred to the ICU for further evaluation and monitoring. Electrolytes, liver enzymes, and an arterial blood gas were obtained on arrival to the ICU and were within normal limits. Electrophysiology was consulted and believed the wide complex tachyarrhythmia was caused by propafenone toxicity and not ventricular tachycardia given cycle length variability and changes in QRS complex width without changes in total cycle length. They recommended discontinuation of propafenone, and avoidance of other antiarrhythmics. The patient was initiated on metoprolol twice a day for rate control. On post-operative day 11 the patient converted to narrow complex atrial fibrillation with slowing of her heart rate (Fig. 3) consistent with the use-dependent nature of Ic antiarrhythmics.

Discussion

We present a case of propafenone toxicity seven days after the initiation of amiodarone in a patient who previously tolerated propafenone. To our knowledge, this is the first reported case. Current

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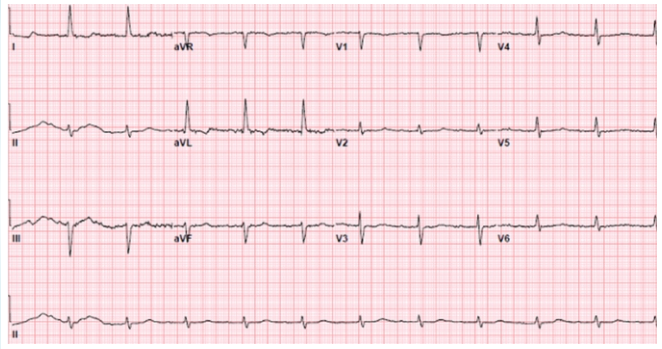

Figure 1: Post-op Day 1 EKG

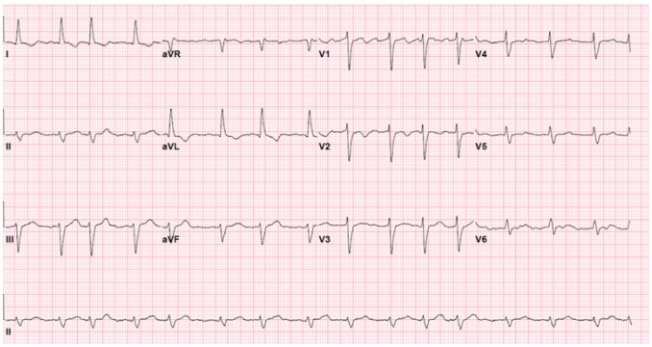

Figure 3: Post op day 11 EKG

propafenone toxicity case reports describe patients who have been recently initiated on propafenone, those who have had a recent dose increase, or those who are slow metabolizers

Propafenone toxicity affects multiple organ systems. Acute cases mainly involve cardiovascular symptoms including hypotension, bradycardia, ventricular dysrhythmias, widening QRS, and heart block. The main concerns with propafenone use are 1) slowing of the atrial fibrillation or tachycardia, and 2) prolongation of the QRS complex. Slowing of the atrial rate facilitates a 1:1 AV conduction with a rapid ventricular response [4]. QRS prolongation is due to rate-dependent ventricular slowing in the His-Purkinje bundle [5, 6]. This 1:1 conduction in the presence of QRS prolongation may present a confusing EKG often misdiagnosed as ventricular tachycardia, as seen

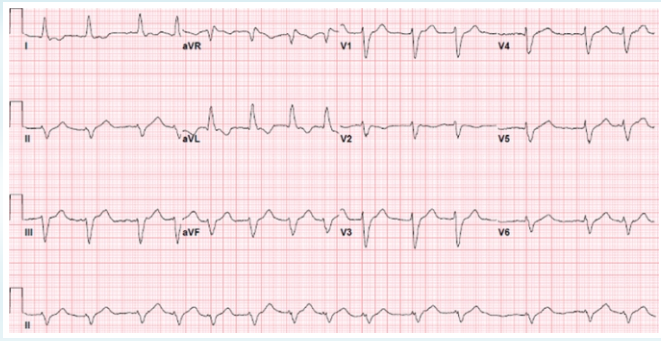

Figure 2: Post op day 9 EKG

in this case. Toxicity of propafenone and other drugs in the 1c antiarrhythmic class come with a high risk of mortality, reported up to 22.5% when compared to an overall mortality of less than 1% in general drug overdose [7].

Amiodarone is a class III antiarrhythmic drug that is often used in the setting of supraventricular and ventricular tachycardias, most commonly used in the setting of atrial fibrillation. The ability of Amiodarone and its metabolites to inhibit multiple cytochrome p450 enzymes is a well-documented phenomenon [8]. It is important to note this inhibition when deciding to initiate a patient on amiodarone and to consider other medications the patient is taking that are metabolized via a cytochrome p450 mechanism. Another important characteristic of amiodarone that must be taken into consideration before administration is its long half-life. The half-life of amiodarone can range from 3.2 to 79.7 hours after a single dose, and up to 100 days after discontinuation after long-term use. This long half-life is caused by its large volume of distribution which ranges between 0.9 to 148 L/kg [9].

Conclusion

We believe the propafenone toxicity in this patient was likely due to cytochrome P450 inhibition caused by post-operative amiodarone administration. This case demonstrates the importance of understanding the pharmacokinetics and pharmacodynamics of specific medications as well as how this may impact drug-drug interactions.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his/her consent for his/her images and other clinical information to be reported in the Journal. The patient understands that his/her name and initials will not be published, and due efforts will be made to conceal his/her identity, but anonymity cannot be guaranteed.

Conflict of interest: Nil **Source of support:** None

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