Flecainide Use in Pacemaker Patient Increases Pacemaker Sensing Threshold: A Case Report

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Abstract

Anti-arrhythmic medications have a narrow therapeutic index which makes the identification of toxic effects critical for patient care. Efforts to mitigate these harmful processes are often impeded due to their difficult to discern from normal cardiac physiology. Here we report a rare complication of flecainide toxicity in an elderly male with a past medical history significant for stage 3 chronic kidney diseases and paroxysmal atrial fibrillation on flecainide therapy that was in our care after having an episode of cardiac syncope. It became apparent after 24-h telemetry monitoring that our patient was suffering from recurrent cardiac syncope. A permanent pacemaker was successfully implanted without complications; however, following the procedure, the patient began experiencing an episode of marked symptomatic bradycardia. His condition rapidly deteriorated progressing to cardiac arrest with an underlying rhythm of pulse less electrical activity. After 2 cycles of CPR, 1 mg of epinephrine, a pulse was reinstated with a stable rhythm. Pacemaker interrogation revealed dual-chamber sensing and pacemaker leads were only capturing at maximum outputs of 7.5 V. This was unusual as normal ranges for capture tend to less than 1 V. It was determined that flecainide levels were starkly above normal therapeutic dosing at the same time of failure of capture. At this point flecainide was discontinued and as its level returned to therapeutic ranges pacing function normalized. It is known that flecainide toxicity can cause a pacemaker to capture failure by increasing the pacemaker sensing threshold. In patients where metabolism of flecainide is impaired particularly in patients with renal insufficiency, close monitoring of flecainide levels and avoidance of the drug in this setting can be effective solutions to ensuring proper capture after pacemaker placement.

Introduction

Flecainide is a class 1C antiarrhythmic drug used to treat paroxysmal supraventricular tachycardia, paroxysmal atrial fibrillation/flutter, and sustained ventricular tachycardia [1,2]. The use of it is limited because of its pro-arrhythmic effects and an increase in mortality in patients with prior myocardial infarction, structural heart disease, and left ventricular dysfunction [3,4]. The half-life of flecainide ranges from 7 h to 23 h, in patients with renal impairment it can be prolonged to 58 h [5]. It is a potent blocker of sodium channels in phase 0 of the cardiac action potential of fast conducting heart fibers and does not prolong the action potential duration or QT interval. Such properties also mediate a reversible negative inotropic effect on the left ventricle and increase myocardial capture thresholds, even at therapeutic doses [6].

Case Presentation

An 86-year-old female with a past medical history significant for paroxysmal atrial fibrillation, hypertension, hypothyroidism, and stage 3 chronic kidney disease who was admitted to the telemetry unit for recurrent cardiac syncope. She is compliant with her current medication regimen and notably takes flecainide 200 mg twice daily. Cardiac monitoring reveals atrial fibrillation with 8 sec of sinus pause along with the symptom of dizziness.

Echocardiogram ruled out structural heart disease and showed an ejection fraction of 55%. At this time the decision to place a dual-chamber pacemaker was made. Electrocardiography (ECG) showed dual-chamber pacing after pacemaker insertion as demonstrated in Figure 1. After 24 h following pacemaker insertion, the patient had an episode of monomorphic broad complex tachycardia on ECG as demonstrated in Figure 2. A few minutes later patient went into cardiac arrest with a presenting rhythm of pulse-less electrical activity. Advance cardiac life support protocol was initiated and CPR continued for 5 min with the successful Return of Spontaneous Circulation (ROSC). First ECG after ROSC revealed capture failure both atrial and ventricular with junctional...
escape rhythm as demonstrated in Figure 3. The differential diagnosis for this scenario includes capture failure due to lead displacement or fracture, metabolic abnormalities, myocardial infarction, or flecainide toxicity. As the leads were confirmed to be intact on repeat X-ray, troponins were within normal limits, and that there were no metabolic abnormalities present. Pacemaker interrogation revealed dual-chamber sensing, capture failure, and leads were only capturing at maximum outputs as demonstrated in Figure 4. The outputs were, therefore programmed to the maximum of 7.5 V. Plasma flecainide levels were starkly elevated. Flecainide discontinued and the pacing function normalized gradually over the next two days. The clinical picture improved as flecainide was cleared, with the ventricular lead threshold falling back to less than 1 V as demonstrated in Figure 5. Flecainide was stopped and she was discharged on diltiazem. The cause of pacemaker capture failure was due to flecainide toxicity increasing the pacemaker sensing threshold. It is however very important to consider close monitoring of flecainide levels in patients with a pacemaker implanted and better to avoid it altogether in patients with renal impairment and structural heart disease.

Discussion

Flecainide is a potent blocker of sodium channels, slows phase 0 in fast response cardiac fibers (cardiac muscles, His-Purkinje system) without any effect on action potential duration. It’s a known fact that flecainide toxicity is common in those with underlying cardiac dysfunction [4]. This was dramatically demonstrated in Cardiac Arrhythmia Suppression Trial (CAST), which was terminated prematurely because of a two and half fold increase in mortality in patients with pre-existing ventricular tachyarrhythmia and those with prior myocardial infarction [4]. The mechanism causes pacemaker capture failure is not fully understood. Failure to capture occurs when a pacing stimulus is generated but fails to trigger myocardial depolarization. Failure to capture is demonstrated on electrocardiogram by the presence of pacing spikes without associated
myocardial depolarization. We report a case of flecainide toxicity, likely mediated by underlying renal insufficiency, which led to a failure of ventricular pacemaker lead capture presented with broad complex tachycardia. In our patient, markedly increased capture thresholds were likely driven predominantly by flecainide toxicity, given that the pacemaker threshold returned to normal (less than 1 V) within 48 h. Experimentally, therapeutic doses of intravenous and oral flecainide have been shown to alter the ventricular pacing capture threshold in healthy subjects, with thresholds rising more than 200% after chronic oral therapy [6].

As with other Class 1 agents, patients treated with flecainide for atrial flutter have been reported with 1:1 atrioventricular conduction due to slowing the atrial rate. A paradoxical increase in the ventricular rate also may occur in patients with atrial fibrillation who receive flecainide. Concomitant negative chronotropic therapy such as digoxin or beta-blockers may lower the risk of this complication. Flecainide’s proarrhythmic effect mediated by rate-dependent blockage of fast sodium channels with subsequent prolongation of phase 0 of the cardiac action potential may promote re-entry circuit formation in ventricular tissue, thus leading to ventricular arrhythmia [7,8]. Moreover, flecainide is known to be a narrow therapeutic index drug, requiring careful patient selection and regular monitoring especially in patients with renal insufficiency [9].

**Conclusion**

This case demonstrates how cardiac pacing can be affected by antiarrhythmic drugs, which can reset the stimulation threshold for the pacemaker leads. Special attention to flecainide dosing is required in a patient with a reduced Glomerular Filtration Rate (GFR) as it can cause a sudden rise in the pacing threshold. Flecainide causes rate-dependent slowing of rapid sodium channel which slows phase 0 of depolarization and in high doses; it inhibits the slow calcium channel. This will slow conduction in atria, ventricles, atrioventricular node, and His-Purkinje system and lead to prolongation of PR and QRS duration. Flecainide toxicity is suggested when there is a 50% increase in QRS duration (0.18 sec) or 30% prolongation in PR interval (0.26 sec). The QTc interval can also be prolonged. After pacemaker implantation, a steady increase in threshold is a normal occurrence during the first 6 weeks after lead implantation, while a sudden loss of capture is most commonly the result of dislodgement of the lead tip.

However, a sudden rise in the pacing threshold that may exceed 200% in patients on long-term therapy with flecainide is another reason. In our case, flecainide dosage of 400 mg/day may be considered excessive in this elderly lady with estimated GFR 40 ml/min.

**References**


