Drug Interaction of Amiodarone, Flecainide, Metoprolol and Diltiazem leading to Heart Block

Vijay Kahajuria, Sanjeev Gupta, Roshi, Neelam Rani

Abstract
Amiodarone, flecainide, metoprolol and diltiazem individually are known to cause heart blocks due to their cardiac depressant property but the current case report is worth reporting because it resulted because of drug interaction of multiple drugs due to possible medication error.

Key Words
Amiodarone, Flecainide, Metoprolol, Diltiazem, Heart Blocks

Introduction
Adverse Drug Reactions (ADRs) in cardiology are common. There are numerous reports of drug induced bradycardia and heart block (1). Co-morbid conditions often coexist with cardiac ailments and results in polypharmacy which enhance the chances of drug interactions culminating to adverse events. In the current study report patient was prescribed multiple drugs for cardiac arrhythmia and he presented with heart block and bradycardia. Though amiodarone, flecainide, metoprolol and diltiazem individually are known to cause heart blocks due to their cardiac depressant property but the current case report is worth reporting because it resulted because of drug interaction of multiple drugs due to possible medication error.

Case Report
A 60 years old male diabetic patient with normal thyroid functions, on oral metformin 500 twice and glimipride 2mg once a day was diagnosed with atrial flutter and was prescribed tab. amiodarone 600 mg once a day orally by the cardiologist. After one year of medication his TSH levels increased to 50uIU/ml. Subsequently exogenous thyroxine 50 micrograms was added to the regimen and the dose of amiodarone was reduced to 300mg once a day. After six months, his TSH reached within normal limits but he started experiencing palpitations. On evaluation he was found to have counter clockwise atrial flutter on ECG which was unrelated to thyroid dysfunction. His hemoglobin levels were 13g/dl, total leucocyte count 6000/UL, neutrophils 56.5%, lymphocytes 30.5%, eosinophils 7.6%, basophils 0.2%, platelet count 1.5 lacs, serum urea-33mg/dl, serum creatinine 0.90mg/dl, prothrombin time 10.9 sec, INR 1.04, hepatitis serology was non reactive, blood sugar random 182 mg/dl, TSH 1.4uIU/ml, serum sodium 142 mmol/L, serum potassium 5 mmol/L.

He was prescribed tab.atenolol 20mg and tab.procaainamide 20mg which did not bring any relief. So radiofrequency ablation was done which was uneventful. The patient was put subsequently on tab. metoprolol 12.5mg XR once a day, tab. atorvastatin 10mg bed time, tab. diltiazem CD 120 once a day, tab. aspirin 75mg once daily, tab. flecainide 100mg morning and 50mg evening. He continued with Tab. thyroxine 50 micrograms once a day empty stomach, tab. metformin 500mg twice a day and tab.glimipride 2mg once daily before breakfast.

After one month of taking above medication the patient developed light headedness, shortness of breath and four episodes of syncpe prompting him to seek medical advice. On ECG (Fig.1) sinus rhythm bradycardia with first degree heart block was seen with PQ duration of 224ms, broad S in V3, V4, V5, V6 and flat T wave in AvL. The said event could not be correlated with any other disease or biochemical abnormality strongly pointing

From the PG Department of Pharmacology, Govt Medical College Jammu J&K-India
Correspondence to: Dr. Vijay Khajuria, Associate Professor, Deptt of Pharmacology, Govt Medical College Jammu- J&K India
to the possibility of drug induced adverse event. Keeping this into consideration tab. metoprolol was stopped but the patient was not relieved of the symptoms. He continued with dizziness, light headedness and occasional syncopal attacks. The dose of flecainide was also reduced to 50mg twice a day. No specific medication was given for first degree heart block other than dechallenge of metoprolol and dose reduction of flecainide.

**Discussion**

The Naranjo causality score was 7 and WHO Causality assessment showed probable correlation with the current adverse event. (2, 3) The severity of reaction was assessed by Hartwig Adverse drug reaction assessment scale (4) which classified it to be mild. Preventability status was worked out by Schumock and Thornton scale (5) which classified it to be definitely preventable. Since the adverse effect was related to the pharmacological action of drugs it can be classified as Type -A.

Amiodarone is a benzofuranic derivative iodine rich, class 3 antiarrythmic drug which blocks inactivated sodium channels and acts as an antiarrythmic. It also decreases calcium current and blocks outward delayed rectifier potassium currents. Since it inhibits 5’deiodinase activity, it decreases peripheral conversion of T4 to T3 and decreases clearance of reverse T3. (6)

Metoprolol is not a pure cardio selective beta blocker, but if prescribed in low doses becomes cardio selective and decreases heart rate, cardiac workload, oxygen demand and diastolic and systolic period (7). In the present case low dose metoprolol was prescribed rather than conventional dose and this could have contributed to bradycardia and heart block.

Diltiazem, a class 4 antiarrythmic drug, is a non dihydropyridine calcium channel blocker which decreases velocity of AV nodal conduction. AV node block can occur as a result of decremental conduction and increased AV Nodal refractoriness. (7)

Flecainide is a class 1c antiarrythmic agent which blocks late opening of sodium channels. It slows conduction of heart and increases time taken to conduct from atrium to ventricle. (8)

Since all the drugs prescribed have cardio depressant action, so cumulative effect of these drugs are more likely to adversely affect heart conduction (9). Since dechallenge of metoprolol could not relieve the patient of the symptoms, dose amelioration of flecainide was done. This brought relief suggesting the drug interaction depressing conduction of the heart to be responsible for bradycardia and heart block rather than single drug to be responsible for this.

**Conclusion**

The current case report highlights potential drug interactions of drugs must kept in mind before prescribing multiple drugs in cardiology.

**References**