CASE REPORT

Moxifloxacin-warfarin Interaction

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INTRODUCTION

Warfarin has its origin as a rat poison and has become one of the widely used anticoagulant drugs to prevent thrombosis and embolism. Many medications, foods and vegetables can interact with warfarin and affect its blood thinning effect in the body. The antibiotic, moxifloxacin official product monograph indicated no interaction with concomitant warfarin treatment as this fourth generation synthetic fluoroquinolone antibiotic does not share the same cytochrome P450 system metabolism pathway with warfarin. However, we report a case of increased anticoagulant activity in a patient treated with moxifloxacin and warfarin causing prolonged hospital stay.

CASE REPORT

A 62 year old lady developed fever and productive cough with whitish sputum for 3 days, associated with worsening symptoms of biventricular heart failure. She went to a private specialist clinic 2 days prior to admission and was treated with oral moxifloxacin 400 mg OD. She was diagnosed to have chronic rheumatic valvular disease with mitral stenosis since the age of 20 years old, for which she underwent closed mitral valvotomy in 1971, balloon valvotomy in 1991 and prosthetic mitral valve replacement in 1992. She also had severe tricuspid regurgitation secondary to non coapting tricuspid leaflets and atrial fibrillation(AF). She was on warfarin 1.5mg OD with relatively stable International Normalised Ratio(INR) levels.

She was admitted for worsening of her cardiac symptoms from New York Heart Association(NYHA) functional class II to class III. She was febrile with temperature of 38.5°C, tachypnoeic, raised jugular venous pressure(JVP), reduced breath sound over the right lower zone and crepitations. Chest x-ray(CXR) showed right lower zone consolidation, and total white cell count was $9.19x10^9$/L. A diagnosis of pneumonia was made and oral moxifloxacin 400 mg OD was continued. Warfarin was initially withheld on admission in view of prolonged INR 4.64. Echocardiography during this admission showed left ventricular ejection fraction of 35-45%, normal prosthetic mitral valve gradients and severe tricuspid regurgitation which were consistent with previous outpatient ECHO studies.

Despite withholding warfarin for 6 days, her INR levels remained elevated ranging from 2.08 to 4.31. There was no untoward bleeding incidence. She quickly became afebrile, her pneumonia resolved and her heart failure symptoms improved by the second day of admission. Moxifloxacin was duly stopped on the 6th day of admission. After stopping moxifloxacin for two days, the INR level dropped to 1.60. Hence, she was bridged with Enoxaparin 40 mg bd in preparation for a pre-operation coronary angiogram (COROS). COROS was done on the 9th day of admission, which interestingly revealed single left coronary artery system with absent right coronary artery and no significant coronary artery disease . After 10 days of hospitalisation, she was discharged with T. Frusemide 40mg BD, T. Digoxin 0.0625mg OD, T. Spironolactone 50mg BD, and T. Warfarin 1.5mg OD.

DISCUSSION

Chronic valvular heart disease is still prevalent in this country especially in the lower socio-economic and indigenous population. It may cause thickening of the mitral leaflets, mitral incompetence or mitral stenosis which can be treated by balloon valvotomy or definitive valvular surgery with prosthetic heart valve replacement. Her indications for warfarin were mechanical prosthetic mitral valve and atrial fibrillation. Warfarin is an oral vitamin K antagonist which inhibits the vitamin K-dependent gamma-carboxylation of coagulation factors II, VII, IX, and X. Its activity is monitored with a blood test called International Normalised Ratio(INR). As warfarin is mainly metabolized by the CYP2C9 hepatic microsomal enzyme system, it is prone to a wide range of drug interactions. There may exist genetic variant(polymorphism) of the CYP2C9 hepatic microsomal enzyme system which affect the way warfarin is metabolized. A host of drugs such as amiodarone, rifampicin, ciprofloxacin, erythromycin, cimetidine, oral contraceptives and fibrates also have been known to interact with warfarin. Moxifloxacin is a newer generation of quinolone which is not metabolized by the cytochrome P450 system and theoretically will not interact with warfarin. Moxifloxacin is commonly prescribed by general practitioners(GP) and physicians alike for community acquired pneumonia(CAP), acute exacerbation of chronic bronchitis(AECB), acute sinusitis and soft tissue infection. Moxifloxacin has broad spectrum bactericidal activity against gram positive and gram negative aerobes.

This patient developed CAP which could temporary worsen her preexisting heart failure and she responded well to moxifloxacin. Initially we didn't suspect moxifloxacin to have probable or possible causal effect for the prolonged INR level. There were no deranged liver function test(LFT) results and no new recent drug introduction except for moxifloxacin. Hypercatabolic states such as sepsis, fever and heart failure with congestive hepatopathy[1] may contribute to prolong INR levels. As her clinical status quickly improved

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and she was not in overt heart failure with significant liver enzymes derangement, we suspected possible drug interaction as the main contributory factor. We used the Drug Interaction Probability Scale(DIPS)[2] to determine the probability of drug interaction and it was assessed to be possible for moxifloxacin to cause interaction with warfarin and prolong the INR levels. Furthermore, an almost similar case about warfarin-moxifloxacin interaction was reported by Yildiz[3].

This is not really an isolated case as there are several other anecdotal reports of significant moxifloxacin-warfarin interaction in the clinical setting[4]. Although moxifloxacin is being touted as relatively safer than older generation of quinolones such as ciprofloxacin in terms of no interaction with warfarin, there exists in vivo interaction as evidenced in this case. It is postulated that moxifloxacillin can cause displacement of warfarin from plasma protein binding site, thus increasing the level of free warfarin and its anticoagulant effect[5].

Therefore, general healthcare practitioners should be aware of the real possible drug interaction between warfarin and moxifloxacin and monitor the INR levels for early detection and avoid the incidence of overwarfarinisation. Instead of quinolones antibiotic, perhaps other suitable antibiotics maybe chosen with no known interaction with warfarin.

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