

Combined Administration of Dabigatran and Clarithromycin: A New Drug Interaction

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Abstract: Anticoagulant agents are primary choice for avoiding and treatment of systemic thromboembolism in patients with atrial fibrillation (AF). Currently, a huge progression in the management of clinical thromboembolism has been made owing to the innovation of new oral anticoagulants (NOACs). They have various useful benefits over the conventional vitamin K antagonists, such as not necessary for classic coagulation follow-up. Although there is a restricted drug and food interaction with NOACs; sometimes, especially using some antibiotics, we can observe some drug reactions in clinical practice.

Keywords: new oral anticoagulants, vitamin K antagonists, drug interactions.

INTRODUCTION

Anticoagulant medications are primary choice for avoiding and treatment of systemic thromboembolism in patients with atrial fibrillation (AF). Firstly, as conventionally known, warfarin which most used one of vitamin K antagonists (VKAs) decreases stroke in patients with AF but increases the risk of bleeding [1]. Because of especially this undesirable side effect, in the recent years, a huge progression in the management of clinical thromboembolism has been made owing to the innovation of new oral anticoagulants (NOACs). These medications act by activated factor X (apixaban, rivaroxaban) or directly inhibiting thrombin (dabigatran).

They offer various useful benefits over the conventional VKA, such as not necessary for classic coagulation follow-up. Although there is a restricted drug and food interaction with NOACs; sometimes, especially using some antibiotics, we can observe some drug reactions in clinical practice. We present here a case of dabigatran-chlaritromycin drug interaction.

CASE REPORT

A 75 year old woman was admitted to the internal medicine department with ecchymosis which width of 5 cm and extending between spina iliaca anterior superior (SIAS) and spina iliaca posterior superior (SIPS). On her history, she was previously treated for chronic obstructive pulmonary disease, heart failure, obstructive sleep apnea and AF. She was prescribed dabigatran 110 mg twice a day for AF two months ago. She had cough for two weeks and her primary care physician prescribed to patient chlaritromycin for acute bronchitis. On third day of chlaritromycin treatment, after severe coughing, she felt pain on her left side of the waist and next day, she noticed that a large ecchymosis on this area. The patient admitted to our clinic after 3 days of her last complaint. On physical examination, fine crackles was auscultated on the basis of lungs and the ecchymosis was observed between SIAS and SIPS. On the laboratory,

hemoglobin: 11.9 gr/dl, platelet count: 206 000/mm³, INR: 1.29, aPTT: 39,57 sec detected. On superficial and abdomen ultrason showed that edematous area under the skin but wasn't detected significant fluid collection. Searching dabigatran and chlaritromycin drug interaction showed that clarithromycin can significantly impair the bioavailability of dabigatran. Her chlaritromycin treatment was discontinued and levofloxacin was started. On follow up, the ecchymosis was resolved and her hemoglobin level wasn't declined. Dabigatran treatment was started again after the cardiology consultation and she was discharged.

CONCLUSION

AF raises the risks of stroke and death. VKAs, such as warfarin, decrease the risk of stroke but increase the risk of hemorrhage [1] for this reason, warfarin is advised for patients who have atrial fibrillation and are at risk for stroke [2]. VKAs are troublesome to apply, because of their various interactions with drugs, and they necessitate close laboratory follow-up. Therefore, rates of discontinuation are high [3-4]. A non-VKA oral anticoagulant, dabigatran is a new oral direct thrombin inhibitor which is invented for the prevention of stroke in patients with nonvalvular atrial fibrillation. Although dabigatran is associated with less serious bleeding than warfarin, [5-7] sometimes up to

lifethreatening levels bleeding can occur with under some drug interactions. Although the number of such drugs is expected to be reasonably lower than those potentially disturbing VKAs metabolism, some remarkable interactions have already been announced [8]. The valid guidelines of European Heart Rhythm Association on the use of NOACs in patients with atrial fibrillation schedule various antibiotics as probably interfering substances, which essentially contains itraconazole, voriconazole, ketoconazole, posaconazole, fluconazole, erythromycin, clarithromycin, and rifampicin [9].

On dabigatran metabolism, dabigatran etexilate is a prodrug, which is quickly transformed after oral implementation to the active form, dabigatran. The prodrug, but not its active metabolite, is a substance of permeability glycoprotein (P-gp), which is an ATP-dependent transmembrane transporter with vast substrate specificity assigned to transferring of substances (i.e., xenobiotics and endogenous compounds) from the lumen of the intestine within the enterocyte [10]. After the adsorbing to the enterocyte, dabigatran etexilate is broken down to dabigatran and then swiftly excreted into the circulation, where it reaches the plasma peak level roughly 2 hour after administration. The drug is primarily removed by renal clearance [9]. According to these pharmacokinetics features, strong P-gp inhibitors (e.g., clarithromycin, erythromycin, itraconazole, and ketoconazole) are drugs that will characteristically enhance dabigatran bioavailability, whereas P-gp inducers (e.g., rifampicin) are supposed to decrease the bioavailability [11]. So, as in our case, clarithromycin can cause dabigatran overdose by this way and can cause hemorrhage.

Finally, NOACs are useful tools for especially prevent stroke in AF. Today, they are increasingly prescribed by physicians. The administration of antibiotics in patients undergoing therapy with NOACs necessitates more detailed evaluation. One must note that, when prescribing a new antibiotic to AF patient who using one of NOACs, a new drug interaction can develop so if needed, checking the potentially interfering substances list may be beneficial for avoiding the drug interactions.

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