


Case Report

Bleeding Following Warfarin and Amoxicillin/Clavulanate Drug Interaction: A Case Report



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ABSTRACT

Background and Objectives: Anticoagulants are drugs that prevent blood clotting; however, inappropriate use can also increase the risk of blood clots or bleeding. Warfarin is a commonly prescribed anticoagulant, but its narrow therapeutic index and potential for drug interactions can make it challenging to manage. Direct oral anticoagulants have reduced the use of warfarin; however, it remains the preferred option for some patients. Clinicians must also be aware of drug-drug interactions, such as those between warfarin and antibacterial agents, such as amoxicillin-clavulanic acid (AMC). A case study is presented where an interaction between warfarin and AMC resulted in an elevated international normalized ratio (INR) and bleeding.

Case Report: A 64-year-old man with a history of hypertension, ischemic heart disease, and atrial fibrillation presented to the emergency department with new onset epistaxis. He was taking aspirin, metoprolol succinate, and warfarin, which had been in the therapeutic range for over a year. Two weeks before, he had been prescribed AMC for acute sinusitis without any dosage adjustments to his warfarin. Laboratory tests revealed an elevated INR of 5.6 and microscopic hematuria. The patient was treated with nasal packing and vitamin K, and his INR returned to normal. The case highlights the importance of monitoring drug interactions when prescribing anticoagulants.

Conclusion: Drug interactions between warfarin and AMC can cause bleeding complications and require close monitoring. Healthcare providers should consider alternative antibiotics for patients taking warfarin.

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Introduction

Anticoagulants are pharmacological agents that aid in the prevention of blood coagulation. Administration of such agents at sub-therapeutic doses may elevate the likelihood of thrombus formation, consequently heightening the risk of stroke or venous thromboembolism. Conversely, the employment of anticoagulants at supra-therapeutic doses may augment the risk of hemorrhage [1].

Warfarin, a vitamin K antagonist, is a commonly prescribed oral anticoagulant for preventing stroke, venous thromboembolism, and other thromboembolic complications in patients with atrial fibrillation and mechanical heart valves. Introducing direct oral anticoagulants (DOAC) into clinical practice has reduced the frequency of warfarin prescribing. However, warfarin remains the preferred anticoagulant for a substantial proportion of patients who choose to continue its use or have medical conditions that necessitate its administration or where the additional expense of DOACs is not feasible [2].

Despite its established effectiveness and longstanding use as the standard of care for anticoagulation therapy, warfarin's pharmacokinetic and pharmacodynamic properties pose certain clinical challenges. Its narrow therapeutic index and potential for drug-herb, drug-food, and drug-drug interactions contribute to the variability of a patient's international normalized ratio (INR) and occasional adverse events. Anticoagulants have consistently ranked among the top drug classes associated with clinical harm necessitating emergency medical evaluation or hospitalization [3].

In addition, clinicians frequently encounter the issue of drug-drug interactions when managing patients with multi-morbid diseases who are concurrently taking multiple medications. Clinicians often encounter the issue of drug-drug interactions when managing patients with multi-morbid diseases who are concurrently taking multiple medications. Those between warfarin and various antibacterial agents are commonly documented among these interactions. In this report, we present a case of an interaction between warfarin and amoxicillin-clavulanic acid (AMC) that resulted in an elevated international normalized ratio (INR) and bleeding and epistaxis.

Case Presentation

A 64-year-old man presented to the emergency department with complaints of new onset epistaxis with

no history. The patient's past medical history included hypertension, ischemic heart disease, and atrial fibrillation. Aspirin tablets (80 mg daily), metoprolol succinate tablets (50 mg daily), and warfarin tablets (5 mg daily) were among the patient's routine drugs. On initial examination, his hemodynamic state was stable; his blood pressure was 130/90 mm Hg, and his heart rate was 72 beats/min. Laboratory tests revealed an elevated INR of 5.6 (microscopic hematuria). The patient had been taking warfarin 5 mg/day for more than one year for stroke prophylaxis because of a history of atrial fibrillation.

Laboratory records revealed that the INR had been in the therapeutic range of 2–3 since the initiation of warfarin. Two weeks before the current events, he was prescribed AMC 500/125 mg tablets to be taken as one tablet three times daily for 14 days for acute sinusitis. The previous INR level one month ago was 2.8. In addition, no dosage adjustments were made at that time. The patient did not experience any adverse effects during the administration of AM/ clavulanate (CL); however, clinical manifestation was revealed three days after the sinusitis treatment period. Nasal packing was performed for epistaxis, 10 mg of vitamin K in one subcutaneous dose prescribed for coagulopathy. As a result, the INR the next day changed to 2.9, which is in the normal range. The patient was discharged with a normal condition three days after admission.

Discussion

Drug-drug interactions are a common occurrence in clinical practice and can have significant consequences for patients [4]. This case report discussed a potential DDI between warfarin and AMC.

AMC is a broad-spectrum antibiotic that is commonly used to treat bacterial infections. Amoxicillin is a penicillin-like antibiotic that inhibits bacterial cell wall synthesis, while CL is a beta-lactamase inhibitor that prevents bacteria from breaking down amoxicillin. AMC is generally well-tolerated but can cause gastrointestinal side effects, such as nausea, vomiting, and diarrhea [5, 6].

Warfarin works by inhibiting the clotting factors necessary for forming blood clots; however, warfarin also has a narrow therapeutic index, which means that the dose must be carefully monitored to prevent bleeding or clotting complications. The efficacy of warfarin is monitored by measuring the INR, which is a standardized measure of the prothrombin time. The clinical significance of the drug-drug interaction between warfarin and AMC is that

it can increase the risk of bleeding, which can be life-threatening in some cases [7, 8].

There have been several case reports and studies that have suggested a potential DDI between warfarin and AMC. The mechanism of this interaction is due to the inhibition of warfarin metabolism by AMC. Warfarin is metabolized by the cytochrome P450 (CYP) enzyme system, specifically CYP2C9. AMC has been shown to inhibit CYP2C9, which can lead to an increase in warfarin levels and an increased risk of bleeding complications [9].

The management of patients who are taking both warfarin and AMC requires careful consideration and monitoring. Patients who are prescribed warfarin and AMC together should be closely monitored for signs of bleeding, such as easy bruising, petechiae, or hematomas [10]. Patients who develop bleeding while taking both medications may require a reduction in their warfarin dose or temporary cessation of warfarin therapy. In addition, alternative antibiotics should be considered for patients who are taking warfarin. Antibiotics that do not inhibit the CYP2C9 enzyme, such as azithromycin or clarithromycin, may be safer for patients who require antibiotic therapy while on warfarin. If AMC is the only appropriate antibiotic choice, the patient's warfarin dose should be closely monitored, and adjustments be made as needed [11, 12].

Conclusion

The potential DDI between warfarin and AMC is a clinically significant issue that requires careful consideration. Healthcare providers should be aware of this interaction's potential and monitor their patients closely for signs of bleeding complications. If necessary, alternative antibiotics should be considered for patients taking warfarin.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Authors' contributions

Data collection and data interpretation: Saeed Kargar-soleimanabad; Writing and final approval: The both authors.

Conflict of interest

The authors declared no conflicts of interest.

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