www.jcimcr.org

JCIMCR OPEN ACCESS Journal of Clinical Images and Medical Case Reports

ISSN 2766-7820

Case Report

Open Access, Volume 3

Rifampin-warfarin interaction in a transcatheter aortic valve replacement patient with septic knee arthritis

Austin J Teel[1]; Nicolas W Shammas[2]*

[1]Des Moines University College of Osteopathic Medicine, Des Moines, IA, USA.

[2]Midwest Cardiovascular Research Foundation, Davenport, IA, USA.

***Corresponding Author:** Nicolas W Shammas*
Research Director, Midwest Cardiovascular Research Foundation, 640 E 4th street, Suite A, Davenport, IA 52801, USA.
Email: shammas@mchsi.com

Received: Nov 28, 2022
Accepted: Dec 20, 2022
Published: Dec 27, 2022
Archived: www.jcimcr.org

DOI: www.doi.org/10.52768/2766-7820/2217

Keywords: Warfarin; Rifampin; Drug interaction; International normalized ratio; Mechanical valve.

Introduction

Warfarin therapy is known to participate in numerous drug-drug interactions that may cause substantial fluctuations in anticoagulation status. Rifampin is a commonly used antibiotic that also possesses the capability to interact with a multitude of medications, including warfarin, due to its strong induction capabilities on the CYP450 system, including CYP2C9, CYP3A4, CYP1A2, and CYP2C19. We present a case of warfarin-rifampin interaction leading to a non-therapeutic International Normalized Ratio (INR) despite continued warfarin escalating dose necessitating the discontinuation of rifampin in a patient with a mechanical heart valve.

Case report

We report a case of a 53-year-old male chronically treated with warfarin for his mechanical aortic valve. He has a history of obstructive sleep apnea, hypertension, hyperlipidemia, left knee replacement, and Transcatheter Aortic Valve Replacement (TAVR) in 2018. The patient developed septic arthritis of the left knee and was started on levofloxacin at 750 mg daily after undergoing left knee irrigation and debridement, antibiotic bead placement, and ancef in the hospital. He was discharged to a skilled nursing facility and subsequently returned to the emergency department with complaints of lower extremity pain, redness, and swelling in the left knee. He was prescribed rifampin at 600 mg twice daily and was continued on levofloxacin at 750 mg after being discharged in a stable condition from the emergency department. His INR at this time was 1.5, and his warfarin dosage was 37.5 mg weekly.

Warfarin dose was gradually increased to a maximum dose of 155 mg weekly. Patient's INR remained unresponsive to increasing dose of warfarin. Rifampin dose was then reduced to 300 mg twice a day. Figure 1 shows the increasing dose of warfarin with no to little change in INR even after reducing Rifampin

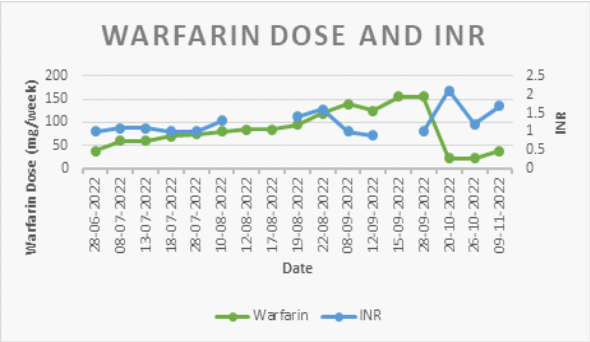

Figure 1:

dose. Rifampin was then discontinued. Enoxaparin bridge therapy was recommended but patient did refuse to take it because of expenses. Luckily he has not developed valve thrombosis or an adverse cardiovascular event.

Discussion

Warfarin is an oral anticoagulant that inhibits the synthesis of factors II, VII, IX, and X, specifically in liver cells at the vitamin K cycloreductase complex subunit 1 [2]. Warfarin is administered in a racemic mixture, where the more potent enantiomer is approximately 90% metabolized through oxidative metabolism via the Cytochrome P450 pathway, nearly entirely via CYP2C9 and to a lesser extent CYP3A4. Conversely, the less potent R enantiomer is approximately 60% metabolized through oxidative metabolism via CYP1A2 and CYP3A4, and to a lesser extent via CYP2C19 [1]. Warfarin is a less expensive anticoagulation option that is widely used in thromboembolic disease, myocardial infarction, atrial fibrillation, and mechanical valve replacement [2].

Rifampin is a widely used antibiotic for treating severe, life-threatening infections, which include tuberculosis, endocarditis, and osteomyelitis. Rifampin has numerous major interactions with a plethora of medications due to its potent P-glycoprotein and induction capabilities on CYP2C9, CYP3A4, CYP1A2, and CYP2C19 [1]. As such, rifampin usage in patients who are dependent on warfarin for anticoagulation purposes results in a clinically substantial drug-drug interaction. Specifically, warfarin clearance is accelerated and leads to a significant reduction in anticoagulation. This has been documented in a few published cases, where warfarin dose has been increased significantly, up to six-fold in some instances, to maintain therapeutic INR. This interaction has been observed to continue for numerous weeks after rifampin cessation, and this finding has also been associated with an increased risk of bleeding due to presumed alterations in warfarin dosage and metabolism [1].

Our patient continued to have a very low INR despite increasing dosing of warfarin in the setting of Rifampin. When Rifampin was discontinued, the INR gradually increased as noted in Figure 1. In patients with mechanical valves, it is critical that INR remains in the therapeutic range to avoid valve thrombosis and stroke. Luckily adverse events did not happen in our patient who resisted bridging with low molecular weight heparin. Careful monitoring of INR is necessary when Rifampin is administered to a patient on warfarin. This may require almost once or twice a week monitoring of INR with rapid adjustment of warfarin dosing. Similar to our case, a few published reports have described the interaction between rifampin and warfarin, which have resulted in a reduced anticoagulation effect of warfarin throughout the duration of tandem usage of these two medications [4]. Lee et al. discussed a case where a patient was started on rifampin for active tuberculosis and was started on warfarin 4 months later for treating a left ventricular thrombus. When attempting to attain therapeutic INR in this patient, the warfarin dosage that was required was 233% higher while on rifampin when compared to the warfarin dosage used after rifampin was discontinued.

Apart from drug-drug interactions, there are additional causes of inadequate control of anticoagulation with vitamin K antagonists. Antibiotics are known to reduce vitamin K-producing bacteria in the gut microbiome which could further increase levels of INR. In our patient, Levaquin did not increase INR because of the likely dominant warfarin-Rifampin interaction. This latter interaction lasts from 15 days [6] to 5 weeks [1] in recent case reports. The onset of interaction and subsequent requirement to increase warfarin dose appears to occur at around 7 – 14 days after beginning rifampin when compared to the offset of the interaction [1]. Furthermore, additional case studies have described patients who were started on rifampin at 600 mg daily while being started on warfarin at a similar timeframe, and their warfarin dose was reduced by nearly 50% after discontinuing rifampin to maintain therapeutic INR levels [3]. This intensive follow-up requirement may pose additional difficulties in patients with financial concerns and a history of medical noncompliance.

Conclusion

In summary, our case is an illustration to the strong interaction between rifampin and warfarin that requires close monitoring of warfarin therapy potentially 2-5 weeks post-rifampin therapy. This drug-drug interaction can be particularly problematic in patients with mechanical valve replacement, venothromboembolic disease or atrial fibrillation.

References

1. Fahmi AM, Elewa H, Abdelsamad O. Rifampin-warfarin interaction in a mitral valve replacement patient receiving rifampin for infective endocarditis: A case report. SpringerPlus. Retrieved September 28, 2022, from https://pubmed.ncbi.nlm.nih.gov/26759747/

2. Hu YN, Zhou BT, Yang HR, Peng QL, Gu XR, Sun SS. (2021, February 16). Effect of rifampicin on anticoagulation of warfarin: A case report. World journal of clinical cases. Retrieved September 28, 2022, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7896655/

3. Krajewski KC. Inability to achieve a therapeutic INR value while on concurrent warfarin and rifampin. J ClinPharmacol2010, 50(6): 710–713.

4. Lee CR, Thrasher KA. Difficulties in anticoagulation management during coadministration of warfarin and rifampin. Pharmacotherapy. 2001; 21: 1240–1246.

5. Martins MA, Reis AM, Sales MF, Nobre V, Ribeiro DD, Rocha MO, Ribeiro AL. Rifampicin-warfarin interaction leading to macroscopic hematuria: a case report and review of the literature. BMC PharmacolToxicol. 2013; 14: 27.

6. Mizera L, Geisler T, Mörike K, Gawaz M, Steeg M, et al. Problems in anticoagulation of a patient with antibiotic treatment for endocarditis: Interaction of rifampicin and Vitamin K antagonists. 2018; BMJ case reports. Retrieved September 28, 2022, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5836613/