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LETTER

Warfarin and Thrombotic Mechanical Aortic Valve – Be Cautious to Avoid Severe Warfarin Drug Interactions in Patients with Suspected Infective Endocarditis after Mechanical Aortic Valve Replacement [Letter]

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Dear editor

We read with great interest the case report presented by Ababneh et al,[1] which shows a patient with mechanical aortic valve thrombosis and heart failure was entirely treated with warfarin. We especially appreciate their successful experiences. We found several points worthy of discussion, and we would like to share our perspectives in the following paragraphs.

Clinicians should be cautious when 6 weeks of antibiotic therapy (rifampin, gentamicin and vancomycin) was prescribed for the patient on warfarin maintenance therapy suffering from suspected infective endocarditis (IE). Rifampin is a strong inducer of cytochrome P450 2C9, which is the primary metabolizing enzyme responsible for warfarin metabolism. There is a severe drug–drug interaction between warfarin and rifampin, therefore, patients coadministered with rifampin and warfarin necessitate vigilant monitoring. However, achieving a therapeutic level of anticoagulation was difficult despite escalating doses of warfarin, even a 5- to 6-fold increase in warfarin dose was insufficient to maintain the international normalized ratio (INR) in the therapeutic range.[2] Similarly in this case,[1] the patient had recurrent sub-therapeutic INR readings of 1.2–1.8 despite warfarin dosage adjustment. Furthermore, an excessively high INR would be observed after rifampin discontinuation due to the disappearance of enzyme induction.

We suggest that the combination of warfarin and rifampin should be avoided whenever possible. If clinically indicated, daptomycin may be an alternative for the treatment of IE. In an IE model of biofilm-forming methicillin-resistant *Staphylococcus aureus* (MRSA), daptomycin monotherapy has better in vitro bactericidal activity than daptomycin in combination with rifampin or gentamicin or any vancomycin-containing regimen.[3] Daptomycin at a dose of 6 mg per kilogram once daily is not inferior to standard therapy for the treatment of right-sided endocarditis caused by *Staphylococcus aureus*.[4] Daptomycin has been recommended for treating staphylococcal and enterococcal endocarditis, and it is given at high doses (10 mg/kg once daily) and combined with a second antibiotic (beta-lactams or fosfomycin in beta-lactam allergic patients).[5] Although there is not enough evidence to support or reject any regimen of antibiotic therapy for the treatment of IE, it may be wise to choose an antimicrobial regimen without rifampin for special patients, such as those being treated with warfarin.

Very recently, warfarin-rifampin-gene interaction was revealed by a retrospective, genetic, case–control study.[6] The warfarin-sensitizing *CYP2C9/Vitamin K epoxide reductase complex subunit 1 (VKORC1)* genotypes were associated with modest warfarin dose requirements in patients receiving rifampin concomitantly, whereas the noncarriers would have

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required more than double these doses to respond. Therefore, it is necessary to perform genotyping of *CYP2C9/VKORC1* prior to initiation of rifampin in patients on warfarin maintenance therapy.

Ababneh et al is remarkable for successfully treating such a complex patient. The purpose of our letter is to further enhance the collaboration between physicians, pharmacists and nurses and to promote individualized rational drug use and the management of drug–drug interactions.

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Disclosure

The authors report no conflicts of interest in this communication.

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