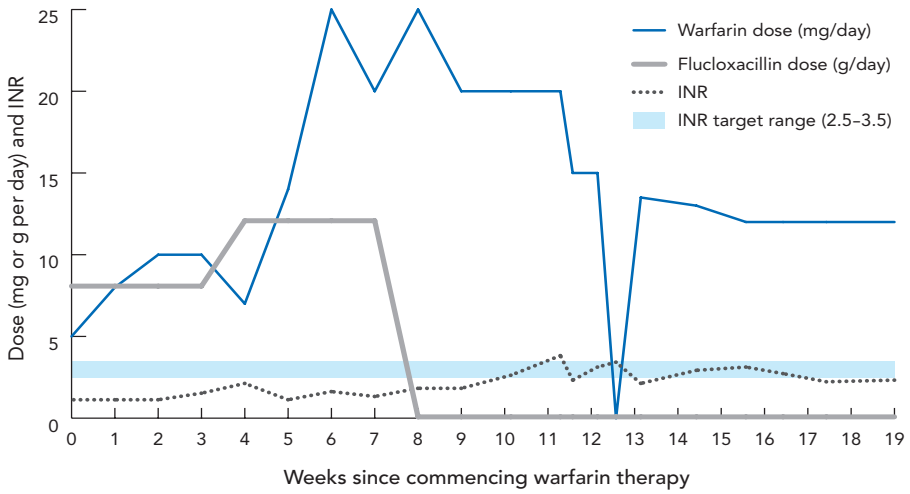
Doses* for oral warfarin and intravenous flucloxacillin administered to a 64-year-old man with infective endocarditis, and corresponding INR



INR = international normalised ratio. * Graph shows abbreviated, not daily, data. Intervals are weekly up to Week 9, then vary according to when INR was measured. ◆

High-dose intravenous flucloxacillin may affect warfarin therapy

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To the Editor: Warfarin is an orally administered vitamin K antagonist and has many well described interactions with commonly prescribed medications.[1] However, only a handful of case reports worldwide have shown that flucloxacillin, a widely used antibiotic, may affect warfarin therapy by reducing its anticoagulant effect — in one instance contributing to the development of ischaemic stroke.[2,3] There are several reports describing potential mechanisms of interaction for flucloxacillin with warfarin.[4,5]

We describe the case of a 64-year-old man who was diagnosed with infective endocarditis on the basis of mitral valve vegetations and blood cultures that were positive for methicillin-sensitive *Staphylococcus aureus*. The patient underwent mitral valve replacement with a prosthetic valve and received prolonged antibiotic therapy with intravenous flucloxacillin for 8 weeks.

Initially, for nearly 4 weeks, therapeutic anticoagulation with warfarin was difficult to achieve with warfarin doses ranging between 5 and 10 mg per day (target international normalised ratio [INR], 2.5–3.5). During this time, the patient was receiving intravenous flucloxacillin at a total daily dose of 8 g (2 g every 6 h). Flucloxacillin was increased to 12 g per day (2 g every 4 h) and there was a subsequent fall in the patient's INR, which was sustained despite increasing the dose of warfarin to 25 mg per day (Box). Completion of flucloxacillin therapy was associated with a rise in the patient's INR and a reduction in his warfarin dose requirement.

No other relevant medications were commenced during this period of observation.

This case highlights the potential for a dose-related effect of intravenous high-dose flucloxacillin (up to 12 g per day) on warfarin metabolism and the need for vigilance when prescribing antibiotics in conjunction with oral vitamin K antagonists. Other penicillins such as amoxicillin can, conversely, enhance the anticoagulant effects of warfarin, so the warfarin–flucloxacillin interaction may not be intuitive for many clinicians.

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