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Severely diminished response to vitamin K-treatment for self-inflicted warfarin intoxication in a patient genotyped as *CYP2C9*3*3*

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Sir, an 86-year-old woman suffering from cardiovascular disease and atrial fibrillation treated with warfarin was admitted to the emergency department following self-inflicted intoxication with warfarin. Her GP had instituted a dementia workup due to episodes of confusion, and during a confusional episode the patient ingested a “large number” of warfarin tablets. When she was admitted to the emergency department approximately 12 h later, she had a PK-INR of 2.2 and was initially treated with Oplex (factor II, VII, IX, X, protein C, protein S) as well as vitamin K. During the first 8 days, she received 20 mg/day of vitamin K i.v. and her PK-INR was stable around 2.2. The ninth day after admission, no vitamin K was administered upon which her PK-INR increased to 4.6, and vitamin K treatment was reinstated. Her maintenance dose of warfarin had been low (5–7.5 mg/week) during warfarin treatment, and a lowered warfarin elimination caused by genetic polymorphism was suspected. Genotyping confirmed a genotype associated with a low clearance of warfarin (*CYP2C9*3*3*). The low maintenance dose of warfarin seen in this patient is in accord with doses seen in most *CYP2C9*3*3* patients described in the literature [1]. Twenty-five days after warfarin intake, the PK-INR was still elevated (1.4) despite ongoing vitamin K treatment.

S-warfarin, the more potent enantiomer of racemic warfarin, is metabolised by the *CYP2C9* enzyme, and polymorphisms in

the *CYP2C9* gene may cause a reduced clearance [2, 3]. In patients who are homozygous for *CYP2C9*3* it has been shown that the clearance of s-warfarin can be reduced by 90%, which would correspond to a 10-fold increase in the normal s-warfarin half-life of 18–35 h [4, 5].

To our knowledge, this is the first report on self-inflicted intoxication with warfarin by an individual with a *CYP2C9* genotype predisposing to slow warfarin elimination. The observed long recovery period with daily vitamin K treatment suggests that *CYP2C9* genotyping in cases of warfarin intoxication may help to better understand the time requirements for adequate monitoring.

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