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Genetic polymorphisms associated with the dose of acenocoumarol

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BACKGROUND

The coumarins have a narrow therapeutic window and there is wide inter- and intra-individual variability in dose requirements. Therefore, patients are monitored by measuring the international normalized ratio (INR). Recent discoveries show relationship between genetic polymorphisms and dose requirements of coumarins. Genetic polymorphisms affect CYP2C9*2(*2/*2), CYP2C9*3 (*1/*3, *3/*3) and VKORC1 (CT, TT) reduce the enzyme activity, requiring a lower dose of anticoagulant drug. Besides, genetic polymorphism in CYPF2 (TT), decreases the enzyme activity but in this case it needs higher doses of anticoagulant.
novel treatments for hepatitis C have been recently approved in Spain. Several studies have confirmed its high efficiency to achieve good virological response.

PURPOSE

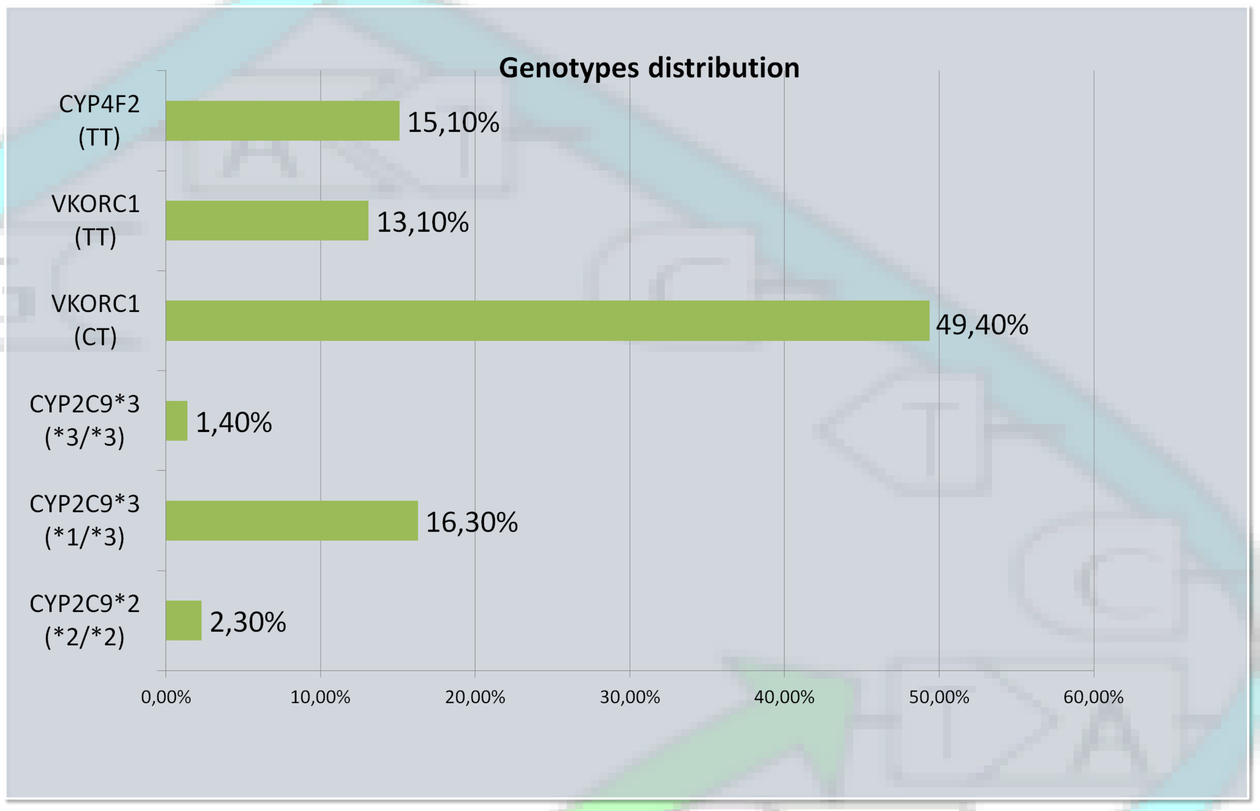
Determine the percentage of potential patients with changing dose taking into account the prevalence of polymorphisms CYP2C9*2 (*2/*2), CYP2C9*3 (*1/*3, *3/*3), VKORC1 (CT, TT) and CYP4F2 (TT) in patients with Thromboembolic Disease, atrial fibrillation and mechanical heart valve prostheses.

MATERIALS AND METHODS

This was an observational, descriptive, transversal study with 344 patients treated with acenocoumarol, from May 2012 to May 2013. Saliva samples were taken from all the patients. For genotyping we used TaqMan probes and allelic discrimination technique. We performed a univariate descriptive analysis of the frequencies of genetic polymorphisms affecting the doses (CYP2C9 * 2, CYP2C9*3, VKORC1, CYP4F2). We focus on the polymorphisms which affect the drug dosage (CYP2C9*2 (*2/*2), CYP2C9*3 (*1/*3, *3/*3), VKORC1 (CT, TT) and CYP4F2 (TT).

RESULTS

Genotypes distribution: CYP2C9*2 (*2/*2): 2.3% patients, CYP2C9*3 (*1/*3): 16.3% and (*3/*3): 1.4% patients. VKORC1 CT: 49.4% and VKORC1 TT: 13.1% and the CYP4F2 TT: 15.1%.
The overall percentage of patients which would need a change in the dose is 75.87% according to the pharmacogenetic guides.



CONCLUSIONS

Due to the high percentage of patients with a potential change in dosage, it is necessary to start genotyping patients on acenocoumarol in order to keep them controlled.