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Pharmacogenomics and Personalized Medicine

Dora Janeth Fonseca mendoza[1]

[1]Center For Research in Genetics and Genomics-CIGGUR, GENIUROS Research Group, School of Medicine and Health Sciences. Universidad del Rosario, Bogotá, Colombia.

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DORA FONSECA

ABSTRACT

Background: Warfarin is an oral anticoagulant associated with adverse reaction drugs due to wide inter- and intra-individual dosage variability. Warfarin dosage has been related to non-genetic and genetic factors. *CYP2C9* and *VKORC1* gene polymorphisms influence warfarin metabolism and dosage. Due to the central role of populations' ethnical and genetic origin on warfarin dosage variability, novel algorithms for Latin American subgroups are necessary to establish safe anticoagulation therapy.

Patients and Methods: We assessed *CYP2C9**2 (c.430C>T), *CYP2C9**3 (c.1075A>C), *CYP4F2* (c.1297G>A) and *VKORC1* (-1639G>A) polymorphisms in 152 patients who received warfarin. We evaluated the impact on the variability of patients' warfarin dose requirements. Multiple linear regression analysis, using genetic and non-genetic variables, was used for creating an algorithm for optimal warfarin maintenance dose.

Results: Median weekly prescribed warfarin dosage was significantly lower in patients having the *VKORC1* -1639 AA genotype and poor *CYP2C9*2/*2,*2/*3* metabolizers than their WT counterparts. We found a 2.3-fold increase in mean dose for normal sensitivity patients (wild type *VKORC1/CYP2C9* genotypes) compared to the other groups (moderate and high sensitivity); 31.5% of the patients in our study group had warfarin sensitivity-related genotypes. The estimated regression equation accounted for 44.4% of overall variability regarding warfarin maintenance dose. The algorithm was validated, giving 45.9% correlation (R^2=0.459).

Conclusions: Our results describe and validate the first algorithm for predicting warfarin dose in a Colombian mestizo population and have contributed towards understanding pharmacogenetics in a Latin America population subgroup.

EXTERNAL LINK

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PROTOCOL STATUS

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