A CLINICAL-GENETIC ALGORITHM FOR CALCULATING THE STABLE THERAPEUTIC DOSE OF ACENOCOUMAROL

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Aim: To develop and validate an algorithm for calculating the stable dose of acenocoumarol in patients diagnosed with acute deep vein thrombosis, atrial fibrillation or valvular prostheses.
Material and methods: The study included 301 patients that necessitated treatment with acenocoumarol for a prolonged time (> three months). The patients were selected from those admitted within the internal medicine, geriatric and cardiology wards of Municipal Hospital of Cluj-Napoca and the Heart Institute "Niculae Stănciou" in Cluj-Napoca, Romania, between October 2009 and December 2011. For each patient we recorded demographic, clinical and pharmacological data that could have influenced the stabile dose of acenocoumarol. The genetic analysis included genotyping the CYP2C9 gene and the VKORC1 gene. Through randomization, patients were included in the algorithm group (200 (66.4%) patients) and in the validation groups (101 (33.6%) patients).
Results: The age and body mass index were responsible for 18.8% (R^2 coefficient) of the acenocoumarol weekly dose variability in patients within the algorithm group. After the inclusion of CYP2C9 and VKORC1 mutations, the R^2 coefficient increased at 43.1%. For the algorithm group we calculated a mean error of -0.6 (±6.4) mg/week and a mean absolute error of 5 mg/week (0.71 mg /day). In the validation group, the clinical parameters explained 22.2% of the acenocoumarol weekly dose variability, and, after adding the genetic factors, the R^2 coefficient increased at 32.8%.
Conclusion: We created and validated an adequate algorithm for the prediction of acenocoumarol therapeutic stable dose.