Impact of CYP2C9 polymorphisms on the vulnerability to pharmacokinetic drug-drug interactions during acenocoumarol treatment

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Aim: The objective of this study was to investigate the impact of CYP2C9 polymorphisms and drug-drug interactions on the risk of overanticoagulation in patients treated with acenocoumarol, a vitamin K antagonist.

Materials and Methods: A prospective observational study was performed on patients starting acenocoumarol (n = 115). CYP2C9 genotypes were assessed. Data on International Normalized Ratio, comedications and doses of acenocoumarol were collected during the first 35 days of therapy. Overanticoagulation was defined as the occurrence of at least one International Normalized Ratio ≥4.

Results: The presence of a CYP2C9 inhibitor or a CYP2C9 polymorphisms statistically increased the risk of overanticoagulation (hazard ratio [HR]: 2.8, $p < 0.001$ and HR: 1.7, $p = 0.04$, respectively). The presence of CYP2C9 polymorphisms almost tripled the risk of overanticoagulation (HR: 2.91, $p = 0.01$) in the presence of a clinically significant drug-drug interaction.

Conclusion: These findings support the fact that CYP2C9 genotyping could be useful to identify patients requiring closer monitoring, especially when a drug-drug interaction is expected

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