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Factors affecting clopidogrel response in the Montenegrin population

Snežana Mugoša[1], Majda Šahman-Zaimović[1], Zoran Todorović[2] and **Nataša Đorđević[3]**

[1]Faculty of Medicine, University of Montenegro, Podgorica, Montenegro

[2]Faculty of Medicine, University of Belgrade, Belgrade, Serbia

[3]Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia

Background: This study addresses the genetic and nongenetic factors associated with increased risk of having major adverse cardiac events in Montenegrians treated with clopidogrel.The aim of this study was to provide the analysis of genetic and non-genetic factors that influence clopidogrel efficacy in cardiology patients.

Methods: We have conducted a prospective study in 200 hospitalized patients. *CYP2C19* genetic testing was conducted, and the PREDICT score was calculated in 102 out of 200 patients treated with clopidogrel in order to determine the influence of genetic and non-genetic factors on outcomes of interest. Adverse cardiovascular events and adverse reactions to clopidogrel were assessed during 12 months follow up period.

Results: In univariate logistic regression model, statistically significant predictors of the outcome of interest are: the PREDICT score ($p < 0.001$), enzymatic activity [slow metabolizers ($p<0.001$) compared to the rapid, extensive and intermediate metabolizers as a reference category] and concomitant use of other drugs that are also metabolized through *CYP2C19* ($p = 0.030$). In multivariate logistic regression model, predictors from the model of univariate logistic regression which were statistically significant at the significance level of 0.05 were included. The model contains three predictors - PREDICT score, enzymatic activity and concomitant administration of other drugs that are metabolized via the same CYP enzyme. The whole model was statistically significant ($p < 0.001$). There is no significant multicollinearity or interaction between the predictors ($p = 0.002$ and 0.009, respectively).

Conclusions: In assessing the clopidogrel resistance in cardiology patients the stepwise approach could be used, combining the PREDICT score, platelet aggregation test, and genetic testing for *CYP2C19* polymorphism.

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