Comparison of three different platelet function tests in patients on P2Y12 inhibitors in correlation to genetic background.

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Background

Residual platelet reactivity (PR) in patients treated with P2Y12-inhibitors can be measured with several platelet function tests (PFTs). However, the agreement between different PFTs is only slight to moderate. Polymorphisms of the CYP2C19 gene have impact on the metabolization of clopidogrel into its active metabolite and, thereby, have impact on the patients' on-treatment PR. The prodrug prasugrel is less affected by genetic variation in CYP2C19, whereas ticagrelor is a direct-acting agent so not influenced by CYP2C19 polymorphism. Aim of this study is to investigate which of three different PFTs correlates best with underlying CYP2C19 metabolism in patients treated with P2Y12-inhibitors.

Methods

In this single-center cohort study, genetic testing and PFTs were performed in 396 patients, treated with either clopidogrel (n=314), prasugrel (n=55) or ticagrelor (n=27). The choice of P2Y12-inhibitor was up to the treating cardiologist. We performed three different PFTs: Multiplate ADP, Light Transmission Aggregometry (LTA, ADP 20 µmol/L) and VerifyNow P2Y12. In whole EDTA-blood, genotyping of the CYP2C19 polymorphisms was performed using the LightCycler (Roche Diagnostics).

Results

In the clopidogrel group, LTA shows a decrease in mean value per group of CYP2C19 metabolism, with the highest value of 45.1 ± 18.1 ADP% for poor metabolizers (PM) and the lowest value of 38.1 ± 16.3 ADP% for rapid metabolizers (RM) *(p=0.063).* Roughly, the VerifyNow P2Y12 shows the same decreasing trend, with the highest value of 178.4 ± 79.6 PRU for intermediate metabolizers (IM) and the lowest value of 128.5 ± 81.3 PRU for rapid metabolizers (p<0.001). However, Multiplate ADP does not show any association between the CYP2C19 metabolism and PR of clopidogrel *(figure 1).* In prasugrel-treated patients, we detected a decrease in mean value of PR in all three PFTs for respectively IM, extensive metabolizers (EM) and RM. As expected, in ticagrelor-treated patients we found no correlation between CYP2C19 metabolism and PR as measured by all three PFTs.

Conclusion

In patients treated with clopidogrel or prasugrel, PR measured by LTA and VerifyNow correspond with underlying CYP2C19 polymorphisms, contrary to PR measured by Multiplate. As expected, no such associations were found in ticagrelor-treated patients.

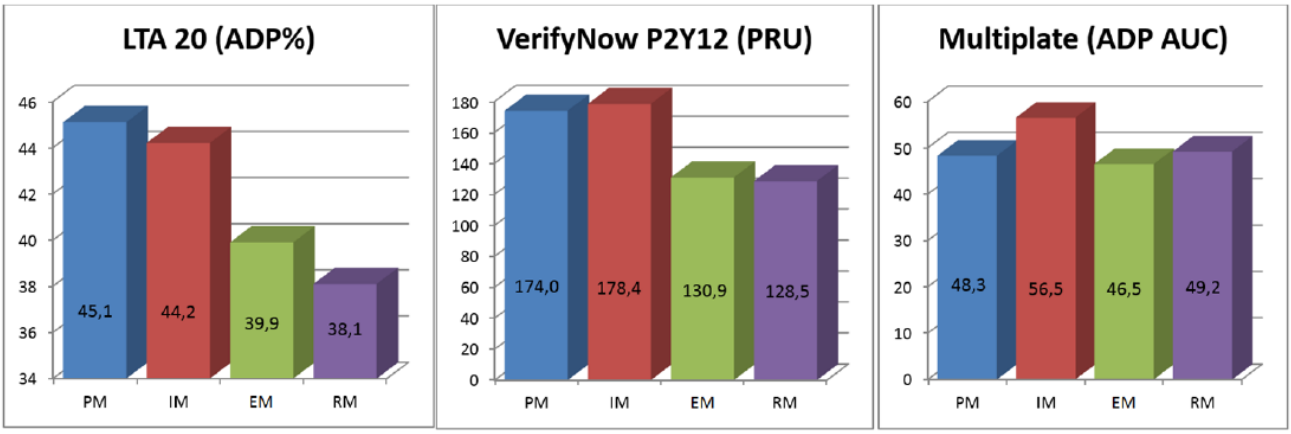

Figure 1: Mean platelet reactivity as measured by the three PFTs in the clopidogrel group; expressed per group of CYP2C19 metabolism. PM: poor metabolizers, IM: intermediate metabolizers, EM: extensive metabolizers, RM: rapid metabolizers.