

Platelet Reactivity in Patients with ESRD Receiving Clopidogrel Compared with Ticagrelor: Results of Platelet Inhibition According to Novel Drug in Patients with ESRD randomized Cross Over Study

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Background: Patients with end stage renal disease (ESRD) on maintenance hemodialysis (HD) are poor responders to clopidogrel. The aim of this study was to assess the functional impact of ticagrelor in ESRD patients receiving maintenance HD.

Methods: In a single-center, prospective, randomized, crossover study, 25 HD patients with HTPR (high on-treatment platelet reactivity) were assigned to receive ticagrelor (180 mg loading, 90 mg twice daily for maintenance dose) or clopidogrel (300 mg loading, 75 mg once daily for maintenance dose) for 14 days, and after a 14 day washout period, crossover treatment assignment for another 14 days. Platelet function was evaluated before and after anti-platelet therapy via light transmittance aggregometry and VerifyNowTM P2Y₁₂ assay, and genotyping was performed for CYP2C19*2 status. P2Y₁₂ reaction units (PRUs) less than 235 after clopidogrel treatment defined as HTPR.

Results: Baseline characteristics, cardiovascular risk factors, and concomitant medications of two groups were not significantly different. Higher inhibition of platelet aggregation (IPA) at both 5 and 20 μ mol/L ADP stimuli occurred with ticagrelor than with clopidogrel at 1, 5, and 48 hours, and 2 weeks after loading. By 5 hours after loading, a greater proportion of patients in the ticagrelor group than in the clopidogrel group achieved IPA >50% (75% versus 12%, respectively, $p < 0.05$), and IPA >70% (44% versus 0%, respectively, $p < 0.05$). The rates (slope) of onset and offset of the antiplatelet effect were faster in patients on ticagrelor than on clopidogrel ($p < 0.05$). By 1 hour after loading, the PRU values were significantly lower in the patients treated with ticagrelor (157.0 ± 57.1) than with clopidogrel (400.8 ± 66.6) therapy ($p < 0.01$). The mean percentage of platelet inhibition was also significantly higher with ticagrelor ($40.4 \pm 22.8\%$) than with clopidogrel ($2.1 \pm 5.2\%$) therapy ($p < 0.01$). The rate of HTPR at 1 hour, 48hr and 14days after loading was significantly lower in the ticagrelor group than in the clopidogrel group ($p < 0.01$). Regardless of status of CYP2C19*2 allele the ticagrelor group showed significantly lower P2Y₁₂ reaction units at all times after loading and during maintenance. No severe adverse events occurred in both groups.

Conclusions: Ticagrelor achieved more rapid and greater platelet inhibition than clopidogrel did in ESRD patients on HD.

Key Words: Platelet, Ticagrelor, Clopidogrel, End stage renal disease