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투석 중인 말기신부전 환자에서 Ticagrelor 용량과 혈소판 반응성의 관계: 무작위 교차 시험

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Relationship of dose of Ticagrelor and Platelet Reactivity in Patients with End Stage Renal Disease on Hemodialysis: A Randomized Crossover Study

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Background: Previous studies have been reported that ticagrelor has superiority on platelet inhibition in compared with clopidogrel. In our recent study, patients with end stage renal disease (ESRD) on hemodialysis (HD) also showed same results and although not serious, bleeding risk of ticagrelor was increased. We hypothesized that there were some relationships between the dose of ticagrelor and platelet inhibition, and investigated the efficacy and safety of standard dose ticagrelor, low dose ticagrelor and clopidogrel in patients with ESRD on HD.

Methods: In a single-center, prospective, randomized, crossover study, 28 patients with ESRD on HD were randomly assigned to receive standard dose ticagrelor (90 mg twice daily) or clopidogrel (75 mg once daily) for 14 days. And after a 14-day washout period, crossover treatment performed for another 14 days. Following a second-washout period, all the patients received low dose ticagrelor (90 mg once daily) for 14 days. Light transmittance aggregometry (LTA), and the Verify Now TM P2Y12 assay were used to serially measure platelet function at various time (baseline, 1, 5, and 48 hours, and 14 days after loading).

Results: Baseline characteristics, cardiovascular risk factors, and concomitant medication of three groups were not significantly different. The two ticagrelor doses showed significant higher IPAs as compared with clopidogrel ($p< 0.05$). There was no significant difference of IPAs between two ticagrelor doses. The PRUs of two ticagrelor doses were lower than clopidogrel. Though there was a significant difference of PRUs between standard dose and low dose ticagrelor at 48 hours after ($p=0.02$), the PRUs at 14 days after loading showed no significant difference between two ticagrelor doses ($p=0.056$). By 5 hours after, a greater proportion of patients in two ticagrelor doses achieved IPA >50% and >70%. The low dose ticagrelor revealed more rapid and potent inhibition of platelet when compared with clopidogrel, but not with standard dose ticagrelor. Two patients of standard dose ticagrelor and one patient of clopidogrel discontinued study due to bleeding events. There was no bleeding event in low dose ticagrelor.

Conclusions: Low dose ticagrelor may result in more rapid and greater platelet inhibition than clopidogrel, but not superior than standard dose ticagrelor in patients with ESRD on HD. Further studies with large number are needed for more definitive results.

Key Words: 티카그렐러, 클로피도그렐, 말기신부전
Ticagrelor, Clopidogrel, End stage renal disease