THE IMPACT OF NON-CYTOCHROME 3A4 METABOLIZED STATIN IN PATIENTS WITH HIGH POST-CLOPIDOGREL PLATELET REACTIVITY

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Background: "High post-clopidogrel platelet reactivity (HPPR)" after percutaneous coronary intervention (PCI) has been associated with the higher risk of peri-procedural and long-term ischemic events. Several mechanisms have been suggested as factors to diminish antiplatelet effect of clopidogrel. Because cytochrome (CYP) 3A4-metabolized statin can interact with activation of clopidogrel, it may contribute to reduced antiplatelet effect of clopidogrel. We sought to assess enhanced platelet inhibition of change with non-CYP3A4-metabolized statin in HPPR patients receiving atorvastatin.

Methods: We enrolled 40 HPPR patients treated with PCI. They all received clopidogrel 75 mg/day and atorvastatin 10 mg/day at least 6 month after PCI. They were randomly assigned to change with either rosuvastatin 10 mg/d; n = 20 and pravastatin 20 mg/d; n = 20. Platelet reactivity (PR) was assessed before change and at 15-days after change with conventional aggregometry and the VerifyNow P2Y12 assay. HPPR was defined as maximal PR (PRmax) ≥ 50% with 20 umol/l ADP stimuli.

Results: All patients completed study protocol without specific side effect. After change with non-CYP3A4-metabolized statin (rosuvastatin 10 mg/d; n = 20 and pravastatin 20 mg/d; n = 20), there were significant reductions of PRmax with 5 and 20 umol/l ADP stimuli (52.7 ± 10.7% to 46.2 ± 16.1%, p = 0.004; 66.9 ± 8.1% vs. 60.5 ± 13.9%, p = 0.001, respectively). Likewise, 5 and 20 umol/l ADP-induced late PRs were significantly decreased (41.7 ± 14.5% to 34.9 ± 19.0%, p = 0.004; 58.7 ± 13.3% vs. 50.6 ± 20.0%, p = 0.002, respectively). P2Y12 reaction unit on non-CYP3A4-metabolized statin showed a reduced value compared with that on atorvastatin (294.8 ± 64.3 vs. 244.5 ± 79.8, p < 0.001). After 15-day therapy, 9 patients (22.5%) could overcome HPPR (p < 0.001). If we divided patients into two sub-groups, the results did not differ between the groups.

Conclusions: Switch administration of non-CYP3A4-metabolized statin in HPPR patients receiving atorvastatin can enhance platelet inhibition and reduce the rate of HPPR. It needed to evaluate whether change with non-CYP3A4-metabolized statin in HPPR patients can be translated into the improved clinical outcomes.