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SERUM COTININE LEVELS ARE ASSOCIATED WITH INCREASED CLOPIDOGREL-INDUCED ANTIPLATELET EFFECTS IN PATIENTS WITH DIABETES MELLITUS AND CORONARY ARTERY DISEASE

i2 Poster Contributions
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Background: Cigarette smoking is an inducer of cytochrome P450 1A2, a hepatic enzyme involved in clopidogrel metabolism, which may explain why smokers have greater clopidogrel-induced antiplatelet effects compared with non-smokers. Clopidogrel metabolism is reduced among patients with diabetes mellitus (DM), which may explain why they commonly present with high on-treatment platelet reactivity while on clopidogrel. However, it is unknown if cigarette smoking can enhance clopidogrel-induced antiplatelet effects among DM patients.

Methods: DM patients (n=107) with stable coronary artery disease on aspirin (81mg/day) and clopidogrel (75mg/day) for at least one-month were studied. Since self-reporting smoking is not always reliable, a more objective assessment based on serum cotinine levels was used to define the degree of exposure to smoked tobacco. Patients were divided into three groups according to serum cotinine levels measured by ELISA: <3 ng/ml (non-smoker; n=71), 3-199 ng/ml (light smoker; n=23), and ≥200 ng/ml (heavy smoker; n=13). Platelet function was assessed by light transmittance aggregometry (LTA) following stimuli with 5 and 20 μmol/L adenosine diphosphate (ADP), VerifyNow P2Y12 assay, and flow cytometric assessment of intraplatelet vasodilator-stimulated phosphoprotein (VASP). LTA, VerifyNow P2Y12 assay, and VASP results were reported as maximal percentage aggregation, P2Y12 reaction units (PRU), and platelet reactivity index (PRI), respectively.

Result: Serum cotinine levels were inversely associated with platelet aggregation following 5μmol/L ADP (43.9±14.3, 35.3±15.9, and 25.8±11.9, respectively; p<0.0001) and 20μmol/L ADP (56.6±12.9, 48.6±17.5, and 35.5±13.2, respectively; p<0.0001). Similar results were found with PRU values (241±102, 184±98, and 144±79, respectively; p=0.001), and PRI values (62.7±19.9, 54.2±19.8, and 50.9±20.5, respectively; p=0.01), indicative of enhanced clopidogrel-induced antiplatelet effects with increased cotinine levels.

Conclusion: Serum cotinine levels, a marker of the degree of exposure to smoked tobacco, are associated with increased clopidogrel-induced antiplatelet effects in patients with DM.