A Study On The Impact Of CYP2C19 Genotype And Platelet Reactivity Assay On Patients Undergoing PCI

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BACKGROUND A thorough understanding of the patient's genotype and their functional response to a medication is necessary for improving event free survival. Several outcome studies support this view particularly if the patient is to be started on clopidogrel due to the prevalence of clopidogrel resistance. Such guided therapy has reduced the incidence of Major Adverse Cardiac Events (MACE) after stent implantation.

METHODS Between August 2013 and August 2014, 200 patients with coronary artery disease undergoing percutaneous coronary intervention (PCI) were prescribed any one of the anti-platelet medications such as clopidogrel, prasugrel or ticagrelor and offered testing to detect CYP2C19 gene mutations along with a platelet reactivity assay (PRA). Intended outcome was modification of anti-platelet therapy defined as either dose escalation of clopidogrel or replacement of clopidogrel with prasugrel or ticagrelor for the patients in clopidogrel arm, and replacement of ticagrelor or prasugrel with clopidogrel if those patients were non-carrier of mutant genes and also if they demonstrated bleeding tendencies in ticagrelor and prasugrel arms.

RESULTS Results obtained with the genotype assay from 200 patients showed 19.5% (n = 39) of patients had normal function of the CYP2C19. The intermediate metabolizers formed 47% (n = 94) with regards to clopidogrel metabolism. Ultra-rapid metabolizers (2.5%, n = 5), rapid metabolizers (14.5%, n = 29), and poor metabolizers (16.5%, n = 33) made up the rest. Our results suggest that up to 80% the patients could benefit from clopidogrel potentially using the PRA to guide optimal dosage. VASP assay showed good correlation of platelet reactivity with the genotype in patients on clopidogrel. Patients responding well to any of the three APTs are expected to have a PRI below 50%. Patients responded well prescribed dose of clopidogrel with a mean PRI value of 20.6% for patients with normal genotype and 23.8% for patients with increased metabolism genotype. Poor metabolizer showed inadequate response in the function test with the mean PRI value of 67%. Patients with intermediate met and were on clopidogrel (n = 30) varied greatly in their response to clopidogrel ranging from 4.5% to 84.6% on the PRI, PRA was valuable in determining which of these patients could be maintained on clopidogrel versus those with PRI >50 needing a change in drug or dosage.

CONCLUSIONS Clopidogrel resistance was observed to be 16.5% in our study population. PRA was useful in monitoring the efficacy of thienopyridines. By having this test, one can be safely maintained on clopidogrel in non-carriers, or with increased dose of clopidogrel in intermediate metabolizers or with newer drugs such as ticagrelor or prasugrel in poor metabolizers. Patients on ticagrelor and prasugrel identified as non-carriers of gene mutations for clopidogrel metabolism could be offered clopidogrel resulting in economic benefits to the patients. Patients at high risk of bleeding were also identified by the PRA.

CATEGORIES CORONARY: Pharmacology/Pharmacotherapy
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Impact of Age on the Disruption of Dual Antiplatelet Therapy: Analysis from the PARIS (Patterns of Non-Adherence to Anti-Platelet Regimens in Stented) Patients Registry

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BACKGROUND Disruption of dual antiplatelet therapy (DAPT) for either bleeding or due to patient non-adherence is associated with increased adverse events. Previous studies have also varying rates of medication adherence according to patient age. The impact of age on DAPT disruption in PCI patients has not been examined in detail.

METHODS The PARIS registry was a multicenter, prospective observational study of patients who had successful percutaneous coronary intervention (PCI) with stents. We compared the incidence of disruption by cause in the three different age groups (<50, 51-70, and >70 years old).

RESULTS Disruption for bleeding progressively increased with age whereas disruption due to patient non-adherence decreased with age. These patterns were consistent among male and female patients.

CONCLUSIONS In this real world PCI registry, older patients had increased incidence of disruption due to bleeding whereas younger patients had the highest rate of disruption due to patient non-adherence.