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RESPONSIVENESS OF CLOPIDOGREL AFTER CORONARY ARTERY STENTING

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Abstract:
Background: *Antiplatelet therapy prescribed in combination has been in practice all over the globe. The non-respondents are then put on interventional procedures like coronary artery stenting. Aspirin and clopidogrel 300mg each are used as anti-ischemic in patients with acute coronary syndrome.*
Objective: *The aim of study is to find resistance of clopidogrel after coronary artery intervention.*
Methods: *Study was conducted at department of cardiology, Mayo Hospital, Lahore, Pakistan. Study duration was one year from June 2016 to July 2017. 4 to 6 hours before PCI all patients were given 600mg clopidogrel and later were advised clopidogrel and aspirin 75mg each. A blocking analysis test was performed on P2Y12 after collecting venous blood sample. Test results were categorized into resistant, hypo-reactive and receiver based on closing time, <106 seconds, between 106 to 224seconds and >225 seconds, respectively. Demographic profile and risk factors for ACS were inquired from all participants.*
Results: *Total study population was 50 patients who were to undergo PCI including 38 males and 12 females. Fifteen were resistant (30%), 5 were hypo-reactive (10%), 30 were receivers (60%). All patients remained free from any coronary event till 4 weeks after PCI.*
Conclusion: *More than one third of post PCI population was resistant or hypo-reactive to clopidogrel.*
Keywords: *Clopidogrel, resistance, percutaneous coronary intervention (PCI), P2Y12 platelet aggregation.*

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INTRODUCTION:

Peraoxonase 1 gene promotor DNA methylation or genetic variations and major adverse events and bleeding or cardiac adverse events have been observed after dual antiplatelet therapy. In a study conducted in 2018 this relationship was studied. Statistically significant relation was observed in that study. It was concluded that hypomethylation of CpGs in the PON1 promotor leads to statistically significant bleeding after use of dual antiplatelet therapy [1,2]. The mechanism behind altered clinical efficacy of using dual antiplatelet therapy was studied by Yan Wu, et al. it was concluded that PXR polymorphisms have impact on clinical efficacy of antiplatelets [3]. Percutaneous Coronary Intervention (PCI) is an effective therapy against myocardial infarction [5].

METHODOLOGY:

Study follows descriptive study design, conducted at mayo hospital Lahore. 4 weeks prior, all patients who were to go through PCI were called and 600mg clopidogrel was prescribed to them 4 to 6 hours before PCI, then clopidogrel and aspirin 75mg daily was given. Patients who were taking drugs which interfere with efficacy of clopidogrel were excluded from selected study sample.

Venous blood was obtained from each patient and 3.2% sodium citrate was collected. Samples were pooled and tested for P2Y12 blockade with PFA, 200 siemens innovance analysis was performed, assess to P2Y12 blockade with a single use cartridge specific test clopidogrel. Closure time in seconds was measured using this method, an alternative to bleeting time measuring technique. Then on the basis of closure time patients were stratified, 106 to 224 as hyporeactives, sensitive (106 and 225 seconds). Demographic profile and risk factors to IHD were studied. Data analysis was done on SPSS 20. Categorical variables were expressed in form of frequencies and percentages. Chi square test was applied. P value <0.05 was considered significant.

RESULTS:

Study sample included 38 males and 12 females, total 50 patients who were to underwent PCI and presented to cardiology department of Mayo Hospital Lahore. All were from 38 to 70 years of age. 32% patients had DM, 22% were smokers, 10% continued smoking even after PCI. According to closure time 15 patients were clopidogrel resistant, 5 were pituitary, remaining 30 patients were sensitive. Despite of these results, no patient suffered ischemia till 4 weeks after PCI.

Characteristics		Results
Gender	Male	38 (76%)
	Female	12 (24%)
Smoker		11 (22%)
Smoker after PCI		5 (10%)
Diabetics		16 (32%)
Clopidogrel responsiveness	Resistant	15 (30%)
	Hyporesponsive	5 (10%)
	Sensitive	30 (60%)

Table 1: Demographic and clinical characteristics.

		Male	Female	P value
Diabetics	Resistant	4(10.5%)	2(16.6%)	0.925
	Hyporesponsive	3(7.8%)	1(8.3%)	
	Sensitive	5(13.1%)	1(8.3%)	
Non-diabetics	Resistant	7(18.4%)	2(16.6%)	0.040
	Hyporesponsive	1(2.6%)	2(16.6%)	
	Sensitive	18(47.3%)	4(33.3%)	

Association of DM and gender with clopidogrel resistance.

DISCUSSION:

High prevalence of non-clopidogrel and aspirin high platelet reactivity was found, and high association with risk of death was found. An Iranian population study was conducted to evaluate the risk of clopidogrel resistance and its effect on clinical outcome of patients with myocardial infarction, there was 24.7% resistance to clopidogrel in Iranian population and no effect on adverse cardiac events during follow up was observed [6,7].

An analysis on 4,587 patients was done for most powerful single nucleotide polymorphisms (CYP2C19, CYP2C9, ABCB1, PON1, P2Y12) related to on treatment platelet reactivity. No association was observed between on platelet

reactivity and bleeding. Thus, CYP2C19 may has significant impact on prognosis of PCI patients [8].

Park K, et al mentioned in a clinical trial the role of ticagrelor on antiplatelet function and efficacy was compared with clopidogrel. A pilot study on similar drug effect was conducted by Gao C, et al. ticagrelor was found to have better efficacy than clopidogrel in stabilizing vascular endothelium and improving stability of atherosclerotic plaques and reduction in ischemic outcomes [9,10].

Ischemic heart disease is notorious for causing most deaths worldwide. Thus more drugs are needed to be tested in terms of efficacy in order to reduce disease burden and to prevent recurrence of adverse cardiac events after PCI.

CONCLUSION:

More than one third of post PCI population was resistant or hypo-reactive to clopidogrel.

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