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TO DETERMINE THE EFFECTS OF CLOPIDOGREL IN PLATELET AGGREGATION INHIBITION

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Abstract:

Objective: *To evaluate the in vivo Clopidogrel 75 mg (Lowplat) therapeutic effects.*

Study Design: *A multicentre and an open study.*

Place and Duration: *In the Medicine Units of Jinnah and Services Hospital Lahore in collaboration with Cardiology department for one-year duration from May-2018 to May-2019.*

Methodology: *This study is multicentre and an open study to conclude the inhibition of aggregation of platelet of analytic drug in adult patients who were taking antiplatelet therapy, ie peripheral vascular disease (PVD), cerebrovascular accident (CVA) and coronary artery disease (CAD).*

Results: *66% inhibition of Mean platelet aggregation is done by Lowplat (P <0.001) with ± 10% standard deviation, which was significant statistically.*

Conclusion: *This analysis demonstrates that (LP) Lowplat is operative in significantly decreasing platelet aggregation in subjects requiring antiplatelet treatment. The price advantage of locally produced drugs can be given to patients.*

Key Words: *Antiplatelet therapy, Clopidogrel, platelet aggregation inhibition.*

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INTRODUCTION:

After vascular injury; first hemostatic plug at sites was the role of platelets. In temporary clot formation 1st step begins with platelets adhesions[1-2]. After adherence and aggregation of additional platelets at injury site, platelets which undergo activation result in number of changes leading to aggregation of platelet, a course that permits platelets to stick together and platelet plug formed at Injury zone[3-4]. Ticlopidine, clopidogrel and thienopyridine derivatives are antiplatelet drugs that prevent aggregation of platelet encouraged by adenosine diphosphate, which reduces ischemic trials.

Several antiplatelet drug assays have been performed in subjects with platelet activation disorders[5-6]. Its determination was to decrease several subsequent risks; myocardial infarction, vascular death and ischemic attack[7]. Patients at high risk for such outcomes include those with transient ischemic attacks or atherothrombotic disease such as severe, moderate and mild stroke, unstable angina, atherosclerotic peripheral arterial disease an MI; (POBA) and percutaneous coronary interventions (PCI) have emerged as assimilated sources of vascular trauma, predisposition to thrombosis and platelet aggregation[8-9]. NSAIDs and Aspirin prevent platelet cyclooxygenase, thus blocking the thromboxane A2 formation. These drugs tend to haemorrhage crisis by affecting aggregation of platelets due to thrombocyte and thus bleeding time increased. Clopidogrel is a platelet aggregation competitor that inhibits selectively the adenosine diphosphate (ADP) binding to the ADP and platelet receptor facilitated glycoprotein complex GPIIb / IIIa activation, thereby preventing aggregation of platelets. Clopidogrel work by irretrievably altering the ADP platelet receptor. As a result, platelets are affected by clopidogrel for the rest of its life span. Dose-dependent platelet aggregation inhibition can be seen 2hrs after one oral dose of Clopidogrel 75 mg. Frequent 75 mg Clopidogrel daily usage prevent ADP-induced aggregation of platelets on the 1st day and reach inhibition. A fixed level between 3rd to 7th days. Clopidogrel has a very high cost in the international market (more than 10 times related to local brands). Recently, in Pakistan there are many local brands, so it is necessary to assess the inhibition of platelet aggregation of new brand in the population of Pakistan and detect cost-effective contrast[10-11].

MATERIALS AND METHODS:

In this study, the Clopidogrel and Lowplat (LP) brand was used. This is an open, multicenter study held in the Medicine Units of Jinnah and Services Hospital Lahore in collaboration with Cardiology department for one year duration from May, 2018 to May, 2019. evaluating the inhibition of aggregation of platelets by Lowplat in mature patients requiring antiplatelet therapy who were suffered from various diseases. The criteria of Inclusion was patients with peripheral vascular disease (PVD), cerebrovascular accident (CVD) and coronary artery disease (CAD), women or men aged eighteen years and older, admitted at various clinics and hospitals in Lahore.

This study was carried out by 14 expert researchers in the field of cardiology, neurology and medicine. Subjects who gave their consent and who met the criteria of inclusion participated in the training were referred to the platelet collection laboratory. Exclusion criteria were uncontrolled hypertension, acute coronary syndrome, hepatic or renal insufficiency, bleeding history disorder, anticoagulant or antiplatelet drugs, clopidogrel hypersensitivity or allergy. Pregnant women and babies were also not included. Initially, on a Chronolog aggregometer in the central laboratory platelet aggregation study of each subject was done, then each subject was given a 75 mg / day tablet (LP) for seven days which was commercially available. The coordinator of study was accountable for distributing the drug of study and recording of study drug in patient file. A drug obligation record was kept, including subject dose, date of manufacture, lot number, and documentation of the termination of the study drug. After therapy completion, all drug / ampoule containers in the study were used, partially used or not collected from patients due to their responsibilities and suitability. The main characteristics of the subjects included at the time of registration are shown in Table I.

Table-I: Baseline characteristic of the patients at time of enrolment

Baseline characteristics	*n*
Total no. of patients enrolled	106
No. of patients who completed the trial	57
Mean Age (Years)	54
Men / Women	33 / 24
Hypertension	40
DM	26
Smokers	16
CAD	11
Stroke	7

Currently, methods of evaluating platelet function (eg, light conduction aggreggometry) have been advanced primarily to distinguish acquired and hereditary abnormalities of platelets and cannot be easily adapted to a point-of-care environment. The main limitations of existing platelet aggregation tests (turbidimetric) are the requirements of multi-component equipment, long time to carry out these analyzes. In contrast, electrical impedance agometry does not require preparation time and minimum cell separation (blood dilution with 1: 1 saline alone and incubation 5 minutes formerly the start of the test) and is a clinical evaluation technique approved by FDA. This procedure determines aggregation as rise in electrical impedance by a divalent metal wire subsequently from the platelets accumulation in the reaction of an agonist. After30 minutes of blood samples are taken; Impedance collection can be completed and the technique gives precise results for up to 3 hrs. Impedance and turbidimetric aggregation reactions in blood samples comparison from healthy donor's shows a good relationship among 2 methods. Electrical impedance aggregation assessment study: On the eighth day of the treatment period; blood samples were taken just before administration of the study drug, and blood was extracted directly by venous puncture using vacuum tubes. After extraction, the blood tubes were mildly shake many times to provide a comprehensive mixture with sodium citrate anticoagulant contained in the vacuum tube. Impedance method: On 591 model of Chronolog total blood aggregometer; electrical impedance aggregation dimensions were done.

Statistical analysis was performed in SPSS, version 18. To determine the variation between the previous and subsequent treatments of the study drug; paired T test was performed. $P \leq 0.05$ was considered significant.

RESULTS:

In this open study, 106 people, 57 of whom fulfilled the eligibility criteria, were included. Many of the subjects stopped during study as it was difficult to return to the final assessment of the test. 66% was the mean reduction in platelets aggregation, 56-76 mean ± SD, P = <0.001, which was significant statistically. During the study; No serious side effects were noted.

DISCUSSION:

The aim of this study was to investigate the effect of platelet aggregation of the study drug in Pakistani patients requiring antiplatelet therapy[12]. A repeated dose of LP 75 mg / day for seven days inhibits the mean platelet aggregation by 66%. The comparison of our results with other international and national data on clopidogrel confirms the results of our study[13]. The data of this study on the total blood aggregometer provide evidence of a decrease in platelet aggregation in the LP population, confirming the antithrombotic efficacy of the drug in the Pakistani population. Antiplatelet therapy is very important in CAD, especially after PCI, CABG and CVA, PVD. In most cases, the outcome of the intervention is based on regular long-term prescription drugs to improve compliance with the socioeconomic status of our patients[14]. Therefore, whenever possible, it is recommended that you prefer local quality generic drugs rather than expensive foreign brands[15].

CONCLUSION:

The median dose-dependent platelet aggregation reticence obtained with the study drug was 66%, with 56-76 mean ± SD and p = <0.001 in patients who were given Lowplat 75 mg / day and were well accepted. The results of this study are consistent with other multinational and local analysis in Clopidogrel that confirm the results of this study. This study authorizes that (Lowplat) clopidogrel is an effective antithrombotic drug. In addition, it shows that LP is effective and safe antiplatelet drug that can be given with full assurance in patients requiring antiplatelet treatment.

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