

## Research Article

## Effect of Clopidogrel Alone and in Combination with Aspirin on Platelet Aggregation in Patients with Heart Failure

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### ABSTRACT

Heart failure is a pathophysiologic state in which the heart is unable to pump blood at a rate sufficient to meet the metabolic needs of the body. Heart failure is caused by any condition which reduces the efficiency of the myocardium through damage or overloading. A cross-sectional descriptive comparative study was done in 45 post discharge patients in the 'Heart City' department of a multispecialty hospital. The main objective of this study is to assess the anti platelet effect of clopidogrel alone and with aspirin, and to assess the better choice to treat heart failure. Blood tests routinely performed include bleeding time (BT), clotting time (CT), prothrombin time (PT), international normalized ratio (INR), and platelet count (PC). The average age of the group under study was 56.25 years. There were 71% male patients. In all the patients 39% were alcoholics and smokers. In the 13 female patients, 9 (24%) were in post menopausal stage. The most affected patients were male. This study analyzes the benefits of combining of clopidogrel with aspirin in heart failure patients. The drug information sources mention that BT, CT, PT, INR, and PC values have been increased by the use of this drug. By combining this result with our result, it is proved that there is a drastic increase in the blood tests. We conclude that treatment with Clopidogrel+Aspirin provides significant synergistic inhibition of platelet activity than clopidogrel alone in patients with heart failure, antiplatelet effect being more in the combination treatment than the single drug.

**Keywords:** Heart Failure, Clopidogrel, Aspirin.

### INTRODUCTION

Heart failure is a pathophysiologic state in which the heart is unable to pump blood at a rate sufficient to meet the metabolic needs of the body. Heart failure is not a classic disease entity, in that it may be caused by numerous cardiac disorders<sup>1</sup>. It is estimated that approximately 18.8 million Indians carry a diagnosis of heart failure; this is equal to 1.76% of population. It is further estimated that 1.75 million (0.15%) new diagnosis of heart failure are made each year.

Platelet aggregation is the clumping of platelets together, using fibrin as the connecting agent. If the number of platelets is too low, that can cause bleeding. If the number is too high, that can cause thrombosis which block blood vessels, and cause strokes and heart attacks<sup>2</sup>.

Oral agents often used to alter/suppress platelet function are aspirin, clopidogrel,

cilostazol, and ticlopidine. Aspirin has proven benefits in primary and secondary prevention of coronary artery disease. Currently aspirin is an established medication for prevention of vascular events. The American diabetes association recommends using aspirin for the primary and secondary prevention of vascular disease in patients with diabetes<sup>3</sup>.

Clopidogrel, an alternative antiplatelet agent used in patients with aspirin intolerance, is especially useful in combination with aspirin after coronary stent procedures. The CURE study (Clopidogrel in Unstable Angina to Prevent Recurrent Events) demonstrated for the first time the benefit of adding clopidogrel to aspirin rather than using aspirin alone in patients having acute coronary syndromes without ST-segment elevation myocardial infarction<sup>4</sup>. However, of late, as a lot of reports are coming up

about clopidogrel's interaction with PPIs which are very commonly prescribed in many of cardiac patients on poly-pharmacy, this work has been taken up to see the superiority of clopidogrel combination with aspirin in prophylactic therapy.

This cross-sectional study compares the inhibitory effects of the combination of aspirin and clopidogrel with clopidogrel alone on platelet aggregation.

### MATERIALS AND METHODS

**Study design:** A cross-sectional descriptive comparative study.

**Study site** : 'Heart City' - department of a 400 bedded multi-speciality hospital.

**Study period:** The study was conducted during a period of 6 months.

**Inclusion/exclusion criteria:** All CHF patients with or without diabetes; LVEF < 40%; NYHA class II-IV; age 40 years and above; both sexes were included. Patients those who have taken fibrinolytic drugs during the past 6 months; patients who had MI within 2 months before the start of study period; rheumatic mitral valvular disease; pregnant women; lactating women; peptic ulcer patients; those who are taking any other antithrombotic agent than aspirin and clopidogrel were excluded.

**Method:** The clinical ethics committee of the institution approved the study. Forty-five patients who accepted to participate were included in a pre and post intervention study. After obtaining consent, the patients were interviewed to gather clinical and demographic details. Blood samples were collected for the evaluation of platelet parameters like bleeding time (BT), clotting time (CT), prothrombin time (PT), international normalized ratio (INR), and platelet count (PC) on 1<sup>st</sup> day (Base) and 30<sup>th</sup> day (Review).

The select patients were randomly divided into two groups receiving 75mg of clopidogrel alone *po* (Group A) or 75mg of clopidogrel with 150mg of aspirin *po* (Group B) every day for 30 days. Blood samples

were obtained with a 19-gauge needle by direct vein puncture and drawn into 7ml vacutainer tubes at room temperature, containing 3.8% trisodium citrate. The vacutainer tube was completely mixed with anti coagulant. Platelet studies were performed at base line and after 30 days. Bleeding time was done by Ivy method, clotting time was done by Modified Lee and White method, prothrombin time was done by "Quick" Time method, INR, and platelet count was done by Pipette method by using "Neubars chamber"<sup>5</sup>.

### STATISTICAL METHODS

The collected data were subjected to statistical analysis and results expressed as mean  $\pm$  standard deviation. 'P' value of <0.0001 was considered statistically significant.

### RESULTS

The average age of the 45 patients under study was 56.25 years. Male patients numbered 32(71%) and female patients were 13(29%). Amongst this, 2(5%) were tobacco smokers, 2(5%) were alcoholics, both smoker and alcoholics were 14(39%), non-vegetarians 10(27%), and patients in post menopausal stage 9(24%). The patients having associated diseases of both hypertension and diabetes mellitus were 8(18%). Patients having family history of CAD were 21(47%).

The base and review value of BT, CT, PT, INR, PC with the mean change value for both the groups A and B are given in Table 1 and graphical representation shown in Figure 1.

### DISCUSSION

Amongst all the subjects (n=45) in this study, 71% were males indicating that men are more likely to have heart failure than women 39%, Smoking with habitual alcohol intake (39%); smoking with alcohol with alcohol and non-vegetarian food habits (69%); and post-menopausal state in females (69%) are considered as risk factors for heart failure.

This study demonstrates that heart failure is associated with some other risk factors, which included 6 patients (13%) with DM, 8 patients (18%) with HT, 8 patients (18%) with both DM and HT.

Out of the selected 45 patients, 21 patients (46.7%) had family history of CAD and the remaining 24 patients (53.3%) were not having family history. Family history may also play a role in heart failure as risk factor precipitations.

The base and review value of BT, CT, PT, INR, PC with the mean change value for both the groups A and B are given in Table 1. In group A there is significant increase in (BT, CT, PT, INR,) and in group B there is drastic increase in (BT, CT, PT, INR,). This is due to the combination with aspirin BT, CT, PT, INR have increased by the synergistic effect of both the drugs. The PC is decreased in both the groups due to

platelet aggregation, there by it increases the blood flow to the heart and decrease the mortality rate.

From this data, it is indicated that the aspirin-clopidogrel in combination shows drastic increase in BT, CT, PT, INR and decrease in PC.

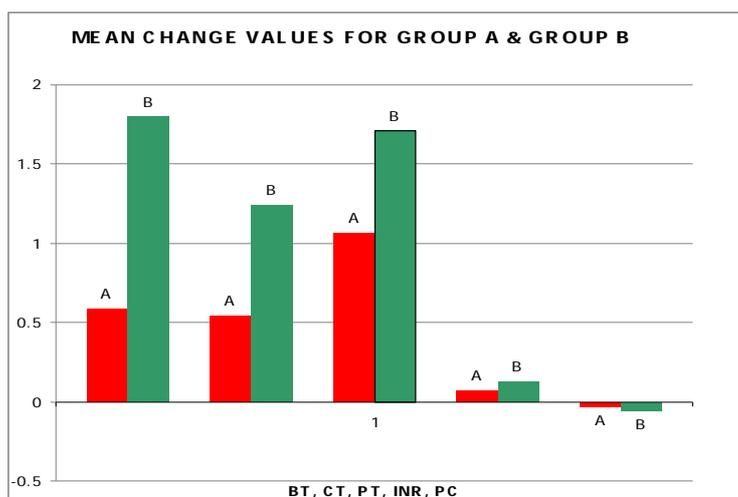
### CONCLUSION

It is concluded that the treatment with clopidogrel and aspirin provides significant synergistic inhibition of platelet activity than clopidogrel alone in patients with heart failure. The antiplatelet effect is more in the combination treatment than with the single drug. By the combination treatment, there is a definite reduction in the risk of myocardial infarction. Therefore, the best choice is the combination of these two drugs in the treatment of heart failure.

**Table 1: Mean  $\pm$ SD and mean change of platelet parameters**

S. No	Blood Parameters	Group A		Mean change	Group B		Mean Change
		Base	Review		Base	Review	
1	Bleeding time (min)	3.282 $\pm$ 0.724	3.783 $\pm$ 0.676*	0.591	3.504 $\pm$ 0.623	5.300 $\pm$ 0.801*	1.796
2	Clotting time (min)	7.300 $\pm$ 1.713	7.841 $\pm$ 1.602	0.541	7.652 $\pm$ 0.935	8.891 $\pm$ 0.894*	1.239
3	Prothrombin time (sec)	12.473 $\pm$ 0.614	13.541 $\pm$ 0.691*	1.068	12.778 $\pm$ 0.735	14.491 $\pm$ 0.782*	1.713
4	INR (sec)	0.9945 $\pm$ 0.0410	1.0627 $\pm$ 0.0719*	0.068	0.9865 $\pm$ 0.069	1.110 $\pm$ 0.0656*	0.126
5	Platelet count (lakh/cu.mm)	2.127 $\pm$ 0.101	2.096 $\pm$ 0.097	-0.031	2.070 $\pm$ 0.389	2.014 $\pm$ 0.085	-0.056

\* <0.0001 Vs Base value using Student's "T" test



**Fig. 1**

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