



Research Article

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Combined Clopidogrel And Aspirin Treatment Up To Surgery Doesn't Increase The Risk Of Postoperative Blood Loss And Reoperation For Bleeding In Patients Undergoing Coronary Artery Bypass Grafting

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ABSTRACT

Dual antiplatelet therapy is widely used in patients with coronary artery disease and the optimal management of aspirin and clopidogrel before surgery in patients with acute coronary syndrome is uncertain. The study was a prospective and randomized trial. Patients undergoing urgent coronary artery bypass graft surgery (CABG) were randomly assigned to one of two groups. Group A of patients operated by an experienced surgeon. Group B of patients that treated precautionary by blood products operated by two recently graduate surgeons. Simultaneously one group of elective patients operated after 5 days of antiplatelet cessation by mentioned experienced surgeon (Group C). Randomly assigned patients were 150 adults whom 50 in each group. The total units of given packed red cell; fresh frozen plasma and platelets in groups of A, B and C were $(0.78 \pm 1.14; 3.60 \pm 2.20; 3.14 \pm 1.90; P < 0.0001 - 0 \pm 0; 5.20 \pm 3.40; 2.34 \pm 2.36; P < 0.0001$ and $0 \pm 0; 2.10 \pm 4.90; 0.06 \pm 0.42; p < 0.005$ respectively). The amount of bleeding in that order was $(987 \pm 443 \text{ ml}; 1210 \pm 830.30 \text{ ml}; 973 \pm 537.50 \text{ ml}; p < 0.204)$. No re-exploration was found in groups A and C while 4 case of group B returned to operating room for control of bleeding and tamponade (8%). Precise CABG with good hemostasis by experienced surgeons can reduce requirement of blood products and bleeding in patients undergoing primary urgent CABG without clopidogrel and aspirin cessation.

Keywords: Clopidogrel, Aspirin, Postoperative Blood Loss, CABG

INTRODUCTION

Coronary artery bypass graft(CABG) is the most frequent cardiac surgery procedure with nearly 1 million operations conducted annually worldwide(1-4). Antiplatelet therapy forms the mainstay of primary and secondary prevention in atherothrombotic disease. In patients with acute coronary syndrome, addition of clopidogrel, a newer and more potent antiplatelet agent to aspirin within 24 hours of onset of symptoms, decreases death from cardiovascular causes, nonfatal myocardial infarction and stroke [5-7]. However in patients with acute coronary syndrome who require in-house urgent surgery, whether to continue or stop aspirin and clopidogrel therapy before surgery is uncertain.

The enhanced antiaggregatory effects of aspirin and clopidogrel raises concern about possible hemorrhagic complications arising from their use in immediate proximity to cardiac surgery. This is reflected in the practice of avoiding oral antiplatelet agents and abruptly reversing anticoagulant therapy before surgery [8-10]. Continuing preoperative antiplatelet therapy increases bleeding and reexploration after CABG [11-13]. This must be balanced against the risks of stopping antiplatelet therapy and delaying surgery.

The purpose of the current study is to assess the effect of experience and precision of the surgeon in patients receiving primary and isolated on-pump CABG with clopidogrel and aspirin ingestion less than 5 days preoperatively. The working hypothesis was that precision in hemostasis would improve transfusion requirements, bleeding and re-exploration in this specific population.

MATERIALS AND METHODS

Patient Recruitment

The study was a prospective, randomized trial. Patients eligible for randomization were men and women aged 38 to 78 years undergoing primary and isolated on-pump CABG who received dual antiplatelet therapy (clopidogrel and aspirin) with their last ingestion less than 5 days preoperatively. Patients excluded from the study were those with previous cardiac surgery, or impaired renal function and warfarin therapy.

Study protocol

Patients admitted from June 2012 to July 2013 with acute coronary syndrome requiring in-house urgent CABG with cardiopulmonary bypass surgery were considered for inclusion and these types of patients divided into two groups. Group A of patients operated by an experienced surgeon (Heidari A). Group B of patients that treated precautionary by blood products operated by two recently graduate surgeons. The randomization sequence was generated by on-call surgeon that was consulted urgently by cath. Lab. Simultaneously one group of elective patients operated after 5 days of antiplatelet cessation by mentioned experienced surgeon (group C). Dual antiplatelet therapy (clopidogrel and aspirin) was continued till surgery in both groups of A and B. Group B was treated perioperatively by platelet and fresh frozen plasma, as a precautionary procedure.

Measurements

The end points included postoperative blood loss, reoperation and postoperative blood requirements transfusion. The threshold of allogenic erythrocyte transfusion was a hemoglobin concentration of less than 6 g/dL during cardiopulmonary bypass and less than 8 g/dL postoperatively.

Postoperative blood loss was recorded as the total volume of chest and mediastinal tube drainage from the end of the operation until the removal of the tubes. Chest tubes were removed when blood loss was less than 100ml in 5 hours.

Reexploration for bleeding was performed when massive bleeding occurred in the early postoperative period with a drainage greater than 10 mL .kg⁻¹ . h⁻¹ or greater than half of this for up to 3 hours, or in the case of cardiac tamponade. Indication for fresh frozen plasma and platelet transfusion in group A and C was excessive bleeding of greater than 3 mL/kg for 2 consecutive hours.

Statistical consideration

The study is done through cross-sectional and comparative (case-witness) methods. For comparing the mean of quantity factors, in case of equality of variances, analysis of variance (ANOVA) test is used, and in case of inequality of variances Welch test is used. Independent-test is used for comparing the mean of the two groups, and chi-square is used for comparison of gender ratio. Analysis of the data is done by SPSS software v.20 with significance level set at 0.05.

RESULTS

Study participants

In the study duration, there were 625 patients who underwent cardiac surgery in the hospital, of whom 514 patients had primary isolated on-pump CABG. When urgent CABG on patients under clopidogrel and aspirin treatment reached to 50 cases in each groups of A and B, the study was stopped and investigated. Simultaneously 50 cases of elective CABG that was done by surgeon of group A brought into the study.

Baseline characteristics and perioperative data baseline characteristics, including demographics, clinical history, preoperative hemoglobin and preoperative international normalized ratio , were fairly balanced between the groups (Table 1).

Table 1. perioperative characteristics

Variable	Clopidogrel & aspirin till surgery ; no precautionary treatment (group A) (n = 50)	Clopidogrel & aspirin till surgery ; with precautionary treatment (group B) (n = 50)	No clopidogrel & aspirin within 5 days of surgery (group C) (n = 50)	P value
age(y)	59.5 ± 9.70	58.3 ± 8.60	57.9 ± 8.70	0/64
gender (% male)	72	62	66	0/56
preoperative hemoglobin(g/dL)	12.6 ± 2.35	12.6 ± 1.85	12.4 ± 1.5	0/75
preoperative platelet ×10 ³	229.5 ± 56.6	252.9 ± 68.3	250.8 ± 54.14	0/10
preoperative international normalized ratio(INR)	1.05 ± 0.11	1.07 ± 0.15	1.07 ± 0.12	0/59
postoperative hemoglobin(g/dL)	9.50 ± 1.65	9.74 ± 1.47	10.30 ± 1.30	0/051

Table 2. perioperative complications (transfusion requirements; amount of bleeding and reexploration)

Variable	Clopidogrel & aspirin till surgery ; no precautionary treatment (group A) (n = 50)	Clopidogrel & aspirin till surgery ; with precautionary treatment (group B) (n = 50)	No clopidogrel & aspirin within 5 days of surgery (group C) (n = 50)	P value
packed Red cell	23(46%)	45(90%)	46(92%)	0/0001
No. of patients (%)				
Total units	0.78 ± 1.14	3.6 ± 2.2	3.14 ± 1.9	0/0001
Fresh Frozen plasma	0(0%)	42(84%)	27(54%)	0/002
No. of patients (%)				
Total units	0 ± 0	5.2 ± 3.4	2.34 ± 2.36	0/0001
Platelet	0(0%)	15(30%)	1(2%)	0/003
No. of patients (%)				
Total units	0 ± 0	2.1 ± 4.9	0.06 ± 0.42	0/005
Amount of bleeding	50(100%)	50(100%)	50(100%)	1
No. of patients (%)				
Total mL	987.9 ± 443	1210 ± 830.3	973 ± 537.5	0/204
Reexploration	0(0%)	4(8%)	0(0%)	
No. of patients (%)				

Bleeding , transfusion and reexploration outcomes analysis between the groups showed no significant difference in amount of bleeding (987 ± 443 mL in group A; 1210 ± 830.30 mL in group B; 973 ± 537.50 mL in group C; p < 0.204) . While the difference of transfusion requirement was significant. The total units of given packed red cell ; frozen plasma and platelets were (0.78 ± 1.14 in group A; 3.60 ± 2.20 in group B; 3.14 ± 1.90 in group C; p < 0.0001 – 0 + 0 in group A; 5.20 ± 3.40 in group B; 2.34 ± 2.36 in group C; p < 0.0001 and 0 + 0 in group A; 2.10 ± 4.90 in group B 0.06 ± 0.42 in group C ; p < 0.005) respectively .

No reexploration was found in groups A and C that was operated by experienced surgeon , while 4 cases of group B returned to operating room for control of bleeding and tamponade (8%)(Table 2) .

Mortality and morbidity

There were no in-hospital mortality and specific major morbidity in groups .no specific follow-up was achieved except for routine 2weeks visit after hospital discharge.

DISCUSSION

Delay of surgery until platelet function has recovered is usually not a feasible option for patients requiring urgent or emergent CABG surgery. Under these circumstances, prophylactic platelet transfusion during surgery may be considered for rapid reversal of any pro-hemorrhagic tendency, even when the platelet count is normal [13].

However, this approach carries the risk of acute reversal of the clinical benefits of platelet inhibition [14] . For this reason, perhaps, it may be more appropriate to reserve platelet transfusion for patients with clinical bleeding after discontinuation of extracorporeal circulation and neutralization of heparin with protamine, an approach adopted in abciximab-treated patients requiring CABG surgery [15]. In this era of aggressive platelet inhibition for treatment of

coronary artery disease, the optimal management of patients presenting for CABG surgery while on oral antiplatelet therapy is still evolving.

As with all therapies, the clinical benefits (fewer preoperative or postoperative ischemic events, and improved graft patency) need to be balanced against the potential clinical drawbacks (a modest increase in blood Loss and transfusion requirements). New evidence suggests that oral antiplatelet therapy can be used with relative safety closer to the time of surgery than the ACC/AHA guidelines recommend. Importantly, aspirin and clopidogrel confer no appreciable bleeding risk if discontinued more than 5 days before CABG surgery; moreover, although their use within 5 days of surgery may increase procedural bleeding in high-risk patients, there is no associated rise in perioperative mortality. We have demonstrated that the strategy of continuing aspirin and clopidogrel therapy with precise surgery and specific attention to left internal thoracic artery bed and sterna steel wire needle holes, by experienced surgeon leads to decreased blood Loss and blood transfusion requirements compared with giving blood products as a precautionary measure and performing surgery by Less experienced surgeons.

In conclusion, for patients with acute coronary syndrome having urgent CABG, a strategy of continuation aspirin and clopidogrel therapy before surgery, coupled with precise surgery by experienced surgeon, may be adopted.

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