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Anticoagulation therapy in intra-aortic balloon counterpulsation: Does IABP really need anti-coagulation ?

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Abstract: Objective: To investigate if intra-aortic balloon pump(IABP) is contraindicated without anticoagulation therapy. Methods: Some 153 IABP patients in the King Abdulaziz Cardiac Center(KSA) were randomly assigned into two groups. Anticoagulation group(Group A) consisted of 71 patients who were given heparin intravenously with target aPTT 50-70 seconds. Non-anticoagulation group(Group B) consisted of 82 patients without intravenous heparin during balloon pumping. Hematological parameters including platelet count, D-dimer, Plasminogen activator inhibitor-1(PAI-1) and fibrinogen degradation products(FDP) were checked respectively at the point of baseline, 24 hours, 48 hours and 24 hours post IABP counterpulsation. Clot deposits on balloon surface, vascular complications from IABP including bleeding and limb ischemia were recorded. Results: Platelet count and PAI-1 level decreased at 24 hours and 48 hours in both groups ($P<0.05$). D-dimer and FDP level increased at 24 hours and 48 hours in both groups($P<0.05$), but returned to the baseline level 24 hours post IABP removal($P>0.05$). Three patients in Group A and 2 patients in Group B developed minor limb ischemia($P>0.05$). No major limb ischemia in either group. Two patients in Group A suffered major bleeding and required blood transfusion or surgical intervention, whereas no patient had major bleeding in Group B. Eight patients had minor bleeding in Group A, but only 2 patients in Group B($P<0.05$). No clot deposit developed on IABP surface in either group. Conclusion: IABP is safe without routine anticoagulation therapy. Selecting appropriate artery approach and early detection intervention are key methods for preventing complications.

Key words: Intra-aortic balloon pump, Anti-coagulation, Ischemia
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INTRODUCTION

The intra-aortic balloon pump(IABP) is the most widely used of all circulatory assist devices today and is routinely used in a wide range of serious cardiovascular conditions, ranging from hemodynamic instability in patients suffering from complications of acute myocardial infarction or cardiogenic shock, to very high risk patients undergoing angioplasty or coronary artery by-pass grafting. Limb ischemia is one of the most serious IABP related complications(Li *et al.*, 2001; Iverson *et al.*, 1988; Alderman *et al.*, 1987; Funk *et al.*, 1989). The major causes for IABP related limb ischemia are peripheral vascular disease, too large diameter of IABP catheter and its duration in aorta. Anticoagulation treatment with heparin was supposed to be reasonable for preventing limb ischemia and is routine mangement in many medical centers throughout the world. IABP was even considered contra-indicated when patients were contra-indicated for anticoagulation (Steven *et al.*, 2000). However, few studies have documented if anti-coagulation therapy can really prevent limb ischemia. Moreover, with technological advance, the IABP catheter has become thinner and thinner; low profile cathether(i.e. 8Fr) was invented and widely used. The inccidence of limb ischemia decreased(Kuki *et al.*, 2001; Jame *et al.*, 2001). The occurrence of IABP related bleeding became a serious issue(Winters *et al.*, 1999; Cohen *et al.*, 2000). Therefore, a randomised

IABP anti-coagulation therapy study was developed in King Abdulaziz Cardiac Center, Kindom of Saudi Arabia.

MATERIALS AND METHODS

Selection of patients

One-hundred fifty-three consecutive IABP patients were enrolled in this prospective study in King Abdulaziz Cardiac Center from Jan 2001 to Aug 2002 (Table 1). It was comprised of 104 male and 49 female patients with mean age of 59.2 ± 12.6. Among them, 68.2% of the patients were diabetic, 27.5% had peripheral vascular disease, 44.4% had acute myocardial infarction. Some 49.7% of the patients underwent percutaneous coronary intervention (PCI), while the rest received coronary artery by-pass grafting (CABG) surgery. They were randomly assigned into two groups. The anticoagulation group (Group A) consisting of 71 patients who were given anticoagulation therapy with heparin given intravenously during IABP therapy with goal aPTT of 50 – 70 seconds and mean IABP use duration of 46.9 ± 19.4h. The non-anticoagulation group (Group B) consisted of 82 patients to whom no intravenous heparin was given during the whole IABP therapy period, with mean IABP use duration of 45.1 ± 22.4h.

Table 1 Baseline demographics

	Total patients (N = 153)	GroupA (N = 71)	GroupB (N = 82)
Age (year)	59.2 ± 12.6	58.7 ± 11.2	59.6 ± 13.8
Female (%)	49 (32.0)	19 (26.8)	30 (36.6)
[b] BSA (M2)	2.0 ± 0.2	2.0 ± 0.3	2.0 ± 0.2
PVD (%)	42 (27.5)	18 (25.4)	24 (29.3)
[c] DM (%)	89 (58.2)	43 (62.0)	46 (56.1)
[a] AMI (%)	68 (44.4)	36 (50.7)	32 (39.0)
PCI (%)	76 (49.7)	35 (49.3)	41 (50)
[d] CABG (%)	77 (50.3)	36 (50.7)	41 (50)
PD (h)	45.9 ± 22.1	46.9 ± 19.4	45.1 ± 22.4

[a] AMI: acute myocardial infarction; [b] BSA: Body surface area; [c] DM: diabetes mellitus; [d] CABG: coronary artery by-pass grafting; N: patient number; PCI: percutaneous coronary intervention; PD: Intra-aortic balloon contrapulsation time; PVD: peripheral vascular disease. On each parameter above between GroupA and GroupB, no statistical difference was found ($P > 0.05$).

IABP catheter and artery approach

All IABP catheters were 8Fr Fidelity (34cc and 40cc) that were heparin-free and manufactured by Datascope Corp., U.S. One-hundred fifty-one patients underwent IABP insertion procedure in the Cath Lab and were then transferred to CCU or CVICU for postprocedure care. Only two patients received emergent IABP insertion procedure out of the Cath Lab. Fifty-six patients had retrograde abdominal aortagraphy before catheter insertion and the side with less peripheral vascular disease in the iliac and femoral artery was chosen as artery approach. The femoral artery approach were applied to 151 patients, but 2 patients received IABP via the left axillary artery.

Hematological parameters

Routine blood test was done every day during IABP counterpulsation. Besides routine blood test, blood sample was drawn and sent to the central lab at the point of beginning , 24 hours, 48 hours and 24 hours post-IABP for special hematological tests including D-dimer (ELISA, D-D1 Asserachrom Stago), PAI-1 (ELISA method) and FDP (Mershey method).

Clinical parameters

(1) Limb ischemia: Major limb ischemia was defined as a loss of pulse or sensation, or abnormal limb temperature or pallor, requiring surgical intervention. Decreased arterial flow as presented by diminished pulse that resolves with balloon removal, and not resulting in any impairment of body function defined as minor limb ischemia. (2) Bleeding: Severe bleeding was defined as bleeding associated with hemodynamic compromise, requiring blood transfusion or surgical intervention. Whereas, minor bleeding involved minor hematomas and oozing from puncture site, and did not require blood transfusion or surgical intervention. (3) IABP thrombus: Positive was defined as any clot deposit developed on the surface of IABP which was detected immediately after IABP removal. No clot deposit was defined as negative.

Statistical methods

Chi-squared analysis and t-test were used to analyze the differences of complication incidence, and demographic and hematological pa-

rameters. For all analysis $P < 0.05$ was taken as statistically significant.

RESULT

1. Hematological results(Table 2)

(1)Platelet count: Compared to the baseline level, platelet count changes were seen at 24 hours and 48 hours in both groups($P < 0.05$). It was not back to baseline level even at 24 hours post-IABP counterpulsation in either group($P < 0.05$). But no significant difference of platelet count was seen between GroupA and GroupB ($P > 0.05$).

(2)D-dimer: Compared to the baseline level, significant increasing of D-dimer was noted at 24 hours and 48 hours in both groups ($P < 0.05$). It returned to baseline level at 24 hours post-IABP counterpulsation in both groups($P > 0.05$). However, no difference was seen between the two groups($P > 0.05$).

(3)PAI-1: Compared to the baseline level, significant decreasing of PAI-1 was detected at 24 hours and 48 hours in both groups ($P < 0.05$). It recovered to baseline level at 24 hours post-IABP counterpulsation in both groups($P > 0.05$). But no difference was found between GroupA and GroupB($P > 0.05$).

(4)FDP: Compared to the baseline level, significant increasing of FDP was noted at 24 hours and 48 hours in both groups($P < 0.05$). No difference of FDP level was noted between the two groups($P > 0.05$).

Table 2 Hematological parameter changes

	Baseline		24 hours		48 hours		24 hours Post-IABP	
	GroupA ($N = 71$)	GroupB ($N = 82$)	GroupA ($N = 62$)	GroupB ($N = 70$)	GroupA ($N = 31$)	GroupB ($N = 37$)	GroupA ($N = 71$)	GroupB ($N = 82$)
Plt(1000/ul)	181.4 ± 76.8	177.6 ± 82.2	167.1 ± 64.5†	165.3 ± 71.5‡	131.7 ± 74.6†	123.0 ± 72.1‡	156.4 ± 74.4†	153.7 ± 70.2‡
DD(mg/L)	0.45 ± 0.51	0.46 ± 0.49	2.65 ± 2.73†	2.71 ± 2.31‡	2.01 ± 1.45†	1.96 ± 1.08‡	0.42 ± 0.39	0.49 ± 0.42
PAI-1(iu/ml)	1.22 ± 0.81	1.31 ± 1.24	0.64 ± 0.43†	0.61 ± 0.46‡	0.51 ± 0.66†	0.48 ± 0.57‡	1.28 ± 0.84	1.24 ± 0.78
FDP(ug/L)	35.2 ± 11.5	36.4 ± 15.2	172.3 ± 97.2†	182.4 ± 93.5‡	144.8 ± 88.6†	159.4 ± 79.4‡	41.2 ± 36.7	40.5 ± 33.8

DD: D-dimer; FDP: fibrinogen degradation products; N: patient number; PAI-1: plasminogen activator inhibitor-1; Plt: platelet; †: compared to Group A at baseline, $P < 0.05$; ‡: compared to Group B at baseline, $P < 0.05$.

2. Vascular complications(Table 3):

(1)Limb ischemia: No major limb ischemia occurred in either group in this study. There were three and two patients suffering minor limb ischemia in Group A and Group B, respectively. However, no statistically significant difference was seen at this point of view($P > 0.05$).

(2) Bleeding: There were two patients who developed major bleeding at the puncture site in Group A. No major bleeding was found in Group B. Eight patients suffered minor bleeding in Group A; whereas two patients had minor bleeding in Group B. There was statistically significant difference at this point of view($P < 0.05$).

(3) IABP thrombus: No clot deposit on IABP surface was detected macroscopically in either group.

Table 3 IABP vascular complications

	GroupA ($N = 71$)	GroupB ($N = 82$)	P
Major limb ischemia(%)	0	0	
Minor limb ischemia(%)	3(4.2)	2(2.4)	>0.05
Bleeding(%)	10(14.1)	2(2.4)	<0.05
Major bleeding(%)	2(2.8)	0	>0.05
Minor bleeding(%)	8(11.3)	2(2.4)	<0.05

N: patient number

DISCUSSION

Heparin was supposed to mainly prevent IABP related limb ischemia. However this study showed that routine anti-coagulation therapy with heparin to prevent IABP related limb ischemia is not essential. No extra limb ischemia induced by IABP was seen in Group B. Among 82 patients in Group B, two developed minor limb ischemia. However, there were 3 cases of minor limb ischemia in Group A which consisted of 71 patients. No statistically significant difference

was seen at this point of view. The Benchmark IABP Registry, a multi-center, randomised, and prospective study, showed that there is an increased risk of major complications in women, older patients and patients with peripheral vascular disease(Ferguson *et al*., 2001). The major causes for IABP related limb ischemia are peripheral vascular disease, too large diameter of IABP catheter and its duration of use in the aorta. Percutaneous placement of an IABP through a femoral artery approach of a patient is associated with a risk of reduction of blood flow distal to the balloon insertion site. Diameters of vessel and catheter have a profound and nonlinear effect on the distal flow. For example, a 12.2Fr catheter in a 5 mm vessel only allows 19.9% of normal flow, whereas a 6.1Fr catheter in the same size vessel allows 92% flow. As catheter diameter increases or vessel diameter decreases, the physical resistance suddenly grows, which causes a significant drop in distal flow. In general, vessels larger than 5 mm in diameter do not exhibit substantial flow reduction for most IABP at modern time(Ohley *et al*., 1998). 8Fr IABP catheter is widely used these days. Therefore, too small femoral artery in diameter is a main factor leading to limb ischemia. Without anti-coagulation therapy, no clot deposit on the surface of working IABP was found even by scanning electron microscopy(Mueller *et al*., 1999). In this study, no clot deposit was found macroscopically in either group. In the neurological field, IABP was successfully used to treat patients with symptomatic cerebral vasospasm after subarachnoid hemorrhage(Sato *et al*., 2001). All evidence above show it is safe to use IABP without routine anti-coagulation therapy.

This study also showed that patients in both groups were prone to bleed and IABP therapy with anti-coagulation medication further increased the inccidence of bleeding. In both groups, platelet count decreased significantly during IABP counterpulsation, even 24 hours after IABP removal. PAI-1 level decreased, indicating fibrinolysis was prone to be activated. Elevation of D-dimer and FDP level during IABP counterpulsation supported activation of fibrinolysis. Decreased platelet count and activation of fibrinolysis resulted in tendency of bleeding. In Group B, there were two patients developed major bleeding and eight patients had minor bleeding. Two patients with major bleeding both suffered acute myocardial infarction. One received rescue PCI after failure of thrombolytic therapy. The other underwent direct PCI. Both of them were given 300 mg Clopidogrel before the procedure. The patient undergoing direct PCI also received intravenous Abaxicimab infusion. IABP activated the internal coagulation path via factor XIIa; meanwhile, it stimulated fibrinolysis and resulted in obvious bleeding tendency at or around 24 hours of IABP therapy and continued throughout the next 24 hours(Suzanne *et al*., 1997). When an arterial sheath is not removed, potent anti-platelet medications (i.e. Clopidogrel, Ticlodipine and Abaxicimab etc.) combined with heparin treatment significantly increased the possibility of puncture site bleeding(Kleiman *et al*., 2000). During IABP counterpulsation, anti-platelet medications further inhibits the platelet function; thrombolytic therapy further stimulates fibrinolysis and diminishes coagulation factors. Furthermore, heparin inhibits coagulation factors' activation and hence leads to bleeding.

The effective measure to prevent limb ischemia is to select an appropriate aterial approach for IABP and careful post-procedure nursing care. In this study, all patients except two underwent IABP insertion procedure in the Cath Lab. Among them, 56 patients had retrograde abdominal aortagraphy before IABP insertion and the side with less peripheral vascular disease in the iliac and femoral artery was chosen as artery approach. There were two patients receiving IABP successfully without any complication via left axillary artery because of either severe arterial stenosis or total occlusion in both femoral arteries. Limb ischemia associated with intra-aortic balloon pumping is preventable (Stavarski, 1996). The critical care nurses should have awareness of potential limb ischemia related to IABP and check the distal arterial pulse and puncture site every one hour. Early detection and rapid intervention serves to decrease the inccidence of more serious and devastating limb ischemia associated with the use of IABP. In this study, five patients developed minor limb ischemia and recovered completely, which was attributed to early discovery and rapid removal of IABP. Anti-coagulation theray with heparin cannot prevent limb ischemia associated with the use

of IABP. In general, it is very important to select appropriate artery aproach for IABP and provide special post-procedure nursing care for early detection and rapid intervention of complications.

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