



Effectiveness of low volume acute normovolemic hemodilution in patients undergoing off pump coronary artery bypass grafting surgery

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Abstract

Background: *The objective of this study was to evaluate the effectiveness of low volume acute normovolemic hemodilution (LVANH) in patients undergoing primary elective off pump coronary artery bypass graft (OPCAB) surgery.*

Methods: *Sixty patients undergoing primary elective OPCAB surgery were prospectively randomized into two groups: Group LVANH (n=30) and Group C (n=30) as control. Autologous blood was removed (< 4 ml/ kg but more than 200 ml) of estimated blood volume in patients with hemoglobin (Hb) >12g% to keep hematocrit more than 30% after acute normovolumic hemodilution for subsequent re-transfusion after protamine administration from group LVANH, while no blood was withdrawn from control group. The autologous blood withdrawn was replaced simultaneously with an equal volume of hydroxyl-ethyl starch solution in group LVANH patients only. Allogenic blood was transfused in both the groups when Hb was ≤8.5g %. Total post operative drain and requirement of postoperative allogenic blood transfusion along with any adverse events were evaluated.*

Results: *The two groups were comparable in regards of demographic data, type of surgical procedures performed, duration of surgery. Both groups have comparable hemaocrit and ACT levels at the time of shifting to post operative cardiac surgery unit without any added ischemic or hemodynamic intraoperative events. During first and fourth hour of recovery period, amount of blood drainage is significantly reduced in LVANH group but after twenty four hours amount of total blood drain is comparable. Perioperative blood transfusion requirements were also not statistically different. No patient in any of the groups suffered major adverse cardiac event. Patients were extubated, shifted out of intensive care unit and discharged home with comparable time periods.*

Conclusion: *We conclude that low volume autologous blood transfusion procedure is safe and can be done without any added risk to selected patients those are posted for off pump cardiac surgery. This method of blood salvage may have importance during first four hours of surgery but had no advantage after that period on perioperative blood loss and transfusion requirements.*

Keywords: *Low volume acute normovolemic hemodilution, off pump coronary artery bypass graft surgery.*

Objective

Blood salvage is a major concern during cardiac surgeries as recent evidence suggests allogenic blood transfusion results in negative outcome in terms of increased morbidity and mortality, prolonged hospital stay and decrease in long-term quality of life¹.

Acute normovolemic autologous blood withdrawal and retransfusion post surgery is one of the strategies for blood salvage during on pump cardiac surgery². Usually 6-8 ml/ kg blood is collected in standard CPDA bag prior to heparinization so that hematocrit remained more than 25% after isovolumic hemodilution during extra corporeal circulation, which is transfused back to patient after hemostasis and protamine.³ This autologous blood provides advantages of not only increases hemoglobin but also replaces platelets and coagulation factors⁴.

Patients planned for off pump coronary artery bypass graft surgeries which are done on beating heart without the use of extra corporeal circulation require more hematocrit (30%). In these patients, myocardium is at the increased risk of ischemia during low cardiac output stages which occurs with manipulation of heart at time of coronary grafting⁵. It is not prudent to take full volume autologous blood in these patients. Our objective is to study utility of low volume acute normovolumic hemodilution (< 4 ml/kg but more than 200ml) with target hematocrit of not less than 30% can be safely collected from these patients and replaced after protamine will able to decrease perioperative drainage and allogenic blood transfusions.

Methods

After getting approval from institutional ethical board, patients who were planned for off pump coronary artery bypass graft surgery with stable cardio vascular status and controlled comorbidities, having preoperative hematocrit more than 36% were included in this study. Informed consent was taken. Preoperative exclusion criteria were body weight less than 50 kg, left ventricular ejection fraction (LVEF) less than 40%,

associated valvular lesions, preoperative hematocrit less than 36% or hemoglobin less than 12 g/dl, history of hematologic diseases, more than mild renal impairment (plasma creatinine >1.4 mg/dl), history of hepatic diseases (e.g. active hepatitis or cirrhosis) and re-do surgeries. Preoperative treatment with aspirin or heparin was not a contraindication to enrolment in this study.

A standardized protocol for anesthesia was applied. Induction and maintenance of anesthesia were performed with propofol (response titrated bolus of 1- 2 mg/kg, midazolam 0.05 mg/ kg and fentanyl (bolus of 3-5 µg/kg). Muscle relaxation was obtained with vecuronium or pancuronium bromide (bolus of 0.1 mg/kg and further administrations of 0.03 mg/kg hourly). Isoflurane was added after induction and patients were ventilated on closed circuit system with end tidal carbon dioxide value of 35mmHg.

By using a computer-generated random number sequence, the 60 patients were prospectively randomized, into two groups: the LVANH group (30 patients) and the control group (30 patients). In the LVANH group patients, less than 4 ml/ kg but above 200 ml of pre calculated blood was withdrawn after the induction of anesthesia and before systemic heparinization to keep hematocrit above 30% after acute normovolumic hemodilution (ANH). Calculation for amount of blood withdrawn was done according to Gross formula¹ that is patient hematocrit minus target hematocrit divided by patients hematocrit and multiply by total blood volume. The blood was withdrawn through a large bore catheter placed into the internal jugular vein, with gravity drainage, to limit shear effects on the platelets. During the withdrawal of the autologous blood, a colloid solution was infused (Volulyte 6% HES 130/0.4, Fresinus Kabi) in 1:1 ratio. This blood was collected into sterile standard CPDA blood collection bags containing citrate phosphate dextrose anticoagulant (Terumo Penpol, India). In group C patients, no autologous blood was withdrawn and hemodilution with colloids was not done. In both groups, crystalloids were infused

if hemodynamic status required. Isovolemia was evaluated through standard monitoring (systemic arterial pressure, electrocardiogram, pulmonary artery pressure and central venous pressure). Autologous blood withdrawn was labeled with the patient's identification and stored at room temperature in the operating room.

The same team of surgeons, with standardized surgical procedures, did all the interventions. All patients were operated on through full median sternotomy. Before coronary arteriotomy, porcine heparin, was administered to keep activated clotting time (ACT) above 300 sec. and off pump coronary artery bypass graft surgery performed using medtronic heart stabilizers (octopus). The blood drawn before surgery from the LVANH group patients was reinfused at the end of surgery after protamine and before transporting patients to the intensive care unit (ICU). Intra- and postoperative criteria for allogeneic transfusions were standardized. These criteria were applied in the LVANH group only after the reinfusion of the autologous blood withdrawn. Packed red blood cells (PRBC) were transfused, during surgery if hemoglobin value was less than 8.5 g/dl and hematocrit value was less than 26% at any point of time to all the patients.

Fresh frozen plasma (FFP) was infused, after protamine administration, if prothrombin time value was 1.5 times the basal in presence of active bleeding. Platelet concentrates (PLTC) were transfused in presence of active bleeding and of a platelet count less than 50,000/mm³. Samples for evaluation of hemoglobin, leucocyte count, platelet count, activated clotting time (ACT), creatinine were performed before the induction of anesthesia (time:T1), on arrival in ICU (time T2), 24 h after the arrival in ICU (time T3), shifting to step down from ICU after surgery (time T4) and at discharge (time T5). Further determinations of these variables were made as the clinical situation required.

Blood loss was recorded during the first 24 h.

Surgical re-exploration was decided on when bleeding in the first 2 h was greater than 300 ml/h or if greater than 200 ml/h for 4 consecutive h, with normal coagulation data. Intubation time, ICU stay, hospitalization, major complications (e.g., perioperative myocardial infarction, renal insufficiency, pulmonary embolism, stroke), and mortality were considered.

Results

Table 1 Demographic data

Variable	Control	LVANH	P value
AGE (years)	59.4±12.9	63.7±17.2	0.278
SEX (M: F)	18:12	16:14	
WEIGHT (kg)	63.6±19.8	69.2±15.3	0.225
LV EF			
40% -50%	12	14	0.27
50%-60%	18	16	
NYHA Class	3	3	
Vessels grafts count			
2 (lima +1 rsv graft)	7	9	
3 (lima +2 rsv graft)	23	21	0.67
Co Morbidity			
I. DM	14	16	0.27
II. HTN	18	19	0.97
III. HYPOTHYROID	9	5	0.38
IV. Rn.Insufficiency	4	3	0.79
Sr.Creat: 1.2-1.4			
Pre op. Asprin up to 2days	6	8	0.27

Table 2 Post operative data

Variable	Control Gr.	LVANH Gr.	P value
Duration of surgery	239 ±67 min	266 ±42 min	0.067
Intervention during grafting	0	0	
Conversion to onpump / iabp	0	0	
Postoperative act	145±23	129±29	0.109
Post operative hct	29±7%	31±9%	0.341
Extubation time	324 ±63 min	347±56 min	0.14

Table 3 Post operative bleeding

Post operative bleeding			
1st hr.	80±45 ml	50±52 ml	0.02
2 nd hr.	68±36 ml	76±32 ml	0.36
3 rd hr	72±45 ml	90±43 ml	0.056
4th hr	90±48 ml	62±57 ml	0.044
Bl loss 24 hr.	553±65	528±45 ml	0.089
Pt. Require BT	19/30	17/30	0.89
Total no. of BT			
PRBC	25	22	1
FFP	Nil	Nil	
PL.	Nil	Nil	

Table 4 Post operative data

	Group C					Group LVANH				
	T1	T2	T3	T4	T5	T1	T2	T3	T4	T5
Hct% (±2SD)	38 (7.2)	28 (5.1)	27.5 (5.7)	28.2 (5.9)	29 (6.1)	37 (6.9)	30 (6.1)	28 (4.9)	27.5 (6.3)	28 (6.6)
TLC10 ³ (±2SD)	10.7 (1.8)	12.3 (2.3)	13.45 (2.6)	13.0 (1.9)	11.37 (2.4)	10.5 (2.1)	11.4 (2.9)	13.7 (2.6)	12.2 (2.9)	11.2 (2.9)
Plt.10 ⁵ (±2SD)	1.58 (0.4)	1.26 (0.2)	1.26 (0.31)	1.20 (0.19)	1.38 (2.7)	1.42 (0.19)	1.38 (0.28)	1.32 (0.25)	1.28 (0.31)	1.32 (0.29)
ACT.sec (±2SD)	128 (23.7)	152 (22.6)	132 (23.8)	130 (27.3)	132 (21.8)	133 (27.9)	146 (32.8)	130 (29.4)	126 (23.9)	128 (27.1)
Cr.mg/dl (±2SD)	1.1 (0.3)	1.2 (0.2)	1.1 (0.1)	1.2 (0.2)	1.2 (0.1)	1.08 (0.2)	1.2 (0.12)	1.18 (0.19)	1.15 (0.17)	1.2 (0.16)

Table 5 Adverse Events Data

	Group C	Group LVANH	
Fever>38.5° C	3	4	>0.05
Leukocytosis	2	3	>0.05
Sternal wound inf.	1	0	>0.05
inotropes> Mild dose	7	9	>0.05
Arrhythmias	0	0	
Reintubation	0	0	
Re Exploration	0	0	
Tamponade	0	0	
LOS ICU > 3d	4	3	>0.05
LOS Hospital > 7d	3	3	>0.05

Discussion

Cardiac surgery is responsible for approximately 20% of allogenic blood transfusion.⁷ However, the transfusion rate has been decreased considerably in recent years.⁸ This has been mainly due to advancement in surgical expertise as well as better understanding of the physiology of blood

transfusion which has led to lower transfusion trigger⁹. In addition, the use of newer antifibrinolytics drug, blood salvage techniques and guidelines by ASA 2015 guidelines have also contributed to the decrease in transfusion requirements.¹⁰ The efficacy of ANH is still controversial with only some studies

demonstrating the benefit of ANH in cardiac surgery¹¹. These have mostly been in patients undergoing coronary artery bypass grafting on cardiopulmonary bypass in whom large volume of autologous blood (700-1000 mL) was withdrawn¹². Few others have demonstrated ANH with withdrawal of 5-8 mL/kg or 400 mL¹³ of blood. But to remove this amount of blood from patients who are at the risk for myocardial ischemia is not approved by most of the cardiac surgeons. Our desire to study the effects of low-volume ANH on patients undergoing OPCAB surgery derives from the fact that these patients are considered to be at increased risk for perioperative excessive bleeding, therefore theoretically more benefits may be achieved by the application of autologous blood transfusion to this group of patients. Segal *et al.*¹⁴ in their meta-analysis report that only a modest hemostatic benefit is seen with ANH and that the clinical benefit of reducing blood loss by small volume is unknown. We designed this study for assessment of benefit gained with the use of low volume acute normovolumic blood transfusion in selected off pump cardiac surgery patients.

In our study both groups were comparable in terms of demographic data, comorbidity, pre operative nature of disease and duration of surgery. (Table 1)

Analysis of post operative data shows both groups have comparable hematocrit and ACT levels at the time of shifting to post operative cardiac surgery unit without any added ischemic or hemodynamic events. (Table 2). This reflects safe method of normovolumic hemodilution with use of 6% 130/0.4 HES colloid solution. As none of the patients in LVA group had intraoperative ischemic episodes and no patients required any blood transfusion during coronary grafting, it can be concluded that low volume autologous blood can be safely withdrawn in selected patient group posted for off pump coronary artery bypass graft surgery without posing additional risk to these vulnerable patients. (Table 2)

Interesting observation is that during first and fourth hour of recovery period, amount of blood

drainage is significantly reduced in LVANH group but after twenty four hours amount of total blood drain is comparable. Possible explanation is this may be due to replacement of transfused platelets and coagulation factor with fresh autologous blood in LVANH group. (Table 3)

Total number of allogenic blood transfusion requirement was also not statistically different. Patients were extubated, shifted out of intensive care unit and discharged home with comparable time periods. (Table 3)

No statistical significant difference was observed in hematocrit, leucocyte count, platelets count, ACT values and serum creatinine values at all predefined point of times. (Table 4).

Authors acknowledge that autologous blood transfusion is not without adverse events. Acute hemolytic reactions has been documented due to mistaken transfusion to a different patient in literature. Bacterial contamination of collected blood, hemodynamic instability and acute coronary events were other reported complication of autologous blood transfusions¹⁵. But no such complications were noted in the present study. This may be due to prudent technique and may also related to low volume of autologous blood withdrawn from the patients. Blood transfusion requirements post off pump coronary bypass surgery were comparable in both groups and amount of blood required not significantly different, this observation annul any conclusive advantage of low volume acute hemodilution transfusion in these cases after four hours of surgery.

No patient in any of the groups suffered major adverse cardiac event and all patients discharged home with satisfactory recovery within 10 day of surgery. (Table 5)

Conclusion

This study suggested that low volume autologous blood transfusion procedure is safe and can be done without any added risk to selected patients those are posted for off pump cardiac surgery. Actual benefit of this technique on reduction of blood loss is seen in first four hours of recovery

but no added advantage is gained in post four hour period. Authors recommended large scale multicentre study with long follow up period for definitive conclusions.

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