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A PROSPECTIVE RANDOMISED CASE CONTROL STUDY OF EFFICIENCY AND SAFETY OF LOW VOLUME ACUTE NORMOVOLUMIC HEMODILUTION IN PATIENT UNDERGOING CARDIAC SURGERY.

Anaesthesiology

Dr. Anita Saini* M.D Anaesthesia Resident Department of Anaesthesiology, Critical Care and Pain Management, Mahatma Gandhi Medical College and Hospital, Jaipur (Rajasthan) Pin 302022, India. *Corresponding Author

Dr. Gaurav Goyal M.D, FNB Cardiac Anaesthesia, Professor Department of Anaesthesiology, Critical Care and Pain Management, Mahatma Gandhi Medical College and Hospital, Jaipur (Rajasthan) Pin 302022, India.

Dr. Durga Jethava M.D Anaesthesia, Professor and Head of Department Department of Anaesthesiology, Critical Care and Pain Management, Mahatma Gandhi Medical College and Hospital, Jaipur (Rajasthan) Pin 302022, India.

ABSTRACT

Background & Aim: Intra-operative autologous blood donation is well known blood conservation technique with limited evidence. Mostly one to two units packed red blood cells are required.

Methods and Material: 60 patients undergoing cardiac surgery were prospectively randomized into two Groups LVANH (n=30) and control (n=30). Autologous blood was removed (2.5ml/kg but above 200ml) in patients with hemoglobin >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hemodilution for subsequent re-transfusion after protamine administration from group LVANH, while no blood was withdrawn from control group. The autologous blood withdrawn was replaced simultaneously with an equal volume of hydroxyl-ethyl starch solution. Allogenic blood was transfused in both the groups when Hb was ≤8g %. Total post operative drain and allogenic blood transfusion along with adverse events were evaluated.

Results: The groups were comparable. They have stable haemodynamics without any added intraoperative events. During initial two hours of recovery period, amount of blood drainage is significantly reduced in LVANH group. Total bleeding was also more in control group (729.33±98.67ml) as compared to LVANH group (656.33±135.71ml). Post-operatively 16 patients in control and 11 patients in LVANH group received 1- and 2- units red blood cells. No patient in any of the groups suffered major adverse event.

Conclusion: Low volume autologous blood transfusion is safe and feasible without any added risk.

KEYWORDS

Allogenic blood, Hematocrit, Bleeding

INTRODUCTION:

Cardio thoracic surgery accounts for around 20% of total blood transfusion requirements in health care facilities, which is significantly more than any other surgery. They are associated with increased risk of perioperative bleeding[1]. With the advancement of surgical skills and blood salvage strategies mostly 1- and 2- units of red blood cell transfusion required. Our aim is to evaluate role of low volume acute normovolumic hemodilution in reducing allogeneic blood requirement and also safety of this technique by analysing outcome. Blood transfusion associated complications[2] and possibility of excessive bleeding which predisposes to subsequent increase in postoperative morbidity and mortality[3] are the two main concern of these patients. Acute normovolemic autologous blood withdrawal and re-transfusion post-surgery is one of the strategies for blood salvage. This not only increases hemoglobin but also replaces platelets and coagulation factors[4]. This helps in decreasing red cell loss during surgery by reducing the patient's red cell mass just before surgery[5]. Usually 6-8 ml/ kg blood is collected in standard CPDA (citrate phosphate dextrose adenine) bag prior to heparinization so that hematocrit remain more than 25% after isovolumic hemodilution during extra corporeal circulation, which is transfused back to patient after hemostasis and protamine.[6] Our hypothesis is that this can safely be achieved with low volume autologous normovolumic hemodilution (LVANH) method. Our objective is to evaluate need of allogeneic blood transfusion and safety of low volume acute normovolumic hemodilution (2.5ml/kg but more than 200ml) with target hematocrit of not less than 30% in patient undergoing cardiac surgery.

MATERIAL AND METHOD:

This is prospective randomized case control study conducted on 60 patients planned for cardiac surgery with NYHA grade 2 and 3 statuses with well optimized co-morbidity and those who can be extubated early.

These patients were randomly divided into two group LVANH (study) and control group. Under standard and invasive monitoring, which includes Spo2, ECG, Heart Rate, end tidal CO2 and invasive blood pressure patients were induced with 3-5µg/ kg of fentanyl, 0.05 mg/ kg midazolam, through intravenous (IV) route. Hypnotic dose of propofol 1-2mg/ Kg was given intra venously as per response with assisted ventilation. All patients were intubated after giving intravenous vecuronium 0.1mg/ Kg with proper size endotracheal tubes and ventilated with oxygen and inhalational anaesthetic agent isoflurane.

For maintenance isoflurane 1% and top up doses of anaesthesia drugs were given throughout operative period and patients were ventilated on closed circuit system with end tidal carbon-dioxide value of 35mmhg.

In the LVANH group patients, 2.5ml/kg but above 200 ml of whole blood was withdrawn after induction of anaesthesia and before systemic heparinization to keep hematocrit above 30% after hemodilution. Patients who did not match criteria were excluded from study.

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 ratio of 1:1. This blood was collected into sterile blood collection bags containing citrate phosphate dextrose anticoagulant over the weighing scale and labelled with patient identification and stored at room temperature in the operating room. In control group patients, no autologous blood was withdrawn and hemodilution with colloids was not done. In both groups, crystalloids were infused if hemodynamic status required.

The same team of surgeons, with standardized surgical procedures, did all interventions. All patients were operated on through full median sternotomy. Before arteriotomy, porcine heparin, 300 U/kg, was administered to keep activated clotting time above 300 sec. The blood withdrawn before surgery from LVANH group patients reinfused at the end of surgery, before transporting patients to the intensive care unit (ICU). Intra and postoperative criteria for allogeneic transfusions was standardized. These criteria were applied in the study group only after their infusion of the autologous blood withdrawn. Packed red blood cells (PRBC) were transfused, during surgery if hemoglobin value was less than 8 g/dl and hematocrit value was less than 24% 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) was transfused in presence of active bleeding and if a platelet count less than 50,000/mm³. Samples for evaluation of hemoglobin, hematocrit, platelet count, prothrombin time were performed before the induction of anaesthesia, on arrival in ICU, 24 h after the arrival in ICU, 48 h after surgery, and at discharge.

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

RESULT:

Table 1. Demographic Data

Variable	Control	LVANH (case)	p-value
AGE (years)	55.9±13.24	56.33±10.107	0.88
GENDER (F/M)	9/21	4/26	0.11
HEIGHT (cm)	162.37±7.72	165.17±7.49	0.15
WEIGHT (kg)	63.37±12.66	68.3±10.97	0.11
LVEF 35%-50% 50%-60%	18 12	16 14	0.6
CO MORBIDITY I.DM II. HTN III.HYPOTHYROID	7 15 10	9 14 2	0.56
HB (gm/dl)	14.71±1.06	15.17±1.15	0.11
HCT (%)	44.66±3.15	45.8±3.63	0.2
PT (sec)	12.85±0.93	12.85±1.28	0.98

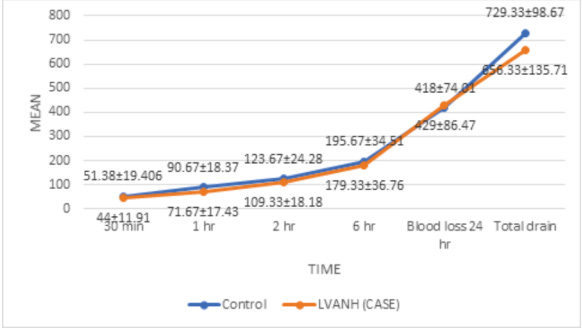
Table 2. Baseline Data

Variable	Control	LVANH (CASE)	p-value
Platelets(10^/mcl)	224.03±69.14	225.36±69.57	0.94
Duration of SX (min)	237.33±24.32	246.53±24.04	0.14
Baseline ACT (sec)	142±16	148±19	0.101
Post-operative ACT (sec)	146±19	143±14	0.52

Table 3. Intraoperative Data

Control					LVANH (CASE)			
Variable	90 min	150 min	210 min	270 min	90 min	150 min	210 min	270 min
Hb	11.48	10.03	9.68	**9.63**	11.26	10.14	9.62	**10.24**
(gm/dl)	±1.75	±1.82	±1.01	**±0.95**	±1.01	±0.75	±0.85	**±1.08**
±2SD								
M.B.P	73.53	70.5	73. 93	73.33	76.63	72.5	71.33	76.97
(mm Hg)	±11.95	±9.48	±11.12	±11.06	±12.8 05	±9.90 6	±12.50 7	±8.9
±2SD								
H.R	80.6	79.97	**88.83**	88.3	81.07	80.87	**79.17**	83.37
(beat/ min)	±14.7 3	±11. 71	**±14.1 2**	±14.2 9	±11.3 07	±9.98	**±8.44**	±10.1 7
±2SD								

***SD = Standard deviation, *H.R = Heart Rate *M.B.P = Mean Blood Pressure Graph 1. POST OPERATIVE BLEEDING (ml)**



Graph 1. showing post operative bleeding at different intervals among the study groups. At 30min, bleeding was approximately similar in control and LVANH group. At 1hr, 2hr and in total drain bleeding was comparatively higher in control group (90.67, 123.67, 729.33ml) as compared to LVANH (71.67, 109.33, 656.33ml).

Table 4. Adverse Events And Transfusion Requirement

	Control	LVANH (CASE)	p- value
Inotropes >mild dose	20	27	0.16
Arrhythmias	4	6	0.36
Reintubation	0	0	NA
Re exploration	0	0	NA
PONV	0	1	0.86
ICU>4 D	3	5	0.73
Hospital stay >7d	6	5	0.45
Pt. received 1- and 2- units PRBCs	16/30	11/30	0.18

DISCUSSION

Bleeding is major concern during cardiac surgery. Severe anemia during perioperative period has been associated with negative outcome. Approximately 50% of cardiac procedures require blood transfusion[7]. Moreover, because of the COVID-19 pandemic (coronavirus disease 2019), blood supply shortage is becoming an important issue globally. Guidelines on protecting blood supply also announced by the World Health Organization during the COVID-19 pandemic.

However, with the advancement of surgical technique as well as better knowledge of blood transfusion physiology, its effect on haemodynamics, the use of antifibrinolytics and autologous blood transfusion led to decrease in blood transfusion rates in recent years[8].

Intraoperative withdrawal of a part of circulating blood volume and simultaneous substitution with colloid and crystalloid solution to obtain fresh whole blood to transfuse after the end of surgery was first proposed in the 1960s[9].

Thus far, no conclusion has been achieved in the results of published studies on ANH. Many trials have confirmed the positive effects of ANH in reducing perioperative allogeneic transfusions; however, othe¹r studies have reported negative effects[10]. Another important controversial point is the degree of ANH performed. Some authors consider that only a large volume of ANH is useful or effective in minimizing the need for allogeneic transfusions; however, Kahraman et al. observed no differences between the effect of mild and high volume of ANH on postoperative bleeding and perioperative blood transfusions[11]. Furthermore, there may be a risk of performing moderate or severe ANH in patients with a lower preoperative hematocrit level in cardiac surgery with cardiopulmonary bypass (CPB) which would lead to hemodilution[12]. We preferred to withdraw 2.5ml/kg but above 200 ml of whole blood after induction of anaesthesia and before systemic heparinization to keep hematocrit above 30% after hemodilution. During withdrawal of the autologous blood, we use colloid solution (volulyte 6% HES 130/0.4, Fresinus kabi) in ratio of 1:1 to prevent hypovolemia. This small volume of colloid does not affect coagulation profile or renal function of patient and give advantage of net diffusing volume more than blood extracted, and colloids may be better in comparison to crystalloids in coronary artery disease patients receiving β-blockers because little replacement is required with colloids and there is no acute overload on the ventricles or dilutional anemia with three- time crystalloid replacement, which may lead to myocardial ischemia and hemodynamic instability[13]. In our study overall characteristics were comparable in both the groups in terms of demographic data, comorbidity, pre operative nature of disease and duration of surgery. Base line hematochemical parameters in both the groups were similar (Table 2).

Haanschoten et al. found that patients with a baseline hemoglobin of more than 11.3 g/dL who underwent isolated CABG surgery without the availability of RBCs in the operating room presented a decrease in complications. In present study also subjects were included, who had baseline Hb(gm/dl) more than 12gm/dl. During intraoperative period at 270min Hemoglobin and hematocrit were higher in LVANH in comparison to control group, possibly due to transfusion of autologous blood at the end of surgery.

In various studies, the acceptable hematocrit has been variable but the current guidelines by The Society of Thoracic Surgeons and The Society of Cardiovascular Anaesthesiologists (STS-SCA) recommend Hb of 7g% unless there is a risk of organ ischemia such as coronary,

cerebrovascular or renal. In present study Hb of 8g% is accepted for transfusion.

Intraoperatively both the groups were hemodynamically stable and mean value of lactate was comparable indicating well maintained tissue perfusion and oxygenation.

Postoperatively during initial hour hemoglobin was higher in LVANH that may be because of transfusion of autologous blood at the end of surgery before shifting of patient to intensive care unit.

Post operative bleeding (ml) in drain was compared in both the groups. There was significant decrease in drain volume in LVANH group at initial 1hr, 2hr and at the end. Total bleeding was also more in control group in comparison to LVANH. This possibly due to replacement of transfused platelets and coagulation factor with fresh autologous blood in LVANH group. Allogenic blood transfusion requirement was slightly higher in control group (16 patients out of 30) as compared to LVANH (11 patients out of 30) but not statistically significant, this observation nullifies any conclusive advantage of low volume acute hemodilution transfusion in these cases.

In our study, the patients undergoing low-volume ANH did not show increased perioperative complications, but this may simply be the result of the low level of hemodilution obtained, judicious procedure and the relatively few patients enrolled.

Patients were extubated, shifted out of intensive care unit and discharged home with satisfactory recovery within 10 days of surgery. No patient suffered major adverse cardiac event.

CONCLUSION

This study suggested that, low volume ANH technique is safe and efficient alternative to allogeneic transfusion. It can be done without any added risk to selected patients those are posted for elective cardiac surgery. Patients with rare blood group phenotypes or allogeneic antibodies can benefit from autologous transfusion because compatible allogeneic blood may not be always available. Potential complications of allogeneic transfusion can be minimized or eliminated when autologous blood is administered. In our study, actual benefit of this technique on reduction of blood loss is seen in first two hours of recovery and total bleeding was also less in LVANH group as compare to control group. However, there was not significant difference in allogeneic transfusions during postoperative and total perioperative period. Further -more prospective and randomized studies are needed to confirm the effects of low volume ANH on perioperative outcomes during cardiac surgery in India.

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