



Retrograde Autologous Priming Reduces Transfusion Requirements During CPB

KEYWORDS

retrograde autologous priming, cardio-pulmonary bypass, blood transfusion

Dr Sneha Ann Ancheri

DEPARTMENT OF ANAESTHESIOLOGY, Christian Medical College, Vellore, India

Dr Shoma Vinay Rao

Division of Critical Care, Christian Medical College, Vellore, India

ABSTRACT *Background:* Retrograde autologous priming involves priming the cardio-pulmonary bypass circuit with the patient's own blood and is being used worldwide to reduce haemodilution and transfusion rates. No literature has emerged from the Indian subcontinent on the usefulness of blood conservation strategies in cardiac surgery in spite of very high transfusion rates. We decided to study the effectiveness of retrograde autologous priming of cardio-pulmonary bypass in reducing transfusion requirements in Indians at our center and to incorporate it into routine practice, if found beneficial.

Aims: To compare the effect of retrograde autologous priming vs. standard priming techniques on peri-operative transfusion requirements and morbidity in patients presenting for elective primary coronary artery bypass grafting.

Methods: A randomized control study, comparing the effect of retrograde autologous priming to standard priming techniques on perioperative transfusion requirements and morbidity, in patients undergoing elective primary coronary artery bypass grafting.

Results: Mean hemoglobin levels during cardio-pulmonary bypass were significantly lower in the standard priming group when compared to retrograde autologous priming group. Number of units of packed red cells transfused per patient was significantly lesser in the retrograde autologous priming group.

Conclusion: Retrograde autologous priming is effective in reducing the number of units of packed cells transfused per patient during cardio-pulmonary bypass although there is no reduction in the transfusion requirements during the entire length of hospital stay.

INTRODUCTION

A majority of cardiac surgical procedures require the heart to be arrested and cardio-pulmonary bypass to be instituted. Even though cardiopulmonary bypass has been around for more than fifty years, it is not without complications or adverse effects. High transfusion requirements and haemodilution are common complications that need to be addressed so as to improve the quality of care.

In our center we perform approximately 30 major cardiac surgical procedures per week. Almost all of these require the use of cardio-pulmonary bypass. We have observed that our transfusion requirements are higher than the global average. The need to reduce our transfusion rates prompted us to incorporate one or more blood conservation strategies into routine practice. We decided to study the effectiveness of retrograde autologous priming of cardio-pulmonary bypass in reducing transfusion requirements in Indians at our center and to incorporate it into routine practice, if found beneficial.

AIM:

To compare the effect of retrograde autologous priming vs. standard priming techniques on peri-operative transfusion requirements and morbidity in patients presenting for elective primary coronary artery bypass grafting.

OBJECTIVES:

1: To study the effect of retrograde autologous priming on peri-operative transfusion requirements.

2: To study the effect of retrograde autologous priming on peri-operative morbidity like renal failure, stroke and gastro-intestinal dysfunction.

3: To look for complications, if any.

4: To study the effect of retrograde autologous priming on duration of stay in the intensive care unit and hospital

MATERIALS AND METHODS

SETTING:

This study was performed exclusively at the Christian Medical College and Hospital, Vellore, Tami Nadu, India. Ours is 2500 bedded tertiary care center which caters to patients from all over India.

The department of Cardio-thoracic surgery performs approximately 1000 heart surgeries per year, almost all of which require the use of cardio-pulmonary bypass. Myocardial revascularization constitutes approximately 30-40% of cardiac surgical procedures performed at our institute, 99% of which use cardio-pulmonary bypass. In our institution we do not have a well-defined protocol for blood conservation strategy during cardiac surgery. It is most commonly based on personal experience or preference.

STUDY DESIGN:

A randomized control study, comparing the effect of retrograde autologous priming to standard priming techniques on perioperative transfusion requirements and morbidity, in patients undergoing elective primary coronary artery bypass grafting.

STUDY POPULATION:

Patients aged between 20 and 70 years presenting for elective primary coronary artery bypass grafting were included in the study. Patients aged <20 or >70 years.

Patients with left ventricular ejection fraction <40%, pre-operative Hemoglobin <10gm%, weight less than 45 kg, pre-existing renal impairment i.e. serum creatinine >1.4mg/dl, pre-existing neurological deficits/ history of stroke, patients presenting for emergency surgery, patients with critical left main disease and those presenting for re-do coronary artery bypass grafting were excluded from the study.

The study recruited patients who met the inclusion criteria from January 2013 to August 2013. The protocol received approval from the Institutional Review Board of Christian Medical College, Vellore and was funded by the fluid research fund of the Christian Medical College, Vellore

METHOD OF RANDOMIZATION:

Computer generated randomized numbers using block randomization with block sizes of 2, 4 & 6 were generated using SAS 9.2. Eligible patients presenting for elective first time coronary artery bypass grafting under general anesthesia were randomly assigned to either the retrograde autologous priming (group A) or standard priming (group B) groups

Primary outcome measured was reduction in peri-operative transfusion requirements. Secondary outcomes included reduction in peri-operative morbidity, incidence of renal impairment/ failure, peak post-operative creatinine, need for dialysis, incidence of cerebro-vascular accidents (CVA), ventilator days, duration of ICU stay and hospital stay.

TRANSFUSION TRIGGERS:

Packed red cells will be transfused if hemoglobin is <6gm% on cardio-pulmonary bypass and if hemoglobin is <8.5gm% at any time after termination of cardio-pulmonary bypass. Packed red cells will also be transfused at higher hemoglobin values if clinically symptomatic anemia develops. At any point of time, transfusion of packed red cells will be performed only after documenting a hemoglobin value. Use of platelets and fresh-frozen plasma (FFP) were performed on clinical evidence of bleeding

STATISTICAL METHODS:

Statistical methods used for primary outcome analysis included description of methods to estimate the strength of the effect (e.g.: Odds ratios, relative risks, etc.). After checking for normality, appropriate parametric tests like 2 independent sample t test were used to assess the mean difference between participants of the retrograde autologous priming and standard priming groups for continuous variables like hemoglobin, lactate, creatinine etc. For categorical variables, like sex, pre-operative diagnosis, comorbidities, etc., Chi square/ Fisher's exact was used. The p-value was computed using 2 proportion Z test for non-continuous variables like number of patients transfused with packed red cells.

The required sample size to show a risk difference of -0.2, 80% of the time between retrograde autologous priming & standard priming techniques using Rosengart et al {Journal of Thoracic and Cardiovascular Surgery (1998; 115:426-439)} was found to be 43 in each arm. The two proportion hypothesis testing formula was used for the above estimation.

A total of 90 patients were approached. Out of the 90 patients, 86 were recruited for the study after getting their informed consent. 4 patients were excluded as 3 refused to participate in the study and one due to violation in study

protocol.

ANAESTHETIC MANAGEMENT

Standard anesthetic techniques for induction, maintenance and inotrope management were followed for both groups. The surgical and perfusion teams were also the same for both groups. All patients in this study received only less than 250ml crystalloid infusion prior to initiation of cardio-pulmonary bypass from the anesthesia team.

CARDIO-PULMONARY BYPASS

Standardized cardio-pulmonary bypass equipment and technique for retrograde autologous priming was used for all patients who participated in this study. Ringer lactate was the priming solution used for all patients, with 1200ml as standard volume in the standard prime group. St. Thomas cardioplegia (1:4 blood cardioplegia) was used to arrest the heart in diastole in all patients. In the retrograde autologous priming group the volume of crystalloid prime displaced from the extracorporeal circuit was based on the clinical discretion of the anesthetist and perfusionist, but an attempt was made to displace approximately 500ml. Extracorporeal circuit volume was documented for all patients.

RETROGRADE AUTOLOGOUS PRIMING TECHNIQUE

For patients randomized to the retrograde autologous priming group, after aortic and venous cannulation, mean arterial blood pressure was hiked up to approximately 100mm of Hg using 50-100µgm bolus doses of phenylephrine. Retrograde autologous priming was performed on the arterial line initially, arterial line was unclamped and crystalloid solution in the arterial line was gradually displaced back into the reservoir using the patients' blood. Just prior to the patients' blood entering the reservoir, the arterial line was clamped. Once this is done, the main cardio-pulmonary bypass pump was switched on and the cardioplegia line was unclamped to push the displaced crystalloid into the collecting bag, connected to the cardioplegia line. The crystalloid solution in the venous line was also displaced in a similar manner after completion of the procedure on the arterial line. Approximately 2-4 minutes were required for institution of retrograde autologous priming on both arterial and venous lines. All through this time, the cardiotomy suction is turned off to avoid mixing of the blood with the crystalloid solution in the reservoir. A GEM Premier 3000® blood gas analyzer was used for measurement of hemoglobin and lactate levels for all patients.

Data was collected intra-operatively and post-operatively by the primary investigator. Clinicians giving post-operative care to patients were unaware of patient randomization, but were advised to strictly adhere to transfusion protocols set for study purposes.

RESULTS

DEMOGRAPHIC VARIABLES

Eighty six patients (70 males and 16 females) presenting for elective primary coronary artery bypass grafting were recruited for this study. 43 patients each were recruited to the retrograde autologous priming group (RAP) and the standard priming group (No RAP). There is no statistically significant difference in demographic variables (age, weight and body surface area) between the two groups.

PRE-OPERATIVE VARIABLES

The pre-operative variables like hemoglobin and creatinine do not show a statistically significant difference between the two groups.

	RAP	No RAP	p Value
Hemoglobin (gm %)	13.167±1.0960	12.909±1.3952	0.343
Creatinine	1.1342±0.16326	1.1249±0.16162	0.791

INTRA-OPERATIVE VARIABLES

Mean cardio-pulmonary bypass volumes were 676.74±61.090ml in the retrograde autologous priming group and 1200.00±21.822ml in the standard priming group. The cardio-pulmonary bypass and the aortic cross clamp times were not significantly different in the two groups.

PARAMETERS DURING CARDIO-PULMONARY BYPASS

	RAP	No RAP	p Value
Hemoglobin (gm %)	7.305±0.9514	6.581±0.7310	0.000
Lactate(mg/dl)	2.893±0.8328	3.128±1.1009	0.268
PRBCs (units/patient)	0.0558±0.25940	0.2586±0.50197	0.022
Patients transfused PRBCs	2	10	0.0126

Table 2

Mean hemoglobin levels during cardio-pulmonary bypass were significantly lower in the standard priming group as depicted in Table:2. Mean lactate levels were lesser in the retrograde autologous priming group but there was no statistical significance (Table: 2). Number of units of packed red cells transfused per patient, each unit being equivalent to 250ml, was significantly lesser in the retrograde autologous priming group (Table: 2). As depicted in Table 2, only 2 patients in the retrograde autologous priming group were transfused packed red cells as compared to 10 patients in the standard priming group, again a statistically significant difference. None of the participants were transfused any platelet concentrates or fresh frozen plasma during cardio-pulmonary bypass.

In the post-cardio-pulmonary bypass period, i.e. in the operating room, mean hemoglobin levels were not statistically different between the two groups. Mean lactate and packed red cells transfused per patient were lower in the retrograde autologous priming group, but again of no statistical significance.

During the post cardio-pulmonary bypass period, 15 patients in the retrograde autologous priming group were transfused packed red cells against 14 in the standard priming group. With regard to fresh frozen plasma, only 2 participants in the retrograde autologous priming group were transfused. In the standard priming group, only one patient was transfused. Only one patient received 150ml of platelet rich concentrate in the retrograde autologous priming group vs. 2 patients with a mean volume of 112.033 ml in the standard priming group. None of these were of statistical significance.

POST-OPERATIVE DAY 1 PARAMETERS

	RAP	No RAP	p Value
Hemoglobin (gm %)	10.081±1.2176	9.614±0.8790	0.045
Lactate(mg/dl)	5.137±1.9349	5.147±1.6895	0.981

PRBCs (units/patient)	0.0698±0.25792	0.0716±0.26484	0.974
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Table3

During the first post-operative day, i.e. from the time of receiving the patient in the intensive care unit till midnight of the same day, hemoglobin levels were significantly higher in the retrograde autologous priming group (Table: 3). There was no statistically significant difference between the two groups with regard to lactate and units of packed red cells transfused per patient at this time (Table: 3).

On the second and third post-operative days, there was no clinically significant difference in the hemoglobin and creatinine values between the retrograde autologous priming group and the standard priming group. There was no statistically significant difference between the amount of packed red cells transfused between the retrograde autologous priming group and the standard priming group for the whole length of hospital stay.

There was no statistically significant difference in the time to extubation between the retrograde autologous priming and the standard priming groups. Duration of ICU admission and hospital stay were not statistically different in both groups.

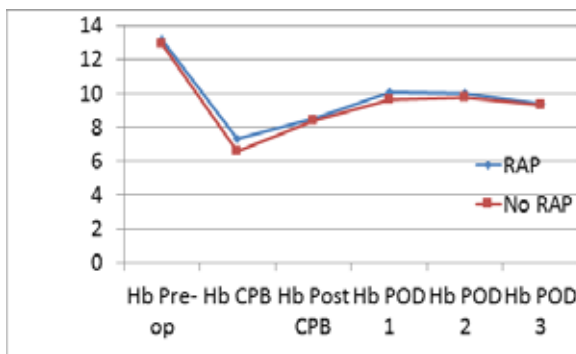


Fig:1

Fig:1 depicts the trend of hemoglobin (gm%) levels in patients of both the groups at various time intervals. Analysis of data revealed that only during cardio-pulmonary bypass and during the first post-operative day there was a statistically significant reduction in hemoglobin levels in the retrograde autologous priming group.

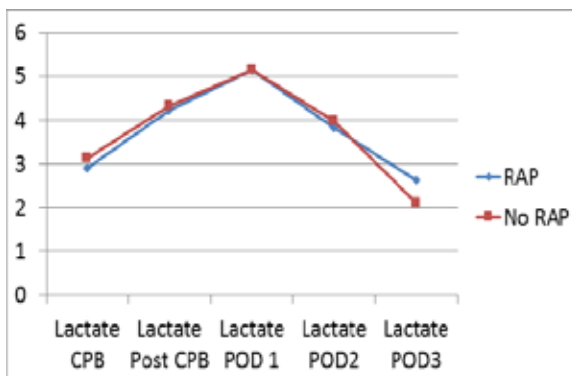


Fig:2 displays the trend in lactate levels (mg/dl) at various intervals for patients of both groups. There was no statistically significant difference for this variable at any point of time between the two groups

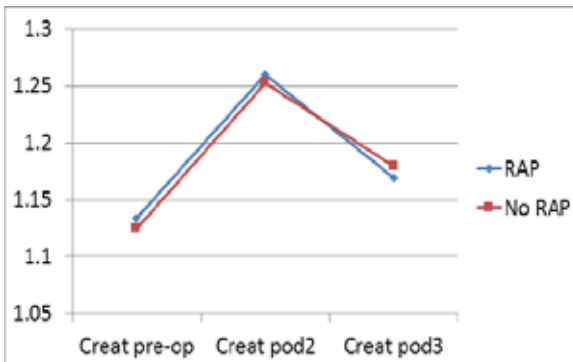


Fig: 3 displays the trend in creatinine levels (mg/dl) at various intervals for patients of both groups. There was no statistically significant difference for this variable at any point of time between the two groups.

Complications

One patient developed severe hypotension on initiation of retrograde autologous priming (only 300ml displaced from arterial line), which could not be controlled with bolus doses of phenylephrine and required the immediate initiation of cardio-pulmonary bypass. This patient had an uneventful intra-operative and post-operative course, but was excluded from the study. There were no other major complications associated with conduct of retrograde autologous priming or during cardio-pulmonary bypass.

DISCUSSION

Retrograde autologous priming of the cardio-pulmonary bypass circuit is recommended as a strategy with level IIa evidence by Society of Cardio-thoracic Surgeons 2011 to reduce haemodilution and transfusion requirements(1). Retrograde autologous priming was first described by Panico and Neptune in 1960(2,3). In 1998, in the USA, Todd K. Rosengart et al performed a prospective randomized control study, on primary coronary artery bypass grafting patients, reviving the technique, to demonstrate the efficiency of retrograde autologous priming in reducing transfusion requirements(2).

In our investigation, the groups were comparable in terms of demographic data. The two groups were similar with respect to surgical, anaesthetic and perfusionist teams and techniques. Cardio-pulmonary bypass and cross clamp times were almost similar for both the groups. Both the groups were similar with respect to risk factors for hemorrhage and transfusions peri-operatively. Out of the 90 patients approached for the study 87 gave consent. One patient was excluded due to hypotension at the beginning of RAP.

We were able to reduce prime volumes by approximately 50% in the retrograde autologous priming group, with a mean prime volume of 676.74 ± 61.09 ml. Korneel Vandewiele et al identified optimal retrograde autologous priming volume as 475 ml in patients with BSA > 1.7 m² and 375 ml in patients with BSA < 1.7 m², for reducing transfusion requirements(4).

Cardio-pulmonary bypass durations were approximately 1.29 ± 0.38 hrs and 1.23 ± 0.35 hrs in the retrograde autologous priming and standard priming groups respectively. Aortic cross clamp times were 0.51 ± 0.17 hrs and 0.53 ± 0.21 hrs in the retrograde autologous priming and standard priming groups respectively.

Retrograde autologous priming has been proven to be an effective method in reducing haemodilution and transfusion requirements during cardiac surgery(2,4–8). The introduction of retrograde autologous priming resulted in significantly lower levels of intra-operative haemodilution; in our study only 2(4.65%) patients in the retrograde autologous priming group vs. 10(23.25%) patients in the standard priming group were transfused packed red cells, during cardio-pulmonary bypass. Hemoglobin levels were also significantly higher in the retrograde autologous priming group during cardio-pulmonary bypass. Haemoglobin levels during cardio-pulmonary bypass were 7.30 ± 0.95 in the retrograde autologous priming group and 6.58 ± 0.73 gm% and standard priming group (p value: 0.00). The number of units of packed red cells transfused per patient was (1 unit being 250ml of packed red cells) 0.0558 ± 0.25940 in the RAP group vs 0.2586 ± 0.50197 units per patient in standard priming group, which was statistically significant (p value: 0.022). These results were comparable to Rosengart et al, Balachandran et al, Hou et al, Saczkowski et al and Vandewiele et al(2,4–7).

In the immediate post cardio-pulmonary bypass period the mean haemoglobin values were comparable between the groups. This may be because of the significantly higher number of patients who received transfusion in standard priming group during cardio-pulmonary bypass. Also as discussed earlier the mean number of units transfused during cardio-pulmonary bypass was significantly higher in the standard priming group during cardio-pulmonary bypass

The Society of Cardio-thoracic Surgeons advocates the use of tranexamic acid as class I(A) recommendation, however its safety profile during coronary artery bypass grafting surgery is still being investigated(1,9). Taking these factors into consideration tranexamic acid was not administered to patients of this study, contrary to most previous trials. The administration of tranexamic acid, by reducing mediastinal bleeding, might have resulted in further reduction of haemorrhage and transfusion requirements in both groups.

Although hemoglobin levels were not statistically different in the immediate post-operative period, during the first post-operative day hemoglobin levels were significantly higher in the retrograde autologous priming group. Mean haemoglobin values were 10.081 ± 1.2176 and 9.614 ± 0.8790 gm% in the retrograde autologous priming and standard priming groups respectively (p value: 0.045).

Reported transfusion rates for cardiac surgical patients (50–60%) are comparable with transfusion rates in our standard priming group (58.14%) group. Use of a single intervention (retrograde autologous priming) resulted in reduction of transfusion requirements by more than 10% (46.5% in the retrograde autologous priming group). This reduction in transfusion requirements, although not statistically significant is lesser than the global average(10).

The transfusion trigger of <8.5gm% for the post-cardio-pulmonary bypass period used in our study accounted for comparatively liberal transfusion protocol, when compared to previous studies. If we had adopted a more restrictive transfusion trigger like 8gm% for the post-cardio-pulmonary bypass period, like previous authors, our transfusion rates would have been much lesser. 17 out of 48 patients who received transfusions in the post-cardio-pulmonary bypass period had haemoglobin concentrations between 8 and 8.5gm%.

On analysis of lactate levels at different intervals, we could not demonstrate any significant advantage of retrograde autologous priming over standard priming techniques. We could not demonstrate any statistically significant difference between the retrograde autologous priming group and the standard priming group with regard to trends of creatinine levels. Both nadir hematocrits and transfusion of packed red cells are associated with renal dysfunction in cardiac surgical patients. The lack of difference between the two groups with respect to lactate and creatinine levels can probably be attributed to very strict maintenance of pump flow rates and perfusion pressures during cardiopulmonary bypass and due to shorter bypass times compared to other investigators. Exclusion of patients with pre-operative renal dysfunction and low ejection fractions may be the reason for the lack of post-operative renal dysfunction in our study population as compared to previous studies where such patients have not been excluded.

Intra-operative transfusion of packed red cells can result in increased risk of adverse effects like sternal wound infection, renal and pulmonary dysfunction, prolonged length of stay in the intensive care unit and hospital. However the trial did not demonstrate any statistically significant difference between the two groups with regard to such complications.

There was also no statistically significant difference between times to extubation, discharge from intensive care unit or hospital between patients of both the groups. These results probably can be attributed to the institutional practice of maintaining mechanical ventilation and intensive care unit admission for minimum fixed durations, for observation.

Among the various intra-operative strategies available to reduce transfusion requirements, retrograde autologous priming and minimalized cardio-pulmonary bypass circuit were based on the principle of reducing haemodilution. The use of a haemo-concentrator will not attenuate the initial drop in haemoglobin concentrations and the correction of haemodilution is slow. Haemo-concentrators require increased pump flows to facilitate filtration and are again expensive. Use of retrograde autologous priming provides on termination of cardio-pulmonary bypass a lower volume of comparatively less haemodiluted blood, which is easier to re-infuse to the patient. Retrograde autologous priming is a safe and inexpensive technique of reduction of transfusion requirements intra-operatively.

LIMITATIONS

Limitations for our study include the fact that our study was underpowered to effectively detect complications and morbidity. Our numbers were not sufficient to perform a multivariate analysis for identification of risk factors of transfusion. Our trial excluded all patients with high risk factors for transfusion of packed red cells, except probably low RBC mass. These high risk patients might have benefitted the most from lower levels of haemodilution and avoidance of transfusion of packed red cells. In our investigation we adopted a liberal transfusion trigger, which might have resulted in higher transfusion rates. A restrictive transfusion policy with a post-cardio-pulmonary bypass transfusion trigger of 8gm% would have been a more appropriate

CONCLUSION:

Retrograde autologous priming is an effective technique in reducing haemodilution and transfusion requirements dur-

ing cardio-pulmonary bypass in elective primary coronary artery bypass grafting. Retrograde autologous priming is effective in reducing the number of units of packed cells transfused per patient during cardio-pulmonary bypass although there is no reduction in the transfusion requirements during the entire length of hospital stay. RAP has no effect on morbidity with respect to renal failure, stroke and gastro-intestinal dysfunction. Retrograde autologous priming has no effect on duration of stay at the hospital or intensive care unit and is not associated with complications. Retrograde autologous priming is a safe and inexpensive intervention. It should be part of a multi-modality blood conservation strategy for reduction of allogeneic transfusions.

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