ORIGINAL ARTICLE

Comparative study of acute normovolaemic haemodilution and acute hypervolaemic haemodilution in major surgical procedures

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ABSTRACT

Background: Ready availability of human blood for transfusion is limited, especially in case of rare blood groups and fraught with many risks necessitating a search for methods of blood conservation. Acute Normovolemic Hemodilution (ANH) and Acute Hypervolemic Hemodilution (HHD) have been found to be useful in this respect but studies related to a direct comparison between the two as regards to time, cost effectiveness in autologous blood conservation, effect on blood loss, hematocrit values and on hemodynamic stability are limited.

Methodology: A prospective, randomized study was designed to compare ANH with HHD at Pravara Hospital, a teaching hospital attached to Pravara Institute of Medical Sciences during a period of six months from July 2008 to January 2009. Sixty adult patients of ASA Grade I and II with haemoglobin percentage $\geq$10 Gms posted for major surgeries, with an estimated blood loss around 1200 to 1500 ml were randomly distributed into two groups, ANH (n = 30) and HHD (n = 30). In ANH group autologous blood was removed using a predefined formula and simultaneously an equal amount of 6% hydroxyethyl starch was infused. Perioperative retransfusion was done after perfect surgical haemostasis. In HHD group 15 ml/kg of 6% hydroxyethyl starch was infused without removing any blood. Mean time required, cost, intra operative blood losses, hemodynamic stability, hematocrit changes, homologous blood requirements and complications (if any) were compared between two groups and data was analyzed statistically.

Results: ANH was found to be costlier (Rs.761.10 ± 61.35) and more time consuming (539.33 ± 128.75 minutes) than HHD (Rs.445.43 ± 32.28 and 20.7 ± 3.34 minutes). (p-value < 0.05) Intraoperative blood loss was comparable (ANH : HHD = 1293.67 ± 124.30 : 1253.67 ± 135.58 ml) between two groups. (p-value > 0.05) Patients in ANH group developed a higher pulse rate but had lower systolic and diastolic blood pressures in comparison to HHD Group patients. Hematocrit values were higher in HHD (29.30 ± 2.77 and 33.56 ± 2.75) than in ANH Group patients (27.00 ± 3.1 and 29.43 ± 2.49) on second and seventh postoperative day respectively. (P-value < 0.05)

Conclusion: Acute hypervolemic hemodilution appears to be a simple, easier, hemodynamically more stabilising, time saving and cost effective alternative to acute normovolemic hemodilution.

Keywords: Acute normovolemic hemodilution, Acute hypervolemic hemodilution, Transfusion, Hydroxyethyl starch, autologous blood transfusion

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INTRODUCTION

Availability of human blood for transfusion is often very limited necessitating blood conservation strategies like preoperative autologous blood collection, intra and postoperative salvage of the patient's blood and retransfusion, acceptance of lower hemoglobin level trigger for transfusion and adopting a very meticulous (asanguinous) surgical technique.[1,2] Additional problems with allogenic transfusion are mismatched transfusion, risk of infection, transmission of many diseases and immunosuppression.[3-6] In acute normovolemic hemodilution (ANH) patient's blood is removed in anticoagulant containing blood bags, either immediately before or shortly after induction of anesthesia and is simultaneously replaced with appropriate volume of crystalloids and/or colloids to maintain normovolemia[7-9]. ANH has been modified by hemodiluting the patients with colloids preoperatively without removing blood, resulting in hypervolemic hemodilution (HHD)[10-12]. Hemodilution techniques have great benefits when a cell saver cannot be used or is not available.

The aim of this study was to compare ANH with HHD techniques in autologous blood transfusion, in respect of time, cost, its effect on hematocrit, on blood loss and on hemodynamic stability in patients undergoing major surgery.

METHODOLOGY

A prospective randomized study was designed to compare ANH with HHD at Pravara Hospital which is a teaching hospital, affiliated to Pravara Institute of Medical Sciences during a period of six months from July 2008 to January 2009. After approval from the hospital ethical committee, this study was carried out in 60 adult ASA Grade I and II patients posted for major surgery having haemoglobin $\geq$ 10 Gms %, and expected to have blood loss around 1200-1500 ml. Exclusion criteria were: anemia (hemoglobin < 10 g/dL), clinically evident cardiac or pulmonary dysfunction, untreated hypertension, liver or kidney disease, sepsis and metabolic, endocrine or coagulation disorders. After valid informed consent, selected patients were randomly allocated to two groups: Group HHD (n = 30) and Group ANH (n = 30). Oral diazepam 10 mg was given to all patients on the night before day of surgery. Premedication was by pentazocine 0.4 mg/kg IV before induction by thiopentone (3-5 mg/kg) intravenously followed by intubation facilitated by 1.5 mg/kg succinylcholine. Mechanical ventilation by a mixture of halothane in 35% to 40% oxygen and 60% to 65% nitrous oxide was done targeting end-tidal PCO_2 of 32-36 mm Hg and end-tidal halothane at 1.0 -1.5 vol %. Muscle relaxation was maintained by inj. pancuronium 0.1mg/kg followed by top-up doses as and when required. Neuromuscular block was reversed at the end of surgery with inj. neostigmin 0.05 – 0.06 mg/kg and inj. glycopyrrolate 0.008-0.01mg/kg. Routine monitoring of all physiological parameters was done. Just after induction of anesthesia and before starting surgery, hemodilution was performed. In ANH group autologous blood was collected in 350 ml disposable blood transfusion bags containing 49 ml of CPD –A as a preservative anticoagulant. Simultaneously, an equal amount of 6% hydroxyethyl starch was transfused in the contra-lateral arm. The total volume of blood collected was based on the following formula proposed by Gross.[13]

Volume withdrawn = EBV x $(Hct_0 - Hct_1)/Hct_{av}$
(EBV = estimated blood volume (calculated as 70 ml/kg body weight); Hct_0 = Hct before hemodilution; Hct_1 = desired Hct after hemodilution (targeted to 27 ± 3 %); Hct_{av} = average of the Hct before and after hemodilution)

It was ensured that autologous blood had clearly identifiable label with necessary patient particulars and sequentially numbering the units removed. The first unit of blood was refrigerated at 4°C. Other units were kept at OR temperature to preserve platelet function. This blood was retransfused, after perfect hemostasis by the surgeon in the reverse order so that the first unit with the highest hematocrit and platelets was administered last.

In the HHD group 15 ml/kg of 6% hydroxyl ethyl starch was rapidly infused after induction of anesthesia and before commencement of surgery without removing any blood. Intra operative blood loss was measured by weighing sponges and measuring suctioned blood. Blood loss on sterile towels at operation site and on the gowns of the operating team was estimated. Pulse rate, systolic and diastolic blood pressure were measured preoperatively [baseline], during hemodilution (average of all readings recorded after every five minutes), five minutes after hemodilution, intra operatively (average of all the readings

recorded after every five minutes), immediately after operation & after completion of retransfusion and on the second and seventh postoperative days. Hematocrit was measured preoperatively [baseline], after hemodilution, immediately after retransfusion, and on the second and seventh postoperative days. Maintenance fluid requirement was administered by lactated Ringer's solution or Dextrose Normal Saline. Mean time required, cost, intra operative blood losses, hemodynamic stability, hematocrit changes, homologous blood requirements and complications (if any) were compared between two groups and data was analyzed statistically. For continuous variables descriptive statistics (mean and standard deviations) were computed. Comparison of means in group 1 and group 2 was done using t-test. For categorical variables proportions were computed. Comparison of proportions in two groups was done using chi-square test. Data analysis was done using STATA 10 IC.

RESULTS

The patients' characteristics are shown in Table 1. There was no significant difference in the two groups (p-value > 0.05). Surgical specialty-wise distribution of cases is shown in Table 2. There was no significant difference with respect to nature of surgery in the two groups (p-value > 0.05). Preoperative hemodynamic parameters and hematocrit values were comparable in both groups. Pulse rates were

Table 1: Patient characteristics, age and gender distribution

Characteristics		ANH Group (n = 30)	HHD Group (n = 30)	P value
		Mean ± SD	Mean ± SD	
Age (in years)		43.76 ± 11.79	44.70 ± 10.76	> 0.05
Weight (in Kgs)		48.43 ± 3.58	50.33 ± 4.99	
Gender	Male [n (%)]	9(30)	12(40)	
	Female [n (%)]	21(70)	18(60)	

ANH = Acute Normovolaemic Haemodilution
HHD= Acute Hypervolaemic Haemodilution
There was no significant difference with respect to age, gender and weight in the two groups (p-value > 0.05).

Table 2: Surgical specialty-wise distribution of cases(n=60)

Specialty	ANH Group *No. of Patients (%)*	HHD Group *No. of Patients (%)*	P value
Gynaecological surgery	12(40)	13(43.34)	**> 0.05**
General surgery	11(36.66)	10(33.33)	
Orthopaedic surgery	5(16.66)	5(16.66)	
Otorhino laryngeal surgery	2(6.67)	2(6.67)	
Total	**30**	**30**	

ANH = Acute Normovolaemic Haemodilution
HHD= Acute Hypervolaemic Haemodilution
There was no significant difference with respect to nature of surgery in the two groups (p-value > 0.05).

Table 3: Perioperative changes of pulse rate, systolic and diastolic blood pressure and hematocrit in the acute normovolemic hemodilution group and hypervolemic hemodilution group

	Heart Rate/minute		Systolic blood pressure (mm Hg)		Diastolic blood pressure (mm Hg)		Hematocrit Values	
	ANH Group (n=30)	HHD Group (n=30)	ANH Group (n=30)	HHD Group (n=30)	ANH Group (n=30)	HHD Group (n=30)	ANH Group (n=30)	HHD Group (n=30)
Preoperative	79.23 ± 8.08	77.60 ± 8.63^{NS}	125.53 ± 12.32	121.26 ±11.53^{NS}	81.13 ± 5.99	79.53 ± 6.52^{NS}	35.66 ± 2.75	35.80 ± 2.65^{NS}
During Hemodilution	93.53 ± 9.12	73.86 ± 8.5**	105.6 ± 9.95	128.00 ± 11.30**	72.66 ± 4.91	81.80 ± 6.78**	-	-
After Hemodilution	95.40 ± 9.44	72.53 ± 8.2**	103.66 ± 9.68	130.40 ± 10.99**	72.47 ± 4.92	82.33 ± 6.57**	26.87 ± 2.60	27.46 ± 2.54^{NS}
Intraoperative.	102.87 ± 9.41	79.80 ± 7.72**	93.80 ± 9.87	116.2 ± 10.73**	68.66 ± 5.20	78.80 ± 6.44**	-	-
Postoperative	100.43 ± 9.47	82.13 ± 7.94**	97.27 ± 9.58	110.53 ± 10.07**	69.67 ± 4.87	76.60 ± 6.22**	-	-
After Re transfusion	94.57 ± 8.55	-	104.33 ± 10.51	-	72.60 ± 5.22	-	-	-
Second Postop. Day	92.2 ± 8.86	77.73 ± 7.93**	106.60 ± 10.62	119.00 ± 9.48**	72.87 ± 5.43	79.60 ± 6.35**	27.00 ± 3.1	29.30 ± 2.77**
Seventh Postop. day	86.73 ± 7.82	75.30 ± 8.14**	113.6 ± 11.26	120.93 ± 10.04 *	75.66 ± 5.51	79.73 ± 6.49 *	29.43 ± 2.49	33.56 ± 2.75**

NS = not significant
*= Significant **= Highly Significant
p-value > 0.05 , * p-value significant at 0.05; ** p-value significant at 0.01

significantly higher where as systolic and diastolic blood pressures are significantly lower in ANH group as compared to HHD Group patients during other stages. Hematocrit values measured preoperatively and just after haemodilution were comparable while these values were significantly higher in HHD Group patients (29.30 ± 2.77 and 33.56 ± 2.75) than in ANH Group patients (27.00 ± 3.1 and 29.43 ± 2.49) on second and seventh postoperative day respectively. (P-value < 0.05) (Table 3).

Table 4: Time required for hemodilution techniques

Process	Time Required (in minutes)	
	ANH Group (n=30)	HHD Group (n=30)
	Mean±SD (Range)	Mean±SD (Range)
Intravenous access	12 ± 1.68 (9-15)	3.33 ± 1.45 (2-7)
Removal of blood	32 ± 3.38 (28-40)	-
Infusion (6% hydroxyethyl starch)	-	17.37 ± 2.98 (14-25)
Retransfusion a) First unit	a) 60 ± 9.58 (50-70)	-
b) Second unit	b) 200.67 ± 27.66 (180-240)	-
c) Third unit	c) 320 ± 24.93 (300-360)	-
Total time required	539.33 ± 128.75 (285-720)	20.7 ± 3.34* (16-29)

ANH =Acute Normovolaemic Haemodilution

HHD=Acute Hypervolaemic Haemodilution

NS = not significant
*= Significant
p-value < 0.05 * p-value < 0.01

Table 5: Cost in Indian rupees required for hemodilution techniques

Cost head	Average cost required in Indian Rupees	
	ANH Group (n=30)	HHD Group (n=30)
Intravenous cannula x1	63	63
Infusion set x1	35	35
Transfusion bag x1	67	-
Blood transfusion set x1	38	-
6% hydroxyl ethyl starch 1xbottle	198	198
Ringer's Lactate solution x1	21	21
Dextrose Normal Saline x1	17	17
Total Cost per patient	761.10 ± 61.35 (589-854)	445.43 ± 32.28 * (397-516)

ANH =Acute Normovolaemic Haemodilution

HHD=Acute Hypervolaemic Haemodilution

NS = not significant
*= Significant
p-value < 0.05 * p-value < 0.01

Intra operative blood loss was 1293.67 ± 124.30 ml in ANH Group and 1253.67 ± 135.58 ml in HHD Group. This difference was not significant (p-value > 0.05).

Mean time required for HHD (20.7 ± 3.34 minutes) was considerably less than that required for ANH (539.33 ± 128.75 minutes) (p-value < 0.01) (Table 4). The total cost of both hemodilution techniques was calculated and compared. It clearly indicates that ANH was significantly costlier than HHD. Total cost in HHD Group patients (445.43 ± 32.28 Indian Rupees) was significantly less than that required in ANH Group patients (761.10 ± 61.35 Indian Rupees). (P-value < 0.01) (Table 5).

DISCUSSION

The search for perfect blood substitutes in the light of worldwide shortage of safe and viable allogenic donor blood is not yet complete[14, 15]. ANH has been used for many years to reduce the requirement of perioperative homologous blood transfusion. [16-20]. This technique has been widely in practice to avoid the risks of allogenic blood like contamination and transmission of diseases like AIDS and HepatitisB&C, clotting disorders , technical errors in typing and cross matching, sensitization and isoimmunization. Provision of fresh whole autologous blood for transfusion at the end of surgery improving tissue perfusion are the main advantages of ANH. However, its limitations like extra time required and the added cost may explain why it remains underutilized[12,21,22]. AHD, by preoperative infusion of colloids or crystalloids without removal of blood to reduce Hct is a much simpler procedure, but HHD is easy, consumes less time and is less expensive than ANH. It is possible to infuse an appropriate volume of colloid solution to induce HHD without any adverse hemodynamic effects by vasodilatory effects of isoflurane or halothane [12, 23]. In fact, HHD may cause a greater degree of hemodynamic stability during isoflurane or halothane anesthesia by augmenting preload and obviating the usual decrease in arterial blood pressures. The use of a starch solution for HHD does not result in excessively high arterial blood pressures, especially in the pulmonary circulation[23]. Signs of excessive intravascular volume after HHD were not seen in our study as well. HHD can also be used very safely in Jehovah's Witnesses. Different workers have used different formulae for removal of blood during ANH. Virmani S et al [21] removed 10% of estimated blood volume in patients with hemoglobin (Hb) > 12g% and 7% when the Hb was < 12g%. We calculated the volume to be removed using formula proposed by Gross[13] targeting hematocrit to 27 ± 3 % [24, 25.] Consistent to the

findings of Mielke L.L.et al [12], our study also indicates the mean time required for HHD (20.7 ± 3.34 minutes) is considerably less than that required for ANH (539.33 ± 128.75 minutes) (p-value < 0.01) which includes the time for retransfusion which needs to be done slowly extending to postoperative period to avoid circulatory overload. Total cost in HHD Group (445.43 ± 32.28 Indian Rupees) is significantly less than that required in ANH Group (761.10 ± 61.35 Indian Rupees). (p-value < 0.01) Intraoperative blood loss is comparable between the two groups (1293.67 ± 124.30 : 1253.67 ± 135.58 ml respectively; p-value > 0.05). Singbartl K et al [10] reported that, hypervolemic hemodilution appears to be superior to normovolemic hemodilution in reducing homologous transfusions, for blood losses <40% of blood volume. Various researchers have reported that preoperative HHD in patients with expected blood loss >30% results in decreased needs for blood transfusion and is a safe and easy-to-use method[26,27]. Chen YQ et al [28] found no significant difference in intra-operative blood loss between HHD and control group. The amount of transfused red blood cells (18 +/- 4) ml/kg and fresh frozen plasma (3.5 +/- 1.1) ml/kg in HHD group, were significantly lower than in the control group [(28 +/- 11) and (5.8 +/- 1.8) ml/kg in children undergoing post spine fusion surgery. They have concluded that HHD successfully reduced intra-operative blood transfusion and medical expenses. Xiao et al [29] who evaluated the security and validity of the acute extreme hypervolaemic hemodilution (AEHH) in spine surgery also had similar findings. In a similar study like ours Saricaoglu and colleagues [30] have found that the HHD group patients are far more haemodynamically stable perioperatively than ANH group patients. They also found that hemodilution (both ANH and HHD) decreased the demand for homologous blood without adversely affecting hemodynamics or coagulation parameters and HHD seemed to be a simple and valuable alternative to ANH in patients undergoing hip replacement.

CONCLUSION

Thus we conclude that, in patients free of systemic diseases and with a hemoglobin level above 10 gm % and with a predicted intraoperative blood loss of 1200-1500 ml, acute hypervolemic hemodilution is simple, easier, more haemodynamically stable, as well as time saving and cost effective alternative to acute normovolemic hemodilution. It has additional benefits of being acceptable to be used in Jehovah's Witnesses and avoidance of complications associated with autologous blood transfusion.

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