Comparison of Hemodynamic Changes After Acute Normovolemic Hemodilution Using Ringer's Lactate Versus 5% Albumin in Patients on β-Blockers Undergoing Coronary Artery Bypass Surgery

Virendra K. Arya, MD,* Navanit G. Nagdeve, MD,* Arun Kumar, MD,* Shyam K. Thingnam, MS, MCh,† and Rajinder S. Dhaliwal, MS, MCh†

Objective: **Acute normovolemic hemodilution (ANH) is used cautiously in coronary artery disease (CAD) patients because of concerns of compromised coronary blood flow. This study aimed to compare hemodynamic changes by using either Ringer's lactate or albumin for ANH in CAD patients receiving β-blockers.**

Design: **Prospective, randomized study.**

Setting: **Postgraduate teaching hospital.**

Participants: **Thirty patients undergoing coronary artery bypass graft surgery (CABG) (hemoglobin >12 g/dL, on chronic β-blocker therapy).**

Interventions: **Monitoring, induction, and anesthesia followed a routine protocol for CABG surgery including pulmonary artery catheter placement. Patients were randomly included in group 1 (ANH by Ringer's lactate) or in group 2 (ANH by 5% albumin). A hemodynamic calculation software program was used for parameters recorded before and after ANH.**

Measurements and Main Results: **ANH could not be completed in 5 patients (33%) in group 1 because of a fall in mean arterial pressure (MAP) of more than 25% from baseline. In both groups posthemodilution MAP, heart rate, systemic vascular resistance, and oxygen delivery index decreased, whereas stroke volume index, cardiac index, and tissue oxygen extraction increased significantly as compared to baseline values ($p < 0.05$). Hemodynamic parameters were better maintained during the study period in group 2 than group 1.**

Conclusions: **Hemodynamic stability was better maintained by 5% albumin than Ringer's lactate for ANH in chronic β-blocked CAD patients. Despite an increase in cardiac index, systemic oxygen delivery was decreased irrespective of the hemodiluting fluid used. ANH to a hemoglobin value of 10 g/dL in chronically β-blocked CAD patients was well tolerated.**

© ***2006 Elsevier Inc. All rights reserved.***

KEY WORDS: acute normovolemic hemodilution, coronary artery disease, β-blockers, crystalloids versus colloids, coronary artery bypass graft surgery

PREOPERATIVE ACUTE normovolemic hemodilution (ANH) is used to reduce the need for allogeneic blood transfusion and to avoid potential complications associated with it. The physiologic effects of ANH using non–oxygen-carrying exchange solutions have been studied in animal models.[1,2] The most important mechanism invoked as physiologic compensation of acute reduction of hemoglobin (Hb) is an increase in cardiac output (CO). The primary factors responsible for the increase in CO are a decrease in viscosity, systemic vascular resistance (SVR), and an increase in venous return.[3,4]

There are little hemodynamic data available in humans undergoing ANH, especially those receiving β-blocker medications for coronary artery disease (CAD).[5-9] Recently, even previously accepted compensatory mechanisms such as increased CO have been questioned.[10] The choice of a better or safer diluent for ANH in CAD patients on chronic β-blocker therapy has also not been addressed. Hence, the authors designed this study using invasive measurements to evaluate and compare the hemodynamic effects of ANH by either Ringer's lactate or 5% albumin in CAD patients receiving chronic β-blocker medications and undergoing coronary artery bypass graft (CABG) surgery.

*From the Departments of *Anaesthesia & Intensive Care and †Cardiothoracic Vascular Surgery, Postgraduate Institute of Medical Education and Research, Chandigarh, India.*

Address reprint requests to Virendra K. Arya, MD, Department of Anaesthesia & Intensive Care, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh–160012, India. E-mail: aryavk_99@yahoo.com

© 2006 Elsevier Inc. All rights reserved.

1053-0770/06/2006-0011$32.00/0

doi:10.1053/j.jvca.2005.04.012

MATERIAL AND METHODS

After obtaining ethics committee approval and informed written consent, 30 patients of New York Heart Association class II and III with Hb values ≥12 g/dL scheduled to undergo CABG for CAD were enrolled in the study. All patients were on chronic β-blocker medications. The adequacy of β-blockade was judged as per generally accepted guidelines, ie, resting heart rate (HR) between 50 and 60 beats/min and an increase in HR of <20 beats/min during exercise.[11] The patients were randomly allocated into 2 groups: group 1 (ANH by Ringer's lactate) or group 2 (ANH by 5% albumin). Patients having a myocardial infarction within 4 weeks, unstable angina (patients on heparin and nitroglycerin infusions), associated valvular lesions, rhythm other than sinus rhythm, presence of left bundle-branch block, pulmonary restrictive or obstructive airway disease, renal dysfunction, and those undergoing emergency CABG surgery were excluded from the study. However, patients were not excluded on the basis of advanced age or low ejection fraction.

All patients were premedicated with diazepam, 5 mg orally, the night before surgery, and received their usual cardiovascular medications, including β-blockers, calcium channel blockers, and nitrates both the evening before as well as on the morning of surgery. However, angiotensin-converting enzyme inhibitors were omitted on the morning of operation as per the institutional practice.

Preinduction continuous monitoring included 5-lead electrocardiogram, pulse oximetry, end-tidal capnometry, and invasive arterial blood pressure through a 20-G catheter inserted in a radial artery. A central venous catheter and a pulmonary arterial thermodilution catheter (Swan-Ganz, Viggo spectramed 7.5F; Becton Dickinson, Singapore) were inserted before or after induction of anesthesia depending on the condition and cooperation of the individual patient. Anesthesia was induced using midazolam, 0.04 mg/kg, morphine, 0.2 mg/kg, fentanyl, 2 μg/kg, and thiopental, 2 to 3 mg/kg. Tracheal intubation was facilitated with vecuronium, 0.1 mg/kg. Anesthesia was maintained with isoflurane (end-tidal concentration 0.5%) along with 66% nitrous oxide in oxygen, and minute ventilation was adjusted to achieve normocapnia. No additional anesthetic drug was given during the study. Patients received a normal saline infusion of 2 mL/kg/h during induction and

Table 1. Demographic Characteristics

	Group 1 (n = 15)	Group 2 (n = 15)
Age (y)	54.4 ± 7.17 (42-66)	55.7 ± 6.01 (44-64)
BSA (m^2)	1.89 ± 0.34 (1.4-2.6)	1.91 ± 0.26 (1.37-2.51)
Preoperative Hb (g/dL)	14.6 ± 0.88 (13-16)	14.7 ± 0.96 (13.6-16)
Preoperative HR (beats/min)	59.8 ± 7.69 (44-72)	57.2 ± 8.63 (42-74)
LVEF %	50 ± 9.28 (35-68)	53.7 ± 9.87 (36-72)
LVEDP (mmHg)	16.8 ± 4.95 (8-24)	16.4 ± 5.78 (6-28)
Median NYHA class	3 (2-3)	3 (2-3)
Previous MI (n) (%)		
Angina only	3 (20)	2 (13.3)
One previous MI	7 (46.7)	9 (60)
Two previous MI	5 (33.3)	4 (26.7)
Affected vessels (n) (%)		
One	1 (6.6)	2 (13.3)
Two	4 (26.7)	4 (26.7)
Three	10 (66.7)	9 (60)
Calcium channel blockers (%)	6 (40)	5 (33.3)
ACE inhibitors (%)	7 (46.7)	9 (60)

NOTE. There were no significant differences between 2 groups for all variables ($p > 0.05$).

Abbreviations: BSA, body surface area; HR, heart rate; LVEF, left ventricular ejection fraction; LVEDP, left ventricular end-diastolic pressure; NYHA, New York Heart Association; MI, myocardial infarction; ACE, angiotensin-converting enzyme.

afterwards until blood collection was started. Before ANH, additional normal saline was infused as per clinical indications (eg, to normalize a decrease in arterial pressure associated with low filling pressures [individual level] or marked ventilation-associated variations in the arterial pressures). A heating mattress was used to maintain body temperature at the basal value.

The pulmonary arterial catheter was used to monitor pulmonary artery pressure (PAP), pulmonary artery wedge pressure (PAWP), central venous pressure (CVP) at end-expiration, and CO by thermodilution (Horizon 2000 monitor; Mennen Medicals Ltd, Jerusalem, Israel). The mean of 3 or more consecutive CO by thermodilution measurements (10 mL of 5% dextrose at room temperature 18°-20°C) were used. Arterial and mixed venous blood samples were analyzed for oxygen saturation (SaO_2 and SvO_2), partial pressure of oxygen (PaO_2 and PvO_2), partial pressure of carbon dioxide ($PaCO_2$ and $PvCO_2$), and acid base status, respectively. A built-in hemodynamic calculation software program (Horizon 2000 monitor) was used to determine ST-segment changes and calculate stroke volume index (SVI), cardiac index (CI), SVR, and pulmonary vascular resistance (PVR). From the directly measured variables, derived parameters were computed according to the following formulae:

1. $CI = CO \div \text{body surface area}$
2. $SVR = 80 \times (\text{mean arterial pressure [MAP]} - CVP) \div CO$
3. $PVR = 80 \times (\text{mean pulmonary arterial pressure} - PAWP) \div CO$
4. $\text{Oxygen delivery index } (DO_2I) = 10 \times CI \times (Hb \times 1.39 \times SaO_2 + PaO_2 \times 0.003)$
5. $\text{Arteriovenous oxygen content difference } (AVDO_2) = (Hb \times 1.39 \times SaO_2 + PaO_2 \times 0.003) - (Hb \times 1.39 \times SvO_2 + PvO_2 \times 0.003)$
6. $\text{Oxygen consumption index } (VO_2I) = 10 \times CI \times AVDO_2$
7. $\text{Oxygen extraction } (O_2\text{-Ex}) = 100 \times AVDO_2 \div (Hb \times 1.39 \times SaO_2 + PaO_2 \times 0.003)$

After sternotomy, 15 minutes for stabilization was allowed, and then ANH was undertaken. To achieve a hemoglobin value of 10 g/dL, the blood volume to be withdrawn was preoperatively calculated from the actual body weight and preoperative hemoglobin level, using a normogram based on the formula: volume lost = blood volume × ln (hemoglobin start ÷ hemoglobin final)[12], where ln denotes the natural logarithm. However, no more than 12 mL/kg of blood was taken out in any patient.[13] Blood withdrawal and volume substitutions were accomplished simultaneously over 20 to 30 minutes in both groups depending on the blood volume to be removed and the flow of blood achieved by gravity. The total infused volume of Ringer's lactate was 3 times that withdrawn in group 1, and in group 2 an equal quantity of 5% albumin to the volume of blood withdrawn was infused.[14,15] Hemodynamic measurements, hemoglobin, and blood gas analysis of arterial as well as mixed venous blood were made at 5 time points: 3 baseline recordings at 5-minute intervals during the stabilization period (mean of these readings was taken as the baseline value for subsequent comparison) and 2 post-ANH recordings at 5 minutes and 20 minutes after completion of ANH. The ANH was stopped if mean arterial pressure fell by 25% of the basal value or new ST-segment changes (new ST depression >0.1 mV or a new ST elevation >0.2 mV) appeared on the electrocardiogram. If the hemodynamics in these patients improved after stopping ANH and remained stable subsequently without inotropic support, their hemodynamic data was included in the analysis; however, they were not hemodiluted any further. Their hemodynamic data were excluded from the analysis only if mean arterial pressure remained low (less than 25% of basal value) despite stopping ANH or they required inotropic support to maintain blood pressure. Both the groups were also compared for number of patients whose target level of blood withdrawal could not be achieved.

An SPSS-10 software program (SPSS Inc, Chicago, IL) was used to analyze the data collected. Analysis of variance was done for repeated measures to identify any changes during the stabilization period or after ANH. The significant changes were subjected to unpaired and paired *t* tests with Bonferroni correction. A p value of <0.05 was considered significant.

RESULTS

All patients in both groups were male, and their demographic data and other variables were comparable (Table 1). There were 11 and 13 patients of New York Heart Association class III in group 1 and group 2, respectively. During the stabilization period, no significant hemodynamic changes were recorded and the mean of 3 readings was taken as the baseline value. ANH could not be completed to the target level in 5 patients in group 1 because of a fall in MAP by 25% without any associated rhythm changes after 350 mL of blood was withdrawn. The MAP improved in these patients once ANH was stopped. Mean

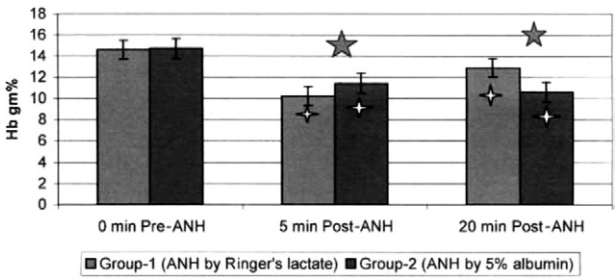

Fig 1. Pre- and postautologous normovolemic hemodilution hemoglobin changes.

Table 2. Hemodynamic Data Before and After ANH in Both Groups (Mean ± SD)

	Group 1 (n = 15)			Group 2 (n = 15)		
	Baseline	5 Minutes Post-ANH	20 Minutes Post-ANH	Baseline	5 Minutes Post-ANH	20 Minutes Post-ANH
Hb (g/dL)	14.6 ± 0.88	10.2 ± 0.62*	12.9 ± 0.94*†	14.7 ± 0.96	11.4 ± 0.35*‡	10.6 ± 0.78*‡
HR (beats/min)	59.8 ± 7.69	53.6 ± 6.94*	54.8 ± 5.06*	57.2 ± 8.63	54.2 ± 7.63	53.8 ± 6.46*
MAP (mmHg)	70.6 ± 8.95	62.6 ± 11.26*	69.6 ± 7.45†	74.6 ± 7.34	71.9 ± 6.85‡	70.82 ± 7.62
MPAP (mmHg)	14.2 ± 4.31	15.75 ± 4.47	14.8 ± 6.1	13.96 ± 4.16	15.2 ± 4.28	15.33 ± 5.31
CVP (mmHg)	6.23 ± 2.98	6.44 ± 3.1	3.65 ± 2.43*	5.86 ± 2.21	6.12 ± 3.32	5.92 ± 3.68‡
PCWP (mmHg)	10.4 ± 4.55	10.5 ± 4.62	6.8 ± 3.86*	11.2 ± 4.84	11.65 ± 5.2	10.43 ± 6.35‡
SVI (mL/m^2)	38.33 ± 6.77	55.7 ± 4.56*	47.9 ± 5.12*†	37.2 ± 5.89	61.45 ± 6.32*‡	60.21 ± 5.98*‡
CI (L/min/m^2) (range)	2.46 ± 0.55 (1.68-3.4)	3.09 ± 0.39* (2.6-4.4)	2.6 ± 0.63† (1.92-3.9)	2.48 ± 0.67 (1.48-3.8)	3.48 ± 0.46*‡ (2.1-4.56)	3.44 ± 0.52*‡ (1.96-4.6)
SVR (dynes/s/cm^{-5})	1,369.7 ± 177.3	860.3 ± 163.8*	1,130.6 ± 173.8†	1,318 ± 180.5	918.5 ± 112.4*	912.8 ± 127.3*‡
PVR (dynes/s/cm^{-5})	84.6 ± 36.8	78.4 ± 44.7	86.9 ± 38.4	76.4 ± 42.7	66.9 ± 39.6	69.6 ± 41.3‡

* $p < 0.05$ with in the group as compared with baseline value.
† $p < 0.05$ with in group at 20 minutes as compared with 5 minutes post-ANH.
‡ $p < 0.05$ between the 2 groups.

volume of blood withdrawn was 690 ± 98.6 mL (range 350-850 mL) in group 1 and 730 ± 94.8 mL (range 400-960 mL) in group 2.

The baseline hemoglobin values of 14.6 ± 0.88 g/dL and 14.7 ± 0.96 g/dL decreased to 10.2 ± 0.62 g/dL and 11.4 ± 0.35 g/dL at 5 minutes post-ANH in groups 1 and 2, respectively ($p < 0.001$) (Fig 1). The fall in hemoglobin values was significantly higher in group 1 as compared with group 2 at this time ($p < 0.05$). After 20 minutes post-ANH, there was a rise in hemoglobin values in group 1 to 12.9 ± 0.94 g/dL that was not seen in group 2 ($p < 0.05$) (Fig 1). There was no significant difference between hemoglobin values at 5 and 20 minutes post-ANH in group 2. None of the patients in either group had significant ST-segment changes in leads II and V_5 during or after ANH.

The filling pressures (CVP, PAWP) were maintained at 5 minutes of ANH; however, CO and CI increased in both groups, which was accompanied by increase in SVI ($p < 0.01$ within groups). These changes were significantly higher and well sustained until 20 minutes after ANH in group 2 ($p < 0.05$ between the groups). In group 1, at 20 minutes post-ANH, filling pressures along with CI and SVI showed significant declines as compared with values at 5 minutes (Table 2). HR did not increase in either group at 5 minutes. A small but statistically significant decrease was observed in both groups at 20 minutes after ANH ($p < 0.05$) (Table 2).

Despite an increase in CI, DO_2I decreased in both groups associated with significant increases in O_2-Ex at 5 and 20 minutes after ANH ($p < 0.001$) (Figs 2 and 3). O_2-Ex was comparable between the groups at 5 minutes but was significantly higher in group 1 as compared with group 2 at 20 minutes after ANH (Fig 3). This was also reflected by a significant decrease in SvO_2 values at similar time intervals as compared with baseline values in both groups (Table 3). $AVDO_2$ showed significant decreases as compared with basal values in both groups ($p < 0.05$) (Table 3). Whole-body oxygen consumption was stable in both groups before and after hemodilution as depicted by VO_2I (Fig 4).

There was a significant fall in MAP in group 1 at 5 minutes as compared with group 2 ($p < 0.05$ between and within the groups) (Table 2). PAP was not affected significantly in either group during and after ANH. SVR fell significantly in both

Fig 2. Pre- and postautologous normovolemic hemodilution oxygen delivery index changes.

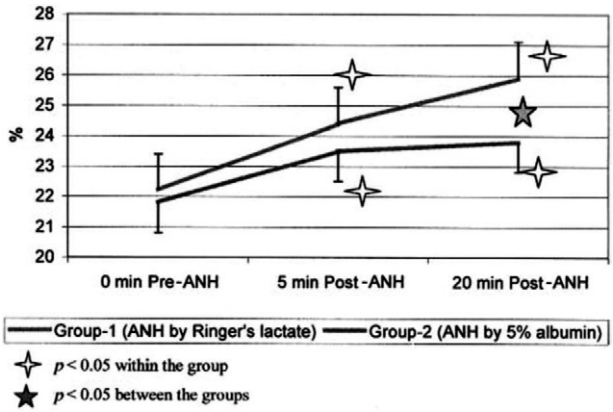

Fig 3. Pre- and postautologous normovolemic hemodilution oxygen extraction changes.

groups 5 minutes after ANH ($p < 0.001$ within groups). However, in group 1, SVR increased at 20 minutes along with significant decreases in CVP and PCWP ($p < 0.05$ between the groups) (Table 2). The changes in PVR were not statistically significant in both groups ($p > 0.05$). Arterial $PaCO_2$ and pH were not affected by hemodilution. However, there was a significant decrease in bicarbonate concentration (HCO_3) and base excess (BE) and an increase in arterial PaO_2 after hemodilution in both groups ($p < 0.05$ within groups) (Table 3).

The early postoperative course was similar in all patients. Three patients in group 1 and 4 patients in group 2 required an intra-aortic balloon pump (IABP) for hemodynamic support. None of the patients in group 1 who could not achieve target hemodilution because of hemodynamic instability required intra-aortic balloon pump support postrevascularization. Patients in both groups received similar amounts of allogeneic blood transfusions during first 24 hours (1.87 ± 0.74 U in group 1 and 1.92 ± 0.81 U in group 2, $p > 0.05$). There was no perioperative mortality in either group.

DISCUSSION

Various studies have documented benefits of hemodilution during CABG, both in terms of decreased number of patients requiring blood transfusion and the amount of blood transfused per patient as compared with control groups.[16-19] In the current study, the authors used invasive measurements to evaluate and compare the hemodynamic effects of ANH by using either Ringer's lactate or 5% albumin in CAD patients receiving β-blocker medications and undergoing CABG.

In ANH, the choice of a diluting fluid can be either a crystalloid and/or colloids. The crystalloids are recommended in a 3:1 ratio to avoid a volume deficit.[14,15] The colloids have a primary advantage of intravascular retention so the amount infused can be approximately equal to the amount of blood removed. Hemodynamic studies comparing various colloids including dextran, albumin, and hydroxyethyl starch have shown no significant difference among these diluents.[20] Jones et al[21] compared Ringer's lactate, 5% albumin, 6% dextran-70, and 6% hydroxyethyl starch for ANH and observed that hemodilution was well tolerated irrespective of the replacement fluid used. However, their study included patients without CAD.[21] In the present study, among the group hemodiluted with Ringer's lactate, ANH had to be stopped in 33% of the patients because of a fall in MAP by more than 25% and a slight rise in PAP as compared with no changes in group 2 who received 5% albumin as the diluting fluid. It can be speculated that group 1 patients did not receive resuscitation as quickly as the colloid group because the rate of infusion was not measured in this study. Had the rate of Ringer's lactate been 3 times faster than 5% albumin, this would most likely not have changed the hemodynamics at 20 minutes, but it might have decreased the number of patients in whom the target ANH could not be achieved because of acute hypotension in group 1. However, because 3 times more volume was infused in group 1 as compared with group 2 within the same time period of blood withdrawal, the rate of infusion was definitely faster in group 1, thus decreasing the possibility of delayed resuscitation in this group. Although no ST-segment changes were noticed in patients when target ANH could not be achieved, it is difficult to rule out early ischemic changes in these patients. The sensitivity of leads II and V_5 to detect intraoperative myocardial ischemia is only approximately 80%.[22] It is therefore possible that undetected myocardial ischemia might have developed in these patients during ANH. However, they became stable once ANH was stopped. This suggests that colloid may be a better alternative than crystalloids in CAD patients receiving β-block-

Table 3. Blood Gas Analysis Values Before and After ANH in Both Groups (Mean ± SD)

	Group 1 (n = 15)			Group 2 (n = 15)		
	Baseline	5 Minutes Post-ANH	20 Minutes Post-ANH	Baseline	5 Minutes Post-ANH	20 Minutes Post-ANH
Pt. temperature (°C)	36.6 ± 0.10	36.6 ± 0.11	36.6 ± 0.10	36.6 ± 0.11	36.5 ± 0.12	36.6 ± 0.10
SvO_2 (%)	78.2 ± 4.24	74 ± 4.15*	72.6 ± 3.95*	80.3 ± 4.65	76.8 ± 4.73*	76.5 ± 4.29*†
PaO_2 (mmHg)	128.2 ± 8.9	132.6 ± 9.68*	133.4 ± 9.23*	125.9 ± 7.85	130.2 ± 6.47*	135.3 ± 6.67*
$PaCO_2$ (mmHg)	36.8 ± 1.32	36.8 ± 1.32	36.8 ± 1.32	34.7 ± 1.42	34.7 ± 1.42	34.7 ± 1.42
pH	7.44 ± 0.02	7.43 ± 0.02	7.42 ± 0.02	7.44 ± 0.02	7.43 ± 0.02	7.43 ± 0.02
HCO_3 (mmol/L)	28.2 ± 0.03	26.1 ± 0.03*	25.0 ± 0.02*	28.0 ± 0.02	26.2 ± 0.03*	26.0 ± 0.03*
BE (mmol/L)	2.4 ± 0.2	1.8 ± 0.02*	1.2 ± 0.02*	2.6 ± 0.02	2.0 ± 0.02*	1.6 ± 0.03*
$AVDO_2$ (mL/dL)	4.7 ± 0.68	3.8 ± 0.72*	4.2 ± 0.67	4.52 ± 0.48	3.36 ± 0.59*	3.40 ± 0.51*

*$p < 0.05$ within the group.
†$p < 0.05$ between the 2 groups.

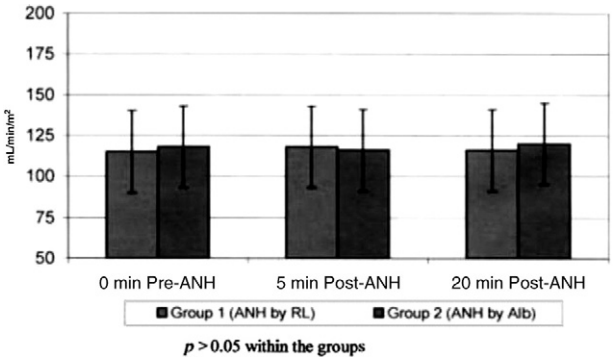

Fig 4. Pre- and postautologous normovolemic hemodilution oxygen consumption index changes.

ers because less replacement is required with colloid and there is no acute overload on the ventricles or excess of dilutional anemia (with 3 times crystalloid replacement), which may lead to myocardial ischemia and hemodynamic instability. This rationale may be even more applicable to CAD patients with poor ejection fraction and low Hb values.

Some studies suggest that preoperative hemodilution using 4% albumin on a 1:1 volume basis for blood substitution enhances the extravasation rate of albumin and fluid into the interstitial tissues and isovolemic conditions are not maintained.[23] This may be because of low colloid oncotic pressure of 4% albumin compared with human serum. Hence, substitution with an identical volume of the 4% albumin solution alone would not be useful for "isovolemic" hemodilution. To obtain a clinically safe and approximately normovolemic hemodilution, the authors replaced the withdrawn blood with an equal volume of 5% albumin solution instead of 4% albumin as reported in previous studies.[23,24]

Anesthesia itself has effects on the cardiovascular response to ANH. However, in the present study, the anesthesia regimen was not altered in any patient during the observation period. Moreover, before ANH and during the stabilization period under anesthesia, hemodynamic variables did not change, and the mean of 3 readings was taken for comparison to rule out any bias because of the anesthesia regimen. The similar choice of anesthetizing agents and the prolonged stabilization period in this study make it less plausible that anesthetics could explain the differences observed after ANH. The small but significant decrease in HR in both groups post-ANH may be attributed to the anesthetic effect in β-blocked patients because there was no surgical stimulation during this period.

There was a significantly greater decrease in hemoglobin at 5 minutes post-ANH in group 1 than group 2 because of different amounts of substitute volume. This indicates the greater effect of hemodilution by Ringer's lactate (crystalloid) than 5% albumin (colloid) immediately after ANH. In contrast to ANH by 5% albumin, hemodilution by Ringer's lactate decreased over time because of further redistribution of fluid into the interstitial space, which led to falls in CVP, PAWP, SVI, and CI accompanied by rises in hemoglobin, SVR, and O_2-Ex at 20 minutes post-ANH. This implied that compensatory increases in SVI and CI were better preserved by colloid solutions in β-blocked CAD patients after ANH.

In this study, the hemodynamic responses to ANH were characterized by compensatory increases in CI and oxygen extraction in both groups that were better preserved in group 2. This is similar to studies conducted on β-blocked experimental animals without CAD, who showed increases in CI and O_2-Ex as compensatory mechanisms for ANH.[25-27] The increase in CI was solely dependent on an increase in SVI because HR did not increase because of the β-blockers. Licker et al[28] studied hemodynamic changes during ANH in anesthetized patients with CAD using a transesophageal Doppler and showed that the primary compensation was by an increase in stroke volume that increased CO similar to that found in the present study. Spahn et al[29] showed that increases in CO in anesthetized humans are achieved primarily by increases in stoke volume, and an increase in heart rate should be viewed as a sign of hypovolemia. Increases in SVI can also be attributed to reduced blood viscosity because it increases venous return and decreases SVR. In the present study, a combined increase of CI and O_2-Ex resulted in maintained whole body VO_2I despite compromised arterial oxygen content because of reduced hemoglobin. This observation is similar to other studies of ANH in which Hb was lowered quickly during hemodilution by clear fluids.[25-29] The capacity of patients with CAD to adapt to lowered Hb levels may be related to an increase in transstenotic coronary artery flow during ANH, maintained myocardial oxygen consumption because of prevention of an increase in HR by β-blockers, and facilitated left ventricular ejection because of a decrease in afterload.[29] Moreover, animal studies have shown that normal coronary arteries respond to acute anemia by substantial dilatation before oxygen delivery is affected.[30]

In a study by Spahn et al,[31] comparing patients undergoing CABG surgery with and without β-blocker therapy, it was observed that chronically β-blocked patients tolerated ANH comparable to non–β-blocked patients. Patients on β-blockers tolerated an acute decrease in arterial oxygen content by increasing CI and oxygen extraction. In their study, the increase in CI was primarily by increases in SVI, similar to the present findings. The increase in SVI in chronically β-blocked patients may be because of an increase in the number of myocardial β-adrenergic receptors, which maintains cardiac contractility as observed during long-term β-adrenergic blocker therapy,[32,33] which may also be responsible for increased exercise tolerance[34] and an exaggerated response to exogenous catecholamines such as dobutamine.[33]

There were no significant changes observed in PVR in both groups. Unchanged as well as decreased PVR have been described during hemodilution.[35] The authors observed an increase in PaO_2 with hemodilution in both groups. During hemodilution, intrapulmonary shunt (Qs/Qt) may increase or decrease, depending on ventilation-perfusion relationships (V/Q).[36] It has been reported that during ANH when V/Q ratio is normal, Qs/Qt may actually decrease because of the increased CI leading to exaggerated perfusion of more lung units with a higher alveolar oxygen partial pressure resulting in higher PaO_2.[37] The comparative changes in HCO_3, BE, SvO_2, and $AVDO_2$ after ANH in both groups of the present study are similar to previous studies on hemodilution.[13,30,31,35]

The postoperative course of patients in both groups was comparable. The requirement for IABP support and need of blood transfusion in the first 24 hours after surgery could be due to a

number of other factors such as the surgeon's experience, skill, difficult dissection, CPB time, prior antiplatelet therapy, adequacy of myocardial preservation, or poor target vessels. In this study, IABP support was required postoperatively in those patients whose CPB time was long because of the surgeon facing technical difficulties in grafting the diseased vessels. None of the 5 patients in group 1 who developed hemodynamic instability during ANH required IABP support postrevascularization.

In conclusion, the present study showed that hemodynamic stability during ANH was better maintained with colloids (5% albumin) as compared with crystalloids (Ringer's lactate) in chronically β-blocked CAD patients. Hence, colloids may be a better or safer diluent for ANH in these patients. The patients tolerated ANH to an Hb value of approximately 10 g/dL before CABG without signs of myocardial ischemia. During the early phase of hemodilution, compensation was primarily by increases in SVI and O_2-Ex and not by an increase in HR. Despite increases in CI resulting from hemodilution, overall systemic oxygen delivery was decreased because of the fall in oxygen content. Because most of the CAD patients in this study were relatively healthy, the results cannot be extrapolated to sicker patients.

REFERENCES

1. Doss DN, Estafanous FG, Ferrario CM, et al: Mechanism of systemic vasodilatation during normovolemic haemodilution. Anesth Analg 81:30-34, 1995
2. Chapler CK, Cain SM: The physiologic reserve in oxygen-carrying capacity: Studies in experimental hemodilution. Can J Physiol Pharmacol 64:7-12, 1986
3. Guyton AC, Richardson TQ: Effect of hematocrit on venous return. Circ Res 9:157-164, 1961
4. Murray JF, Escobar E: Circulatory effects of blood viscosity: Comparison of methemoglobinemia and anemia. J Appl Physiol 25: 594-599,1968
5. Laks H, Pilon RN, Klövekorn WP, et al: Acute hemodilution: Its effect on hemodynamics and oxygen transport in anesthetized man. Ann Surg 42:103-109, 1974
6. Rose D, Coutsoftides T: Intraoperative normovolemic hemodilution. J Surg Res 31:375-381, 1981
7. Fontana JL, Welborn L, Mongan PD, et al: Oxygen consumption and cardiovascular function in children during profound intraoperative normovolemic hemodilution. Anesth Analg 80:219-225, 1995
8. Gisselsson L, Rosberg B, Ericsson M: Myocardial blood flow, oxygen uptake and carbon dioxide release of the human heart during hemodilution. Acta Anaesthesiol Scand 26:589-591, 1982
9. Weiskopf RB, Viele MK, Feiner J, et al: Human cardiovascular and metabolic response to acute, severe isovolemic anemia. JAMA 279:217-221, 1998
10. Gratz I, Carrig T, Goldberg M, et al: Acute normovolemic hemodilution is not accompanied by a compensatory increase in cardiac output in anesthetized patients. Anesth Analg 84:S79, 1997
11. Morgan GE: Anesthesia for patients with cardiovascular disease, in Morgan GE, Mikhail MS, Murray MJ (eds): Clinical Anesthesiology. New York, McGraw-Hill 2002, pp 386-432
12. Zetterström H, Wiklund L: A new nomogram facilitating adequate hemodilution. Acta Anaesthesiol Scand 30:300-304, 1986
13. Spahn DR, Schmid ER, Seifert B, et al: Hemodilution tolerance in patients with coronary artery disease who are receiving chronic beta-adenergic blocker therapy. Anesth Analg 83:687-694, 1996
14. Stehling L: Autologous Transfusion, in Miller RD (ed): Anesthesia (vol 1). Philadelphia, PA, Churchill Livingstone, 2000, pp 1645-1662
15. Goodnough LT, Brecher ME, Monk TG: Acute normovolemic hemodilution in surgery. Hematology 2:413-420, 1992
16. Schonberger JDAM, Breeder JJ, Jjian D, et al: Intraoperative predonation contributes to blood saving. Ann Thorac Surg 56:893-898, 1993
17. Petry AF, Jost J, Siever H: Reduction in homologous blood requirements by blood pooling at the onset of cardiopulmonary bypass. J Thorac Cardiovasc Surg 107:1210-1214, 1994
18. Helm RE, Klempereer JD, Rosengart TK, et al: Intraoperative autologous blood donation preserves red cell mass but does not decrease postoperative bleeding. Ann Thorac Surg 62:1431-1441, 1996
19. Kochamba GS, Pfeffer TA, Sintek CF, et al: Intraoperative autotransfusion reduces blood loss after cardiopulmonary bypass. Ann Thorac Surg 61:900-908, 1996
20. Martin E, Hansen E, Peter K: Acute limited normovolemic hemodilution: A method of avoiding transfusion. World J Surg 11:53-59, 1987
21. Jones SB, Whitten CW, Monk TG: Influence of crystalloid and colloid replacement solutions on hemodynamic variables during acute normovolemic hemodilution. J Clin Anesth 16:11-17, 2004
22. London MJ, Hollenberg M, Wong MG, et al: Intraoperative myocardial ischemia: localization by continuous 12-lead electrocardiography. Anesthesiology 69:232-241, 1988
23. Payen F, Vuillez JP, Geoffray B, et al: Effect of preoperative intentional hemodilution on the extravasation rate of albumen and fluid. Crit Care Med 25:243-248, 1997
24. Tonnesen T, Tollofsrud S, Kongsgaard UE, et al: Colloid osmotic pressure of plasma replacement fluids. Acta Anaesthesiol Scand 37:424-426, 1993
25. Shinoda T, Smith CE, Khairalla PA, et al: Effects of propranolol on myocardial performance during acute normovolemic hemodilution. J Cardiothorac Vasc Anesth 5:15-22, 1991
26. Tarnow J Eberlein HJ, Hess E, et al: Hemodynamic interactions of hemodilution, anesthesia, propranolol pretreatment and hypovolaemia on systemic circulation. Basic Res Cardiol 74:109-122, 1979
27. Chapler CK, Cain SM: Blood flow and O_2 uptake in dog hindlimb with anemia, norepinephrine and propranolol. J Appl Physiol 51:565-570, 1981
28. Licker M, Sierra J, Tassaux D, et al: Continuous haemodynamic monitoring using transoesophageal Doppler during acute normovolaemic haemodilution in patients with coronary artery disease. Anaesthesia 59:108-115, 2004
29. Spahn DR, Lene BT, Reves JG, et al: Cardiovascular and coronary physiology in acute normovolemic hemodilution: A review on non-oxygen-carrying and oxygen-carrying solutions. Anesth Analg 78:1000-1021, 1994
30. von Restorff W, Hofling B, Holtz J, et al: Effect of increased blood fluidity through hemodilution on general circulation at rest and during exercise in dogs. Pflugers Arch 357:25-34, 1975
31. Spahn DR, Seifert B, Pasch T, et al: Effect of chronic β-blockade on compensatory mechanism during acute isovolemic haemodilutionin patients with coronary artery disease. Br J Anaesth 78:381-385, 1997
32. Gilbert EM, Olsen SL, Renlund DG, et al: Beta-adrenergic receptor regulation and left ventricular function in idiopathic dilated cardiomyopathy. Am J Cardiol 71:23C-29C, 1993
33. Heilbrunn SM, Shah P, Bristow MR, et al: Increased β-receptor density and improved haemodynamic response to catecholamine stimulation during long-term metoprolol therapy in heart failure from dilated cardiomyopathy. Circulation 79:483-490, 1989
34. Engelmeier RS, O'Connell JB, Walsh R, et al: Improvement in

symptoms and exercise tolerance by metoprolol in patients with dilated cardiomyopathy: A double-blind, randomized placebo-controlled trial. Circulation 72:536-546, 1985

35. Vara-Thorbeck R, Marcote JAGF: Hemodynamic response of elderly patients undergoing major surgery under moderate normovolemic hemodilution. Eur Surg Res 17:372-376, 1985

36. Salem MR: Blood conservation, in Motoyama EK, Davis PJ (eds): Smith's Anesthesia for Infants and Children. St. Louis, MO, Mosby, 1996, pp 357-361

37. West JB: Ventilation-perfusion ratio inequality and regional gas exchange, in West JB (ed): Ventilation, Blood Flow and Gas Exchange. Oxford, Blackwell, 1990, pp 31-50