The Influence of Crystalloid and Colloid Replacement Solutions in Acute Normovolemic Hemodilution: A Preliminary Survey of Hemostatic Markers

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Acute normovolemic hemodilution (ANH), in which blood for autologous use is collected immediately before the onset of surgical blood loss, is a recommended autologous blood procurement technique for blood conservation. Both crystalloid and colloid replacement fluids have been used to maintain normovolemia during ANH, but few data are available to justify the use of a particular replacement fluid. Therefore, we designed a prospective, randomized study to determine if the replacement fluid choice affects various coagulation variables and perioperative blood loss. Forty adult patients, ASA physical status 1-3, scheduled for ANH during radical prostatectomy were randomly assigned to one of four replacement fluid groups: (a) Ringer's lactate, (b) 5% albumin, (c) 6% dextran 70 (DEX), or (d) 6% hetastarch (HES). After the induction of a standardized general anesthetic, all patients underwent ANH to a final hemoglobin level of 9 g/dL.

cute normovolemic hemodilution (ANH) is a useful and cost-effective blood conservation strategy in procedures with an expected blood loss of more than 1 L (1,2). The red blood cell (RBC) loss is decreased in the hemodiluted patient because blood that is lost during surgery has a reduced hematocrit (2). This technique effectively reduces the need for allogeneic blood transfusion and the accompanying risk of transfusionrelated infection and transfusion reactions (3). There is

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Complete blood count, prothrombin time, partial thromboplastin time, fibrinogen, factors V and VIII levels, bleeding time, and thromboelastography (TEG[®]) measurements were obtained at similar time points in the procedure. When compared with baseline, activated partial thromboplastin time decreased and factor VIII levels increased in the postanesthesia care unit in both the Ringer's lactate and 5% albumin groups. The DEX and HES groups demonstrated a decrease in TEG[®] maximum amplitude between preoperative and postanesthesia care unit measurements and TEG[®] α (angle) was decreased from baseline in the DEX group. The changes in factor VIII, activated partial thromboplastin time, and TEG[®] measurements indicate that HES and DEX may attenuate the hypercoagulability related to surgery.

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also evidence that the transfusion of allogeneic blood may induce immunosuppression, which may be detrimental with respect to perioperative infection and patients undergoing surgery for malignancies (4). ANH is less expensive than preoperative autologous donation (PAD) (1,5) and eliminates the risk of administrative error that may occur whenever banked blood is used.

ANH involves the removal of blood from the patient shortly after the induction of anesthesia and before the start of major surgical blood loss. A replacement fluid is simultaneously transfused to maintain intravascular volume. The stored blood is returned to the patient when a threshold hematocrit (Hct) is reached, or sooner, if clinically indicated. Ideally, this is after most of the blood loss has occurred.

Both crystalloid and colloid replacement fluids have been successfully used to maintain normovolemia during ANH. Colloids such as hetastarch and dextran decrease hypercoagulability in some studies (6–8), whereas crystalloid administration may not (9,10). Less is known about the effects of these fluids

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on hemostasis within the context of ANH. This prospective, randomized study was designed to determine if the replacement fluid choice impacts measured coagulation values and perioperative blood loss.

Methods

After IRB approval, written informed consent was obtained from 40 adult patients, ASA physical status I-III, scheduled to undergo radical retropubic prostatectomy. Patients were excluded from participation if they had a history of a known coagulation disorder, platelet count <100,000/mm³, preoperative hemoglobin (Hb) <12 g/dL, anticoagulant therapy within 10 days before surgery, aspirin or nonsteroidal antiinflammatory drug use <10 days before surgery, or if they had a documented allergy to any of the IV fluids used in the protocol. Enrolled patients were randomly assigned to one of four fluid replacement groups using a computer-generated random numbers table: (a) lactated Ringer's solution (LR), (b) 5% albumin (ALB; Baxter HC Corporation, Glendale, CA), (c) 6% dextran 70 (DEX; Abbot Laboratories, Chicago, IL), or (d) 6% hetastarch 450/0.7 (HES; Hespan®, Du Pont Merck, Wilmington, DE). Surgeons were blinded with respect to the study fluid, although the primary anesthesiologist was aware of the fluid administered to any given patient in the protocol.

All patients were premedicated with midazolam in the preoperative holding area and received a standardized general anesthetic induction consisting of thiopental (3–4 mg/kg), vecuronium (0.1 mg/kg), and fentanyl (2.5 μ g/kg). After tracheal intubation, anesthesia was maintained with isoflurane, nitrous oxide (67% in oxygen), and a continuous fentanyl infusion (1–3 μ g · kg⁻¹ · h⁻¹).

All patients underwent moderate hemodilution to a target Hb of 9 g/dL. ANH was performed in conjunction with prepping and draping of the patient and pelvic lymph node dissection. Whole blood was collected in standard citrate-phosphatedextrose (CPDA-1) blood collection bags while simultaneously infusing the replacement fluid. LR was administered in a 3:1 volume replacement ratio and the colloids in a 1:1 ratio. The colloid groups received a maximum of 20 mL/kg of the study fluid during hemodilution to adhere to the maximum recommended doses of HES and DEX. If further hemodilution was required to achieve the target Hb value in patients who received the maximum amount of colloid infusion, LR was used in a 3:1 ratio. The blood collected during hemodilution was returned to the patient when Hb < 8 g/dL or when the attending anesthesiologist felt it was clinically indicated, primarily for persistent decreases in blood pressure. All hemodiluted blood was returned to the patient before leaving the operating room (OR). If Hb <8 g/dL in the operating room or during the hospital stay, any PAD was transfused, followed by allogeneic blood if required.

Blood samples for coagulation testing and Hb levels were collected before induction, preANH, postANH, and upon arrival to the recovery room (postanesthesia) care unit [PACU]). Prothrombin time, activated partial thromboplastin time (aPTT), and fibrinogen concentration were determined on citrated plasma using an automated coagulation analyzer. Platelets were counted in EDTA-anticoagulated blood. Factor V and factor VIII activity was determined using a functional assay supplied by Diagnostica Stago (Asnieres, France). Celiteactivated thromboelastography (TEG®) (Haemoscope Corp, Skokie, IL) was performed immediately after collecting each blood sample, and standard TEG[®] variables were obtained using software provided by the manufacturer. The primary investigator measured Ivy bleeding times before surgery and upon arrival to the PACU using a Simplate device (Organon Teknika Corp, Durham, NC). A complete blood count was drawn on postoperative Day 3 (POD 3) to estimate total perioperative RBC loss using the formula (where IBW is ideal body weight) (11):

 $[\{70 \text{ mL/kg} \times \text{IBW (kg)}\}]$

× {preop Hct/100 – POD 3 Hct/100}]

+ [200 mL/unit

 \times no. of allogeneic units transfused]

+ [177 mL/unit \times no. of PAD units transfused]

Data were analyzed using SPSS for Windows software (release 6.1; SPSS, Inc, Chicago, IL). One-way analysis of variance was performed for all continuous variables. When a significant difference was noted, a Bonferroni test was performed for *post hoc* comparisons within and between groups. Nonparametric variables were analyzed using χ^2 testing. *P* values <0.05 were considered significant. Data are expressed as mean \pm sp.

Results

There were no significant differences in demographic data (Table 1). Length of stay averaged 4 days in all groups. The volume of blood removed, the number of autologous units predonated, and the percent of these predonated units discarded did not differ among the groups (Table 2). Three patients (two ALB and one HES) received LR to complete hemodilution after reaching the maximum colloid dose of 20 mL/kg. The

Table 1. Clinical Characteristics

	LR (n = 10)	$\begin{array}{l} \text{ALB} \\ (n = 10) \end{array}$	$\begin{array}{l} \text{DEX} \\ (n = 10) \end{array}$	$\begin{array}{l} \text{HES} \\ (n = 10) \end{array}$
Age (yr)	59 ± 11	59 ± 5	62 ± 5	59 ± 8
Weight (kg)	91 ± 13	86 ± 11	87 ± 10	90 ± 13
ASA status	2 (2-3)	2 (1–3)	2 (1–2)	2 (1–3)
Hx antihypertensive use (n)	0	4	3	3
Estimated patient blood volume (mL)	5621 ± 554	5460 ± 515	5558 ± 462	5404 ± 546

Values are mean \pm sp, except ASA (median and range).

LR = lactate Ringer's group; ALB = 5% albumin; DEX = 6% dextran 70; HES = 6% hetastarch; Hx = history of.

Table 2. Hemodilution Pro	cess and Transfusion Outcomes
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	LR (n = 10)	$\begin{array}{l} \text{ALB} \\ (n = 10) \end{array}$	$\begin{array}{l} \text{DEX} \\ (n = 10) \end{array}$	HES $(n = 10)$
	(n = 10)	(n - 10)	(n = 10)	(n - 10)
Admission hematocrit (%)	38.7 ± 2.2	41.1 ± 2.5	37.8 ± 2.9	39.2 ± 3.4
Discharge hematocrit (%)	30.9 ± 4.1	29.8 ± 5.0	27.8 ± 3.1	$25.8 \pm 3.3^{*}$
Estimated surgical blood loss (mL)	1240 ± 453	1150 ± 389	1400 ± 400	1445 ± 600
Calculated RBC loss during hospitalization (mL)	604 ± 251	712 ± 276	758 ± 243	901 ± 284
Median number of units obtained by ANH (range)	3 (2–3.5)	3 (2–4)	2 (2–3)	3 (2–4)
Volume of blood removed during ANH (mL)	1265 ± 286	1372 ± 280	1140 ± 245	1282 ± 321
Percent of EBV removed	23 ± 5	25 ± 5	21 ± 4	24 ± 6
Median number of predonated autologous units (range)	1 (1–2)	1 (0–2)	1 (0–2)	1 (0–2)
Median number of PAD units transfused (range)	1 (0–2)	0.5 (0-1)	1 (0–2)	1 (0–2)
Patients exposed to allogeneic blood (n)	0	0	2	0
Cost of fluid used for ANH (\$)	$3.79\pm0.82\dagger$	239.85 ± 38.95	36.82 ± 7.92†*	61.03 ± 11.0 †*

Values are mean \pm sp.

LR = lactate Ringers; ALB = 5% albumin; DEX = 6% dextran 70; HES = 6% hetastarch; RBC = red blood cells; ANH = acute normovolemic hemodilution; EBV = estimated whole blood volume; PAD = preoperative autologous donation.

* P < 0.05 when compared to LR; + P < 0.05 when compared to ALB.

2 patients in the ALB group donated 3 and 4 U of ANH and received 420 and 1000 mL of additional LR, respectively, whereas the patient in the HES group donated 4 U of ANH and received an additional 1500 mL of LR. Hct levels were lower in HES compared with LR on POD 3. Although estimated total RBC loss tended to be larger in the HES group, this difference did not reach significance (P = 0.1). In addition, although estimated surgical blood loss tended to be larger in DEX (13% for LR and 22% for ALB) and HES (17% for LR and 26% for ALB), these differences did not attain statistical significance (DEX versus LR, P = 0.41; DEX versus ALB, P = 0.17; HES versus LR, P = 0.40; HES versus ALB, P = 0.21). ALB was significantly more expensive than the other fluids. DEX and HES were also more expensive than LR (Table 2). The cost calculations for fluid resuscitation were derived from hospital acquisition costs in 2001.

Prothrombin time increased relative to preoperative baseline in all groups. The platelet count postANH decreased from preoperative to a statistically significant extent in all except the DEX group. In the PACU, LR and ALB aPTT values were significantly decreased from both preoperative and preANH, whereas DEX and HES remained unchanged. Fibrinogen decreased from preoperative to postANH in all groups. The Ivy bleeding time increased in all but the LR group (P < 0.05) but remained within the normal range in each study group (Table 3).

Factor VIII activity significantly decreased post-ANH in the LR and HES groups and increased in the PACU in the LR, ALB, and DEX groups. When viewed as a percent change from preANH baseline values (Fig. 1), the influence of HES on factor VIII seems evident. However, a statistically significant difference among groups was not achieved, likely because of wide interpatient variation in factor VIII activity. Factor V activity decreased in all groups.

TEG[®] yielded several notable findings (Table 4). Administration of DEX resulted in an increased coagulation time and decreased maximum amplitude (MA) compared with the other groups ($P \le 0.05$) as well as a decreased α angle relative to LR and ALB. HES demonstrated less of an overall influence on the TEG[®]. The MA for HES decreased relative to LR in the PACU, and the α angle was unchanged relative to an increase in the LR group. The LR and ALB results illustrate the expected TEG[®] findings of decreased

Table 3. Coagulation Values

	LR $(n = 10)$	ALB $(n = 10)$	DEX $(n = 10)$	HES $(n = 10)$
Platelet count (k \sim mm ⁻³) [140–415]				
Preop	229 ± 47	190 ± 43	203 ± 71	210 ± 44
PreANH	210 ± 39	177 ± 37	190 ± 69	198 ± 39
PostANH	$162 \pm 37*8$	$152 \pm 25^{*}$	151 ± 49	$143 \pm 34*$ §
PACU	198 ± 52	158 ± 37	159 ± 74	$169 \pm 43^{*}$
PT (s) [10.5–14.0]				
Preop	12.2 ± 0.6	12.2 ± 0.8	12.2 ± 0.3	12.3 ± 0.3
PreANH	12.7 ± 0.6	12.8 ± 0.4	12.8 ± 0.4	12.4 ± 0.6
PostANH	13.5 ± 0.6 *§	13.6 ± 0.4 *§	13.5 ± 0.3 *§	$13.6 \pm 0.9^{*}$ §
PACU	$13.0 \pm 0.6^{*}$	$13.3 \pm 0.5 * \$$	$13.6 \pm 0.5 * \$$	$13.9 \pm 1.3*$ §
aPTT (s) [20.0–35.0]		0	6	0
Preop	27.5 ± 1.0	27.0 ± 2.0	26.8 ± 2.5	27.9 ± 3.0
PreANH	28.0 ± 1.4	29.8 ± 4.2	27.6 ± 1.4	28.8 ± 3.2
PostANH	29.8 ± 1.7 *§	28.5 ± 2.6	30.2 ± 2.1 *§	31.8 ± 4.5
PACU	$24.2 \pm 2.5*8$	$24.7 \pm 2.7*$ §	25.5 ± 2.5	26.8 ± 3.9
Fibrinogen (mg \sim dL ⁻¹) [180–460]	U	U		
Preop	291 ± 91	252 ± 66	250 ± 62	329 ± 76
PreANH	240 ± 65	241 ± 38	205 ± 37	268 ± 73
PostANH	$179 \pm 55^{*}$ §	$138 \pm 40^{*}$ §	$158 \pm 50^{*}$ §	$223 \pm 45^{*}$
PACU	$187 \pm 64^{*}$	$155 \pm 44^{*}$ §	$154 \pm 29^{*}$ §	$190 \pm 58 * \$$
Factor V (%) [60–140]				
Preop	87 ± 20	87 ± 15	84 ± 24	94 ± 31
PreÂNH	80 ± 13	80 ± 13	80 ± 18	83 ± 23
PostANH	$53 \pm 8^{*}$ §	$49 \pm 8^{*}$ §	$52 \pm 18^{*}$ §	$57 \pm 25^{*}$ §
PACU	$54 \pm 12^{*}$ §	$54 \pm 9^{*}$ §	$50 \pm 17^{*}$ §	$54 \pm 18^{*}$ §
Factor VIII (%) [50–150]				
Preop	53 ± 21	51 ± 33	81 ± 44	63 ± 36
PreÂNH	68 ± 25	56 ± 29	71 ± 28	67 ± 33
PostANH	44 ± 11 §	53 ± 33	54 ± 27	$31 \pm 16^{*}$ §
PACU	$135 \pm 94*$ §	$108 \pm 53^{*}$ §	139 ± 80 §	111 ± 103
BT (min) [4–9]				
Preop	5 ± 1	4 ± 1	4 ± 1	5 ± 2
PACÛ	5 ± 2	$6 \pm 1^{*}$	$5 \pm 2^{*}$	$6 \pm 1^{*}$
HGB (g/dL)				
Preop	13.4 ± 0.8	$14.2 \pm 0.8 \ddagger$	13.0 ± 1.0	13.4 ± 1.1
PreÂNH	$12.5 \pm 0.8^{*}$	$13.5 \pm 0.8^{++}$	$11.9 \pm 1.0^{*}$	$12.5 \pm 0.7^{*}$
PostANH	$9.2 \pm 0.6^{*}$	$9.7 \pm 0.7^{*}$ ‡§	8.6 ± 0.7 *§	$8.9 \pm 0.5^{\$}$
PACU	$10.2 \pm 1.0^{*}$ ‡§	$10.4 \pm 0.6^{*}$ ‡§	$8.8 \pm 0.6 * \bar{\$}$	$9.2 \pm 0.7*$ †§
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Values are mean \pm sp. [] indicates normal values. LR = lactate Ringer's; ALB = 5% albumin; DEX = 6% dextran 70; HES = 6% hetastarch; Preop = preoperative; ANH = acute normovolemic hemodilution; PT = prothrombin time; aPTT = activated partial thromboplastin time; BT = bleeding time; HGB = hemoglobin; PACU = postanesthesia care unit. * P < 0.05 when compared to preop; § P < 0.05 when compared to preANH; † P < 0.05 when compared to LR; ‡ P < 0.05 when compared to DEX; || P < 0.05when compared to ALB.

coagulability after the induction of general anesthesia (preANH) then increased coagulability after surgical stress (postANH and PACU) (12,13).

Discussion

When one analyzes the influence that ANH had on the coagulation variables investigated, including routine laboratory studies, factor V and VIII analyses, and TEG[®], it is important to remember that the blood was harvested with gentle agitation and then maintained at room temperature while stored in CPDA bags. The influence that ANH may have had on these variables could have been influenced by storage in another substance such as acid citrate dextrose (14). The purpose

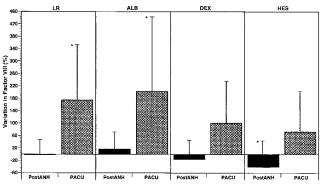


Figure 1. Factor VIII activities as a percent change from preANH (acute normovolemic hemodilution) baseline to immediately after withdrawal of final hemodilution unit (postANH) and upon arrival to the postanesthesia care unit (PACU). LR, Ringer's lactate; ALB, 5% albumin; DEX, 6% dextran 70; and HES, 6% hetastarch. *P < 0.05when compared with baseline.

	LR $(n = 10)$	ALB $(n = 10)$	DEX $(n = 10)$	HES $(n = 10)$
R (mm) [10.4 ± 1.8]				
Preop	$15.9 \pm 4.1 (10.5 - 23.0)$	$13.6 \pm 4.9 \ (8.5 - 23.0)$	$13.9 \pm 6.6 \ (6.5-24.5)$	$16.8 \pm 6.8 \ (10.5 - 32.5)$
PreÂNH	$26.1 \pm 21.0 (11.0 - 76.5)$	$20.6 \pm 14.7 \ (8.5 - 52.0)$	$24.1 \pm 16.0 (10.0-61.0)$	$17.4 \pm 5.8 (12.0 - 27.0)$
PostANH	$9.1 \pm 3.6 \ (4.5 - 15.0)^{*1}$	$9.3 \pm 4.2 (4.5 - 17.5)^{*}$	$12.8 \pm 3.5 (7.5 - 17.0)$	$11.4 \pm 2.3 (8.0 - 16.0)^{*}$
PACU	$8.4 \pm 2.4 (5.0 - 11.5)^{*}$	$7.1 \pm 2.3 (4.5 - 12.5)^{*}$	$10.1 \pm 4.7 (5.0 - 20.5) \ddagger$	$8.8 \pm 3.3 (2.5 - 13.5)^{*}$
K (mm) [3.0 ± 7.0]				
Preop	$5.2 \pm 1.5 (3.0 - 8.0)$	4.2 ± 1.5 (2.5–7.0)	4.9 ± 1.8 (2.0–7.5)	4.8 ± 3.2 (2.5–13.0)
PreÂNH	9.6 ± 7.8 (2.5–27.0)	$7.9 \pm 7.0 (2.5 - 23.5)$	8.9 ± 8.9 (3.0–29.5)	$5.3 \pm 2.6 (3.0 - 10.0)$
PostANH	$3.2 \pm 0.7 (2.0 - 4.0)^{*}$	4.0 ± 1.1 (2.5–5.5)§	$7.5 \pm 3.0 \ (4.5 - 14.0)^*$	$5.2 \pm 1.2 (3.5 - 7.0)$ §
PACU	$3.0 \pm 0.9 (2.0 - 4.5)^{*}$	$3.9 \pm 1.2 (2.5 - 5.5)$ §	$10.7 \pm 6.3 (3.5 - 22.0)^*$	$5.6 \pm 2.6 (3.0 - 11.0)$ §
α (°) [69.0 ± 4.0]				
Preop	$58.2 \pm 7.1 \ (48.0 - 70.5)$	$62.1 \pm 8.0 \ (47.5 - 74.0)$	$59.6 \pm 9.4 \ (45.5 - 72.0)$	$61.1 \pm 11.7 (32.5 - 72.0)$
PreÂNH	$47.7 \pm 19.0 (17.0 - 71.5)$	$53.2 \pm 19.7 (18.5 - 71.5)$	$51.4 \pm 20.0 (14.0 - 70.5)$	$58.9 \pm 12.6 (38.0-71.0)$
PostANH	$68.8 \pm 4.2 \ (61.5 - 76.0)^{*} \pm \$$	$64.9 \pm 6.3 (54.5 - 75.0)$ §	49.9 ± 9.2 (33.0-62.0)*	$57.7 \pm 6.1 (51.0 - 68.0)^{+-1}$
PACU	$69.2 \pm 5.1 \ (61.5 - 76.5)^{*} \pm \$$	$64.7 \pm 7.2 (55.5 - 74.5)$ §	$44.6 \pm 12.7 \ (26.5-66.5)^*$	55.2 ± 11.2 (31.5–69.5)†
MA (mm) $[63.0 \pm 6.0]$				
Preop	$64.8 \pm 3.1 \ (60.5 - 70.0)$	$64.3 \pm 3.7 (59.0 - 70.0)$	$64.3 \pm 5.1 (56.0 - 70.5)$	$68.0 \pm 5.6 (56.0 - 78.0)$
PreÂNH	$62.4 \pm 6.9 (50.5 - 72.5)$	$62.6 \pm 7.1 \ (48.5 - 69.5)$	$60.4 \pm 9.6 (44.0 - 70.0)$	$66.1 \pm 4.1 (58.0 - 72.5)$
PostANH	$63.8 \pm 4.8 (57.0 - 71.5)$ §	$62.4 \pm 3.7 (58.5 - 68.0)$ §	50.6 ± 6.8 (37.0-60.0)*‡	$59.9 \pm 4.3 (52.5 - 65.0)^{*}$
PACU	$66.0 \pm 2.7 (62.5 - 69.5)$ §	$63.5 \pm 4.7 (56.5 - 71.5)$ §	$49.6 \pm 7.1 (41.5 - 65.0)^{*}$	$58.0 \pm 5.6 (51.5 - 66.5) * + §$
HGB (gm/dL)				
Preop	$13.4 \pm 0.8 \ (11.5 - 14.0)$	$14.2 \pm 0.8 (13.0 - 15.3)$ §	$13.0 \pm 1.0 (11.3 - 14.9)$	$13.4 \pm 1.1 \ (11.9 - 15.1)$
PreANH	$12.5 \pm 0.8 (10.9 - 13.3)$	$13.5 \pm 0.8 (12.3 - 14.6)$ §	$11.9 \pm 1.0 (10.0 - 13.4)$	$12.5 \pm 0.7 (11.4 - 13.8)$
PostANH	$9.2 \pm 0.6 (7.9 - 9.9)$	$9.7 \pm 0.65 (8.3 - 9.8)$ §	8.6 ± 0.7 (7.2–9.8)	$8.9 \pm 0.5 (8.6 - 10.5)$
PACU	$10.2 \pm 1.0 \ (8.8-11.6)$ §	$10.4 \pm 0.6 \ (9.7 - 11.5)$ §	8.8 ± 0.6 (8.1–9.8)	$9.2 \pm 0.7 (7.7 - 10.2)^{+}$

Table 4. Thromboelastography Variables

Values are mean \pm sp. [] indicates normal range.

LR = lactate Ringer's; ALB = 5% albumin; DEX = 6% dextran 70; HES = 6% hetastarch; R = reaction time; K = coagulation time; MA = maximum amplitude; α = alpha angle; HGB = hemoglobin; preop = preoperative; PACU = postanesthesia care unit. * P < 0.05 when compared to preop; $\ddagger P < 0.05$ when compared to preANH; $\ddagger P < 0.05$ when compared to DEX; $\parallel P < 0.05$

when compared to ALB.

of this investigation was not to determine which storage medium best suited ANH harvesting but to better understand the influence of four different replacement fluids in an ANH protocol.

The choice of replacement fluid during hemodilution has varying effects on coagulation values. A larger decrease in factor VIII levels might have been expected in the HES and DEX groups based upon previous studies (15-17). This effect may have been masked by the stress response to surgery, which tends to increase factor VIII (18,19), as seen in the LR and ALB groups. TEG[®] measurements demonstrate the interaction of DEX and platelets with an increase in coagulation time and decreased MA when compared with LR and ALB. HES also decreased MA relative to LR and ALB. The significant decrease in postANH reaction time in the LR group compared with the DEX group is in agreement with studies indicating that moderate hemodilution with crystalloid may not suppress surgery-induced hypercoagulability (10,13). This response seems to be blunted to some extent by HES and DEX because DEX has platelet antiaggregatory properties (8,17) and HES is felt to influence platelet activity via von Willebrand Factor and factor VIII (15). Although the three colloid solutions were normal saline based, no patients developed significant acidosis that might have contributed to coagulation changes. A

recent study comparing normal saline and LR for fluid resuscitation was unable to find any differences in TEG^{\mathbb{R}} values or blood loss (20).

There was no significant difference in total RBC loss or transfusion requirements among groups. However, the trend for more surgical blood loss and hospitalization RBC loss in the DEX and HES groups may be important based on the hematologic findings in this study. The lack of achievement of statistical significance for these clinical outcomes may be related to a type II statistical error because of inadequate power for the small series enrollment in this study. The higher POD 3 Hct in the LR group compared with the HES group may have been caused by early diureses of crystalloid. Use of HES or DEX in ANH may be beneficial if reduced coagulability leads to decreased thromboembolic complications without significantly increasing perioperative blood loss. However, patients at risk for bleeding because of congenital (e.g., von Willebrand's disease in up to 1% of the population) or acquired abnormalities (e.g., warfarin or clopidogrel) may be at risk for increased bleeding with HES or DEX. Whether patients would benefit from the administration of HES or DEX from the standpoint of limiting potential prothrombotic episodes after surgery again was not the purpose of this investigation. This

could be more clearly delineated in future investigations.

There were limitations of this study design. There was no power analysis performed on a predetermined outcome marker because this was an initial survey of coagulation markers designed to direct future studies. Although the surgeon was blinded to the replacement fluid used, the primary investigator was not. However, this should not have affected the results of the coagulation studies. There was no nonhemodilution group included in the study. At Washington University, ANH is the standard of care for patients undergoing radical retropubic prostatectomy. It has essentially replaced PAD in these patients. ANH is an equally effective blood conservation strategy and is more cost-effective than PAD (1,5,21,22).

In conclusion, data from our hematologic analysis reveal that use of DEX and HES when compared with either LR or ALB can attenuate hypercoagulability. This is reflected by increased aPTT values, decreased TEG[®] MA and α angle values, and a reduction in the anticipated increase in factor VIII levels. This is paralleled by clinical data that demonstrated a trend towards increased bleeding in patients receiving these replacement fluids. The changes observed may be either beneficial or detrimental depending on the status of a given patient. For most of the patients who demonstrate perioperative hypercoagulability and who are at risk for development of thrombotic complications, administration of either DEX or HES may reduce the incidence of these complications. However, use of these fluids may also result in slightly more blood loss and transfusion in patients at low risk for bleeding. For the patient at risk for excessive perioperative bleeding, use of these fluids may lead to substantial increases in bleeding or transfusion. Further, larger studies that are adequately powered to examine bleeding and thrombotic outcomes are required to support our preliminary findings.

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