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Preoperative acute hypervolemic hemodilution with hydroxyethylstarch in a Jehovah's Witness: effects on hemodynamics and coagulation systems

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Introduction

The increased attention to the risks associated with homologous blood transfusion has provided the impetus for the development of techniques to minimize transfusion. Transfusion with donor blood may be diminished by the use of predeposited autologous blood, intraoperative autotransfusion with a cell-saving device, and hemodilution techniques. Preoperative hemodilution can be achieved either by withdrawal of blood and simultaneous infusion of fluid, i.e., normovolemic hemodilution (ANH), or by rapid infusion of fluid without blood withdrawal, i.e., acute hypervolemic hemodilution (AHH). AHH is induced by hemodilution with hydroxyethylstarch preoperatively without removing autologous blood, and in order to prevent the hemodynamic effect of a large intravascular volume, we must use vasodilators [1–3]. Hypervolemic hemodilution is not time-consuming and requires no special procedure, such as collection and storage of the patient's blood [2]. Patients who refuse ANH, such as Jehovah's Witnesses, are particularly good candidates for AHH. However, in patients who suffer from cardiovascular disease, coagulation disorder, renal dysfunction, particular attention should be paid to AHH.

We treated a patient who was a Jehovah's Witness and underwent major surgery under general anesthesia. The patient refused blood transfusion on religious grounds, not only homologous blood transfusion but also normovolemic hemodilution. Therefore, we chose the AHH technique for this patient.

Thrombelastography (TEG) provides useful information on the functional integrity of the coagulation system from initial clot formation to clot retraction or dissolution [4]. We studied the effects of AHH on the hemodynamics and coagulation systems evaluated by TEG in this patient.

Case report

A 40-year-old female Jehovah's Witness (height, 158 cm; weight, 43.5 kg) was scheduled for total gastrectomy and pancreatosplenectomy for advanced gastric cancer under general anesthesia. She had no history of other disease, including coagulopathy. On admission, she had anemia, with a hemoglobin (Hb) concentration of 8.0 g·dl^{-1}. Erythropoietin was administered, and her Hb concentration increased to 13 g·dl^{-1} just before the operation. Other preoperative laboratory data were within the normal range. She refused transfusion of homologous blood and any form of autologous blood transfusion. However, she agreed to transfusion of some kinds of blood-derived products, such as albumin and coagulation factors, if necessary. Therefore, after obtaining her fully informed consent, we decided to employ preoperative AHH. We informed her that we would do everything possible to avoid homologous blood transfusion, but that if her life was threatened by massive hemorrhage we could not help taking blood transfusion into consideration. She did not consent to blood transfusion under these conditions. In practice, we did not prepare any blood products except albumin, because the estimated volume of hemorrhage in this procedure was not grant.

Atropine sulfate (0.5 mg) and midazolam (3 mg) were given intramuscularly as premedications. A peripheral

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vein and the radial artery were cannulated for continuous blood pressure monitoring and blood sampling. An epidural catheter was inserted at Th9–10 for postoperative pain relief with a balloon infuser containing a mixture of fentanyl (800 μg, 16 ml) and 0.25% bupivacaine (80 ml) infused at the rate of 2 ml·h^{-1}. A pulmonary arterial catheter was introduced via the right internal jugular vein. Anesthesia was induced with intravenous fentanyl (100 μg) and thiamylal (225 mg), and vecuronium (5 mg) was administered to facilitate tracheal intubation. Anesthesia was maintained with the inhalation of oxygen, nitrous oxide (2 l·min^{-1} each), and isoflurane (end-tidal 1.0–1.5%) supplemented with intravenous fentanyl and vecuronium as required. Intraoperative monitoring included electrocardiogram, blood pressure, SpO_2, $ETCO_2$, rectal temperature, and urinary output.

Following the induction of anesthesia, AHH was induced by infusing 1000 ml of 6% hydroxyethylstarch (HES) solution over 30 min in the supine position. Prostaglandin E_1 (PGE_1, 0.01–0.03 μg·kg^{-1}·min^{-1}) was simultaneously infused as a vasodilator to compensate for the volume overload effects of HES. Positive end-expiratory pressure and Fowler's positioning were not applied during AHH. Albumin (25 g) was administered immediately following AHH. The following measurements were recorded before AHH, immediately after AHH, 2 h after AHH, 4 h after AHH, and 1 h after the operation: heart rate (HR), mean arterial pressure (MAP), mean pulmonary artery pressure (MPAP), pulmonary wedge pressure (PWP), Hb, hematocrit (Ht), platelet count (Plt), total protein concentration (TP), and PaO_2/F_IO_2. The values recorded during the study periods are shown in Table 1. The hypervolemic hemodilution resulted in immediate decreases in Hb (from 12.2 to 9.6 g·dl^{-1}) and Ht (from 39% to 30%), and increases in MPAP (from 11 to 32 mmHg) and PWP (from 15 to 30 mmHg). However, the elevated PWP gradually returned to the normal range in about 60 min. Heart rate, MAP, Plt, TP, and PaO_2/F_IO_2 showed no substantial changes during AHH. After AHH, MPAP still remained high and TP fell markedly.

The durations of operation and anesthesia were 6 h 30 min and 9 h, respectively. The intraoperative blood loss was about 700 g. During anesthesia, a total of 3350 ml of crystalloid, mainly acetated Ringer's solution and an additional 25 g of albumin (for a total of 50 g), was infused, and the urine output was 660 ml. After the operation, furosemide was given to facilitate diuresis, and Hb recovered to 11.4 g·dl^{-1}.

The thrombelastograms were obtained using a computerized coagulation analyzer (Thrombelastograph, Haemoscope Corporation, Skokie, IL, USA) before AHH, immediately after AHH, at the end of surgery, and on postoperative day 1 (Fig. 1). A normal thrombelastogram was observed before AHH. Acute hypervolemic hemodilution induced hypocoagulability as detected by reaction time, clot formation time, alpha angle, and maximum amplitude. This hypocoagulability was observed even at the end of surgery, when hemodynamics had been restored to the pre-AHH level. These values returned to normal on postoperative day 1.

The patient recovered from anesthesia uneventfully. Hb was 10.9 g·dl^{-1} 4 weeks after the operation.

Discussion

Several methods have been employed as alternatives to homologous blood transfusion during surgery. Normovolemic hemodilution not only provides a stock of the patient's own blood but also decreases net loss of red cells with hemorrhage [5]. On the other hand, preoperative AHH seems to be a simple as well as time- and cost-saving alternative for normovolemic hemodilution [1,2], and it can be accepted by Jehovah's Witnesses [3].

Hypervolemic hemodilution without combined treatment with vasodilators can cause pulmonary congestion and edema due to volume overload [1]. During AHH in

Table 1. Changes in hemodynamics, hemogram, total protein, and P_aO_2/F_IO_2

Time	HR (bpm)	MAP (mmHg)	MPAP (mmHg)	PWP (mmHg)	Hb (g·dl^{-1})	Ht (%)	Plt (×10^4 mm^{-3})	TP (g·dl^{-1})	P_aO_2/F_IO_2 (mmHg)
Before AHH	65	78	11	15	12.2	39	10.9	6.2	480
Immediately after AHH	68	92	32	30	9.6	30	10.2	6.0	590
2 h after AHH (blood loss, 400 g)	85	90	23	18	9.8	31	9.6	4.1	606
4 h after AHH (blood loss, 700 g)	85	73	24	14	9.9	31	9.4	3.6	564
1 h after operation	75	73	22	12	11.4	35	12.8	4.5	589

HR, heart rate; MAP, mean arterial pressure; MPAP, mean pulmonary arterial pressure; PWP, pulmonary wedge pressure; Hb, hemoglobin concentration; Ht, hematocrit; Plt, platelet count; TP, total protein concentration; AHH, acute hypervolemic hemodilution.

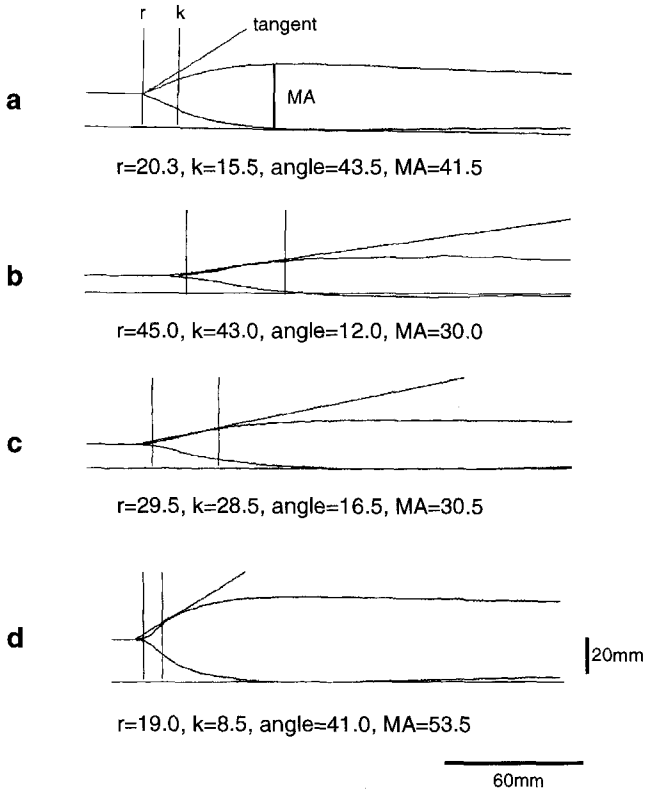

Fig. 1. Changes in the thrombelastogram (TEG). **a** Before acute hypervolemic hemodilution (AHH); **b** immediately after AHH; **c** at the end of surgery; and **d** on postoperative day 1. *r*, Reaction time, defined as the time from blood sampling until the TEG tracing amplitude reaches 2 mm (normal range, 13–21 mm); *k*, clot formation time, defined as the time from the end of *r* until the amplitude of the TEG tracing reaches 20 mm (normal range, 6–18 mm); *angle*, angle calculated from the slope of the TEG tracing from *r* to *k* by the computer (normal range, 50°–60°); *MA*, maximum amplitude, defined as the greatest amplitude on the TEG trace (normal range, 35–60 mm)

our patient, MPAP and PWP considerably increased despite infusion of PGE_1. Further infusions of PGE_1 or other vasodilators such as nitroglycerine or the use of epidural block should have been considered to ameliorate the increases in MPAP and PWP [6]. A transesophageal echocardiographic study indicated that AHH caused no progressive cardiac dilation and dysfunction, while increasing PWP from 5.9 to 22.6 mmHg [7].

We employed a 6% HES solution for AHH because of its safety and potency of intravascular retention. Less concentrated HES and crystalloid solutions are less useful, and low-molecular-weight dextran, an alternative colloid solution, may cause allergic reactions and renal impairment [2].

Both normovolemic and hypervolemic hemodilution have a dilution effect on platelet count and coagulation variables. However, the prothrombin time (PT) and activated partial thromboplastin time (APTT) have been reported to remain within normal ranges in AHH with a 6% HES solution at 15 ml·kg^{-1} [2]. Routine coagulation tests, including platelet count, PT, and APTT, do not assess the interaction of the coagulation cascade with the platelet surface. On the other hand, TEG is a simple test of overall coagulation and allows for diagnosis of specific problems for the hemostatic system [8]. In liver transplantation or after cardiopulmonary bypass, TEG has been reported to be more informative than routine coagulation tests for the assessment of viscoelastic conditions [8,9]. Recently, sonoclot analysis (SCT) has been recommended for the assessment of coagulation systems. SCT provides useful information on platelet function monitoring for perioperative bleeding disorders [10]. In vitro hemodilution significantly compromised blood coagulation and clot lysis measured by TEG, showing that the maximum effect was found with HES as compared with gelatin and albumin [11]. Interestingly, moderate hemodilution with normal saline demonstrated a hypercoagulable state, as evidenced by a shortened reaction time and an increased rapidity of clot formation [12]. In our patient, hypocoagulability was observed by the TEG following AHH despite the normal Plt, and there were no clinical symptoms of a bleeding tendency. Routine coagulation tests might not have detected her coagulation disturbance.

In summary, the technique of AHH safely allowed major surgery without blood transfusion and was tolerated safely by a Jehovah's Witness. However, meticulous attention should be paid to the effects of hypervolemia on the cardiovascular, renal, and coagulation systems, particularly when one or more of these systems are preoperatively compromised. It is of great importance to monitor viscoelasticity using TEG and/or SCT when performing AHH.

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