Anesthesiology
1997; 87:985-7

Extreme Hemodilution Due to Massive Blood Loss in Tumor Surgery

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ACCEPTING minimal intraoperative hemoglobin levels is an important concept to minimize allogeneic blood transfusions.[1-3] A fundamental question is the definition of the "critical hemoglobin value," which has not been defined at present time.[3,4] We report a case of massive intraoperative blood loss, resulting in a nadir hemoglobin of 1.1 g/dl.

Case Report

The patient was a 58-yr-old man with renal cell carcinoma and metastases in L2-L4. The patient had undergone a nephrectomy 16 months before the present operation (see below). A palliative debulking of tumor metastases with dorsal stabilization of the lumbar spine between L2 and L4 was performed 10 months previous. History was unremarkable for pulmonary or cardiac diseases. Preoperatively, hemoglobin was 14.2 g/dl; blood pressure was 145/80 mmHg, and creatinine was slightly elevated at 137 μM (upper normal limit, 105 μM). After developing a progressive and immobilizing neurologic deficit, the patient was scheduled for a second palliative tumor debulking at the lumbar spinal nerve roots L2 and L3.

Anesthesia was induced with fentanyl, propofol, and pancuronium and was maintained with fentanyl and pancuronium boluses and with a propofol infusion. Significant blood loss was expected, and thus two 14-gauge peripheral venous catheters were inserted. Additionally, a double 12-gauge catheter (Arrow International Inc., Reading, PA) was inserted *via* the right internal jugular vein, and a 20-gauge catheter was inserted into the radial artery. Preoperatively blood gases were normal (table 1). The patient was turned into a prone position. Before incision, the patient received approximately 2 l of Ringer's lactate. Methylprednisolone was given as an initial bolus of 30 mg/kg followed by a continuous infusion of 5.4 $mg \cdot kg^{-1} \cdot h^{-1}$ for 23 h.[5] Mean arterial blood pressure during anesthesia initially was 70-80 mmHg with central venous pressures in the prone position of approximately 15 mmHg. Shortly after the start of the operation, massive bleeding from epidural blood vessels in close proximity to the tumor occurred, and 6 l of succinylated gelatin (Physiogel 4%, Braun Medical, Emmenbrücke, Switzerland), and 6 units of packed erythrocytes (PRBC) (1,800 ml) were transfused within 60 min. Dopamine (2.3-5.7 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was also given. At this time, hemoglobin was 5.1 g/dl as determined by a CO-Oximeter (IL 482, Instrumentation Laboratory, Lexington, MA), and a mild metabolic acidosis was present (table 1). Mean arterial blood pressure was 68 mmHg, and central venous pressure was 15 mmHg. Massive blood loss continued. We were then informed by the blood bank that additional units of PRBC and fresh frozen plasma (FFP) would only be ready in approximately 20 min. To maintain normovolemia, an additional 10 l gelatin was infused during this period. Also, the inspiratory O_2 concentration was increased from 40% to 100%. Central venous pressure was maintained above 15 mmHg. Mean arterial pressure remained between 50 and 60 mm Hg, and heart rate between 80 and 115 beats/min without any dysrhythmias. After 30 min, hemoglobin was 1.1 g/dl. With a heart rate of 84 beats/min, the simultaneously recorded (electrocardiograph) ECG did not reveal any signs of myocardial ischemia (fig. 1A). After 10 min, with a heart rate of 111 beats/min and a hemoglobin concentration of (most likely) less than 1.1 g/dl (ongoing blood loss exclusively replaced with gelatin), an ST segment depression was observed (fig. 1B). Also a pronounced metabolic acidosis was apparent with a base excess of −11.9 mM/l and a pH of 7.20 (table 1). The duration of the low hemoglobin concentration (< 5.0 g/dl) was approximately 45 min, 30 min thereof with a hemoglobin concentration of approximately 1.1 g/dl. ST segment depression lasted for approximately 20 min. Finally, AB0 compatible but uncrossmatched PRBC and shortly crossmatched PRBC and other blood products arrived, and 22 units of PRBC (6,600 ml), 14 units of FFP (3,500 ml), and 18 units of platelets (2,700 ml) were transfused. The metabolic acidosis that developed during progressive hemodilution did not immediately improve with transfusion of PRBC. In contrast, the acidosis deteriorated (table 1) and was only corrected by infusion of 200 mmol NaHCO3. Finally, surgical hemostasis was achieved, and the patient was transferred to a surgical intensive care unit.

The patient was extubated 10 h postoperatively and transferred to a regular surgical ward on postoperative day 2. There were no signs of postoperative myocardial ischemia such as ST segment depressions or elevation of serum creatine kinase isoenzyme (CK-MB) activity.

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Received from University Hospital, Zürich, Switzerland. Submitted for publication January 10, 1997. Accepted for publication May 15, 1997.

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Key words: Tumor surgery. Spine, complication: massive blood loss. Blood: hemodilution; anemia.

Table 1. Hemodynamics, Arterial Blood Gas Values, and Ventilatory Data Recorded in the Prone Position

Time	Temperature (°C)	MAP (mmHg)	CVP (mmHg)	pH	Pa_{CO_2} (mmHg)	Pa_{O_2} (mmHg)	HCO_3^- (mM/l)	BE (mM/l)	FI_{O_2}	Hb ($g \cdot dl^{-1}$)	$\%O_{2pl}$ (%)	Comment
09.25	36.5	65	15	7.42	36	151	23.3	−0.2	0.4	14.1	2.4	Mechanical ventilation
12.15	35.9	68	15	7.30	37	221	18.2	−6.7	0.5	5.1	8.8	—
12.45	34.0	60	15	7.20	35	431	13.8	−11.9	1.0	1.1	46.6	—
13.05	33.9	87	31	7.04	50	400	13.6	−15.3	1.0	7.7	10.4	After PRC transfusion only
13.12	33.9	82	32	7.07	50	407	14.5	−14.5	1.0	11.1	7.6	After PCR transfusion only
13.50	34.2	80	28	7.37	38	416	21.5	−2.8	1.0	10.1	8.4	After 200 mmol $NaHCO_3$
15.30	35.0	61	ND	7.38	39	133	23.5	−0.8	0.5	10.1	2.9	After 100 mmol $NaHCO_3$

MAP = mean arterial pressure; CVP = central venous pressure; Pa_{CO_2} = arterial CO_2 partial pressure; Pa_{O_2} = arterial O_2 partial pressure; HCO_3^- = bicarbonate concentration; BE = base excess; FI_{O_2} = fraction of inspiratory O_2; Hb = hemoglobin concentration; $\%O_{2pl}$ = % O_2 dissolved in plasma; ND = not documented.

The maximum postoperative CK-MB value was 12 U/l compared with the preoperative CK-MB value of 13 U/l. There was no neurologic dysfunction or late signs of renal or hepatic dysfunctions. The patient was finally discharged from the hospital on postoperative day 8 without any neurologic deficit.

Discussion

To our knowledge, an intraoperative hemoglobin concentration of 1.1 g/dl is the lowest value ever reported in a surgical patient who survived.[1,6] This extremely low value was tolerated without persistent ischemic organ dysfunction. No ST segment depression was observed at a heart rate of 84 beats/min, but with a heart rate of 111 beats/min, intraoperative myocardial ischemia developed as evidenced by ST segment depression occurring at the time of the lowest hemoglobin concentration. ST segment recovered promptly with transfusion of PRBC. Degree of hemodilution and heart rate thus appear to determine onset of ECG signs of myocardial ischemia.

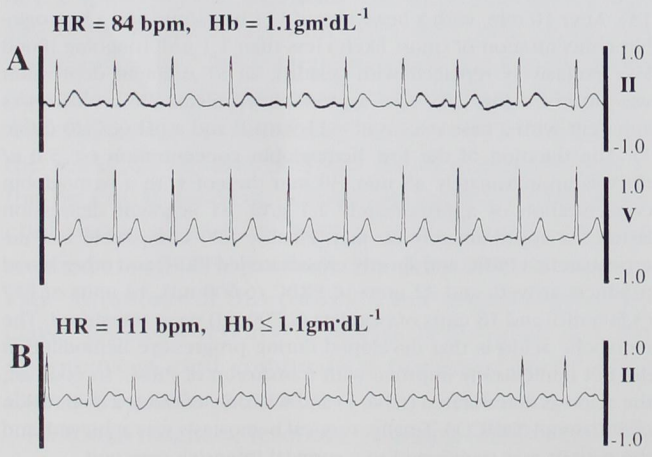

Fig. 1. (*A*) Electrocardiographic (ECG) recorded at a hemoglobin of 1.1 g/dl with a heart rate of 84 beats/min. Note there are no ST segment changes, neither in lead II nor in lead V5. (*B*) ECG (lead II) recorded at a hemoglobin of < 1.1 g/dl with a heart rate of 111 beats/min.

Despite the mild preoperative renal insufficiency after the nephrectomy 16 months before the present operation, no clinical renal insufficiency was encountered postoperatively. The postoperative creatinine values were all below the preoperative level. Also, no signs of late hepatic dysfunction were observed in the postoperative period as evidenced by normal liver enzymes. This indicates that the kidneys and the liver appear to tolerate even extreme forms of hemodilution for a limited period. It remains unknown to what degree the mild intraoperative hypothermia (table 1) contributed to this favorable outcome.

The metabolic acidosis developing during progressive hemodilution may represent lactic acidosis due to tissue hypoxia or a loss of buffering capacity of the blood. No lactate levels were measured in the present case. However, after transfusion of PRBC to a hemoglobin of 7.7 g/dl, the metabolic acidosis further deteriorated, and a parallel increase in $PaCO_2$ was observed (table 1). This might indicate improved perfusion and oxygen delivery to tissue with reduced metabolism during extreme hemodilution. On the other hand, a dilutional acidosis resulting from a loss of buffering capacity due to a loss of erythrocytes is also likely to play a major role.

During profound hemodilution in humans, Singbartl *et al.*[7] observed metabolic acidosis that was not associated with increased lactate levels. Thereby, changes in pH, base excess, and HCO3- correlated with the decrease in hemoglobin concentration.

Maintaining normovolemia is considered of paramount importance during extreme hemodilution for hemodynamic stabilization and prevention of tachycardia. Low-dose dopamine (2.3–5.7 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was used for further stabilization of the circulation and also for blood pressure support. A sufficient coronary and cerebral perfusion pressure is considered essential during such excessive hemodilution. Also increasing the inspiratory O_2 concentration to 100% is an important measure to optimize O_2 delivery during excessive hemodilution. In this patient, 46.6% of the O_2 content was physically dissolved at a hemoglobin of 1.1 g/dl (table 1).

A fundamental question in hemodilution and perioperative anemia remains definition of the "critical hemoglobin value" below which organ dysfunction is encountered. In the present case of a 58-yr-old patient with a nadir hemoglobin of 1.1 g/dl, this "critical hemoglobin value," unintentionally, was probably reached. This is at a lower level compared with a critical hemoglobin concentration of 4 g/dl found in an 84-yr-old patient.[8] At extremely low hemoglobin concentrations, age thus may be an additional factor determining tolerance of acute anemia.[6]

Maintaining normovolemia is of prime importance during extreme hemodilution. This not only supports compensatory mechanisms such as the increase in cardiac output and thus mean arterial pressure, it also prevents relevant tachycardia with potential consecutive myocardial ischemia. In addition, it may be necessary to support a minimal perfusion pressure with catecholamines. Increasing the inspiratory O_2 concentration to 100% may increase the arterial O_2 content significantly. The physically dissolved O_2 may be particularly important for cellular metabolism because its availability is independent of hemoglobin dissociation characteristics. These principles may be at least as important for surviving extreme hemodilution than the actual level of hemoglobin *per se*.

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