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References

1. Rosow C, Manberg PJ: Bispectral Index Monitoring. *Anesthesiology Clinics of North America: Ann Anesth Pharmacol* 1998; 2:89-107
2. Glass P, Bloom M, Kearse L, Rosow C, Sebel P, Manberg P: Bispectral analysis measures sedation and memory effects of propofol,

midazolam, isoflurane, and alfenanil in healthy volunteers. *ANESTHESIOLOGY* 1997; 86:836-47

3. England MR, Murphy MC, Court M: How much is enough: Titrating to the Bispectral Index during cardiac anesthesia. *Anesth Analg* 1997; 84(suppl 2):S73.
4. Song D, van Vlymen J, White PF: Is the Bispectral Index useful in predicting fast-track eligibility after ambulatory anesthesia with propofol and desflurane? *Anesth Analg* 1998; 87:1245-8. (Aspect Medical Systems, Natick, MA)

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Extreme Intraoperative Blood Loss and Hemodilution in a Jehovah's Witness: New Aspects in Postoperative Management

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IN patients who refuse any blood components, global oxygen transport, cerebral oxygen delivery, and blood coagulation may be compromised during massive blood loss. This case report describes potential therapeutic options to improve blood coagulation and to monitor the adequacy of cerebral oxygen delivery by using the patient's own consciousness.

Case Report

We report the case of an 41-yr-old female Jehovah's Witness. Her body weight was 47 kg and her height was 160 cm. She was admitted for elective hysterectomy as a result of a uterine and intraligamentary myoma and failed intubation that occurred at the referring hospital. Her history was remarkable for a severe primary chronic polyarthritis.

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A preoperative echocardiography indicated a slight aortic insufficiency (regurgitation < 30%) caused by degenerative alterations of the aortic valve. Ejection fraction was normal, and the patient was not limited in her physical activity. At the preoperative visit she provided a signed statement documenting her wish to refuse any blood components. Her hematocrit was 37.4% (hemoglobin, 12.6 g/dl), platelet count was 273,000/ μ l, and prothrombin time was < 10.6 s (normal, 10.6-12.9 s). Other laboratory findings were in the normal range. Blood pressure was 115/75 mmHg, and heart rate was 100 beats/min.

An awake fiberoptic intubation was planned. After successful tracheal intubation, anesthesia was induced with fentanyl, etomidate, and midazolam, and muscle paralysis was achieved with atracurium. Anesthesia was maintained with continuous propofol and remifentanyl infusions. Blood pressure was measured noninvasively.

A large myoma was found during laparotomy (diameter, 12 cm; 865 g) that extended into the broad ligament and displaced the right ureter. Massive bleeding occurred from numerous blood vessels from the pelvic floor, supplying the intraligamentous myoma. To maintain normovolemia and blood pressure, a total of 5,000 ml of Ringer's lactate, 1,000 ml of 6% hydroxyethyl starch with a mean molecular weight of 200 kd (Fresenius, Bad Homburg, Germany), and 2,000 ml of 4% modified fluid gelatin (Braun Medical, Melsungen, Germany) was infused. In addition, norepinephrine (up to 170 ng \cdot kg⁻¹ \cdot min⁻¹) and dopamine (4.3 μ g \cdot kg⁻¹ \cdot min⁻¹) were infused, and supplementary bolus doses of epinephrine and norepinephrine were administered. Hematocrit was 10% 2 h after incision and 8% at the end of the surgery. A severe coagulopathy developed, as evidenced by a prothrombin time of 39.5 s, a nonmeasurable activated partial prothrombin time, and a fibrinogen < 0.5 g/l. Platelet count was 113,000/ μ l. Two million units of aprotinin (Bayer, Leverkusen, Germany) were administered, followed by 500,000 U/h (total of 3 million units). In addition, metabolic acidosis was apparent with a pH of 7.28 and a base excess of -8.3 mm/l.

Finally, surgical hemostasis was achieved. A central venous access

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Table 1. Perioperative Laboratory Values

Day	Preop	OD	POD1	POD2	POD4	POD8	POD12	POD23
Hematocrit (%)	37.4	8.4 ⁽¹⁾	6.8	6.4	10.2	11.8	20.9	31.0
Thrombocytes (1,000 · μl^{-1})	273	113 ⁽²⁾	158	—	224	—	350	267
Prothrombin time (s)*	<10.6	39.5 ⁽²⁾	15.2	—	—	—	—	—

Preop = preoperative day; OD = day of operation; lowest value after ICU admission⁽¹⁾ and intraoperative values⁽²⁾; POD(n) = postoperative day(n).

* Normal range, 10.6–12.9 s.

was established after surgery, and the ventilated and mildly sedated patient was transferred to the surgical intensive care unit (ICU). At ICU admission, mean arterial pressure was 55 mmHg, heart rate was 105 beats/min, central venous pressure was 1 mmHg, base excess was -5.6 mmol/L, pH 7.23, and serum lactate concentration was 1.1 mmol/L. Urine output during the first 4 h was $5 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ and $1\text{--}3 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ thereafter. Continuous infusions of norepinephrine ($255 \text{ ng} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$), dopamine ($4.3 \text{ } \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$), propofol ($0.64 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$), and remifentanyl ($0.1 \text{ } \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) were administered. Sedation was stopped 1 h after arrival in the ICU, and when the patient was awake and still intubated, we discussed the critical situation with her and her husband. Again, they refused any transfusion of blood components; therefore, no blood components were administered.

We elected to keep the patient intubated, and assisted spontaneous breathing was planned for the first days in the ICU. Fraction of inspired oxygen (FiO_2) was adjusted to keep arterial oxygen partial pressure > 200 mmHg for the first 24 h and arterial saturation $\geq 99\%$ for the next 3 days.

A mean arterial blood pressure of 50 mmHg was tolerated because urine output was adequate ($> 1 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$) and serum lactate concentration was < 2.4 mmol/L (upper limit of normal). Nevertheless, catecholamines (norepinephrine up to $426 \text{ ng} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ until postoperative day 1, dopamine $4.3 \text{ } \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ until postoperative day 6) and moderate volume loading with 550 ml of 6% hydroxyethyl starch and 250 ml of Ringer's lactate during the first night were necessary to maintain minimal blood pressure and guarantee sufficient urinary output.

Baseline hematocrit at ICU admission was 8.9%. To stimulate erythropoiesis, intravenous therapy with 7,500 U erythropoietin (Janssen-Cilag, Baar, Switzerland; 160 IU/kg) three times per week was started, accompanied by intravenous infusion of 200 mg iron salt (Vifor International, St. Gallen, Switzerland) three times per week, intravenous administration of 5 mg folic acid (Lederle, St. Davids, PA) daily, and intramuscular administration of 1,000 mg vitamin B₁₂ (Streuli, Uznach, Switzerland) three times per week. Although hematocrit decreased from 8.9% to 6.8%, platelet count normalized at $158,000/\mu\text{l}$, and prothrombin time was 15.2 s on postoperative day 1. Even on postoperative day 2, hematocrit was only 6.4% before a definitive increase was observed (table 1). The patient was extubated on postoperative day 5 with a hematocrit of 11.6%. She was discharged from the ICU (hematocrit 11.8%) on postoperative day 8 and was discharged from the hospital (hematocrit 31.0%) without sequelae on postoperative day 23. Serum iron and serum transferrin levels were normal, and serum ferritin level was slightly supranormal. No further complications occurred, and there was no neurologic dysfunction or late signs of renal or hepatic dysfunction.

Interestingly, during the first 24 h we observed a loss of consciousness several times when heart rate decreased to < 100 beats/min.

Accordingly, heart rate was maintained at > 100 beats/min with dopamine.

Discussion

Lower intraoperative hematocrit levels have been reported in surgical patients who survived.¹⁻³ Nevertheless, this case is remarkable for certain specific therapeutic approaches.

Over several days, hematocrit levels remained low and increased only slowly despite therapy with erythropoietin, iron, vitamin B₁₂, and folic acid. Postoperative recovery of platelets was much faster than the increase in hematocrit, with platelet count normalizing within 12 h after surgery. In contrast, 12 days were necessary to reach a hematocrit of 20.9% (table 1). Even on postoperative day 23 hematocrit was not yet in the normal range. The immediate release of sequestered platelets in the spleen caused by sympathetic activity, the stimulating effect of erythropoietin on megakaryocytes, platelet production in bone marrow,^{4,5} and the different turnover rates of erythrocytes (120 days) and platelets (7-10 days) may have facilitated platelet count recovery and may explain the faster postoperative recovery of platelets.

Prothrombin time improved from 39.5 s (intraoperatively) to 15.2 s on postoperative day 1, reflecting an intact capacity of the liver to restore coagulation factors. This contrasts with experimental data in pigs suggesting inadequate liver tissue oxygenation at much higher hematocrit levels.⁶

The intraoperative use of aprotinin during severe coagulopathy resulted in an improved blood coagulation. Nevertheless, the clinical efficacy of this empirical treatment lacks confirmation by laboratory tests and requires future confirmation.

In the ICU, the patient lost consciousness when her heart rate decreased to < 100 beats/min, and higher heart rates were necessary for an adequate cerebral perfusion. These heart rates were not accompanied by signs of myocardial ischemia on electrocardiogram. This is in

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contrast to the findings of Zollinger *et al.*,³ who described an intraoperative hemoglobin concentration of 1.1 g/dl in a 58-yr-old man and observed an ST segment depression at a heart rate of 111 beats/min but not 84 beats/min.

Tissue oxygen delivery can be optimized by increasing $F_{I_{O_2}}$. Habler *et al.*⁷ described the importance of hyperoxic ventilation in acute normovolemic hemodilution, and in the case described by Zollinger *et al.*,³ 46.6% of total oxygen content was due to physically dissolved oxygen. However, prolonged therapy with high $F_{I_{O_2}}$ may also have harmful respiratory and nonrespiratory effects.⁸ Therefore, we decided to reduce $F_{I_{O_2}}$ carefully. With an $F_{I_{O_2}}$ between 0.4 and 0.6, we were able to maintain arterial oxygen partial pressure > 260 mmHg during the first night and between 210 and 165 mmHg for the remaining time that the patient required mechanical ventilation. Such arterial oxygen partial pressure values thus represented a compromise between the benefit in terms of oxygen transport and the risk of associated side effects.

If oxygen delivery is limited because of severe anemia, reduction of systemic oxygen consumption by anesthetics, neuromuscular blockade, mechanical ventilation, and hypothermia may be beneficial. In this case, cerebral perfusion seemed critical because the patient lost consciousness several times at heart rates < 100 beats/min. Therefore, it was essential that the patient be awake to monitor cerebral oxygenation, and the aforementioned measures were not real options.

Provided that normovolemia is maintained, extremely low hematocrit levels can be tolerated over several days. Normovolemia supports compensatory mechanisms

such as the increase in cardiac output and thus mean arterial pressure. In addition, catecholamines may be necessary to support adequate tissue perfusion. These principles are important in the management of extreme anemia, if substitution of blood components is not possible.

References

1. Spahn DR, Leone BJ, Reves JG, Pasch T: Cardiovascular and coronary physiology of acute isovolemic hemodilution: A review of nonoxygen-carrying and oxygen-carrying solutions. *Anesth Analg* 1994; 78:1000-21
2. Viele MK, Weiskopf RB: What can we learn about the need for transfusion from patients who refuse blood? The experience with Jehovah's Witnesses. *Transfusion* 1994; 34:396-401
3. Zollinger A, Hager P, Singer T, Friedl HP, Pasch T, Spahn DR: Extreme hemodilution due to massive blood loss in tumor surgery. *ANESTHESIOLOGY* 1997; 87:985-7
4. Fabris F, Cordiano I, Randi ML, Casonato A, Montini G, Zacchello G, Girolami A: Effect of human recombinant erythropoietin on bleeding time, platelet number and function in children with end-stage renal disease maintained by haemodialysis. *Pediatr Nephrol* 1991; 5:225-8
5. Wolf RF, Peng J, Friese P, Gilmore LS, Burstein SA, Dale GL: Erythropoietin administration increases production and reactivity of platelets in dogs. *Thromb Haemost* 1997; 78:1505-9
6. Nöldge GF, Priebe HJ, Bohle W, Buttler KJ, Geiger K: Effects of acute normovolemic hemodilution on splanchnic oxygenation and on hepatic histology and metabolism in anesthetized pigs. *ANESTHESIOLOGY* 1991; 74:908-18
7. Habler OP, Kleen MS, Hutter JW, Podtschaske AH, Tiede M, Kemming GI, Welte MV, Corso CO, Batra S, Keipert PE, Faithfull NS, Messmer KF: Effects of hyperoxic ventilation on hemodilution-induced changes in anesthetized dogs. *Transfusion* 1998; 38:135-44
8. Lodato RF: Oxygen toxicity, Principles and Practice of Mechanical Ventilation. Edited by Tobin MJ. New York, McGraw-Hill, 1994, pp 837-55