

Vasopressin in Hemorrhagic Shock

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We describe the treatment of two patients with hemorrhagic shock unresponsive to volume replacement and catecholamines. Both patients responded to a small-dose infusion of vasopressin, which allowed tapering off of the catecholamines. The possible role

of small-dose infusions of vasopressin in fluid- and catecholamine-resistant hemorrhagic shock is discussed.

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Fluid resuscitation is the standard of care for hemorrhagic shock. However, a state of resistant hypotension that is not responsive to fluid resuscitation occasionally develops in patients who have prolonged hypotension resulting from massive blood loss. This is presumably caused by accumulation of vasodilatory metabolites as the result of ischemia-reperfusion injury. This hypotension is also not responsive to catecholamines because of coexisting severe acidosis, which inactivates catecholamine receptors. As this situation is analogous to the hypotension seen in septic shock, where vasopressin has been used advantageously, it was presumed that a vasopressin infusion would be beneficial in patients with fluid-resistant hypotension after prolonged hemorrhagic shock. Two cases managed with this approach are described.

Case Reports

Case 1

A 61-yr-old male patient presented with periampullary carcinoma and was scheduled for a Whipple procedure. He was hypertensive on amlodipine 5 mg daily, with a preoperative arterial blood pressure of 130/90. His preoperative hemoglobin (Hb) was 8.6 g%.

Induction and maintenance of anesthesia were uneventful. After 2 h of surgery, there was an accidental laceration of the portal vein, leading to profuse bleeding. The patient's arterial blood pressure decreased to 80/40 mm Hg. Ringer's lactate solution, gelfusine, packed red blood cells and fresh-frozen plasma were transfused, and more blood

was ordered. His arterial blood pressure decreased to 50/30 mm Hg and his end-tidal CO₂ (ETco₂) decreased to 15 mm Hg. The patient developed severe bradycardia. Epinephrine 1 mg in 10 mL of saline was administered. A norepinephrine infusion at 0.2 μg · kg⁻¹ · min⁻¹ was started, while fluid replacement was continued with whole blood. His arterial blood pressure remained around 50/30 mm Hg. An arterial blood gas (ABG) at this point showed a pH of 6.9, Pco₂ of 44, PaO₂ of 185.7, bicarbonate 10.7, and a base deficit of -21. Ninety mEq of sodium bicarbonate was administered and fluid resuscitation was continued for a cumulative total of 11 L of crystalloids, 3 L of colloids, and 3.5 L of blood.

Three hours after the laceration took place the surgeons were able to repair the portal vein and control the hemorrhage. The surgery proceeded. Five hours after laceration of the portal vein his central venous pressure (CVP) was 14 cm H₂O. However, his arterial blood pressure remained at approximately 70/40 mm Hg. At this point it was judged that adequate fluid resuscitation had taken place and that there was no response to fluid resuscitation and norepinephrine infusion, indicating resistant vasodilation secondary to prolonged hypovolemic shock.

Vasopressin 0.04 U/min along with dobutamine 5 μg · kg⁻¹ · min⁻¹ was started, and the norepinephrine was gradually discontinued. His arterial blood pressure started increasing after 6 h of intraoperative resuscitation and 1 h of vasopressin. The patient was moved to the intensive care unit (ICU) with an arterial blood pressure of 90/60 mm Hg and a heart rate of 130/min. An ABG at this time showed a pH of 7.27, Pco₂ of 20 mm Hg, Po₂ of 70.6 mm Hg, Hb of 12.6, and a base deficit of -17.6. Postoperatively, 1.4 L of packed red blood cells and 2 U of platelets were transfused for continuing ooze from the abdominal drains.

After 6 h in the ICU the patient was awake and obeying commands. He had an arterial blood pressure of 104/61, an ABG pH of 7.4, a base deficit of -4, Pco₂ of 35, Po₂ of 160, Hb 12.0. The vasopressin and dobutamine infusions were tapered off over 8 h and the patient maintained a normal arterial blood pressure. The patient was tracheally extubated the next morning and had an uneventful recovery with no postoperative neurological sequelae.

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Case 2

A 53-yr-old patient with stomach carcinoma underwent a distal gastrectomy, gastrojejunostomy, pancreatojejunostomy, and sleeve resection of the neck of the pancreas. His immediate postoperative period was uneventful. On the seventh postoperative day he developed secondary hemorrhage and had 2 L of hematemesis. He had a cardiac arrest while being endotracheally intubated. He was defibrillated, resuscitated with IV colloids, and rushed to the operating room within 30 min. There, a distal pancreaticosplenectomy to control multiple bleeding vessels was performed and a feeding jejunostomy was inserted. Intraoperatively the patient had severe hypotension and asystolic cardiac arrest after 15 min of laparotomy. He was resuscitated with internal cardiac massage and crystalloid, blood and fresh-frozen plasma transfusions and epinephrine boluses. Bleeding was controlled 2 h after surgery started.

The patient's total blood loss was estimated to be approximately 6 L. His CVP was 10 cm after cumulative transfusion of 13 L of crystalloids and 11 L colloids, including 5 L of blood and 1 L of fresh-frozen plasma. He continued to be severely hypotensive, and dobutamine at $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and norepinephrine at $0.5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ were added. He remained hypotensive at an arterial blood pressure of 80/50 mm Hg despite these measures.

Five hours after surgery started, vasopressin was started at a dose of 0.04 U/min. Within half an hour the patient's arterial blood pressure increased to 110/70 mm Hg. A blood gas analysis performed at this time revealed severe metabolic acidosis (pH, 7.1; base deficit, -11.4). Ventilation was continued and sodium bicarbonate was administered to correct the base deficit.

The patient was moved to the ICU. His mean arterial blood pressure remained more than 65 mm Hg. His base deficit was corrected over the next 24 h. Vasopressin was tapered off over 24 h and norepinephrine over 48 h. The patient remained hemodynamically stable and was tracheally extubated on the third day. After this, however, he developed an anastomotic leak and intraabdominal sepsis and died of multiorgan failure on postoperative day 15.

Discussion

Hypovolemic shock of marked severity and duration may progress to cardiovascular collapse that is unresponsive to volume replacement and catecholamine infusion (1). Vasopressin deficiency may contribute to the pathogenesis of irreversible shock (2). The two patients described had severe bleeding with prolonged and severe hypotension that could not be reversed despite volume replacement and catecholamine pressors.

Vasopressin has been found to be of use in the irreversible phase of hemorrhagic shock in animal studies (3,4) and in isolated case reports (5). Under normal conditions, the doses of vasopressin used have little or no pressor action (3,6), and significant increase of plasma vasopressin as a result of unregulated release of the hormone (i.e., in the syndrome of inappropriate secretion of antidiuretic hormone) does not cause hypertension (4,7). Vasopressin may be effective in resistant hemorrhagic shock resulting from inhibition of K_{ATP} channels and inhibition of nitric oxide-induced accumulation of cGMP. Replacement of depleted stores of vasopressin in the neurohypophysis may also contribute to reversal of shock (8).

Fluid-resistant hemorrhagic shock is not common, and adequate volume resuscitation is nearly always effective in resuscitation of hypovolemic patients. However, hemorrhagic shock, when advanced, can become poorly responsive to both volume and catecholamine pressors because of resistant vasodilatation and acidosis. Vasopressin may be a useful adjunct in the treatment of such cases.

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