Hypotension Related to Desmopressin Administration Following Cardiopulmonary Bypass

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Bleeding following cardiopulmonary bypass remains a significant complication and is related to vascular injury from the surgery and acquired acute hemostatic abnormalities. The defects in hemostasis following cardiopulmonary bypass are complex but are largely thought to represent a functional platelet impairment.1

Desmopressin, also known as DDAVP (1-deamino-8-D-arginine vasopressin), is a synthetic polypeptide structurally related to vasopressin and plays an important role in promoting platelet adhesion by increasing the release of von Willebrand’s factor (Factor VIII) from endothelial cells.2 In addition to its use in the hereditary bleeding disorders, hemophilia A, and von Willebrand’s disease, desmopressin shortens bleeding time and decreases surgical blood loss in patients with many conditions associated with platelet dysfunction.3,4

Two recent studies5,6 in patients undergoing surgery requiring cardiopulmonary bypass suggest that treatment with desmopressin increases von Willebrand’s factor and reduces early postoperative blood loss and transfusion requirements without apparent adverse hemodynamic effects.

We have observed two patients in the postcardiopulmonary bypass period who experienced a sudden unexpected decrease in arterial blood pressure shortly after receiving desmopressin.

REPORT OF TWO CASES

A 73-yr-old woman who had an anteroseptal myocardial infarction ten years earlier was admitted for unstable angina. Cardiac catheterization showed a normal left ventriculogram with 80% left main and 90% right coronary artery stenoses. During catheterization the patient developed chest pain with severe ventricular dyskinesia, which was treated with iv nitroglycerin and an intraaortic balloon pump. She underwent emergency coronary artery bypass grafting with a nitrous oxide and fentanyl anesthetic. Her prebypass and bypass courses were uneventful. The intraaortic balloon pump was maintained at a 1:1 rate before and after bypass. Five minutes following cardiopulmonary bypass, arterial blood pressure was 98/60 mmHg and protamine was administered as a 10 mg iv test dose followed by a 225 mg infusion over a 15 min period. Hemodynamic parameters remained stable after protamine administration. Thirty minutes following cardiopulmonary bypass, desmopressin, 0.3 µg/kg, in 50 ml of 5% dextrose in water was started as an infusion through the central venous port. Immediately prior to beginning desmopressin infusion, the following parameters were obtained: arterial blood pressure 101/47 mmHg, central venous pressure 13 mmHg; pulmonary artery pressure 32/12 mmHg, pulmonary capillary wedge pressure 12 mmHg, cardiac output 5.0 l/min, and systemic vascular resistance 920 dyne·s·cm⁻². Five minutes following desmopressin infusion, blood pressure was 70/36 mmHg, central venous pressure 12 mmHg, pulmonary artery pressure 12 mmHg, pulmonary capillary wedge pressure 14 mmHg, cardiac output 5.4 I/min, and systemic vascular resistance 590 dyne·s·cm⁻². Desmopressin infusion was stopped and arterial blood pressure increased to 95/60 mmHg. Reinfusion of desmopressin again decreased blood pressure to 80/34 mmHg. The remainder of the drug was infused without significant blood pressure change. Postoperatively, the intraaortic balloon pump and nitroglycerin infusion were discontinued without difficulty. Based on an elevated CPK with 12% MB fraction, the patient was considered to have had a perioperative myocardial infarction. She was discharged on the sixth postoperative day and remains in good health six months following surgery.

A 63-yr-old man with unstable angina underwent cardiac catheterization, which demonstrated 80% left main, 90% left anterior descending, and 90% right coronary artery lesions with inferior hypokinesia and mildly depressed ventricular function. Three vessel CABG was performed with sufentanil-oxygen anesthesia. Prior to the discontinuation of the coronary artery bypass a dobutamine, 5 µg·kg⁻¹·min⁻¹ infusion was started, which was continued into the postbypass period. Ten minutes following cardiopulmonary bypass protamine was administered as a 10 mg test dose followed by an iv infusion of 275 mg over a 15 min period. After the protamine infusion blood pressure was 95/58 mmHg and remained stable until the time of the desmopressin infusion. Thirty-five minutes following cardiopulmonary bypass, desmopressin 0.3 µg/kg in 50 ml of 5% dextrose in water was started as a continuous infusion at 100 ml/h through the central venous port of a pulmonary artery catheter. Prior to infusion, the following parameters were measured: blood pressure 105/57 mmHg, pulmonary artery diastolic pressure 12 mmHg, pulmonary capillary wedge pressure 10 mmHg, central venous pressure 10 mmHg, cardiac output 4.8 l/min, and systemic vascular resistance 1050 dyne·s·cm⁻². Five minutes following the initiation of desmopressin, the following hemodynamic values were obtained: blood pressure 83/51 mmHg, pulmonary artery diastolic pressure 12 mmHg, pulmonary capillary wedge pressure 12 mmHg, central venous pressure 14 mmHg, cardiac output 4.8 l/min, and systemic vascular resistance 800 dyne·s·cm⁻². Moderate hypotension not associated with blood loss persisted, and 15 min after beginning desmopressin infusion a blood pressure of 78/48 mmHg was recorded. Arterial blood pressure rose to 107/60 mmHg five minutes after desmopressin infusion was completed. No change in the dobutamine infusion was made, although 2 units of packed red blood cells were administered to maintain filling pressures. The patient’s postoperative course was uneventful.

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DISCUSSION

In the cases we have described, a decrease in arterial blood pressure and systemic vascular resistance appeared within five minutes after desmopressin infusion was begun and resolved after cessation of the desmopressin infusion. Ventricular filling pressures and cardiac output did not significantly change and inotropic support was maintained constant during desmopressin infusion. These findings suggest that the observed hypotension is directly related to desmopressin administration. However, in the postbypass period there are many confounding factors that can lower arterial blood pressure, and it is difficult to definitely rule out unrecognized hypovolemia, myocardial depression, or delayed protamine reaction as contributing to the hypotension.

These results contrast with the studies of Salzman et al.\(^5\) and Czer et al.\(^6\) who initially reported the use of desmopressin in the postbypass period. Although their work was concerned primarily with the effect of desmopressin on bleeding variables, both studies suggested that desmopressin administration was not associated with significant hemodynamic side effects.

Other investigators have noted hemodynamic changes with desmopressin under different circumstances. Facial flushing and a feeling of facial warmth, suggestive of vasodilation, accompanied by a decrease in diastolic blood pressure of 5–30 mmHg and an increase in heart rate, was seen after infusion of desmopressin 0.4 μg/kg in awake volunteers.\(^7\) Williams et al.\(^8\) observed a decrease in blood pressure by an average of 13% and an increase in heart rate by an average of 18% after iv desmopressin. In one healthy volunteer blood pressure decreased from 120/80 mmHg to unmeasurably low levels after the rapid infusion of 30 μg/kg desmopressin.\(^9\)

Our experience suggests that desmopressin can cause significant hypotension. This could have adverse consequences in the postbypass period during which the heart is recovering from the insult of cardioplegia and hypothermia and maintenance of adequate arterial coronary perfusion pressure is critical. A sudden unexpected decrease in arterial blood pressure might lead to ischemia.

We have described two cases in which desmopressin, administered to improve platelet function following cardiopulmonary bypass, was associated with hypotension. In light of our findings, it seems prudent to be cautious in administering desmopressin in the postbypass period. Further study of desmopressin is needed to define the nature and mechanism of these observed hemodynamic effects in the postbypass patient.

REFERENCES