Intractable Hypotension in Septic Shock: Successful Treatment with Vasopressin in an Infant

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Sepsis and septic shock constitute an important cause of morbidity and mortality in critically ill children worldwide. The mortality rate of septic shock remains over 50%. Apart from antibiotic administration, most available therapies are limited to supportive strategies. Early mortality is usually due to refractory hypotension with progressive acidosis, which is unresponsive to fluid resuscitation and catecholamine infusions [1].

In case of no response to fluid resuscitation, inotropic and vasoactive agents are commonly used to increase cardiac output, maintain adequate blood pressure and enhance oxygen delivery to the tissues [1]. Recently, several case reports have described the potential benefits of vaso-

pressin in vasodilatory shock in adults [2]. We present the case of a child with septic shock, in whom vasopressin resolved intractable hypotension unresponsive to traditional high dose catecholamine therapy.

Patient Description

A 17 month old child was admitted to the Pediatric Intensive Care Unit following complete repair of transposition of great arteries. Shortly after her birth, at the age of 6 days, she had a palliative repair of coarctation of aorta and a banding of the pulmonary artery. Suffering from low saturation and failure to thrive for more than a year, she was admitted for complete repair. The patient's intraoperative course was unremarkable. Following a stormy postoperative course she was gradually weaned off inotropic support and mechanical ventilation on day 7.

However, on the ninth postoperative day the child developed fever and leukocytosis (36,000 white blood cells/mm^3, polymorphonuclears 90.6%) along with disseminated intravascular coagulation and progressive lactic acidosis. *Bacillus cereus* was recovered from blood cultures and the infant was treated with meropenem and vancomycin. Despite the treatment, the patient's condition progressed to overwhelming hemodynamic deterioration with tachycardia and hypotension to a systolic pressure of 40 mmHg. The patient became increasingly lethargic, hypotensive, tachycardic, anuric (urea 93 mg/dl, creatinine 1.2 mg/dl, potassium 4.5 mEq/L) and developed diminished peripheral perfusion and no urine output despite volume replacement to keep left atrial pressure at 12 mmHg. Inotropic and vasoactive agents were administered: dopamine 20 μg/kg/minute, dobutamine 20 μg/kg/min, milrinone 0.75 μg/kg/min, and adrenalin 0.05 μg/kg/min. The patient continued to show hemodynamic instability refractory to further fluid resuscitation, with central venous pressures >15 mmHg and escalation in vasopressor support.

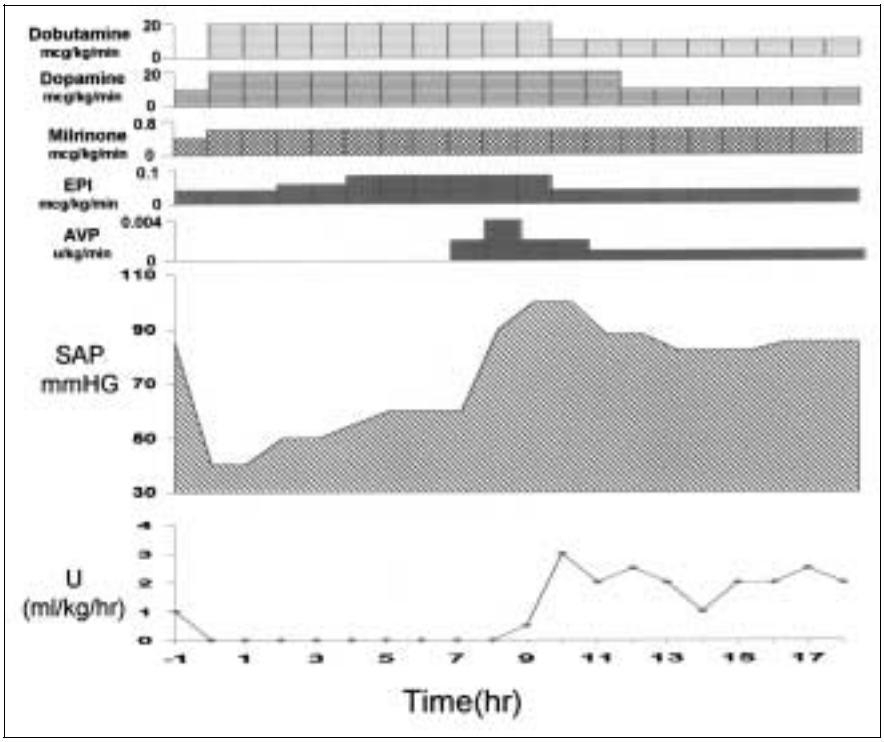
Intravenous vasopressin was added at 0.002 units/kg/min and titrated to a maximal dose of 0.004 units/kg/min, and within minutes her blood pressure increased to 101/80 mmHg. After 10 hours of anuria, urinary output reached 3 ml/kg/hour. Catecholamine pressors were decreased gradually. Administration of volume replacement was stopped, and the dose of vasopressin was decreased to 0.001 units/kg/min, with the blood pressure remaining at 85/60 mmHg. Vasopressin was discontinued uneventfully after 36 hours of administration. The child was weaned from mechanical ventilation and extubated 6 days later. The remainder of the course in the intensive care unit was unremarkable.

Comment

We have presented a child with severe septic shock in whom vasopressin produced an immediate increase of blood pressure allowing downward titration and discontinuation of catecholamines. Vasopressin, known as an antidiuretic hormone, is one of the first described and structurally characterized peptide hormones and is essential for cardiovascular homeostasis [Figure]. It is used mainly to treat variceal hemorrhage and diabetes insipidus.

Vasopressin is a direct vasoconstrictor of the systemic vasculature mediated by V1 receptors, and an osmoregulator by V2 receptors in the kidney [3]. Under normal conditions and at normal concentrations vasopressin has little effect on blood pressure. However, during hypovolemia and hypotension, vasopressin is released from the posterior pituitary, and its concentration in plasma markedly increases to maintain arterial blood pressure. Both hemorrhagic and septic shock are associated with a biphasic response of vasopressin levels. In early shock, appropriately high levels of vasopressin are produced to defend organ perfusion. As the shock state progresses, plasma vasopressin levels fall low for its vascular action but well within the range of its antidiuretic effect [3].

Sepsis is the most frequent cause of vasodilatory shock. In septic shock, hypotension occurs as a result of vasodilatation due to the failure of the vascular smooth muscle to constrict [1]. One of the possible mechanisms is relative deficiency of the hormone vasopressin. This relative deficiency can be explained by depletion of pituitary stores of vasopressin after exhaustive release in early septic shock, or by elevated norepinephrine levels that have a central inhibitory effect on vasopressin release. Finally, increased vascular endothelial release of nitric oxide within the



Systolic arterial pressure before and during vasopressin administration. AVP = arginine vasopressin, SAP = systolic arterial pressure, U = urine output

posterior pituitary during sepsis may down-regulate vasopressin production [1].

Several reports have previously described the beneficial effect of vasopressin for septic shock in patients receiving inotropic and maximal pressor therapy who failed to maintain adequate blood pressure [4]. When vasopressin was administered at very small doses by continuous intravenous infusion (0.04 units/min in adult patients), a marked improvement occurred in blood pressure, and exogenous catecholamine vasopressor requirement decreased, as happened in our case. Furthermore, systemic vascular resistance increased without significant changes to cardiac output. The study by Malay and colleagues [5] (0.04 units/min in adult patients) further highlights the increased pressor sensitivity to vasopressin in patients with vasodilatory shock, supporting the theory of autonomic insufficiency in septic shock. Rosenzwieg et al. [4] evaluated vasopressin administration in 11 profoundly ill infants and children with hypotension refractory to treatment with multiple pressor agents after cardiac surgery. Vasopressin administration (0.0003–0.002 unit/kg/min) increased mean arterial pressure in all patients and decreased pressor agents in five of eight patients. Tsuneyoshi and co-workers [2] demonstrated that low dose vasopressin infusions (0.04 units/min in adult patients) increased mean arterial pressure, systemic vascular resistance, and urine output in patients with vasodilatory septic shock and hyporesponsiveness to catecholamines.

We have shown a dramatic improvement of arterial pressure and organ perfusion following treatment with vasopressin in a child with septic shock. We suggest that exogenous vasopressin is a potential additive to traditional high dose catecholamine therapy for septic children with vascular hyporeactivity to catecholamines [2]. Further studies investigating the effect of vasopressin in children with septic shock should be conducted.

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