The Pivotal Role of Vasopressin in Refractory Anaphylactic Shock

Claudia Schummer, MD*

Melanie Wirsing, MD†

Wolfram Schummer, MD, DEAA, EDIC‡

BACKGROUND: Severe anaphylaxis can be associated with cardiovascular collapse that is difficult to manage and does not respond to treatment with epinephrine. Because anaphylaxis is uncommon, unpredictable and may be fatal, a prospective, randomized, controlled trial in humans on the best management is difficult and guidelines are based on theory and anecdotes only.

METHODS AND RESULTS: We report six cases in which the use of vasopressin was successful in the treatment of anaphylactic shock.

CONCLUSIONS: Standard treatment of anaphylactic shock, including discontinuation of the causative agent, administration of epinephrine, and infusion of IV fluids, did not stabilize cardiocirculatory function, and adding arginine vasopressors resulted in prompt hemodynamic stabilization.

(Anesth Analg 2008;107:620–4)

Most episodes of anaphylaxis respond to treatment with a single dose of epinephrine; however, severe anaphylaxis can be associated with cardiovascular collapse that is difficult to manage.[1] Severe reactions are unexpected and may progress so fast that no treatment can be given before respiratory or cardiac arrest.[2] Because anaphylaxis is uncommon, unpredictable, and may be fatal, a prospective, randomized, controlled trial in humans on the best management is difficult and guidelines are based on theory and anecdotes only.[3,4]

In 2004, we reported the management of anaphylactic shock due to succinylated gelatin solution in a 59-yr-old woman with coronary artery disease.[5] The clinical response while following the Advanced Cardiac Life Support resuscitation guidelines was disappointing. After the administration of vasopressin, hemodynamic function was restored almost immediately. After that experience, we introduced the "early" use of vasopressin into the Advanced Cardiac Life Support resuscitation guidelines at our institution. On a small scale, we now add to the knowledge of treatment of anaphylactic shock by reporting six more cases in which we used vasopressin during treatment of anaphylactic shock (Table 1).

All incidents took place during general anesthesia for major surgery. They all have in common that causes of shock, other than anaphylaxis stemming from the respective drug, could be excluded with great probability.

CASE REPORTS

Case 1

A 63-yr-old woman with a history of cervix carcinoma was scheduled for major hepatic resection due to metastasis. She had no allergies in her medical history. She was taking no regular medication apart from oral aspirin 100 mg. At the start of surgery, her vital signs were stable, with sinus rhythm (SR) 62/min and mean arterial blood pressure (MAP) 91 mm Hg (Table 2). As requested by the surgeon, aprotinin 1 million IU in 100 mL normal saline was infused at a rate of 3.3 mL/min without a test injection. Twenty minutes later, her hemodynamic function deteriorated rapidly: SR 130/min, MAP 30 mm Hg. An anaphylactic reaction to aprotinin was suspected, and the infusion was stopped. Resuscitation was started with epinephrine (cumulative dose 1 mg), methylprednisolone 1000 mg, infusion of 2000 mL crystalloids, 1000 mL 6% hydroxyethylstarch (molecular weight [MW] 130,000 D), and vasopressor support with norepinephrine 0.44 $\mu g \cdot kg^{-1} \cdot min^{-1}$. With these measures, a MAP of 55 mm Hg was achieved (Table 2). A transesophageal echocardiography excluded other reasons for hemodynamic deterioration. After 2 U of vasopressin, hemodynamic function quickly stabilized, and norepinephrine was reduced to 0.044 $\mu g \cdot kg^{-1} \cdot min^{-1}$, which resulted in SR 81/min and MAP 79 mm Hg (Table 2). Surgery was continued and terminated 4 h later without any further adverse events.

Case 2

A 53-yr-old man was scheduled for major liver re-resection due to colon carcinoma. During the first liver resection, the patient had received aprotinin. There were no reports of drug or food allergies. He was taking no regular medication. Induction of general anesthesia and surgery were uneventful until the administration of the test

From the *Department for Anesthesiology and Intensive Care Medicine, Friedrich-Schiller-University of Jena, Germany; †Department of Anesthesiology, Medical Faculty of the University of Heidelberg, Germany; and ‡Department for Anesthesiology and Intensive Care Medicine, Klinikum Quedlinburg, Academic Teaching Hospital of the University Hospital of Magdeburg, Quedlinburg, Germany.

Accepted for publication March 18, 2008.

Reprints will not be available from the author.

Address correspondence to Wolfram Schummer, MD, DEAA, EDIC, Department for Anesthesiology and Intensive Care Medicine, SRH Zentralklinikum Suhl, Albert-Schweitzer str. 2, 98527 Suhl, Germany. Address e-mail to cwsm.schummer@gmx.de.

DOI: 10.1213/ane.0b013e3181770b42

Table 1. Demographic Data and Overview of Treatment of Our Six New Cases and Previously Published Case of Refractory Anaphylactic Shock

Case	Weight (kg)	U Vasopressin	Vasopressin U/kg	Age (yrs)	Gender	Trigger substance
0[b]	68	2	0.03	59	W	Gelatin
1	79	2	0.03	63	W	Aprotinin
2	66	2	0.03	53	M	Aprotinin
3	95	5	0.05	58	M	Metamizol
4	100	15	0.15	47	M	Metamizol
5	75	8	0.11	73	M	Metamizol
6	53	2	0.04	43	W	Gelatin
Mean			0.06			

[a] Single doses given were 100 μg.

[b] Already published case.

[c] Hyperoncotic solution (HyperHES).

dose of aprotinin (1 mL). Thereafter, his hemodynamic function deteriorated rapidly (Table 2): SR 160/min, MAP 30 mm Hg. Anaphylaxis due to aprotinin was suspected. Resuscitation was started with epinephrine (1 mg), methylprednisolone (1000 mg), 1500 mL crystalloid fluid, 1000 mL hydroxyethylstarch 10% MW 200,000 D, and norepinephrine (0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$). Because hemodynamic function could not be stabilized, two units of vasopressin were administered. Subsequently, norepinephrine was reduced to 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (heart rate [HR] 84/min, MAP 75 mm Hg). Liver resection was completed 3 h later without further incidents.

Case 3

A 58-yr-old man with a medical history of arterial hypertension, insulin-dependent diabetes mellitus, obesity, and vascular occlusive disease was scheduled for vascular surgery. General anesthesia and surgery were uneventful until an infusion of 1000 mg of metamizol. Within 5 min, the patient became severely hypotensive (MAP 30 mm Hg, HR 160/min), and bronchospasm and generalized erythema developed. His lungs were ventilated with 100% O_2, and he was given epinephrine (total, 400 μg), methylprednisolone (1000 mg), and 1000 mL crystalloid fluids. The patient then became pulseless. Chest compressions were initiated, and epinephrine (1 mg) was given, accompanied by a norepinephrine infusion (0.4 $\mu g \cdot kg^{-1} \cdot min^{-1}$), resulting in ventricular tachycardia (HR >200/min). Vasopressin (5 U) stabilized his hemodynamic function almost immediately: SR was restored (110/min), and MAP increased to 75 mm Hg. Thirty minutes later, the patient was tracheally extubated and he made an uneventful recovery.

Case 4

A 47-yr-old man was scheduled for posterior lumbar intervertebral fusion. His medical history was unremarkable, and there were no reports of allergies. At the end of an uneventful surgical procedure, he received an infusion of metamizol (2000 mg). About 10 min later, the patient suffered cardiac arrest, accompanied by bronchospasm and generalized erythema. Chest compressions were started, and epinephrine (total, 3 mg), methylprednisolone (1000 mg), dimitenden (8 mg), ranitidine (50 mg), lidocaine (100 mg), and norepinephrine (0.75 $\mu g \cdot kg^{-1} \cdot min^{-1}$) were injected. His MAP (30 mm Hg) was only restored after 5 U vasopressin. Two additional doses of vasopressin (5 U) were required to stabilize his hemodynamic function at SR 85/min, MAP 70 mm Hg on norepinephrine 0.04 $\mu g \cdot kg^{-1} \cdot min^{-1}$.

Case 5

During craniotomy for evacuation of an intracerebral hematoma, hemodynamic function of a 73-yr-old man remained stable. On completion of surgery, the patient received an infusion of metamizol (1000 mg). Shortly thereafter, the norepinephrine infusion had to be increased from 0.1 to 0.8 $\mu g \cdot kg^{-1} \cdot min^{-1}$, and the metamizol infusion was stopped; however, his MAP decreased to 25 mm Hg. Epinephrine (total, 1.6 mg), methylprednisolone (1000 mg), as well as histamine H1 and H2 blocker were administered without restoring normal hemodynamic function. After 8 U of vasopressin, his hemodynamic function stabilized to a MAP of 90 mm Hg at a HR of 80/min with minimal norepinephrine support (0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$).

Case 6

A 43-yr-old woman with chronic pancreatitis was scheduled for Whipple's procedure. Her medical history was unremarkable. Two hours after the start of combined general and epidural anesthesia, the patient was given a gelatin infusion. When 200 mL were infused, her hemodynamic function collapsed (MAP 30 mm Hg, HR increased to 95/min). There was no bronchospasm and no cutaneous reaction. The gelatin infusion was stopped immediately. Epinephrine (3 × 100 μg) was injected along with methylprednisolone (1000 mg), and 1000 mL crystalloids and 250 mL 7.2% sodium chloride/6% hydroxyethylstarch MW 200,000 D were infused rapidly. Norepinephrine was infused (1.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$) along with a further bolus of epinephrine (500 μg). After 2 U of vasopressin, her hemodynamic function stabilized quickly to MAP 65 mm Hg, SR 60/min at a norepinephrine infusion rate of 0.07 $\mu g \cdot kg^{-1} \cdot min^{-1}$.

DISCUSSION

Pharaoh Menes' death in 2600 BC after a wasp sting is renowned as the first report of anaphylaxis.[6] However, not all Egyptologists followed this "translation" of hieroglyphs on two ebony plates.[7] Instead, this account must be seen as one of the first of many anecdotes about anaphylaxis. Even today, data about the incidence and severity of anaphylaxis are limited; the estimated incidence during anesthesia ranges between 1 in 10,000 and 1 in 20,000 anesthesia cases.[8]

Anaphylactic shock occurring during anesthesia is lethal in about 3%–10% of cases, even in previously healthy individuals,[9–11] with neuromuscular blocking drugs being responsible for more than half of these events.[12] Metamizol, aprotinin, and gelatin, the drugs presumed to have caused the anaphylactic reactions in our cases, are known for their anaphylactic potential as well, with the incidence of aprotinin anaphylaxis after re-exposure reported to be 3%–17%.[13,14]

Table 1. Continued

Total epinephrine[a] (mg)	Norepinephrine ($\mu g \cdot kg^{-1} \cdot min^{-1}$)	Crystalloid fluids (mL)	Hydroxyethylstarch (mL)	Methylprednisolone (g)
1.5	1.00		1000	1.0
1.0	0.44	2000	1000	1.0
1.0	0.50	1500	1000	1.0
1.4	0.40	1000		1.0
3.0	0.75		1000	1.0
1.6	0.80	1000	250[c]	1.0
0.8	1.20	1000	250[c]	1.0
1.5	0.70			1.0

Table 2. Hemodynamic Data of Case 1 and 2

	Case 1			Case 2		
	Baseline	After conventional therapy (see text)	After administration of 2 U vasopressin	Baseline	After conventional therapy (see text)	After administration of 2 U vasopressin
HR	62	99	81	78	130	84
MAP	91	55	79	74	43	75
MPAP	25	29	23	20	26	24
CVP	12	14	12	6	5	11
SVRI	2300	550	1600	1813	422	1163
SVI	43	60	48	28	55	52
PVRI	267	203	144	373	233	236
CI	2.7	5.9	3.9	3	7.2	4.4

Note that the systemic vascular resistance was restored immediately after the administration of vasopressin.

HR = heart rate (bpm); MAP = mean arterial blood pressure (mm Hg); MPAP = mean pulmonary artery pressure (mm Hg); CVP = central venous pressure (mm Hg); SVRI = systemic vascular resistance index (dyne $s \cdot cm^{-5} \cdot m^{-2}$); SV = stroke volume index ($mL \cdot m^{-2} \cdot beat$); PVRI = pulmonary vascular resistance index (dyne $s \cdot cm^{-5} \cdot m^{-2}$); CI = cardiac index ($L \cdot m^{-2} \cdot min^{-1}$).

Anaphylactic shock is associated with systemic vasodilation and increased vascular permeability, causing a mixed distributive-hypovolemic shock pattern.[15,16] Circulating blood volume may decrease by as much as 35% within 10 min because of extravasation resulting in poor venous return, hypotension, tissue hypoperfusion, and cellular anoxia.[1,17]

Epinephrine has been considered useful in the treatment of anaphylaxis since 1925.[18] Retrospective analyses have indicated that epinephrine and fluid resuscitation are effective treatments for anaphylaxis occurring during anesthesia.[17] Injection of epinephrine counteracts the systemic vasodilation and inhibits further release of anaphylactic mediators from mast and basophil cells.[19–23] Luckily, most episodes of anaphylaxis respond to treatment with a single dose of epinephrine. However, evidence in the literature suggests that a poor outcome during anaphylactic shock is associated with late administration of epinephrine.[2,24]

There is not a great deal of evidence in the literature, however. In 2005, the American Heart Association conceded that their guidelines for treatment of anaphylaxis consisted of "therapies that are commonly used and widely accepted but are based more on consensus than evidence."[3] When little or no evidence is available, recommendations based on clinical experience and physiological rationale should be considered. Our cases demonstrate clearly that vasopressin may help if circulatory function deteriorates quickly despite adequate standard treatment.

Sympathetic excess, either therapeutic or due to endogenous release, frequently results in hemodynamically significant tachycardia. This itself can result in myocardial or cerebrovascular ischemia, decreased cardiac output, or degeneration into ventricular dysrhythmias, even in the absence of coronary artery disease.[25] This scenario is exemplified by our third case, in which loss of SR occurred immediately after repeated injection of epinephrine.

Patients receiving β-blockers, such as our index patient (case 0),[5] may not respond adequately to epinephrine.[3,9,12,26] Regardless of the undesired effects associated with epinephrine (e.g., increased myocardial oxygen consumption, ventricular arrhythmias, and myocardial dysfunction), even high doses are recommended as first-line treatment of severe anaphylactic shock, along with aggressive intravascular volume expansion. This is followed by antihistamines and steroids and cardiopulmonary resuscitation if needed.

A significant issue faced by clinicians is how to proceed if epinephrine and fluid resuscitation are unsuccessful, or excessive use of these interventions is not suitable. In case of profound hypotension, a decision needs to be made promptly. The available evidence, although largely anecdotal, is compelling and favors an empirical addition of a potent vasoconstrictor bolus to resuscitate patients with severe anaphylaxis. Drugs successfully used have included norepinephrine,[27] the α1-agonists methoxamine,[28] and metaraminol,[29] and the pituitary hormone vasopressin.[5,30] Our cases clearly demonstrate the immediate positive effect of vasopressin in restoring normal hemodynamic function.

The primary role of vasopressin is fluid homeostasis. The strongest release stimuli are increasing plasma osmolarity and severe hypovolemia.[31] When osmolarity of the extracellular fluid increases, the plasma concentration of vasopressin increases only moderately. However, vasopressin synthesis in the hypothalamus and secretion from the posterior pituitary gland are also controlled by the sympathetic nervous system; i.e., the baroreflex, so that, regardless of extracellular osmolarity, vasopressin will be secreted if cardiovascular stability is threatened (e.g., hypotension, hypovolemia). Indeed, during the initial phase of profound hypotension and shock, the plasma vasopressin concentration can reach extremely high levels, e.g., 100–500 pg/mL. In the late phase of septic and hemorrhagic shock, approximately 1/10th of maximal plasma concentrations have been measured.[32]

The precise mechanism of the vasopressor action induced by vasopressin remains unclear. In vasoplegic shock states, vasopressin restores vascular tone by at least four mechanisms: (1) activation of V1 receptors (previously called V1a) that mediate vasoconstriction via Gq protein activation of phospholipase C, (2) the ability to close adenosine triphosphate-sensitive K channels while activation of adenosine triphosphate-sensitive K channels produces cellular hyperpolarization resulting in vasodilatation, (3) modulation of nitric oxide, and (4) enhancement of adrenergic and other vasoconstrictor drugs.[33,34] In addition, vasopressin could act during anaphylactic shock as an "anti-inflammatory drug" by antagonizing the effects of nitric oxide. During anaphylactic shock, distribution in vasoactive action of vasopressin seems to be optimal: vasoconstriction in skin, skeletal muscle, intestine and fat, with relatively less constriction of coronary and renal vasculature, and cerebral vasodilation.[35,36]

In hemodynamically compromised patients, circulatory homeostasis is disrupted by factors that primarily diminish venous return or those that impair compensatory responses, which restore cardiac preload.[37] It has been estimated that an 80% reduction in splanchnic blood flow, e.g., from 1500 to 300 mL/min, would increase MAP by 32 mm Hg when cardiac output is 5 L/min, but only by 6 mm Hg when cardiac output is 25 L/min. Thus, the effect of translocated volume on MAP is only marginal when there is low resistance to flow, as in anaphylactic shock.[38,39]

Considering this pathomechanism, a potent vasopressor such as vasopressin is needed. Hemodynamic measurements in our cases 1 and 2 confirmed an immediate effect of vasopressin on systemic vascular resistance (+200%) when epinephrine and norepinephrine had failed.

Infusion of vasopressin in patients with advanced vasodilatory shock after surgery did not appear to compromise cutaneous microcirculation.[40] In a recent study, reduction in regional flow in the superior mesenteric artery and microcirculatory blood flow in the upper gastrointestinal tract of septic pigs receiving low-dose vasopressin ($0.06\ U \cdot kg^{-1} \cdot h^{-1}$) suggest compromised mucosal blood flow.[38] This could possibly contribute to gut mucosal barrier dysfunction and subsequent multiple organ failure. However, in both studies, vasopressin was infused continuously, whereas our experiences are based on administration of a few small bolus doses during a short time (total dose, 0.03–0.11 U/kg body weight). Mobilization and redistribution of splanchnic blood flow/volume by vasopressin, a hormone with a plasma half-life of about 10 to 35 min,[39] seems to restore cardiac preload immediately. Assuming that the anaphylactic reaction can be stopped and coronary and cerebral perfusion pressures can be maintained, there will only be a short-term reduction in microcirculatory blood flow.

Cases 4 and 5 needed far more vasopressor support than the other patients (Table 1). Both received H1 and H2 antagonists in the hope of lessening the severity of anaphylaxis. However, like β-adrenergic drugs, histamine increases myocardial contractility by increasing myocardial levels of cAMP.[41] In a rat model, pretreatment with H1-receptor blockade, with or without concurrent H2-receptor blockade, worsened hypotension and decreased survival time.[42] In anaphylactic shock, the need for more extensive vasopressor support should be expected in patients receiving β-blockers or those who received H1 and H2 antagonists.

CONCLUSION

In our opinion, there are three principal therapeutic principles in the treatment of anaphylactic shock:

1. Termination of mast cell degranulation and interruption of the mediator-related vicious cycle.
2. Pharmacological modulation of vascular tone (e.g., reduction of peripheral blood flow demands).
3. Intravascular volume replacement.

Appropriate measures are

1. Discontinuation of the causative agent and administration of epinephrine,
2. Administration of vasopressin, and
3. Reasonable administration of IV fluids.

We advocate that our recommendations regarding the management of anaphylactic shock be incorporated in the upcoming guidelines for cardiopulmonary resuscitation and emergency cardiovascular care.

ACKNOWLEDGMENTS

The authors thank Don Bredle, PhD (Professor for Kinesiology, Department of Kinesiology, University of WI-Eau Claire, WI), for his helpful suggestions in the preparation of this article.

REFERENCES

1. Brown SG. Cardiovascular aspects of anaphylaxis: implications for treatment and diagnosis. Curr Opin Allergy Clin Immunol 2005;5:359–64
2. Pumphrey RS. Lessons for management of anaphylaxis from a study of fatal reactions. Clin Exp Allergy 2000;30:1144–50
3. American Heart Association: guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Part 10.6: anaphylaxis. Circulation 2005;112:IV143–5
4. Hepner DL, Castells MC. Anaphylaxis during the perioperative period. Anesth Analg 2003;97:1381–95
5. Schummer W, Schummer C, Wippermann J, Fuchs J. Anaphylactic shock: is vasopressin the drug of choice? Anesthesiology 2004;101:1025–7
6. Wadell LA. Egyptian civilization: it's sumerian original & real chronology. London: Luzac & Co, 1930
7. Krombach JW, Kampe S, Keller CA, Wright PM. Pharaoh Menes' death after an anaphylactic reaction—the end of a myth. Allergy 2004;59:1234–5
8. Mertes PM, Laxenaire MC, Alla F. Anaphylactic and anaphylactoid reactions occurring during anesthesia in France in 1999–2000. Anesthesiology 2003;99:536–45
9. Currie M, Webb RK, Williamson JA, Russell WJ, Mackay P. The Australian Incident Monitoring Study. Clinical anaphylaxis: an analysis of 2000 incident reports. Anaesth Intensive Care 1993; 21:621–5
10. Lienhart A, Auroy Y, Pequignot F, Benhamou D, Warszawski J, Bovet M, Jougla E. Survey of anesthesia-related mortality in France. Anesthesiology 2006;105:1087–97
11. Mitsuhata H, Matsumoto S, Hasegawa J. [The epidemiology and clinical features of anaphylactic and anaphylactoid reactions in the perioperative period in Japan]. Masui 1992;41:1664–9
12. Laxenaire MC, Mertes PM. Anaphylaxis during anaesthesia. Results of a two-year survey in France. Br J Anaesth 2001;87: 549–58
13. Dietrich W, Spath P, Ebell A, Richter JA. Prevalence of anaphylactic reactions to aprotinin: analysis of two hundred forty-eight reexposures to aprotinin in heart operations. J Thorac Cardiovasc Surg 1997;113:194–201
14. Beierlein W, Scheule AM, Dietrich W, Ziemer G. Forty years of clinical aprotinin use: a review of 124 hypersensitivity reactions. Ann Thorac Surg 2005;79:741–8
15. Abbas AK. Diseases of immunity. In: Kumar V, Abbas AK, Fausto N, eds. Robbins and Cotran pathophysiologic basis of disease. 7th ed. Philadelphia: Elsevier, 2005:193–267. Chap 6
16. Kay AB. Allergy and allergic diseases. Second of two parts. N Engl J Med 2001;344:109–13
17. Fisher MM. Clinical observations on the pathophysiology and treatment of anaphylactic cardiovascular collapse. Anaesth Intensive Care 1986;14:17–21
18. Braun LIB. Notes on desensitisation of a patient hypersensitive to bee stings. S Afr Med Rec 1925;23:408–9
19. Barach EM, Nowak RM, Lee TG, Tomlanovich MC. Epinephrine for treatment of anaphylactic shock. JAMA 1984;251:2118–22
20. Bautista E, Simons FE, Simons KJ, Becker AB, Duke K, Tillett M, Kepron W, Mink SN. Epinephrine fails to hasten hemodynamic recovery in fully developed canine anaphylactic shock. Int Arch Allergy Immunol 2002;128:151–64
21. Mink SN, Simons FE, Simons KJ, Becker AB, Duke K. Constant infusion of epinephrine, but not bolus treatment, improves haemodynamic recovery in anaphylactic shock in dogs. Clin Exp Allergy 2004;34:1776–83
22. Sullivan TJI. Systemic anaphylaxis. In: Lichtenstein LM, Fauci AS, eds. Current therapy in allergy, immunology, and rheumatology Toronto: B.C. Decker, 1988:91–8
23. Wasserman SI, Marquardt DL. Anaphylaxis. In: Middleton EJ, Reed CE, Ellis EF, Adkinson NFJ, Yunginge JW, eds. Allergy: principles and practice. St. Louis: C. V. Mosby, 1988:1365–76
24. Sampson HA, Mendelson L, Rosen JP. Fatal and near-fatal anaphylactic reactions to food in children and adolescents. N Engl J Med 1992;327:380–4
25. Wittstein IS, Thiemann DR, Lima JA, Baughman KL, Schulman SP, Gerstenblith G, Wu KC, Rade JJ, Bivalacqua TJ, Champion HC. Neurohumoral features of myocardial stunning due to sudden emotional stress. N Engl J Med 2005;352:539–48
26. Ellis AK, Day JH. Diagnosis and management of anaphylaxis. CMAJ 2003;169:307–11
27. Sneyd JR. Catecholamine-resistant cardiovascular collapse after propofol, atracurium and gentamicin. Eur J Anaesthesiol 1998;15: 600–2
28. McBrien ME, Breslin DS, Atkinson S, Johnston JR. Use of methoxamine in the resuscitation of epinephrine-resistant electromechanical dissociation. Anaesthesia 2001;56:1085–9
29. Heytman M, Rainbird A. Use of alpha-agonists for management of anaphylaxis occurring under anaesthesia: case studies and review. Anaesthesia 2004;59:1210–5
30. Kill C, Wranze E, Wulf H. Successful treatment of severe anaphylactic shock with vasopressin. Two case reports. Int Arch Allergy Immunol 2004;134:260–1
31. Smith AM, Elliot CM, Kiely DG, Channer KS. The role of vasopressin in cardiorespiratory arrest and pulmonary hypertension. QJM 2006;99:127–33
32. Oliver JA, Landry DW. Endogenous and exogenous vasopressin in shock. Curr Opin Crit Care 2007;13:376–82
33. Landry DW, Oliver JA. The pathogenesis of vasodilatory shock. N Engl J Med 2001;345:588–95
34. Landry DW, Levin HR, Gallant EM, Seo S, D'Alessandro D, Oz MC, Oliver JA. Vasopressin pressor hypersensitivity in vasodilatory septic shock. Crit Care Med 1997;25:1279–82
35. Fox AW, May RE, Mitch WE. Comparison of peptide and nonpeptide receptor-mediated responses in rat tail artery. J Cardiovasc Pharmacol 1992;20:282–9
36. Oyama H, Suzuki Y, Satoh S, Kajita Y, Takayasu M, Shibuya M, Sugita K. Role of nitric oxide in the cerebral vasodilatory responses to vasopressin and oxytocin in dogs. J Cereb Blood Flow Metab 1993;13:285–90
37. Peters J, Mack GW, Lister G. The importance of the peripheral circulation in critical illnesses. Intensive Care Med 2001;27: 1446–58
38. Hiltebrand LB, Krejci V, Jakob SM, Takala J, Sigurdsson GH. Effects of vasopressin on microcirculatory blood flow in the gastrointestinal tract in anesthetized pigs in septic shock. Anesthesiology 2007;106:1156–67
39. Kam PC, Williams S, Yoong FF. Vasopressin and terlipressin: pharmacology and its clinical relevance. Anaesthesia 2004;59: 993–1001
40. Luckner G, Dunser MW, Stadlbauer KH, Mayr VD, Jochberger S, Wenzel V, Ulmer H, Pajk W, Hasibeder WR, Friesenecker B, Knotzer H. Cutaneous vascular reactivity and flow motion response to vasopressin in advanced vasodilatory shock and severe postoperative multiple organ dysfunction syndrome. Crit Care 2006;10:R40
41. Opie LH. Receptors and signal transduction. In: Opie LH, ed. The heart: physiology, from cell to circulation. 3rd ed. Philadelphia: Lippincott-Raven, 1998:173–207
42. Bellou A, Lambert H, Gillois P, Montemont C, Gerard P, Vauthier E, Sainte-Laudy J, Longrois D, Gueant JL, Mallie JP. Constitutive nitric oxide synthase inhibition combined with histamine and serotonin receptor blockade improves the initial ovalbumin-induced arterial hypotension but decreases the survival time in brown norway rats anaphylactic shock. Shock 2003;19:71–8