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Case report

Successful treatment by vasopressin of a refractory rocuronium-induced anaphylactic shock: Case report

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Abstract Epinephrine is the recommended treatment in anaphylactic shock. Recently cases of anaphylactic shock refractory to epinephrine have been reported. The authors report the efficacy of a bolus of vasopressin in a refractory anaphylactic shock caused by rocuronium after failure the epinephrine. Thought this case report and review of literature, the authors discuss the mechanism of action and the effectiveness of this alternative treatment, vasopressin, in refractory anaphylactic shock to epinephrine.

1. Introduction

Anaphylaxis is a severe life-threatening generalized or systemic hypersensitivity reaction [1]. The incidence of anaphylactic reactions during anesthesia was variable [2,3]. Epinephrine is considered as the first line of treatment. However, clinical cases of resistance to epinephrine treatment have been reported. In these situations, management is variable and no codified. The use of different therapeutic alternatives to epinephrine seems justified given the risk of serious complications in uncontrolled anaphylactic shock. We describe a case in which a bolus of vasopressin established hemodynamic stability in anaphylactic shock caused by rocuronium after failure of fluid therapy and epinephrine.

2. Case report

A 42-year-old female, weighing 74 kg, was scheduled for elective laparoscopic surgery of gallbladder. Her past history included a diabetes mellitus stabilized by diet alone and arterial hypertension treated with amlodipin, but had no personal or family history of allergy. Preoperative evaluation noted a weight of 74 kg, height 169 cm with a body mass index of 25.91 kg/m^2. Her blood pressure was 143/81 mm Hg, heart rate was 76 beats/min, oxygen saturation was 99% in ambient air and temperature at 37.3 °C. Cardiovascular exam noted a dyspnea grade I of New York Heart Association classification (NYHA) without angina, with a metabolic equivalent (MET) > 4METs. Electrocardiogram noted a left ventricular hypertrophy without conduction or rhythm disorders. The echocardiography showed a

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moderate disorder of left ventricular relaxation, a normal global and segmental contractility without valvular or pericardial disease. Ejection fraction was estimated to 71%. Exam and chest-X-ray were unremarkable. Laboratory tests noted blood glucose at 130 mg/dL, urea plasma at 34 mg/dL, creatinine at 1.2 mg/dL and C-reactive protein (CRP) at 5 μg/mL, hemoglobin concentration at 13gm/dL and platelet count at 231,000/mm^3. Instructions during the pre anesthetic visit consist of a preoperative fasting of six hours with a premedication orally hydroxysine (75 mg). In the operating room a standard monitoring was installed (Zeus Infinity Empowered Dräger Medical AG &CO.KG Lübeck Germany). Non invasive blood pressure (BP) was 145/65 mm Hg, heart rate (HR) was 69 beats/min and her oxygen saturation (SPO2) was 98%. Venous access was secured with an 18 gauge cannula. After a fluid resuscitation with 300 ml of saline solution (0.9%) and preoxygenation (expired fraction of oxygen > 92%), general anesthesia was induced using midazolam (2 mg), fentanyl (250 μg), etomidate (18 mg), lidocaine 2% (80 mg). Rocuronium (35 mg) was administered after efficient mask ventilation. Three minutes later, the trachea was intubated with a single tube of 7 mm in diameter without problems. The patient was connected to the anesthesia machine, (Zeus Infinity Empowered Dräger Medical AG &CO.KG Lübeck Germany), with a tidal volume of 550 ml and a respiratory rate of 14 cycles/min. General anesthesia was continued with isoflurane (1–1.3%) in a mixture of nitrous oxide (50%) and oxygen (50%). Continuous monitoring included electrocardiography (ECG), pulse oximetry (SpO_2), non invasive blood pressure (BP) and capnography [endtidal carbon dioxide ($EtCO_2$)]. Within minutes of anesthetic induction, the patient developed severe hypotension (67/32 mm Hg) associated with sinus-tachycardia at rates varying between 145–157 beats/min. Hypotension related to induction of anesthesia was suspected. Isoflurane and nitrous oxide were stopped and 100% inspired oxygen was started. Intravenous rapid infusion of crystalloids was started with a bolus of ephedrine and operating table was placed in Trendelenburg position. Pulmonary auscultation revealed clear breaths sounds and no wheezing. Peak airway pressure (PAwP) was normal and remained unchanged (21–22 cm H_2O). There were no changes in pulse oximetry (99–98%), capnography (36–38 mmHg) and nasopharyngeal temperature was normal (36.5 °C). A total of 2500 ml of crystalloids, 30 mg of ephedrine and 5 mg of epinephrine was administered without success. Provisional diagnosis of distributive shock caused by anaphylaxis was made. The internal jugular central venous catheter and femoral arterial catheter were placed. Infusion of epinephrine was started at 0.03 μg/kg/min and increase to 0.5 μg/kg/min. The patient's conditions remained unchanged (blood pressure at 71/39 mm Hg, sinus-tachycardia at 149 beats/min). The addition of dobutamine did not allow any hemodynamic improvement. After failure of these means and increasing dose of vasopressor support, an injection a bolus of 2UI vasopressin was decided. Within 5 min, the patient was stabilized with a blood pressure 114/52 mm Hg and heart rate 89 beats/min. The surgery was cancelled. The vasopressor drugs were continued. The patient was transferred to intensive care unit with a propofol infusion. A bolus of dexamethasone (8 mg) was administrated. The vasopressor infusions were gradually withdrawn over three hours. One hour later the patient was extubated without problems. She was discharged home on day 2. Six weeks later, during follow-up skin allergy testing for rocuronium was positive at dilution 1/100. Skin testing for all the administered drugs including latex and others muscle relaxant was negative. Two months later, the patient underwent the primary scheduled surgery under general anesthesia using isoflurane, fentanyl and vecuronium. The anesthetic course was unremarkable.

3. Discussion

Anaphylaxis is a severe life-threatening generalized or systemic hypersensitivity reaction [1]. Its' occurrence during anesthesia is uncommon. The true incidence of this complication is difficult to determine due to uncertainties over the completeness of the data. The estimated overall frequency has been reported to vary between 1 in 5000 and 1 in 20,000 procedures [2,3]. The mortality from these reactions is in the range from 3% to 6%, and an additional 2% of patients experience significant residual brain damage [4]. All the anesthetic drugs may be implicated in the anaphylactic reactions. It is difficult to identify the responsible agent because a large number of drugs have been administered to the patient in most cases such antibiotic, opioids, and neuromuscular blocking agents (NMBAs). A follow-up investigation must be made to determine the responsible agent. We describe a case in which a bolus of vasopressin established hemodynamic stability in a refractory anaphylactic shock to catecholamine's caused by rocuronium. Various etiologies can explain a cardiovascular collapse during anesthesia such a myocardial infarction, a septic shock or anaphylaxis. The absence of fever in our patient and the rapidly hemodynamic degradation were not in favor of the diagnosis of the septic shock. In the same way, the absence of modification of electrocardiogram and normal level of troponin were not in favor of cardiogenic shock. Any ventricular kinetics disorders have not reveled in intensive care unit by echocardiography. Our patient has received midazolam, fentanyl, lidocaine, isoflurane and rocuronium. A severe hemodynamic instability during the use of isoflurane in a patient with idiopathic scoliosis was reported; the suspected mechanism was anaphylaxis reaction or uncommon cardiovascular sensitivity to isoflurane [5]. The incidence of anaphylactic reactions to fentanyl, lidocaine and midazolam is very low [6,7]. In our case, patient was stabilized with isoflurane and a bolus of fentanyl was given without problems. The prophylactic antibiotic was not given yet.

The rocuronium was highly suspected because of high incidence of allergy to NMBAs. The incidence of anaphylactic reactions to NMBAs differs between countries (1/5000–1/150,000) [6,7,2]. Responsibility of pholcodine in these reactions is suspected [8]. This variability in the incidence of anaphylactic reactions between countries could be explained by the variability in consumption of pholcodine them [9]. These agents can induce two types of reactions. One is driven by an immunological mechanism and is IgE-dependent and second one result from nonspecific stimulation of mast cells [10,11].

In anaphylactic shock, the symptomatology was predominant by cardiovascular collapse and arrhythmia, respiratory symptoms are slightly less common, but may predominant in patients with pr-existing asthma, cutaneous symptoms are usually hidden by surgical drapings. In our case were noted only cardiovascular collapse and tachycardia. Increases blood histamine and tryptase concentrations confirmed the diagnosis of anaphylaxis reaction. Skin prick testing is the gold standard,

and has a high sensitivity and specificity [6]. In our case we have no documented elevation of histamine or tryptase because it is not available in our hospital; the skin test was positive confirming the diagnosis of anaphylactic shock induced by rocuronium.

The guidelines treatments of anaphylaxis reaction during anesthesia include fluids therapy and vasopressor. This treatment was facilitated because the patient is usually monitored and has intravenous access in operative room. All guidelines recommend epinephrine for perioperative management of anaphylaxis [1,6,12–14]. However this recommendation was based in experimental and clinical data [10]. Using the criteria evidence-based medicine, epinephrine was classed Level C in treatment of anaphylactic shock [15]. A clinical case with resistance of epinephrine in this shock was reported. In some cases of refractory anaphylactic shock; new pharmacological approaches treatments have been described recently [16–18].

Vasopressin, a nona-peptide, is synthesized as a large prohormone in the paraventricular and supraoptic nuclei of the hypothalamus. This agent is a direct systemic vasoconstrictor. It is important for osmoregulation and maintenance of normovolemia [19]. Septic shock cause biphasic changes in its concentration. In early shock, high concentration of vasopressin is produced to maintain organ perfusion. As the shock state progresses, plasma vasopressin concentration decrease. The mechanism of this depletion was variable [20,21]. The use of vasopressin in second phase of the septic shock, when the catecholamine's and fluid were inefficient, seems logical to make up this deficit. The pathophysiological mechanism of cardiovascular failure in anaphylactic shock is similar of septic shock, including vasodilatation and hypovolemia resulting from endothelial permeability. In severe anaphylactic shock, refractory to epinephrine and fluid, vasopressin can be used is like in advanced septic shock. The efficacy of this administration in this situation was reported in some cases reports [17,22–25]. The comparison between epinephrine and vasopressin reveled that epinephrine was only partially effective in reversing histamine-induced vasodilatation but vasopressin was able to completely reverse histamine-induced vasodilatation in an experimental study [26]. This advantage of vasopressin in anaphylactic shock should be confirmed by the futures study. The optimum dose and the mode of delivery were variable. A comparison of two doses of vasopressin in an experimental study (0.08 vs 0.8 U/kg), the use a high dose (0.8 U/kg) was associated with decreasing the survival rate [27]. In some cases, vasopressin was administered by bolus (1 for 3), in another, she was administered by bolus following by infusion. Based on the experiences of authors, we decided, in our case, to administer 2U (0.02 U/kg). The blood pressure had been stabilized with this only bolus. Any infusion was necessary. Vasopressin should be considered in second line after epinephrine, her administration early in a model of anaphylactic shock induced a mortality of 100%, but administration of epinephrine followed by vasopressin has a rate of survival better (100%) than to epinephrine alone (80%) [28].

4. Conclusion

Through this case report and the review of the literature, we can say that epinephrine remains the first-line treatment of the anaphylactic shock, the vasopressin must be considered, secondary, after failure of epinephrine.

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