CARDIOVASCULAR COLLAPSE AFTER GENERAL ANESTHETIC INDUCTION COMBINED WITH ESMOLOL

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Abstract

Esmolol chloride was commonly used in anesthetic induction to blunt cardiovascular responses of tracheal intubation. Because of its short half-life, esmolol was considered as a relative safe agent in anesthetic practice. Here, we present a 49-year-old diabetic female patient scheduled for vitrectomy. She suffered from a cardiovascular collapse after general anesthetic induction combined with esmolol. The bradycardia and shock cannot be corrected with repeated doses of adrenergic agents including epinephrine. Cardiopulmonary resuscitation persisted for forty minutes to regain the vital sign. The followed examinations didn’t reveal definite pathology such as acute myocardial infarction or anaphylaxis. In this report, we discussed the possible causes of shock and reviewed the esmolol-related cardiovascular collapse and its treatment.

Key words: General Anesthesia, Adrenergic β-antagonists, Heart arrest

Introduction

Bradycardia and hypotension sometimes occurred after general anesthetic induction especially in the old-aged or poor-conditioned patients. However, anesthesia-related cardiovascular collapse is rare.1,2 Esmolol hydrochloride, characterized by its short action duration, was commonly used in anesthetic induction to blunt cardiovascular responses to tracheal intubation.3 Esmolol hydrochloride was considered to be relative safe in treatment of intraoperative hypertension and tachycardia even in patients with compromised left ventricular function.4,5 Here, we reported a 49-year-old patient who was scheduled for vitrectomy. She developed an unexpected profound cardiovascular collapse after induction of general anesthesia combined with esmolol chloride. The bradycardia and shock was refractory to repeated doses of adrenergic agents.

Case Report

A 49-year-old woman, with body weight 42 kg and body height 152 cm, has 12-year history of non-insulin-dependent diabetes mellitus. She was scheduled for vitrectomy due to progressive diabetic retinopathy and vitreous hemorrhage. The patient's diabetes was irregularly controlled with oral hypoglycemic agents and insulin. Except
diabetes, the patient denied any other systemic disease. Her preoperative electrocardiography showed normal sinus rhythm. Chest X-ray film reported a normal heart size. Fasting blood glucose was 242 mg/dl. Other preoperative routines were unremarkable. After admission, the patient’s blood glucose was controlled with rapidly acting insulin. Before the operation, the blood sugar was 229 mg/dl.

At the operation room, the patient’s heart rate was 78 beats per minute and arterial blood pressure was 183/91 mmHg. General anesthesia was induced with fentanyl 150 μg, lidocaine 50 mg, rocuronium 30 mg, thiamylal 250 mg. Esmolol 40 mg was added for controlling the high blood pressure. These drugs were administered within 1-2 minutes in the sequence. Once the induction agents were given, the patient’s blood pressure was monitored continually with the pressure cuff. About one minute after the administration of rocuronium, tracheal intubation was finished smoothly. Within the 1-2 minute period between induction and intubation, the heart rate and blood pressure was decreased slightly but still remained within an acceptable range. However, after the tracheal intubation, the heart rate and blood pressure dropped persistently. The isoflurane was discontinued. Incremental doses of intravenous ephedrine 8, 16 mg, followed by phenylephrine 0.2, 0.4 mg, were given when the systolic pressure was lower than 100 mmHg. Because of ineffectiveness of the above agents, epinephrine 0.2 and then 1 mg were administered. Five minutes after intubation, even under the repeated doses of epinephrine, the patient’s blood pressure was decreased to an immeasurable level. At the same time, the progressive bradycardia occurred and asystole followed. Cardiopulmonary resuscitation commenced and the repeated doses of adrenaline, sodium bicarbonate, and calcium chloride were administered. About ten minutes later, ventricular fibrillation appeared and total five attempts of cardioversion (300J once and 360J 4 times) were given to restore the heart beat. The status of shock persisted about forty minutes. Finally, the patient regained spontaneous heart rate and blood pressure. During the resuscitation, the patient’s extremities are cold and pale. Examination of the patient failed to find any evidence of cutaneous flush, mucosa edema or bronchospasm. Radial arterial line and central venous catheters were inserted after the resuscitation. The Initial arterial blood gas data showed severe acidosis with pH 7.038. Central venous pressure was 12 mmHg. After the patient’s condition turned to be stable, she was transferred to an intensive care unit and the operation was cancelled.

At the intensive care unit, the patient’s consciousness returned ten hours later. The electrocardiography showed non-specific ST-T abnormalities. The echocardiographic report revealed normal chambers size and normal wall motion with preserved left ventricular function. Slightly elevated creatine kinase-MB suggested mild myocardiac injury during ressuscitation. Under aggressive treatment, the patient’s condition became stable and the symptoms of ARDS were gradually improved. She was transferred to ordinary ward about two weeks later.

In the following days, several additional studies including autonomic neurological tests were performed. But the results were inclusive. After one month’s admission, the patient was discharged with stable condition. Due to progressive proliferative diabetic retinopathy and vitreous hemorrhage, she received twice vitrectomy surgery under local block four months later smoothly.

**Discussion**

We reported a patient suffered from cardiovascular collapse happened immediately after the induction of general anesthesia. This patient didn’t have any history of heart disease and other major systemic diseases except diabetes. There was also no evidence of human mistakes during induction or intubation. The cause of this cardiovascular collapse is obscure. The time sequence of this event suggests the induction agents may response to this event. Otteni JC et al had reported that
anesthetic agents can result in cardiac arrest by 1) overdose (absolute, relative), 2) anaphylactoid/ anaphylactic reactions, 3) specific effects (acetylcholine-like effect, hyperkalemia and malignant hyperthermia for succinylcholine; vagal effect of vecuronium and atracurium; cardiotoxicity of bupivacaine) and 4) drug interaction. However, the other possible causes, such as acute myocardial infarction, pulmonary embolism should be ruled out first.

Acute myocardial infarction was once considered as one of the most possible causes when the shock happened. Patients with diabetes mellitus are known to have higher risks of coronary artery disease and death rate than the general population. In order to rule out the possibility of acute myocardial infarction, this patient had been arranged a series of examinations. However, the complete electrocardiographs after resuscitation didn’t reveal ST elevation or abnormal Q waves. The echocardiography showed normal wall motion without any evidence of hypokinesia or akinesia. The cardiac enzyme, creatine kinase-MB, suggested the resuscitation-associated cardiac injury. The above examinations didn’t support the acute myocardial infarction as a cause of this cardiovascular collapse.

Massive pulmonary embolism can also induce cardiovascular collapse and shock. But the patient didn’t have any risk factors of pulmonary embolism, such as estrogen treatment, varicose veins, obesity, prolonged immobility, leg fracture, paralysis, heart failure, abnormal hematological condition, or the history of venous thromboembolism. Echocardiography didn’t find any intraluminal thrombi, signs of right heart failure or pulmonary hypertension. Central venous pressure was not elevated. This patient’s the arterial blood gas during the resuscitation showed normal PaO₂. Because massive pulmonary embolism without hypoxemia is so rare that if the arterial oxygen pressure is normal an alternative diagnosis should be considered. In addition, there were no compatible findings of pulmonary embolism in chest radiograph. Because the diagnosis of pulmonary embolism was not favored, the specific tests for pulmonary embolism, including pulmonary angiography, perfusion lung scan, and spiral computed tomography, were not ordered.

Anaphylaxis could occur during general anesthesia and cause cardiac arrest and shock. The incidence of anaphylactic reactions during anesthesia has been reported to range from 1 in 4,000 to 1 in 25,000. Allergy to thiopental, local anesthetics, neuromuscular blocking agents that used in this patient’s induction all had been documented. Anaphylaxis can appear as cardiovascular collapse, airway obstruction, flushing and/or edema of the skin. Diagnosis of anaphylaxis is usually made on clinical grounds. In this patient, except to cardiovascular collapse, there are no symptoms of airway congestion, bronchospasm, skin flushing or erythema. Even though anaphylaxis could happen without the signs of airway and cutaneous involvement, it was a rare condition.

Previous study showed that intravenous 150 mg bolus of esmolol is superior to high-dose lidocaine or low-dose fentanyl in preventing the tachycardia associated with intubation. Because of the patient’s high blood pressure before induction, 40 mg of esmolol was administered with other induction agents to control blood pressure. Usually esmolol is thought to be a safe anti-hypertensive agent and doesn’t produce prolonged and intracerebral hypotensive effects because of its ultra-short half-life. Peak effects of an intravenous loading dose of esmolol are seen within 5-10 minutes and then diminish rapidly. After literature review of the studies of β-blocker intoxication, we found there were few reports concerning the esmolol intoxication. Herschman and coauthors described a case, the young healthy patient who died after receiving esmolol treatment for postoperative supraventricular tachycardia. In this case, the esmolol-induced bradycardia and asystole are characterized by no response to repeated doses of epinephrine and dopamine. Another case reported by Litman and coauthors was an 11-year-old girl who developed asystole after induction of general anesthesia and administration of a standard dose of intravenous esmolol hy-
drochloride (0.5 mg/kg). Although the ephedrine, epinephrine, and atropine sulfate were given immediately, the patient's cardiac rhythm could not be restored until calcium chloride was administered. In the two cases, the esmolol, even used with recommended dosage, produced prolonged and intractable cardiac arrest and the cardiac arrest is unresponsive to adrenergic agents. The same condition also happened on our case. In this case, the patient developed cardiac arrest which didn’t response to atropine sulfate, ephedrine, phenylephrine and repeated doses of epinephrine. These combined symptoms of hypotension and bradycardia suggests long-lived sympathetic blockade.

Data from self-poisoning of propranolol showed that acute symptoms of β-blocker intoxication include myocardial depression and hypotension. The recommended treatment for β-blocker intoxication is fluid replacement, administration of atropine, and α-adrenergic agents such as epinephrine or isoproterenol. The experience, coming from propranolol overdose, showed that glucagon and calcium chloride also appears to be useful agents. Glucagon causes an increase of cAMP in myocardial cells and then activates the calcium channels. Glucagon and calcium chloride both produce calcium influx and increase intracellular calcium levels. With increased intracellular calcium, the heart rate and myocardial contractivity are also increased. Patients may response to glucagons and calcium chloride, when the adrenergic agents were proved to be ineffective. However, repeated doses of calcium chloride were unsuccessful on our patient.

Among the induction agents used in this patient, barbiturate had been showed to have strong negative inotropic effect. Barbiturate can depress myocardial function by inhibition of the adenyl cyclase cascade. Also, via suppression of total calcium concentration of myocardium, barbiturate can act like beta blockers and calcium antagonists on cardiac mechanoenergetics. In this patient, the dose of thiamylal used in induction is 250 mg, equivalent to 6 mg/kg. This induction dosage is larger than the recent recommended dosage, 3-4 mg/kg. Although there are some suggestion thiamylal induction dosages of 3-6 mg/kg in the other textbook, the dose of 6 mg/kg is the highest suggestion value. The induction dose of fentanyl, 150 μg (around 4 μg/kg) used in this patient was also not low. The recent recommendation of the loading dose used in induction is 2-6 μg/kg. Fentanyl also have significant negative inotropic effect when combined with other anesthetic agents. Diabetic patients are at high risk for perioperative cardiovascular instability. Even no esmolol usage, hypotension frequently occurs during the induction of anesthesia on the long-term diabetic patients. Diabetic patients usually suffer from some degree of autonomic neuropathy. Combination usage of large doses of negative inotropic agents such as barbiturate and fentanyl with esmolol on this patient may produce the synergic negative inotropic effects on the cardiovascular system. If we titrated the induction agents carefully and applied lower dosage of fentanyl and thiamylal, it is possible to avoid this catastrophic event.

In conclusion, after carefully rule out the possibility of other causes, it is most likely that the drug interaction of esmolol and the relative-overdose of negative inotropic induction agents may response for this event. For patients with poor general condition, we recommend utilization of low doses of induction and applying careful titration of these agents when esmolol is used. If large amount of adrenergic agents could not correct the esmolol-induced bradycardia or hypotension, calcium chloride and glucagons is the drugs of choice.

References

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在全身麻醉誘導時併用Esmolol發生心血管塌陷之病例報告

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摘要

esmolol常用於麻醉的誘導中，以減少置放氣管內管時所引起的心臟血管反應。由於esmolol的半衰期相當短，它被認爲是一個相對安全的藥物。在此我們報告一個四十九歲患有糖尿病並將接受玻璃體切除手術的女性病人，她在合併使用esmolol的全身麻醉誘導之後，突然發生嚴重的休克與心跳停止。即使一再給予包括腎上腺素在內的升壓藥物，仍無法避免休克的發生。此病患在經過大約四十分鐘的急救之後，才恢復生命徵象。事後的各種檢查並無發現心肌梗塞或過敏性休克等病因。在此報告中，我們探討了休克可能的發生原因，並回顧esmolol的相關毒性反應及其處理方法。

關鍵詞：全身麻醉，乙型腎上腺素阻斷劑，心跳停止

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