Continuous Veno-Venous Hemofiltration for Massive Rhabdomyolysis After Malignant Hyperthermia: Report of 2 Cases

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We present 2 cases of fulminant malignant hyperthermia (MH), complicated with massive rhabdomyolysis. The patients were successfully treated in the intensive care unit of our university teaching hospital, despite the lack of availability of dantrolene in our country, by early application of continuous veno-venous hemofiltration (CVVH). Both male patients developed fulminant malignant hyperthermia during anesthesia for oromaxillofacial surgery. CVVH was employed when the values of creatine phosphokinase (CPK), myoglobin (Mb), and lactate dehydrogenase (LDH) increased significantly. After emergency treatment and CVVH therapy, the values of CPK, Mb, and LDH in the blood plasma of the patients decreased significantly. The complications, including acute renal failure, disseminated intravascular coagulation, and acute respiratory distress syndrome were also treated without any obvious organ damage. Early detection and management are the keys to treat MH successfully. CVVH is a valuable therapeutic application in the initial/critical management of severe rhabdomyolysis. If these complications occur even with initial treatment with dantrolene, our experiences may be useful adjunctive treatments to consider.

Key Words: Malignant hyperthermia; Continuous veno-venous hemofiltration.

Malignant hyperthermia (MH) is an abnormal hypermetabolic state of skeletal muscle induced by exposure to potent inhalation anesthetics and succinylcholine. Signs of MH include increases in carbon dioxide production and oxygen consumption, metabolic acidosis, hyperthermia, tachycardia, muscle rigidity, and rhabdomyolysis. The mortality is extremely high, up to 90% if early diagnosis and treatment is unavailable.¹ We report 2 cases of acute fulminant MH complicated with massive rhabdomyolysis during anesthesia for oral and maxillofacial surgery, which were managed successfully by administration of continuous veno-venous hemofiltration (CVVH) in the absence of availability of dantrolene.

CASE REPORT

Case 1

A 25-year-old man with dentofacial deformities, weighing 60 kg, was scheduled for a maxillary osteotomy. His initial axillary temperature was 36.5°C. He had not been diagnosed with any muscular disorder, nor had he experienced chronic muscle pain previously, and his family's medical history was noncontributory. The patient was premedicated with 100 mg of phenobarbital sodium and 0.5 mg of atropine intramuscularly, 1 hour prior to surgery. When the patient arrived in the operating room, routine monitors were applied and intravenous access was secured. Anesthesia was induced with propofol (2 mg/kg) and fentanyl (1.5 µg/kg); vecuronium (0.1 mg/kg) was used for tracheal intubation. Anesthesia was maintained with isoflurane (1–2

Received June 4, 2011; accepted for publication December 2, 2012
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Anesth Prog 60:21–24 2013
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ISSN 0003-3006/13
SSDI 0003-3006(13)

vol%) in oxygen using a circle system with a carbon dioxide absorber.

After the patient underwent mechanical ventilation for 40 minutes, a sinus tachycardia of 150–170 beats/min developed, and arterial blood pressure decreased to 80/38 mm Hg. The value of capnograph readings increased from 35 to 90 mm Hg. The patient began to sweat profusely, accompanied by an increase in nasopharyngeal temperature from 36.9°C to 43°C; extreme rigidity of his extremities was observed. Arterial blood gases showed severe acidemia and hyperkalemia (pH 6.94; PaCO₂ 97.4 mm Hg; base excess –6.9 mM; K⁺ 5.65 mmol/L). We concluded that the patient was experiencing MH.

Emergency treatment was initiated immediately, although dantrolene was not administered since it is generally unavailable in China. The isoflurane was immediately discontinued and 100% O₂ was given. Also administered were 100 mL of 5% sodium bicarbonate and 100 mg of hydrocortisone, along with 500 mL of ice-cold normal saline through the intravenous lines; ice packs were placed in the axillary and groin areas of the patient for cooling. A size 12 French nasogastric tube was placed via the left naris for iced gastric lavage and suctioning. With these therapeutic and supportive measures, the value of end-tidal carbon dioxide (E_tCO₂) of the patient declined to 45 mm Hg and rectal temperature dropped to 37.8°C. The patient was transferred to the intensive care unit (ICU) for further observation.

In the ICU, the status of patient deteriorated over the next 48 hours, with creatine phosphokinase (CPK), myoglobin (Mb), and lactate dehydrogenase (LDH) increasing despite diuresis with 60 mg of furosemide and urine alkalization with 250 mL of 5% sodium bicarbonate. Maximal plasma concentrations of CPK and Mb were 119,000 IU/L and 194,550 ng/mL after anesthesia, respectively. Accordingly, the diagnosis of severe rhabdomyolysis syndrome was ascertained for the patient. CVVH was then initiated, 48 hours after the start of the event. A size 13 French dual-lumen catheter was inserted into a femoral vein and CVVH was performed (Baxter, ACCURA System, USA). The hemofilter was a 1.3 m² polyamide S-membrane Polyflux (Fresenius, Bad Homburg, Germany). The replacement solution was a bicarbonate-based solution containing 1.1 g/L glucose and 2.0 mM potassium. Blood flow and ultrafiltrate rates were 160 mL/min and 1.8 L/h, respectively. Replacement fluid was infused after dilution at a rate that matched the hourly ultrafiltration.

The patient was administered CVVH for 28 consecutive days. The values of CPK, Mb, and LDH gradually returned to normal through continuous treatment of 28

days. Anuria occurred 8 days after the operation and lasted for 10 days. Complications, including disseminated intravascular coagulation, adult respiratory distress syndrome, and acute renal failure also occurred. The disseminated intravascular coagulation resolved with plasma and platelet replacement therapy, and adult respiratory distress syndrome and acute renal failure were managed effectively with mechanical ventilation and CVVH, respectively. The patient was discharged after 60 days without any neurologic sequelae but with markedly reduced muscle mass and generalized muscle weakness. The pathologic evaluation of striated muscle indicated that some muscle fibers displayed disintegration and necrosis.

Case 2

A 15-year-old boy, weighing 35 kg, was scheduled for resection of a parotid tumor. His medical history and laboratory investigations were normal. Similar to case 1, the patient developed signs of MH after 3 hours, with his nasopharyngeal temperature rising to 42.9°C. After emergency treatment similar to that in case 1, he was transferred to the ICU. With rescue experiences from case 1, CVVH was conducted on the second day. His CPK peaked at 92,600 μ/L, Mb at 129,600 ng/mL, and LDH at 4350 μmol/L on day 4, with the same series of complications including disseminated intravascular coagulation, adult respiratory distress syndrome, and acute renal failure as in case 1. Oliguria occurred on day 4 and developed further to anuria soon thereafter and lasted for 12 days. The CPK, Mb, and LDH values returned to their normal levels after 21 treatments of hemofiltration and 2 treatments of plasmapheresis over 28 days. The patient recovered completely after further treatment lasting more than 1 month. The pathologic diagnosis of his striated muscle was similar to case 1.

RESULTS

Both patients were rescued successfully. The values of Mb, CPK, and LDH before and after CVVH administration are shown in Tables 1 and 2.

DISCUSSION

Malignant hyperthermia is an abnormal hypermetabolic state of skeletal muscle induced by exposure to potent inhalation anesthetics and succinylcholine.^{1,2} MH mortality was extremely high, up to 90%, in the 1960s. The

Table 1. The Changes of Myoglobin (Mb), Creatine Phosphokinase (CPK), and Lactate Dehydrogenase (LDH) Values After Continuous Veno-venous Hemofiltration (CVVH) in Case 1

	Mb, ng/mL	CPK, μ L	LDH, μ mol/L
Pre-CVVH	10,480	69,125	6558
6 h after CVVH	13,490	55,950	13,170
24 h after CVVH	74,750	119,000	6075
48 h after CVVH	194,550	22,000	6178
1 wk after CVVH	43,200	27,000	1820
4 wk after CVVH	1975	525	738

present mortality has remained below 10% in developed countries with the administration of the specific remedy, dantrolene. There have been occasional reports of MH cases in China, but successful rescues were rare due to the lack of dantrolene.³ Therefore, early diagnosis and timely supportive therapy are critical for MH patients to survive.

The critical issue in the early diagnosis of MH is careful monitoring of the patient's electrocardiogram, blood pressure, pulse oxyhemoglobin saturation, $E_T\text{-CO}_2$ inhaled anesthetic concentration, and body temperature throughout the entire operation. Other clinical manifestations and results of blood biochemistry evaluations could further be helpful in the diagnosis of MH. The combination of hyperthermia, hypermetabolism, hyperkalemia, and significantly elevated levels of serum CPK strongly indicated MH in our patients.

Larach et al⁴ reported a clinical grading scale to predict susceptibility to malignant hyperthermia. The patients were evaluated according to the presence of rigidity, features of muscle injury, respiratory acidosis, increased temperature, cardiac rhythm abnormalities, and family history. The results were graded as a MH rank score, which ranged from 1 to 6. In both of our cases, the MH rank was 6, so the diagnosis of MH was almost certain. Significantly elevated CPK blood levels (higher than 50,000 U/L) and myoglobinuria supported the diagnosis of rhabdomyolysis.

Persistent muscular spasms and contractions in MH patients are late signs of MH and may result in serious rhabdomyolysis.^{5,6} Rhabdomyolysis and myoglobinuria

are responsible for approximately 5% of all causes of acute renal failure.⁷ The myoglobin released during rhabdomyolysis is thought to cause renal dysfunction by producing renal tubular obstruction, lipid peroxidation within the tubular cells, and renal vasoconstriction.⁷ Intravascular volume expansion, urinary alkalization, and forced diuresis are currently administered as renal-protective measures.⁸ These treatments are not effective in severe oliguria where removal of myoglobin using blood purification techniques may be advantageous.

Continuous renal replacement treatment is a hemofiltration method to eliminate water and toxins slowly and continuously and is regarded recently as an important development of critical care medicine.^{9,10} Hemofiltration is effective in removing larger-molecular-weight substances such as myoglobin (17,000 daltons). In an animal model (swine), 4 g of equine myoglobin were administered intravenously. Within 6 hours, 17% and 24% of the administered dose was removed by CVVH with ultrafiltration rates of 1.8 and 2.9 L/h, respectively.¹¹ In our 2 patients, CVVH was provided early and timely. A critical amount of metabolic products and toxins from skeletal muscle spasm and destruction, such as CPK, Mb, and LDH, were eliminated effectively by CVVH. All severe complications such as acute renal failure, adult respiratory distress syndrome, and disseminated intravascular coagulation were appropriately managed, and both patients recovered.

CONCLUSIONS

We conclude that the administration of CVVH can clear metabolic products and toxins such as myoglobin effectively in patients with rhabdomyolysis and acute renal failure after MH. The technique may also be advantageous in patients with oliguric renal failure, multiple organ failures, or if these complications develop despite the availability of dantrolene being administered for MH.

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Table 2. The Changes of Myoglobin (Mb), Creatine Phosphokinase (CPK), and Lactate Dehydrogenase (LDH) Values After Continuous Veno-venous Hemofiltration (CVVH) in Case 2

	Mb, ng/mL	CPK, μ L	LDH, μ mol/L
Pre-CVVH	8660	77,000	4230
24 h after CVVH	53,000	69,800	3940
48 h after CVVH	58,400	74,200	2570
72 h after CVVH	129,600	92,600	1530
1 wk after CVVH	27,800	26,400	1570
3 wk after CVVH	1868	528	201

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