

Early intensive treatment to prevent kidney failure in post-traumatic rhabdomyolysis: Case report

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Abstract

Traumatic rhabdomyolysis is a clinical and biological syndrome secondary to lysis of striated muscle fibers resulting in extended musculoskeletal damage. An acute muscle damage causes the release of constituent elements of the sarcoplasmic reticulum, such as muscle enzymes, potassium, and myoglobin in plasma circulation; these conditions are at great risk of dangerous systemic complications for life such as hypovolemic shock, hyperkalemia, and acute kidney injury. We describe the case of a patient who suffered a severe musculoskeletal and vascular trauma with elevated creatine kinase values and myoglobinemia treated early with coupled plasma filtration adsorption in order to prevent kidney damage, associated with volume replacement, loop diuretics, and correction of metabolic acidosis.

Keywords

Critical care/emergency medicine, nephrology, traumatic rhabdomyolysis, acute kidney injury, coupled plasma filtration adsorption

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Introduction

The mechanism of muscle injury after major trauma determines edema and hemorrhage at the level of muscle fibers. The accumulation of fluid inside the muscle compartments and the increase in local pressure decrease the capillary perfusion of the muscular fiber; these mechanisms trigger the process of necrosis with the subsequent release of muscular components.¹

If the process is not reversed, necrosis continues to produce cardiovascular and renal effects; the latter by secondary occlusion of myoglobin deposit at the level of the distal convoluted tubule. Visible myoglobinuria occurs when it exceeds 250 mg/mL, which corresponds to the destruction of approximately 100 g of muscle.

The circulatory flow of muscle fibers associated with the consumption of glycogen and creatinine phosphokinase leads to the depletion of adenosine triphosphate (ATP), which causes alterations in ionic homeostasis within the cell. Thereafter, dysfunction occurs in membrane transport with the consequent accumulation of intracellular calcium that activates phospholipases and proteases, which in turn leads to mitochondrial dysfunction and formation of free radicals that continue muscle damage.^{2,3}

Myoglobin is a single-peptide protein with a molecular weight of 17.8 kDa composed of 153 amino acids with a single heme prosthetic group. It counts to about 1%–3% of the dry weight of the muscles. Myoglobin binds to oxygen and facilitates the transport of oxygen in muscle cells working under low oxygen tension. Myoglobin is catabolized by glomerular filtration and absorption of the proximal tubule by endocytosis and proteolysis. When injured, muscle tissue releases myoglobin, and this goes into bloodstream and binds haptoglobin and alpha-2 globulins.

The removal from blood circulation is by the reticuloendothelial system. In rhabdomyolysis, the concentration of free myoglobin in blood exceeds the purification capacity of the reticuloendothelial system.^{4–6}

The renal insufficiency described in rhabdomyolysis is acute tubular necrosis. The origin of all tubular necrosis is a

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Figure 1. Right upper limb after surgery.

physiological hypoperfusion of the renal medulla, which makes it extremely sensitive to ischemia.

There are three direct toxic mechanisms of myoglobin that aggravate tubular ischemia and are comparable to the renal effects of free hemoglobin after hemolysis. The first mechanism is a worsening of vasoconstriction caused by hypovolemia (the heme group included in the myoglobin is vasoconstrictor). The second mechanism is intratubular precipitation of myoglobin and uric acid. This phenomenon depends on the acidity of the urine, acidity correlated with the importance of hypovolemia. Finally, iron from myoglobin catalyses reactions that produce free radicals, reactions initiated by ischemia and responsible for a direct toxic effect on tubular cells.⁷

The therapeutic approach consists of treating the three causes of renal failure: an early and strong correction of blood volume (such as the muscular edema condition hypovolemia); the urine alkalization until a higher urinary pH is achieved and the use of diuretics to prevent fluid overload;^{8,9} protect in this way the lungs in the severely traumatized patient with rhabdomyolysis.

Alkalization of urine as a therapy remains controversial. Retrospective studies have failed to demonstrate a benefit in the use of this intervention.¹⁰

Based on these points, the therapeutics approach will have to take into account the following actions to restore the kidney function:

- Rapid and effective restoration of blood volume;
- Improvement of renal blood perfusion;
- Administration of diuretics with normal volume to prevent fluid overload;
- Control of acidosis;
- Monitoring and correction of hyperkalemia.

Intermittent dialysis is not useful for removing myoglobin and for preventing kidney damage. It should be considered in patients with rhabdomyolysis who develop acute renal failure. Indications include a hypercatabolic state, volume overload, acidosis, and significant hyperkalemia.

Continuous hemodialysis with biocompatible membranes (polysulfones, polyacrylonitrile, and polymethyl methacrylate) instead of intermittent dialysis with cuprofan improves recovery of renal function and reduces the incidence of mortality.^{11,12} This method is more effective in removing medium molecules with a molecular mass of approximately 15–20 kDa such as myoglobin.^{13,14}

Intermittent dialysis in the critically ill patient with cardiovascular instability may cause hypotension resulting in multi-organ hypoperfusion.

Among the advantages of continuous therapy, in the critical patient, we can find a more precise control of fluids and metabolites, decreased hemodynamic instability, and removal of harmful cytokines in patients with sepsis; another advantage reported is the possibility of administering an unlimited nutritional support.^{9,15}

Clinical case

This clinical case concerns a patient, a 33-year-old male, who arrived at emergency room due to a severe crushing trauma that occurred during work involving the upper and lower right limbs.

The trauma caused an exposed fracture in the right lower limb in the medial third of the leg, which was treated surgically by intramedullary nail placement and screws for osteosynthesis. The clinical picture was more complex in the right upper limb where, after radiographic, tomographic, and angiographic examinations, a fracture of the proximal third of the humerus, with lesion and flow arrest of the axillary artery, was observed. Reconstruction was performed by the vascular surgeon using autologous venous grafts, while the fracture was treated with an external fixator (Figure 1). A fasciotomy of the right arm was also performed due to extensive collapse and muscle edema.

In intensive care, the patient was sedated with a continuous infusion of midazolam and remifentanyl and subjected to artificial ventilation, continuous infusions of epinephrine at 0.07 mcg/kg/min plus dopamine at 5 mcg/kg/min, and broad-spectrum antibiotic therapy.

The patient began invasive monitoring of central arterial and venous pressure, fluid therapy at 300 mL/h, correction of metabolic acidosis with urine alkalization, and

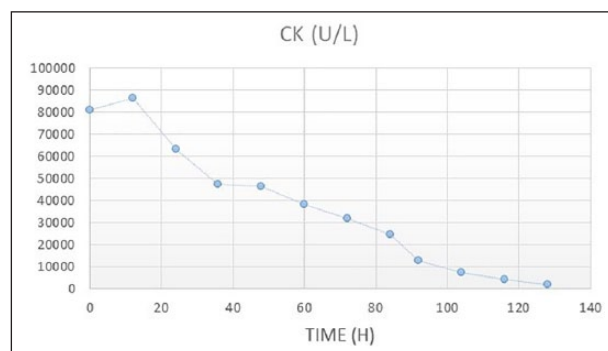
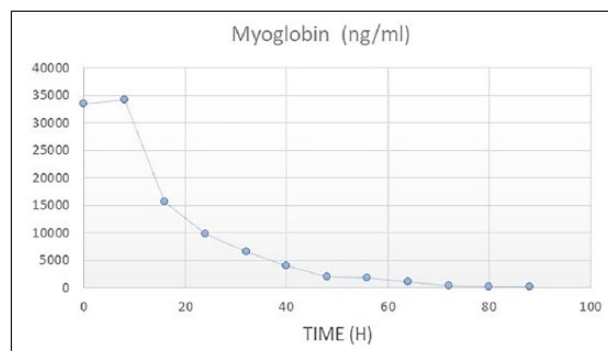
Table 1. Creatine kinase (CK) values measured every 12 h.

Time (h)	CK (U/L)
0	81,250
12	86,354
24	63,458
36	47,298
48	46,355
60	38,452
72	32,123
84	24,555
92	12,986
104	7543
116	4367
128	2145

Table 2. Myoglobin values measured every 8 h.

Time (h)	Myoglobin (ng/mL)
0	33,470
8	34,322
16	15,670
24	9893
32	6543
40	4004
48	2012
56	1840
64	1189
72	456
80	320
88	312
96	289
104	198
112	188
120	156
128	122

furosemide as a continuous infusion at 20 mg/h such that for the first 6 days of hospitalization, the mean hourly diuresis oscillated between 3.2 and 3.7 mL/kg/h. Creatinine values were maintained below 0.9 mg/dL throughout the entire intensive care unit (ICU) admission. On admission to ICU and then, in the immediate post-operative period, the value of creatine kinase (CK) was 86,354 U/L, while the myoglobin level was 33,470 ng/mL. The CK value^{15,16} was checked every 12 h (Table 1), while the myoglobin value was checked every 8 h (Table 2). Coupled plasma filtration adsorption (CPFA) was started with Lynda (Bellco®, Mirandola, Italy) after 6 h from the end of surgery, and after stabilization of the hemodynamic parameters. Six consecutive sessions of CPFA were performed for a duration of 12 h per session, maintaining a plasma target of 0.2 L/kg, blood flow (Q_b) of 150 mL/min, and plasma flow (Q_p) of 15% of blood flow (22.5 mL/min).

**Graphic 1.** Trend of creatine kinase values after CPFA.**Graphic 2.** Trend of myoglobin values after CPFA.

The trend of CK is summarized in Table 1 and Graphic 1, and the trend of myoglobin values after CPFA treatment is summarized in Table 2 and Graphic 2.

On day 5, the infusion of inotropic drugs was suspended, while on day 7, the process of weaning from mechanical ventilation began with a positive result and a return to spontaneous breathing.

The patient was discharged on day 15 to the orthopedics department, where he continued his treatment.

Discussion

Intermittent hemodialysis does not effectively remove myoglobin in rhabdomyolysis due to the size of the protein. Conventional membranes easily remove small water-soluble molecules, such as urea (0.06 kDa) and creatinine (0.113 kDa), but not medium molecules such as myoglobin (about 18 kDa) and cytokines (~5–30 kDa). Instead, the continuous venovenous hemofiltration or hemodiafiltration has shown some effectiveness in the removal of myoglobin, primarily with the use of super high-flow filters and high-volume ultrafiltration (convection).^{17,18}

CPFA is an extracorporeal blood purification treatment that uses a plasma filter for separating plasma from blood, and then allows the passage of plasma through an adsorbent cartridge for removal of various non-specific mediators.

Following purification, the plasma is returned to the blood: this can then go through a hemofilter for further blood purification by conventional hemofiltration in patients with acute renal failure. The therapeutic goal of CPFA is to hit the excess of circulating mediators (both pro- and anti-inflammatory) in order to restore a normal immune function. CPFA combines the first stage of plasma separation and adsorption of cytokines, inflammatory mediators, and/or toxins, followed by the second stage of hemofiltration for volume control and removal of small water-soluble mediators in the range of the medium molecules such as myoglobin, triiodothyronine (FT3) and free thyroxine (FT4), and bilirubin.¹⁹

In CPFA, a synthetic resin made of a styrene-divinylbenzene copolymer is used that interacts with the hydrophobic sites on the molecules.

CPFA is performed using a modular device with four pumps (Lynda; Bellco) which consists of a plasma filter (0.45 m² polyethersulfone with a cut-off of approximately 800 kDa), a hydrophobic resin cartridge not selective (140 mL) with a surface area of about 700 m²/g, and a high-permeability synthetic hemofilter (1.4 m² polyethersulfone) in which the convective exchanges can be applied to the blood reconstituted in post-dilution.^{20–22}

The maximum efficacy is obtained especially in the case of substances with high–medium molecular weight, such as myoglobin and cytokines.

Conclusion

The experience of CPFA in rhabdomyolysis is limited. The use of CPFA in rhabdomyolysis resulting in kidney transplantation has been described.²³ In a limited number of cases, we have described the use of CPFA in post-traumatic rhabdomyolysis with renal damage, elevated blood levels of creatinine, and contraction or absence of diuresis.²⁴

In the case described, we used CPFA early in order to prevent kidney damage, 6 h after the surgical revascularization along with the infusion therapy, diuretic, and correction of metabolic acidosis. The serum creatinine and potassium values remained normal. Diuresis has always been present, and the blood levels of CK and myoglobin decreased rapidly. The patient recovered without sequelae.

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Informed consent

Written informed consent was obtained from the patient for his anonymized information to be published in this article.

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