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Short-Term High-Dose Steroid Therapy in a Case of Rhabdomyolysis Refractory to Intravenous Fluids

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Study Design A
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Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Male, 35
Final Diagnosis: Rhabdomyolysis
Symptoms: Muscle pain • nausea
Medication: —
Clinical Procedure: Intravenous fluids
Specialty: Family Medicine

Objective: Unusual or unexpected effect of treatment

Background: Rhabdomyolysis is a syndrome characterized by skeletal muscle breakdown, that involves the release of intracellular contents into the circulation, including creatine kinase (CK), myoglobin, electrolytes, organic acids, and purines. Causes of rhabdomyolysis include trauma, exertion, drugs, and toxins (including alcohol), and electrolyte abnormalities. The treatment of rhabdomyolysis is to remove the cause and use intravenous (IV) fluids. When this treatment strategy fails to work, high-dose IV steroids may be used.

Case Report: We present a case of rhabdomyolysis following the use of 3,4-methylenedioxy-methamphetamine (MDMA) or 'ecstasy' with hypophosphatemia, which was found to be refractory to intravenous hydration. In this case, pulsed dosing of steroid therapy was found to be effective.

Conclusions: Rhabdomyolysis that is refractory to treatment with IV fluids may respond to a short-term, high-dose course of IV steroids.

MeSH Keywords: Creatine Kinase • N-Methyl-3,4-methylenedioxyamphetamine • Rhabdomyolysis

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/905196

Background

Rhabdomyolysis is a syndrome characterized by skeletal muscle necrosis and the release of the intracellular muscle constituents into the circulation. The severity of the illness ranges from an asymptomatic elevation in serum muscle enzymes to life threatening disease associated with raised serum enzymes, electrolyte imbalance, and acute kidney injury [1].

The standard of care is to treat any underlying etiology and provide aggressive intravenous (IV) hydration with crystalloids.

We present a case of a 35-year-old male, who presented with rhabdomyolysis refractory to intravenous fluids. The purpose of presenting this case is to highlight the potential role of intravenous high-dose glucocorticoids in cases of rhabdomyolysis that do not respond to IV fluids.

Case Report

A 35-year-old male African American patient with the history of asthma, epilepsy, anti-social personality disorder, and poly-substance abuse presented with generalized muscle aches and nausea. Patient denied any other symptoms and confirmed use of ethanol, marijuana and 3,4-methylenedioxy-methamphetamine(MDMA) or 'ecstasy' the night prior to admission. No similar episodes in the past. Patient was not taking any medications at home.

On examination, temperature was 98°F (36.6°C), heart rate 188 bpm, respiratory rate 33 breaths/minute, blood pressure 134/75 and oxygen saturation was 91% on room air. Patient was diaphoretic, agitated and had generalized muscle tenderness. The rest of physical exam was normal. Laboratory results are shown in Table 1. Urine analysis showed clear yellow urine, with a specific gravity of 1.023, hematuria 3+, proteinuria 2+, negative nitrites and leukocyte esterase, WBC 2–5/hpf, and RBC 2–5/hpf. Urine toxicology was positive for cannabinoids and 3, 4-methylenedioxy-methamphetamine (MDMA). Serum alcohol level was negative.

Patient was started on generous IV fluids and had had aggressive electrolyte replacement.

Although the acute renal injury and electrolyte abnormalities resolved on the second day of hospital admission, yet patient continued to complain of generalized muscle aches with persistently elevated creatine kinase (CK) levels (Table 2).

Subsequently patient was given a single IV dose of 1,000 mg methylprednisolone, which resulted in clinical improvement and a significant reduction in serum Ck levels. (Figure 1). Before steroid treatment, serum CK level was 36,650 U/L, serum myoglobin was 1560 mcg/L, and urine myoglobin 4910 mcg/L. At 12 hours following intravenous steroid therapy, serum CK levels came down to 20,040 U/L, serum myoglobin to 837 mcg/L, and urine myoglobin to 112 mcg/L. At 36 hours following intravenous steroid therapy, serum CK was 4,069 U/L.

Table 1. Laboratory investigations.

Sodium 141	mmol/L (135–145)
Potassium	5.0 mmol/L (3.5–5.0)
Urea nitrogen	16 mg/dl (7–20)
Creatinine	2.70 mg/dl (0.6–1.2)
Phosphate	0.6 mg/dl (2.5–4.5)
Bicarbonate	8 mmol/L (24–30)
Anion Gap	31 mEq/L (3–11)
GFR*	33ml/min (90–120)
Calcium	5.2 mg/dL (8.5–10.2)
Creatine Kinase	Initially 1171 U/L (52–336 male) (later 36,900U/L)
Hemoglobin	14.6 g/dL (13.5–17.5)
Hematocrit	59.3% (38.8–50)
White cells	30.1.1×10^3 (3,500–10,500 cells/mcL)
Platelets	264×10^3 (150,000–500,000 cells/mcL)
Lactic Acid	8.7
Liver function tests: within normal limits.	
Arterial blood gases:	
pH: 7.24 (7.35–7.45)	
PO_2 67 mmHg (80–100)	
PCO_2 31 mmHg (38-42)	
O_2 saturation: 90%	

Table 2. Daily creatine kinase (CK) levels while on intravenous fluids only.

Time	Creatine kinase (CK) levels
Day 1	1,171 U/L
Day 2	36,900 U/L
Day 3	29,690 U/L
Day 4	28,380 U/L
Day 5	20,500 U/L
Day 6	24,690 U/L
Day 7	31,330 U/L
Day 8	45,900 U/L
Day 9	36,650 U/L

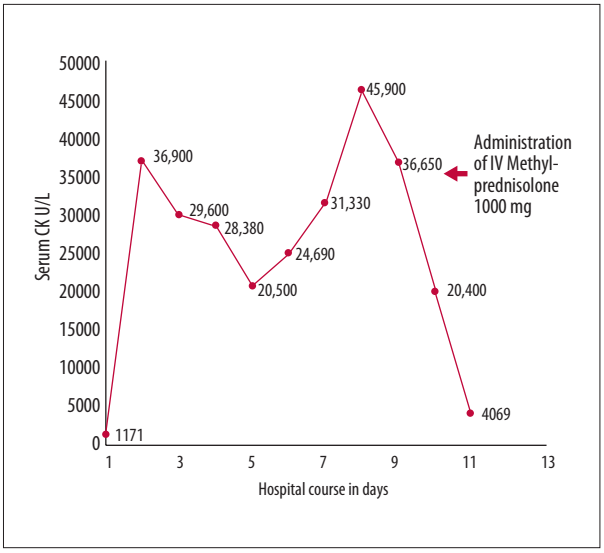

Figure 1. Graph showing the effect of intravenous (IV) corticosteroids on the serum creatine kinase (CK) levels

Patient was later discharged home with a follow up appointment in medicine clinic which he did not keep.

Discussion

Rhabdomyolysis has many different causes and has been reported following the use of 3,4-methylenedioxy-methamphetamine (MDMA) or 'ecstasy' [4–8]. Unlike other drugs, MDMA demonstrates a pattern of toxicity that is independent of dose [9]. Possible mechanisms of rhabdomyolysis due to MDMA include extreme exertion, malignant hyperpyrexia, seizures, or because of direct toxic effects of the drug on the muscle cells [9]. Severe hypophosphatemia has also been described as a cause of rhabdomyolysis [10].

The exact mechanism by which hypophosphatemia induces rhabdomyolysis is unclear, but a possible cause is inhibition of conversion of ADP to ATP and resultant deprivation of energy to the muscle fibers, resulting in rhabdomyolysis [11]. Ethanol-induced rhabdomyolysis may develop from the direct toxic effects on the sarcoplasmic reticulum by increasing sodium permeability and disruption of calcium homeostasis or indirectly due to prolonged immobilization and muscle compression caused by altered mental status, loss of consciousness, and coma [12]. Ethanol ingestion is also associated with hypokalemia, and hypophosphatemia, which can predispose the patient to rhabdomyolysis [12]. There are also case reports of rhabdomyolysis due to the use of synthetic marijuana [13,14].

Our patient had four known risk factors for the development of rhabdomyolysis, including the use of MDMA (ecstasy), marijuana, ethanol abuse, and hypophosphatemia, with no other signs or symptoms suggestive of any underlying inflammatory or immunologic disease. This was patient's first episode of rhabdomyolysis that occurred after illicit drug use. Patient's signs and symptoms and family history was not supporting an underlying genetic abnormality. We do not know if any of the four risk factors in our patient played any role in making rhabdomyolysis refractory to IV fluids, and responsive to IV corticosteroids.

Irrespective of the underlying cause, management of rhabdomyolysis involves treating the underlying cause, and prevention and treatment of acute kidney injury through generous and aggressive intravenous hydration that will restore volume status, as well as prevent formation and deposition of intratubular renal casts [15]. However, as in this case, some patients do not respond to intravenous hydration alone, and in such cases, high dose intravenous steroids may be beneficial. Other factors causing persistent rhabdomyolysis need to be ruled out first. Although the primary pharmacologic effects of corticosteroids are both immunosuppressive and anti-inflammatory, the exact mechanism of IV steroids in treating rhabdomyolysis is unclear [16].

Literature review shows only a few cases of IV corticosteroid use in treating rhabdomyolysis. Of the reported cases, one is associated with alcohol abuse, 2 cases with cytomegalovirus(CMV) infection and one with exertion [16–20]. The successful use of IV corticosteroids in these cases leads to the hypothesis that muscle damage in rhabdomyolysis is associated with an inflammatory component. One study that compares reported cases of CMV-associated rhabdomyolysis shows that patients who received IV corticosteroids had a comparatively shorter recovery time in terms of clinical improvement and improvement in CK levels [21]. In our patient clinical improvement and laboratory improvement in CK levels occurred in only 36 hours after the administration of IV steroids.

In short, although first-line management for rhabdomyolysis remains generous IV fluid administration, IV corticosteroid may prove beneficial if the patient fails to respond to IV fluids.

Conclusions

This case report, together with previously reported cases, demonstrate that rhabdomyolysis that is refractory to treatment with IV fluids may respond to a short-term, high-dose course of IV steroids.

Conflict of interest

None.

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