The Journal of Emergency Medicine, Vol. 50, No. 2, pp. e71–e74, 2016

0736-4679/$ - see front matter

http://dx.doi.org/10.1016/j.jemermed.2015.09.006

Selected Topics: Toxicology

RHABDOMYOLYSIS SECONDARY TO CLENBUTEROL USE AND EXERCISE

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☐ **Abstract—Background: The literature regarding rhabdomyolysis secondary to illicit drug use is sparse. Clenbuterol is a bronchodilator approved for veterinary use, which in high doses can increase protein deposition and lipolysis similarly to anabolic steroids, and is thereby abused for bodybuilding and weight loss effects. Clenbuterol has previously been described in case reports to be cardiotoxic, with patient presentations similar to overdoses of sympathomimetic substances, but reports of rhabdomyolysis are limited to a single case series in horses. Case Report: We report the first case of rhabdomyolysis secondary to clenbuterol in a human. Our patient used clenbuterol for muscle-building effects in addition to exercise for multiple days prior to presentation. The patient's chief complaint at Emergency Department (ED) presentation was discolored urine. Workup for rhabdomyolysis was initiated, and an initial creatine kinase was measured at 122,933 units/L. Our patient's rhabdomyolysis was successfully treated with supportive therapy, and the patient was eventually discharged to home with no identifiable disability. The patient's kidney function remained at baseline, and no acute kidney injury was experienced secondary to rhabdomyolysis. Why Should an Emergency Physician Be Aware of This?: Patients presenting to the ED may have been unintentionally exposed through cutting of illicit substances or through intentional use in bodybuilding. Clenbuterol has well-described cardiotoxic effects, and we report the additional toxicity of rhabdomyolysis with its use.** © **2016 Elsevier Inc.**

☐ **Keywords—clenbuterol; rhabdomyolysis; toxicity; beta-2 agonist; ingestion**

INTRODUCTION

Clenbuterol is a long-acting beta-1, beta-2, and beta-3 adrenergic agonist that has several pharmacologic actions in humans and animals. It is used as a bronchodilator for the treatment of asthma in humans and horses (1–6). Clenbuterol has been shown in animal and human studies to have pharmacodynamic effects of increased protein deposition to skeletal and cardiac muscle as well as increased lipolysis, similar to anabolic steroids, but does not impact growth hormone, testosterone, or insulin levels in the same manner. The mechanism of action for these effects is unknown, with inconclusive studies to date (7). Beta-3 receptors are found on adipocytes, and agonism has been shown to encourage lipolysis; thus, beta-3 activity may be one of the mechanisms responsible (4). Clenbuterol is not approved for human use in the United States (US), but is available as an orally administered tablet and liquid product in Europe and Mexico (4). The Food and Drug Administration (FDA) banned the use of clenbuterol in food animals in 1991 and the European Union followed in 1996. The ban was created due to toxicity in humans after consumption of clenbuterol-contaminated meat (1,8). There have been several US outbreaks of heroin or cocaine adulterated with clenbuterol over the last 10 years (6). Misuse by body builders and high-profile athletes as a performance-enhancing drug has spread rampantly with

RECEIVED: 15 April 2015; FINAL SUBMISSION RECEIVED: 11 August 2015;
ACCEPTED: 4 September 2015

illegal availability over the Internet (9). More recently, exposure has spread into the general public with recreational use as a stimulant or weight loss agent (4,9). The National Poison Data System (NPDS) 2013 annual report lists no mention of clenbuterol toxicity, and the 2012 annual report notes only one fatality involving clenbuterol in combination with several other medications, but no other instances of known exposure are noted (10,11). However, the 2013 NPDS does list 1530 "other beta-2 agonist cases" (11). This suggests there may be underreporting of the extent of the illicit use of clenbuterol. We present a case of a 29-year-old previously healthy man who was taking clenbuterol as part of a self-initiated training program, which resulted in rhabdomyolysis that required hospital admission and supportive care.

CASE REPORT

The patient, a 29-year-old Hispanic man with no significant past medical history, presented to the Emergency Department (ED) with a chief complaint of dark-colored urine that developed earlier that day. The patient denied taking any prescription medications other than clenbuterol 40 μg twice daily, glutamine, fiber supplements, and protein shakes. The patient purchased clenbuterol tablets from Mexico 4 months prior and used the tablets for 5 days without issue prior to discontinuing for unknown reasons at that time. In the ED, the patient stated that he had restarted clenbuterol for weight loss 3 days prior to this presentation. The clenbuterol was not taken at the direction of a prescriber either in the US or in Mexico. He had additionally started a new exercise regimen to lose weight the day prior to presentation. The regimen consisted of 90 min of strenuous activity, including weight lifting, the day prior to and the day of presentation to the ED. Additional complaints noted on physical examination included headache, subjective fever, tachycardia, thirstiness, diaphoresis, and shortness of breath. Vital signs were altered at presentation, with a heart rate of 118 beats/min and blood pressure of 141/91 mm Hg. Although shortness of breath was subjectively identified, objective parameters were within normal limits: his respiratory rate was 16 breaths/min and oxygen saturations were 96%. A physical examination was unremarkable; the patient was noted to be alert and oriented in no acute distress. His mucous membranes were moist, heart sounds regular although tachycardic, with upper extremity soreness but no deficits. The patient's initial laboratory results were significant for a creatine kinase (CK) level of 122,933 units/L, aspartate transaminase 774 units/L, and alanine transaminase 125 units/L, and mild leukocytosis with a white blood cell count of 14,100 cells/μL. The patient's kidney function was within normal limits, with serum creatinine of 1.02 mg/dL and normal urine output. All other chemistries were within normal limits and an initial urinalysis was read as red in color with large blood, 3 red blood cells, protein 100 mg/dL, positive ketones, and a specific gravity of 1.014. Subsequent urinalyses showed resolution of these abnormalities.

The patient was admitted for workup of the markedly elevated CK level and initiation of supportive therapy to protect against renal sequelae from presumed rhabdomyolysis. Aggressive hydration was started in the ED, initially with three 1-L boluses of normal saline followed by an infusion at 200 mL/h. This was quickly changed to dextrose 5% in water with 100 mEq sodium bicarbonate at 200 mL/h after the patient developed iatrogenic hyperchloremia. Twenty-four hours after admission, the patient's bicarbonate drip was stopped and hydration with Plasma-Lyte A (Abbott Laboratories, Chicago, IL) was started, which continued at a rate of 200–300 mL/h until discharge. He received five additional fluid boluses with 1 L of Plasma-Lyte A during his admission. His CK declined steadily with treatment over the 5-day period to 6307 units/L on the day of hospital discharge. The patient maintained urine output above goal, with 28–42 mL/kg/h throughout his admission. The patient's only prescribed medications during his admission were heparin for prophylaxis of deep vein thrombosis and as needed acetaminophen for pain control. The patient was discharged without myalgia or other related complaints. Clenbuterol levels were unable to be obtained to confirm the active component of the tablets. The patient was additionally unable to provide the tablets for confirmation. The patient was counseled by the clinical pharmacist and the medical resident regarding discontinuation of clenbuterol both in the ED and again at discharge.

DISCUSSION

The literature regarding toxicity from clenbuterol is sparse. The medication carries approval for airway disease in veterinary medicine, but is not approved for use in humans. Clenbuterol dilates the bronchi for therapeutic efficacy, but has dose-dependent anabolic effects. In the United States, it is banned by the FDA for human consumption through both food and medications. Clenbuterol has been used illicitly by athletes for bodybuilding and is consequently monitored by the International Olympic Committee (12). The drug causes lipolysis and is noted to be a nutrient partitioning agent in skeletal muscle fiber, leading to increased muscle deposition (13).

The causes of rhabdomyolysis are variable, and can include chemical damage by medications. The precipitant causes direct sarcolemmic injury, resulting in the eventual destruction of myofibrillar, cytoskeletal, and membrane proteins. As the myofibrillar network breaks