Case Report

Received: 2024/03/13    Revised: 2024/06/13    Accepted: 2024/06/13

DOI: https://doi.org/10.15441/ceem.24.217

Mortality case due to minimal bentazone intoxication

Authors
Yumin Jeon MD¹, Sejoong Ahn MD¹, Jong-Hak Park MD¹, PhD, Hanjin Cho, MD, PhD ¹, Sungwoo Moon MD, PhD¹, Sukyo Lee, MD¹*

Affiliations:
1 Department of Emergency Medicine, Korea University Ansan Hospital, 15355, Ansan-si, Republic of Korea

Declaration of interest: None.

Correspondence:
Sukyo Lee
Emergency department, Korea University Ansan Hospital
123, Jeokgeum-ro, Danwon-gu, Ansan-si, Gyeonggi-do, Republic of Korea
E-mail: sukyolee@korea.ac.kr; sukyolee@kumc.or.kr
Abstract
Bentazone is a widely used herbicide and is considered a moderate hazard. Fatalities are rarely reported, with reports of deaths occurring in doses of 200 ml or more. In some literature, it is accompanied by generalized rigidity. Malignant hyperthermia (MH) is a pharmacogenetic diseases that presents a hypermetabolic response to anesthetic gases or depolarizing muscle relaxant due to calcium channel dysfunction. The classic symptom of MH include hyperthermia and muscle rigidity. In this article, we report a case of a 65-year-old man who died 4 hours after presenting to the emergency department after taking approximately 75 ml of Basagran M60 (bentazone 33.6%, 25.2 g). This is the smallest dose (364 mg/kg) reported in a fatal case to date. Electrocardiogram changes, including QRS widening and QT prolongation, were present, and hypocalcemia was confirmed. We propose the possibility that bentazone intoxication causes patient deterioration by a mechanism similar to malignant hyperthermia.

Introduction
Many cases of acute overdose in Korea are attributed to deliberate consumption of agricultural pesticides and herbicides as a means of suicide. [1] Bentazone is an acidic herbicide classified as moderately hazardous by the World Health Organization (WHO). [2] There have been only two cases have reported fatal outcomes and muscle rigidity within a few hours. [3, 4] We report a mortality case after bentazone intoxication, leading to death within 4 h of ingestion. This study was approved by the Institutional Review Board (IRB) of Korea University Ansan Hospital (IRB no. 2024AS0012). Informed consent was obtained from the legal guardian of the patient for the use of clinical photograph.

Case History
A 65-year-old male visited the emergency department (ED) 40 min after ingesting approximately 75 ml of Basagran M60 (bentazone 33.6%, 25.2 g) to commit suicide. There were no other co-ingestions, except for alcohol. He had no medical history.
The patient was alert and did not report any symptoms. Vital signs were as follows: blood pressure, 128/64 mmHg; heart rate, 106 beats/min; respiratory rate, 20 breaths/min; body temperature, 37.3 °C;
and oxygen saturation, 94%. Physical examination was unremarkable including chest auscultation. Initial arterial blood gas analysis (ABGA) revealed respiratory alkalosis (pH 7.482, PCO2 32.3, PO2 68, HCO3 24.2). Notably, the ionized calcium was 1.4 mg/dL. Other abnormal laboratory results included lactic acid at 2.3 mmol/L, osmolality at 329 mOsmol/kg, and ammonia at 149 µg/dL. Serum potassium level was 3.9 mmol/L and creatine kinase was 56 U/L. Serum glucose was 114 mg/dL. Blood urea nitrogen and serum creatinine level was 9mg/dL and 1.1mg/dL respectively. Otherwise, other laboratory results were normal. Electrocardiography (ECG) revealed sinus tachycardia with significant QT prolongation (Figure 1A). Chest plain radiographs was normal. The patient was offensive and it was not possible to perform gastric lavage or administer activated charcoal. Normal saline 500 ml and sodium bicarbonate 60 mEq were administered. Calcium replacement was not done.

Approximately 90 min after ED admission, the patient had a body temperature of 38.7 °C. The patient was treated with evaporative external cooling and urinary bladder irrigation with cold saline. Acetaminophen 1000mg was also intravenously injected. One hour later, tachypnea was aggravated with a respiratory rate exceeding 30 and rapid deterioration of mental status, with a Glasgow Coma Scale of 3. Subsequent ABGA revealed a pH of 7.555, PCO2 of 24.2 mmHg, PO2 of 81 mmHg, and HCO3 of 21.0 mmol/L. Moreover, lactate level increased to 7.49 mmol/L. Brain computed tomography (CT) was performed because of comatose mentality but showed no acute lesions. The patient's body temperature rose to 41.0 °C right after the CT scan. An additional 1000ml of normal saline was administered.

After 163 min of ED admission, endotracheal intubation was performed for airway protection. The patient was intubated with 20mg of etomidate without a neuromuscular blocker. At this time, the patient did not exhibit any muscle rigidity. The patient’s blood pressure decreased to 63/34 5 min after endotracheal intubation. Despite the administration of norepinephrine up to 0.34µg/min/kg, cardiac arrest occurred 10 min after endotracheal intubation, with the initial rhythm being pulseless electrical activity. ABGA before the arrest showed a pH of 7.237, PCO2 of 56.7 mmHg, PO2 of 90 mmHg, and HCO3 of 24.1 mmol/L. The lactate level was 10.21 mmol/L and an ionized calcium showed less < 1.0 mg/dL. Serum potassium level was 5.5 mmol/L and serum glucose was 41 mg/dL. Blood urea nitrogen
and serum creatinine level was 12mg/dL and 1.3mg/dL respectively. Creatine kinase was not rechecked. ECG showed QRS widening and QT prolongation (Figure 1B).

Two minutes after the cardiac arrest, asystole was observed in every cycle. Despite the resuscitation, the patient expired. Muscle rigidity was observed throughout the body at the time of death (Figure 2).

**Discussion**

Bentazone, a herbicide of thiadiazine group, interferes with photosynthesis by preventing carbon dioxide fixation. [5] It is widely used as for the cultivation of rice, perilla, barley, and corn. [6] The WHO classifies bentazone as moderately hazardous, and fatal cases are very rare. [2] Muller et al. suggested a lethal dose of 686–1371 mg/kg in humans. [7] Fatal cases of liver failure, kidney injury, and muscle rigidity with failed or delayed airway access have been reported. [3-7] Of the five fatal cases acute bentazone intoxication reported to date, the smallest dose was 100–200 ml (48%), and all other cases involved more than 200 ml of bentazone. [3-7] However, in this case, the dose was 364 mg/kg. Previous studies reported delayed airway establishment due to muscle rigidity. Lee et al. reported no improvement in rigidity despite succinylcholine administration, suggesting a need for early surgical airway. [3, 4] However, in this case, despite achieving a definite airway before muscle rigidity developed, the patient eventually expired. This suggests that the cause of death is other than respiratory failure and the recommendation of early advanced airway is questionable.

Neuroleptic malignant syndrome (NMS) and malignant hyperthermia (MH) are similar in that they cause symptoms such as fever, muscle rigidity, and autonomic dysfunction. Lin et al. reported that bentazone intoxication mimics NMS.[8] However, we propose that bentazone intoxication mimics MH rather than NMS. First, MH occurs only in a small percentage of genetically susceptible individuals. While bentazone is classified as a moderately hazardous, and most patients have insidious course after consumption, few patients have been reported to develop muscle rigidity and fatal course. The reported fatal cases may have been genetically susceptible to bentazone. Second, hypocalcemia and QT prolongation in our patient were consistent with the pathophysiology of MH, which is based on calcium release from the sarcoplasmic reticulum and extracellular calcium influx. This indicates that bentazone
may induce a potential influx of extracellular calcium. In this regard, the case of bentazone intoxication of fatal course may be candidates for dantrolene. Dantrolene inhibits calcium ions release from sarcoplasmic reticulum by antagonizing ryanodine receptors. Therefore, it is a key part of the treatment of MH and is also used in other conditions that cause muscle contraction and heat production including NMS. Despite hypocalcemia, the benefit of calcium administration is questionable. Because there is a possibility of administration of calcium could increase intracellular calcium concentration which may lead to vicious outcome. Also, since Succinylcholine is one of the causes of MH, it should be avoided.

To our knowledge, this case report is the lowest dose of fatal bentazone intoxication reported to date. It is also the first to report hypocalcemia and ECG changes following bentazone intoxication. In addition, we suggested an association between bentazone intoxication and MH. A limitation of our case is that, although we propose dantrolene as a therapeutic candidate, it has not been applied in practice. Future studies are required to validate this therapeutic effect. Furthermore, it will be necessary to investigate the presence of ryanodine receptor mutations to confirm that those who have been fatally affected by bentazone intoxication are indeed MH.

ETHICALS STATEMENT
This study was approved by the Institutional Review Board (IRB) of Korea University Ansan Hospital (IRB no. 2024AS0012). Informed consent was obtained from the legal guardian of the patient for the use of clinical photograph.

CONFLICT OF INTEREST
None

FUNDING
None
AUTHOR CONTRIBUTION

Conceptualization: all authors; Methodology: all authors; Formal analysis: all authors; Data curation: YJ; Writing-Original Draft: YJ, Writing-Review & Editing: SA, JHP, HC, SM, SL; Supervision: SL.

ORCID

Yumin Jeon https://orcid.org/0009-0000-7584-4601
Sejoong Ahn https://orcid.org/0000-0002-6003-2552
Jong-Hak Park https://orcid.org/0000-0001-9481-6358
Hanjin Cho https://orcid.org/0000-0003-1303-304X
Sungwoo Moon https://orcid.org/0000-0001-9950-3449
Sukyo Lee https://orcid.org/0000-0002-7105-1951
References


2. WHO G. The WHO recommended classification of pesticides by hazard and guidelines to classification 2009 2010.


Fig. 1. Electrocardiogram of the patient.

(A) 101 minutes after emergency department admission. Corrected QT was 615 milliseconds. (B) 235 minutes after emergency department admission. QRS duration was 184 milliseconds.
Fig. 2. Clinical photo after the termination of resuscitation.

The patient developed generalized rigidity due to bentazone intoxication at the time of death. The left arm is rigid with the elbow flexed and the hand in the air, and both feet are rigid with plantar flexion.