

Case Report

# Rhabdomyolysis and acute renal failure as a result of bentazone intoxication

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**Abstract.** Bentazone (Basagran®) is a commonly used and easily available agricultural herbicide. We report a 41-year-old-man who developed rhabdomyolysis with acute renal failure after bentazone toxicity. Four hours later after oral intake of liquid bentazone for suicidal attempt, the patient admitted to emergency service and his initial renal function tests were in normal range. However on the 15<sup>th</sup> hour of intake, urine output decreased, and blood urine nitrogen, creatinine and creatinine kinase levels were increased. On the fifth day of hospitalization, creatinine and creatinine kinase levels had turned to normal levels. As a result, bentazone intoxication may cause rhabdomyolysis with acute renal failure. Thus, renal functions must be followed up closely.

Key words: Bentazone intoxication; rhabdomyolysis; acute renal failure

## 1. Introduction

Bentazone (Basagran®) (C<sub>10</sub> H<sub>12</sub> N<sub>2</sub> O<sub>3</sub> S) is a common used and easily available herbicide. The determined acute oral toxicity (LD50) was 1139 mg/kg in rabbits and 2918 mg/kg of live weight in pheasants. In rats given a single dose, 83-94% appeared in the urine by 24 h and 90-97% by 120 h after dosing. Bentazone is more acutely toxic to rats than its hydroxylated metabolites when given by oral route. In animal studies bentazone had a diuretic effect and increase protrombin time and partial thromboplastin time as a result of systemic toxicity. WHO has classified bentazone as slightly hazardous (1-3). On animal models, lethal doses of bentazone were declared to cause dispnea, central nervous system depression, fever, convulsions and death. In humans, the literature about bentazone toxicity is limited and consists of neuroleptic malign syndrome, sudden cardiac arrest, acute heart or renal insufficiency and rhabdomyolysis (4-9). Here, we present a case of bentazone exposure presenting as elevated

liver enzyme and acute renal failure due to rhabdomyolysis.

## 2. Case report

Half an hour after a 41-year-old man accidentally drank one spoonful of herbicide which includes approximetaly 36 grams of bentazone, complaints of vomiting, palpitation, fever and somnolence developed. Additionally the patient did not ingest any other toxicants (e.g. ethanol, anticoagulants). In his first emergency service (ES) admission, gastric lavage was performed and activated charcoal applied through nasogastric tube. He was transferred to our ES four hours after ingestion. On initial physical examination, he was conscious, oriented and cooperated. His vitals were as follows: blood pressure 130/80 mmHg, heart rate 110/min, body temperature 37.5°C and respiration rate 18/min. Epigastric tenderness was present with palpation, but rebound and muscular defense were absent. On initial laboratory findings, mild leukocytosis and respiratory alkalosis (pH: 7.52, HCO<sub>3</sub>: 21.8 mEq/L, pO<sub>2</sub>: 91.7 mmHg, pCO<sub>2</sub>: 26.7 mmHg) were prominent. Electrocardiography showed sinus rhythm. Renal ultrasonography and urine sediment was normal. Echocardiographic evaluation was in normal limits. Laboratory changes on follow up were given in Table 1. After fifteen hours of ingestion, urine output was decreased, blood urine nitrogen (BUN), creatinine

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and creatinine kinase (CK) levels were elevated and prothrombin time (PT) was increased. Serologic markers of hepatitis A, B, C and other hepatotropic viruses were all negative. The patient was referred to nephrology clinic with the diagnoses of rhabdomyolysis and renal failure. Intravenous hydration was provided to maintain a

central venous pressure of about 8-12 cmH<sub>2</sub>O. Vitamin K replacement (intramuscularly 30 mg) was applied due to prolongation of PT measured in international normalized ratio (INR). On the eighth day of hospitalization, his creatinine, PT measured in INR and CK levels decreased to normal levels.

Table 1. Changes in laboratory findings in the follow up

|     | Range                        | Initial | 1 <sup>th</sup> day | 2 <sup>nd</sup> day | 3 <sup>th</sup> day | 5 <sup>th</sup> day | 8 <sup>th</sup> day | 15 <sup>th</sup> day |
|-----|------------------------------|---------|---------------------|---------------------|---------------------|---------------------|---------------------|----------------------|
| WBC | 4.3-10.3 10 <sup>3</sup> μ/L | 13.9    | 8.0                 | -                   | -                   | -                   | -                   | -                    |
| CK  | 30-171 U/L                   | 168     | 1965                | 3809                | 2437                | 820                 | 201                 | 102                  |
| BUN | 6-20 mg/dl                   | 14      | 25                  | 42                  | 38                  | 32                  | 26                  | 11                   |
| Cr  | 0.8-1.25 mg/dl               | 1.2     | 2.0                 | 3.4                 | 3                   | 2.3                 | 1.9                 | 0.9                  |
| ALT | <45 U/L                      | 28      | 33                  | 45                  | 53                  | 71                  | 68                  | 43                   |
| AST | <35 U/L                      | 23      | 60                  | 118                 | 101                 | 79                  | 36                  | 25                   |
| INR |                              | 0.96    | 1.54                | 3.2                 | 2.1                 | 1.5                 | 1.1                 |                      |

CK: creatinine kinase, Cr: Creatinine, BUN: blood urine nitrogen, AST: aspartate aminotransferase

ALT: alanine aminotransferase, INR: International Normalized Ratio, WBC: white blood cell

### 3. Discussion

Bentazone is a polar, weak acidic and soluble pesticide that can rapidly be absorbed by warm-blooded animals and excreted by the kidneys via metabolizing to 6-OH- bentazone and 8-OH-bentazone (10,11). Bentazone is regarded as slightly toxic according to WHO guideline. According to animal models its no-observed-adverse-effect level (NOAEL) dose for systemic toxicity is 3600mg/kg. Bentazone has diuretic and anticoagulant effect as toxicity (3). Lethal doses may cause dispnea, central nervous system depression, fever and neuroleptic malign syndrome in animals. Bentazone intoxication may induce vomiting, fever, perspiration, muscle rigidity, sinus tachycardia, somnolence, leukocytosis, rhabdomyolysis, renal and hepatic damage (5,7,10). Apart from rhabdomyolysis and ARF; sudden cardiac arrest and acute heart failure has also been described with bentazone intoxication (7,8).

Lin et al. (4) declared a patient who ingested 132.3 grams of bentazone. This poisoning resulted in acute renal insufficiency due to rhabdomyolysis. They concluded that rhabdomyolysis in the bentazone poisoning may mimic muscle rigidity of neuroleptic malignant syndrome. Our patient took lesser amount of bentazone and although no muscle rigidity was observed, CK levels were moderately elevated on the second day.

As Wu et al. (9) mentioned in two cases, bentazone intoxication may also cause nephrotoxicity without rhabdomyolysis. The first case ingested 35.3 gr. of bentazone. His creatinine and BUN increased to 1.8 and 34 mg/dL, respectively. After adequate hydration, acute renal failure was improved on the fifth day of exposure. The second case took 88.2 gr of bentazone. His creatinine and BUN levels were 17.2 and 162 mg/dL, respectively. His ARF was with oliguria. Hemodialysis was applied, however respiratory failure occurred and he died on the fourth day of hospitalization. Both these cases had ARF and their CK levels were within normal limits. They assessed ARF to renal hypoperfusion due to severe vomiting, rhabdomyolysis and direct nephrotoxic effect of the agent (9).

Our case also admitted to ES with the complaints of nausea and vomiting, but initial examination did not reveal hypovolemia symptoms, moreover the peripheral venous pressure was 6-7 cm-H<sub>2</sub>O. Thus, we think that the reason of renal failure in our case was due to direct nephrotoxic effect or rhabdomyolysis.

It is reported that bentazone may ruin liver function tests and may lead to acute hepatitis (4,9). On the other hand, Bentazone has anticoagulant effect as toxicity (3). Our patient's aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were elevated, and PT levels that measured in INR were prolonged. Gamma Glutamyl Transferase (GGT) and hepatitis markers (Hbs-Ag, Hbs-Ab, Anti HCV

and HIV) were in normal ranges. After vitamin K therapy, patient's PT level that measured in INR and ALT levels decreased to normal ranges on the 3<sup>th</sup> and 15<sup>th</sup> days, respectively. When examined mortality associated with Bentazone, death was more frequent by intake of higher doses of Bentazone. Among these cases, 88.2 gr bentazone intake caused respiratory failure, 96 gr intake caused sudden cardiac arrest and 240 gr intake caused acute heart failure and severe muscle rigidity (7-9). In another case who took 132.3 gr of bentazone, neuroleptic malignant syndrome was detected and the patient was cured with bromocriptine therapy (4).

As a result of bentazone metabolism, it is thought that unstable OH<sup>-</sup> radicals occur. These free radicals form oxidative stress, bind to cell proteins and this process result in organ damage. In addition, Bentazone is a nephrotoxic agent as it includes benzothiadiazine acting as a diuretic. Benzothiadiazine increases the blood urea by reducing hepatic glucose production in rats and benzothiadiazine is inhibitor of oxidative mechanisms. Bentazone-induced acute renal failure may develop as a result of renal hypoperfusion due to severe vomiting, rhabdomyolysis and direct nephrotoxic effect of the agent (9,11).

In conclusion, bentazone intoxication may cause rhabdomyolysis which leads to ARF. On the other hand, direct nephrotoxic effect and hypovolemia may also cause ARF. In bentazone ingestion, renal functions should be closely followed up and hydration should be started early and immediately. With this treatment approach, patients may be discharged without need of hemodialysis.

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