

A Case Report of Fatal Oral Ingestion of Resorcinol

MEHTAP BULUT, M.D.¹, NURSEL TURKMEN, M.D.², RECEP FEDAKAR, M.D.², AND SULE AKKOSE AYDIN, M.D.¹

Abstract

Resorcinol is a pharmaceutical agent used topically in dermatological treatments for acne, eczema, psoriasis and related skin conditions. Although there are a few studies that indicate chronic toxic effects of resorcinol on humans after topical application, information on the effects of resorcinol in acute poisoning after oral ingestion is limited. Thus, we wish to report the clinical and laboratory findings of a patient who was admitted to our emergency department (ED) after inadvertent oral ingestion of resorcinol and later died, as well as the patient's autopsy findings. The major clinical and laboratory findings were unconsciousness, respiratory failure that required mechanical ventilation, generalized tonic-clonic seizures, leukocytosis and severe metabolic acidosis. In the blood sample taken at the autopsy, a high level of methemoglobin was found. In the serum, resorcinol was revealed by gas chromatography-mass spectrometry. It can be concluded that the basic approach to patients with resorcinol poisoning should include initial stabilization of the patient by supporting the airway, respiration and circulation, and treating complications such as seizures or metabolic acidosis in the ED, as soon as possible after oral ingestion.

Key Words: Resorcinol, oral ingestion, toxicity, fatal.

Introduction

RESORCINOL is a chemical used in photography and tanning, and in the manufacture of tires and other rubber products; it is a component of adhesives, hair dyes and cosmetics. Resorcinol is also a pharmaceutical agent used topically in dermatological treatments for acne, seborrhoea, eczema and psoriasis. It has been found in roasted barley, canned molasses, coffee, cigarette smoke, effluents from production of coal tar products, and waters from aquifers rich in coal and shale deposits (1).

Resorcinol is rapidly and completely absorbed following oral exposure. Studies of oral application have reported rapid absorption and excretion, mainly in the form of glucuronide and sulfate conjugates. These studies indicate rapid and extensive first-pass metabolism of resorcinol following absorption into portal blood flow (1). Resorcinol may be absorbed through the skin or the lungs. The

threshold limit value for occupational exposure is 10 ppm (45 mg/m³) in air as a time-weighted average, with a short-time exposure limit of 20 ppm (90 mg/m³) (2).

Although there are a few studies that indicate chronic toxic effects of resorcinol on humans after topical application (3–5), information on the effects of resorcinol in acute poisoning after oral ingestion is limited. Thus, we wish to report the clinical and laboratory and autopsy findings of a patient who had been admitted to our ED after an inadvertent oral ingestion of resorcinol.

Case

At 12:10 PM, a 46-year-old woman was admitted to the ED of Uludag University Medical Faculty Hospital, Bursa, Turkey with loss of consciousness and convulsions, shortly after having a glucose challenge test because of a recent high blood glucose level. Just before her transfer to our service, she had been intubated because of persistent convulsions and coma.

On her arrival, her pupils were isocoric and miotic, pupillary light reflexes were negative bilaterally, blood pressure was 110/70 mm Hg, pulse rate 120 beats/min, and temperature was 37°C. The Glasgow Coma Scale reading was 3 points. She

Department of ¹Emergency Medicine, and ²Forensic Medicine, Uludag University Medical School, Gorukle Bursa, Turkey.

Address all correspondence to Mehtap Bulut, M.D., Department of Emergency Medicine, Uludag University Medical School, 16059 Gorukle Bursa, Turkey; e-mail: mbulut94@yahoo.com

Accepted for publication May 2006.

had generalized tonic-clonic seizures and negative deep tendon reflexes. She was intubated and had spontaneous but inefficient respiration. Systemic physical examination revealed no pathology. ECG demonstrated normal sinus rhythm with a pulse rate of 120. Gastric lavage with activated charcoal (1 g/kg) was performed, since we did not know the exact time of oral ingestion, and it had not been performed in the hospital where she was originally admitted. We obtained a complete blood count: white blood cells 42,900/mm³, hemoglobin 11.8 g/dL, hematocrit 35.4%, platelets 611,000/mm³, glucose 329 mg/dL, electrolytes (Na 149 mEq/L, K 4.9 mEq/L). We also did a urinalysis (pH 6.5, protein 30 mg/dL, glucose 250 mg/dL, negative results of ketones, blood, bilirubin and nitrite), and baseline renal and liver measurements (urea 17 mg/dL, creatinine 1.2 mg/dL, aspartate aminotransferase (AST) 47 IU/L, alanine aminotransferase (ALT) 23 U/L). The first arterial blood gas levels were as follows: pH 7.021, pCO₂ 60.5 mm Hg, pO₂ 45.5 mm Hg, HCO₃ 15.3 mmol/L, base excess (BE) 16.2 mmol/L. After resuscitation, in order to eliminate the possibility of brain lesions, a cranial computerized tomography scan was performed. It did not show any pathological finding.

We were informed that resorcinol (Rezorsine, 75 g, EGAS A.S. Ankara, Turkey) had been given to the patient by a pharmacist instead of glucose, which had been prescribed for a 75 g glucose challenge test. She had been admitted to our ED 2 hours after ingestion.

The patient was supported by mechanical ventilation, due to her respiratory insufficiency. For treatment of her seizures, diazepam IV was administered, and due to recurrent seizures after diazepam, phenytoin infusion was started. We monitored acid-base balance closely. To treat metabolic acidosis, NaHCO₃ IV infusion was administered under arterial blood gas control. A central venous line was established and a Foley catheter inserted. The central venous pressure was 4 cm H₂O. Liquid support was continued with central venous pressure observation. Diuresis was performed in order to enhance resorcinol elimination from the plasma via urine. After the patient was transferred to an intensive care unit, hypotension, pulmonary edema and oliguria occurred. Metabolic acidosis was not corrected in spite of the treatments. Cardiopulmonary arrest occurred, although cardiopulmonary resuscitation was performed; as a result, the patient died at 6:00 PM.

A medico-legal autopsy was performed at the Morgue Department of the Bursa branch of the Council of Forensic Medicine of Turkey. At macroscopic examination, there were nonspecific

findings such as diffuse pulmonary edema, and evidence of the medical treatment, such as activated charcoal in the stomach. Microscopic examination revealed pulmonary edema, renal congestion, an eosinophilic substance in renal cortical tubular lumens, and hyperemia in all organs. The Toxicology Department found neither alcohol in her blood nor toxic substances in her tissue samples. Screening and identification of drugs (amphetamines, barbiturates, benzodiazepines, cannabinoids, opiates) in the urine and blood samples were also performed by cloned enzyme donor immunoassay (CEDIA), and none of them were found. In her blood, 10% methemoglobin was estimated by CO-oximetry. However, in her serum, and in the plastic cup that she had used, resorcinol was revealed by gas chromatography-mass spectrometry.

Discussion

The toxic effects of resorcinol and treatment are similar to those of phenol. Resorcinol, with a pleasant scent and a sweetish taste, is used to treat acne and similar skin conditions (2). Kim et al. reported that, following oral administration, resorcinol was readily absorbed from the gastrointestinal tract, rapidly metabolized, and excreted by male and female rats. In both sexes, most of the dose of resorcinol (more than 90%) was excreted in the urine within 24 hr after oral administration of 112 mg/kg, indicating little potential for bioaccumulation in animal tissues (6). Pharmacokinetic data on resorcinol were obtained in rat studies (2).

The human data consist of anecdotal and case reports and several epidemiology studies. The anecdotal reports refer to acute poisoning, often through attempted suicides. The case reports document sensitization reactions in occupationally exposed persons and thyroid effects in persons using dermatological ointments containing resorcinol. The epidemiology studies have focused on effects of resorcinol in occupationally exposed persons and in populations living in geographic regions where drinking water contained resorcinol and other phenolics derived from natural sources (1).

Resorcinol is of moderately acute toxicity. Acute oral lethal dose 50% (LD₅₀) values of 980 mg/kg and 300 mg/kg have been reported for rats. Death was associated with convulsions, salivation, dyspnea, emaciation, and hyperemia of the gastrointestinal tract. A single-dose dermal LD₅₀ value of 3360 mg/kg has been reported in rabbits (1). The lowest lethal dose (LDL₀) of resorcinol in humans has been reported as 29 mg/kg (2). While the LDL₀ was 2.6 g in our patient (90 kg), the ingested amount was 75 g, which could have caused an avoidable death.

In acute exposure, concentrated phenol is extremely corrosive and may cause oral, esophageal, and gastric burns following ingestion. Systemic manifestations of toxicity may include nausea, vomiting, diarrhea, dyspnea, methemoglobinemia, hypothermia, tachypnea, pallor, and profuse sweating. Hypotension and tachycardia are commonly reported (7). While our patient had only sinus tachycardia on arrival, hypotension occurred a few hours after. Tachypnea is commonly reported; pulmonary edema and bronchospasm may also occur. Respiratory arrest occurred 30 minutes after ingestion of 26.7 grams of phenol in one case. A short time after ingestion, our patient's respiration became insufficient and she had to be intubated. Her autopsy also revealed diffused pulmonary edema.

In neurologic acute exposure, initial central nervous system excitations, including seizures, are commonly followed by central nervous system depression ranging from lethargy to coma and death (7, 8). There have been reports of methemoglobinemia and acute poisoning, in some cases with fatal outcome, in children, even when limited areas were exposed to resorcinol (3). Seizures were observed in our patient in her acute exposure after oral ingestion. A major antiepileptic drug infusion was started due to the failure to stop the seizures, by administering diazepam. In the blood sample taken at the autopsy, a high level of methemoglobin was found.

Pathology reported for humans includes marked siderosis of the spleen and marked tubular injury in the kidney, fatty changes and edema of the liver, degenerative changes in the kidney, fatty changes of the heart muscle, moderate enlargement and pigmentations of the spleen, and edema and emphysema of the lungs (9). Autopsy findings in our case displayed a similarity to those noted above, especially for the kidney and lungs.

In Turkey, resorcinol is bought in kilogram bulk and then packed into small plastic packets and labeled, as is the case with glucose in some pharmacological products; this task is done by nonspecialized workers employed by the pharmacists. The similarity in packets and employee carelessness led to this medication error. In an earlier case, also in Turkey, resorcinol was mistakenly administered instead of glucose in a glucose oral test for a pregnant woman. This patient was discharged fifteen days after being admitted to the hospital, but her fetus was lost. The main reason why our patient died is that she came to our hospital too late (2 hours after oral ingestion).

According to the legal system of our country, all cases of death by poison are recorded as unnatural deaths and are subject to medico-legal au-

topsy. Thus, medico-legal autopsies are one source of reliable data on fatal poisoning cases. The punishment for responsibility for the situation in our case is stipulated in the Turkish Penal Code: if any person causes someone to die through an incautious and inattentive act, the guilty person shall be imprisoned for three to six years.

This is the first case report on fatal oral resorcinol poisoning in a woman, with clinical and laboratory findings along with autopsy findings. It suggests the need to take better precautions, such as labeling items more carefully in pharmacy, selling different items in plastic bags of different colors and employing better trained and better informed persons in the pharmacy, etc., for preventing inadvertent oral ingestion of resorcinol. However, bearing in mind that there is neither an antidote nor a specific therapy for resorcinol poisoning other than the supportive treatment, the present report suggests that the basic approach to patients with resorcinol poisoning should include initial stabilization of the patient by supporting the airway, respiration and circulation, and treatment of any complications such as seizures or metabolic acidosis in the emergency department as soon as possible after inadvertent oral ingestion. Then the patient should be transferred to the intensive care unit, to further control any life-threatening complications, as well as to observe the patient closely.

References

1. Lynch BS, Delzell ES, Bechtel DH. Toxicology review and risk assessment of resorcinol: thyroid effects. *Regul Toxicol Pharmacol* 2002; 36(2):198–210.
2. Duran B, Gursoy S, Cetin M, et al. The oral toxicity of resorcinol during pregnancy: a case report. *J Toxicol Clin Toxicol* 2004; 42(5):663–666.
3. Cassano N, Alessandrini G, Mastrodonardo M, Vena GA. Peeling agents: toxicological and allergological aspects. *J Eur Acad Dermatol Venereol* 1999; 13(1):14–23.
4. Yeung D, Kantor S, Nacht S, Gans EH. Percutaneous absorption, blood levels and urinary excretion of resorcinol applied topically in humans. *Int J Dermatol* 1983; 22(5):321–324.
5. De Groot AC, Weyland JW, Nater JP. Unwanted effects of cosmetics and drugs used in dermatology. Amsterdam: Elsevier; 1994.
6. Kim YC, Matthews HB. Comparative metabolism and excretion of resorcinol in male and female in F344 rats. *Fundam Appl Toxicol* 1987; 9(3):409–414.
7. Rumack BH, Sayre NK, Gelman CR: Phenol (Emergency Medical Treatment). In: Klasco RK, editor. POISINDEX (R) Information System (Internet database). Englewood (CO): Thomson Micromedex, Inc.; 2003. CCIS volume 118. Updated periodically. [Nov 2003].
8. American Conference of Governmental Industrial Hygienists, Inc. Documentation of the threshold limit values and biological exposure indices. 6th ed. Volumes I, II, III. Cincinnati (OH): ACGIH; 1991. p. 1335.
9. Clayton GD, FE Clayton, editors. Patty's industrial hygiene and toxicology. Vol. 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York: John Wiley & Sons, Inc.; 1993–1994. p. 1588.