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CARDIAC ARREST WITH RESIDUAL BLINDNESS AFTER OVERDOSE OF TESSALON® (BENZONATATE) PERLES

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□ **Abstract—Background: The extent to which benzonatate (Tessalon®), a structurally similar agent to other local anesthetics including tetracaine and procaine, poses a risk to the public is not fully appreciated as it is still one of the most widely prescribed antitussives available. Objectives: To report a case of cardiac arrest with residual blindness after Tessalon® overdose, review its clinical manifestations, toxicology and management considerations, and describe the need for rational prescribing. Case Report: A 17-year-old woman with no previous medical history presented to the Emergency Department (ED) status post cardiac arrest. One to two hours prior, the patient had ingested at least 10 200-mg Tessalon® capsules as part of a suicide attempt. The patient was sedated, intubated, and given magnesium as prophylaxis against recurrent dysrhythmias. Emergent gastric lavage was performed and well tolerated. A 24-h hypothermia protocol with 6-h cooling period was initiated. Toxicological studies, chest radiograph, and a computed tomography scan of the head were all unremarkable. The patient was admitted to the Pediatric Intensive Care Unit for further work-up and supportive care. The patient was extubated and able to follow some commands 1 week post-admission. The patient developed blindness and experienced generalized confabulations, which did not resolve. Conclusion: Ingestion of Tessalon®, a seemingly innocuous and widely prescribed antitussive, may pose a risk to patients due to its potential for the rapid development of life-threatening adverse events and limited treatment options in the overdose setting. Rational prescribing and patient education is needed. © 2011 Elsevier Inc.**

□ **Keywords— Tessalon®; overdose; survival; clinical manifestations; management; rational prescribing**

INTRODUCTION

Benzonatate was first synthesized in 1956 and first licensed as a cough suppressant in 1958 (1). Benzonatate is a peripherally acting antitussive that directly anesthetizes the vagal stretch receptors in the respiratory passages, lungs, and pleura (1). It is a long-chain polyglycol derivative chemically related to the ester-linked class of drugs such as procaine and tetracaine (2,3). In the United States, benzonatate is marketed under the brand name Tessalon® Perles (Forest Pharmaceuticals, St. Louis, MO) and is available generically as 100- and 200-mg liquid-filled oral gold-color perles. Benzonatate is licensed in the United States, Mexico, and Hungary, but not in Canada or the remainder of Europe (3). Outside of the United States, benzonatate is sold under 23 other brand names and is available in rectal, intravenous, and subcutaneous formulations (4). The recommended dose for adults and children older than 10 years is 100 to 200 mg orally three times daily as needed, with a maximum daily dose of 600 mg (5). Its onset of action is 15–20 min, with a duration of action of 3–8 h (4,5). Adverse effects include nausea, dizziness, headache, sedation, and somnolence (5). Serious reactions such as broncho-

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spasm, laryngospasm, and cardiovascular collapse resulting in death due to overdose have been reported (6,7).

The extent to which benzonatate poses a risk to the public is not fully appreciated. It is one of the most widely prescribed antitussives, yet cardiopulmonary arrest may rapidly develop after over-ingestion (8). This rapid development of life-threatening symptoms may often preclude any possibility of instituting supportive measures, as often it is the case that ingestions occur at home where emergency care cannot be immediately instituted (9–15).

We describe a case of cardiac arrest with residual blindness in a woman who, in a suicidal attempt, ingested a handful of benzonatate soft gelatin capsules. A review of the current literature is provided.

CASE REPORT

A 17-year-old woman with no previous medical history presented to the Emergency Department (ED) status post cardiac arrest resuscitated in the field. As per her family, the patient went to the bathroom to wash her face when her father heard her collapse and witnessed her seizing for 1 min. The patient's father proceeded to apply pressure to the upper lip, a Chinese remedy for convulsions, after which the seizure is believed to have abated. The patient seized twice more for periods of 11 min, as per the father, before Emergency Medical Services' arrival. Upon their arrival, the patient was placed on an automated external defibrillator, was found with no pulse in asystole, and Advanced Cardiac Life Support was initiated.

Pre-hospital providers initiated supportive measures: two doses of epinephrine 1 mg of a 1:10,000 were given, one dose of atropine 1 mg, which lead the monitor to report pulseless ventricular tachycardia that was then defibrillated. A third dose of epinephrine was administered, followed by two additional defibrillations and a dose of vasopressin 40 mg followed again by defibrillation; the patient was converted to a sinus rhythm with a pulse. Dopamine infusion and sodium bicarbonate 44 mEq/50 mL and amiodarone 300-mg intravenous boluses were administered; however, because the patient was normotensive, dopamine was subsequently discontinued. Return of spontaneous circulation was achieved, pulse was regular, and the patient was intubated for further airway management.

Upon presentation to the ED, the patient was sedated with midazolam 2 mg, paralyzed with vecuronium 10 mg for maintenance of sedation post-intubation, and given magnesium sulfate as prophylaxis against recurrent dysrhythmias. Emergent gastric lavage was performed after placement of an 18-French-gauge tube. Aspiration of gastric contents confirmed placement. Lavage was carried out using 200-mL aliquots of normal saline, which returned food particles. The procedure was well tolerated. A 24-h hypothermia protocol with 6-h cooling period was initiated. Toxicological studies were all unremarkable, including quantitative blood salicylate, acetaminophen, tricyclic, alcohol, and urine qualitative barbiturate, benzodiazepine, cocaine, cannabinoids, methadone, opiate, phencyclidine, and amphetamine/meth II studies. Further laboratory data revealed: an arterial blood gas with a pH of 6.85, pCO_2 of 46 mm Hg, pO_2 of 101 mm Hg, a bicarbonate level of 8, and 90% oxygen saturation. A Nova lactic acid level was high at $>$ 20 mmol/L (normal 0.7–2.5 mmol/L). The white blood cell count was 17.4 K/UL, hemoglobin was 11.9 gm/dL and hematocrit 36%, and platelet count was 236 K/UL. The sodium was 149 mmol/L, potassium 3.1 mmol/L, chloride 104 mmol/L, bicarbonate 8 mmol/L, and blood urea nitrogen was 14 mg/dL and serum creatinine 1.1 mg/dL, with a blood glucose of 268 mg/dL.

Chest radiograph and a computed tomography scan of the head were both unremarkable. No other medications were given. The patient was admitted to the Pediatric Intensive Care Unit (PICU) for further work-up.

On the first day of admission, the parents and an English-speaking uncle were re-interviewed. It was revealed that the patient had a minor argument with her mother on the day of presentation to the ED. An empty bottle of 200-mg Tessalon® soft gelatin capsules was found in the patient's room, which the patient had obtained from a friend for treatment of symptoms from an upper respiratory tract infection. The bottle is believed to have contained 10 or more capsules. One to two hours before cardiac arrest, the patient admitted to her friend that she had taken all the capsules simultaneously as part of a suicide attempt. No serum benzonatate levels were obtained.

Supportive care was continued in the PICU. Continuous cardiac monitoring with arterial line placement allowed for strict blood pressure control, as the patient's blood pressures had been intermittently high (maximum systolic blood pressure was 196 mm Hg). A combination of propofol and mannitol were prescribed when the hypertension was thought to be due to subclinical agitation and elevated intracranial pressure, respectively. Ultimately, the high blood pressure readings were believed to be a result of arterial line movement, as blood pressures measured using a blood pressure cuff were all normal. Propofol and mannitol were subsequently discontinued. Creatinine phosphokinase levels were initially elevated and peaked at 3842 IU/L, prompting the administration of intravenous fluids with sodium bicarbonate for urine alkalinization. The patient also became febrile during her stay in the PICU, prompting work-up for