

CASE REPORT

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Dispensing Error Causing Fatal Chlorpropamide Intoxication in a Nondiabetic

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ABSTRACT: A 38-year-old nondiabetic female developed fatal hypoglycemia when chlorpropamide (Diabinese[®]) was accidentally substituted for acetaminophen (Tylenol[®]) with codeine no. 3 in a pharmacy dispensing error. When found, the patient's serum glucose was less than 20 mg/dL. The serum chlorpropamide level on hospital admission was 124 µg/mL. The possibility of dispensing error should be considered whenever unexpected drug effects are encountered. In cases of suspected drug overdose, labels and contents of medicine vials found at the scene should be checked for discrepancy.

KEYWORDS: pathology and biology, accidents, chlorpropamide, iatrogenic injury, dispensing error, hypoglycemia

Chlorpropamide is a widely used oral hypoglycemic agent of the sulfonylurea group. The drug acts by stimulating or increasing the release of endogenous insulin from the islet cells of the pancreas. Diabetics taking chlorpropamide must possess functioning pancreatic islet cells for the drug to work. Accidental nonfatal ingestions of chlorpropamide by nondiabetics have occurred [1, 2]. Intentional fatal overdoses of chlorpropamide in nondiabetics have also been reported [3, 4]. We would like to report a case of fatal accidental chlorpropamide intoxication in a nondiabetic caused by a pharmacy dispensing error.

Case Report

A 38-year-old, single, nondiabetic female with prior suicidal ideation was discharged from the hospital following an uncomplicated bilateral tubal ligation. On discharge, her physician prescribed acetaminophen (Tylenol[®]) with codeine no. 3, one to two tablets every 4 h as needed for pain. The patient filled this prescription at a local pharmacy. She took the medicine every 3 to 4 h without relief, and indicated this fact in a diary which she kept. A grocery delivery boy who saw the patient during this time related that she was stumbling in what appeared to be a drunken stupor. On the third day following hospital discharge, concerned neighbors forced entry to her apartment and found her unconscious on the floor. They noted

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a medicine vial labelled "Tylenol #3" and another vial containing acetaminophen (Pana-dol®) near her body.

Paramedics responded and found the patient unconscious with pale dry skin. The pulse was 76; the blood pressure, 130/90 mm Hg; the respirations, 24. A Chemstrip® test for glucose showed a level of 20 mg/dL in the blood. Paramedics drew a blood sample, administered 50 cm³ of 50% dextrose intravenously and 0.4 mg of naloxone hydrochloride (Narcan®) intravenously, and transported her to the hospital.

On admission to the hospital the patient was in coma, unresponsive to deep pain, and incontinent. Her pupils were dilated. Emergency room personnel inspected the vial marked "Tylenol #3" and found it to contain blue, D-shaped chlorpropamide (Diabinese®) tablets. They administered naloxone hydrochloride and 50% dextrose intravenously without response.

Analysis of the blood sample drawn by paramedics before treatment revealed a serum glucose of less than 20 mg/dL. The sodium was 135 meq/L, the potassium 4.0 meq/L, the chloride 106 meq/L, and the bicarbonate 27 meq/L. The urea nitrogen was 15 mg/dL, the creatinine 1.1 mg/dL, the calcium 8.3 mg/dL, and the phosphorus 1.9 mg/dL. The white cell count was $14.0 \times 10^9/L$ with 90% neutrophils. Urinalysis revealed a specific gravity 1.025, pH 6, 1+ protein, and 2+ occult blood. A chest X-ray showed an infiltrate in the right upper lobe of the lung. Physicians treated the patient with intravenous glucose, positive pressure ventilation, mannitol, steroids, antibiotics, hyperalimentation, and anticholinergic agents. They also administered acetylcysteine (Mucomyst®) because of the possibility of acetaminophen intoxication. The creatine phosphokinase, lactate dehydrogenase, and glutaminoxalic transaminase were elevated during the hospitalization and this was felt to be the result of muscle lysis caused by pressure during coma. The patient expired on her eighth day of hospitalization.

At autopsy, the brain was dark, dusky, and fell apart upon removal. The pathologist also noted bilateral bronchopneumonia and the recent tubal ligation. The liver and pancreas showed no abnormalities. Toxicologic studies performed on the hospital admission blood sample showed the following: chlorpropamide 124 µg/mL, acetaminophen negative. Post-mortem blood showed 23 µg/mL of chlorpropamide.

Further investigation revealed that the pharmacist had substituted chlorpropamide for the prescribed acetaminophen with codeine no. 3 when the prescription was filled. The error apparently occurred because he was filling another patient's prescription for chlorpropamide at the same time. The container labelled "Tylenol #3" was rinsed with methanol and the effluent was found to be negative for acetaminophen and opiate residues.

Discussion

Peak plasma concentrations after a single oral dose of 200 to 250 mg of chlorpropamide range from 20 to 30 µg/mL [5,6]. Plasma levels in four diabetics receiving daily doses of 250 to 500 mg of chlorpropamide ranged from 76 to 246 µg/mL [7]. Severe hypoglycemic effects of chlorpropamide in nondiabetics are seen at plasma concentrations of 200 µg/mL [8]. The initial plasma concentration of chlorpropamide in an intentional fatal ingestion by a nondiabetic was 700 µg/mL [4]. Recovery after treatment occurred in a 19-year-old female nondiabetic who showed an initial plasma concentration of 1100 µg/mL following ingestion of 150 100-mg tablets [9]. The normal plasma half-life of chlorpropamide is 25 to 42 h [7]. Chlorpropamide half-lives of up to 72 h have been reported in two overdose cases [3,8].

Initially, this case appeared to be an intentional overdose. Further investigation revealed that the pharmacist had accidentally substituted chlorpropamide for the prescribed acetaminophen with codeine no. 3 when the prescription was filled. The error was discovered when emergency room personnel checked the contents of the medicine vials found at the scene against their labels. The blue, D-shaped chlorpropamide tablets found bear little resemblance to the white, round acetaminophen with codeine no. 3 tablets prescribed (Fig. 1).

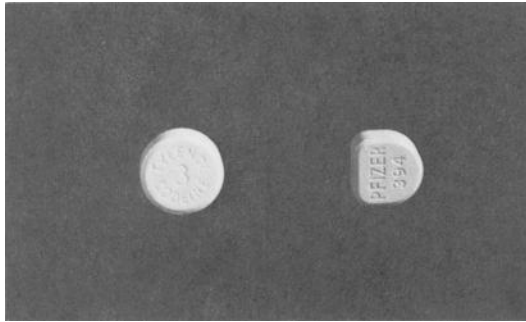


FIG. 1—Note the striking dissimilarity between the prescribed acetaminophen with codeine no. 3 tablet (left) and the blue, D-shaped chlorpropamide tablet (right) which was dispensed.

Pharmacy errors in dispensing are not uncommon and this possibility needs to be considered whenever unexpected drug effects are encountered. In a 12-day study involving the filling of 9394 prescriptions, 1165 dispensing errors were noted, including 141 which were considered potentially serious [10].

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