

Dextromethorphan Poisoning Reversed by Naloxone

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Dextromethorphan, a common ingredient in cough syrups, has rarely been described to cause toxicity. The authors describe an unusual case of a known asthmatic presenting with somnolence, who appeared to be in ad-stage respiratory failure. Her partial response to routine naloxone, 1 M, was surprising. However, additional naloxone was required to completely normalize the patient's mental status. The authors suggest naloxone be administered in doses of 0.4 mg or more intravenously in inspected dextromethorphan overdose. (Am J Emerg Med 1991;9:237-18. Copyright © 1991 by W.B. Saunders Company)

Dextromethorphan, a common ingredient in many cough syrups, is considered one of the most effective cough suppressants commercially available. Dextromethorphan is the methylated dextro-isomer of levorphanol, a codeine analog. Because dextromethorphan is an opioid derivative of morphine, naloxone hydrochloride (Narcan, DuPont Pharmaceuticals, Wilmington, DE) should be an effective antidote. We describe successful naloxone reversal of central nervous system (CNS) depression in an adult patient after overdose with a dextromethorphan containing cough medication.

CASE REPORT

A 41-year-old black woman with a long standing history of asthma including frequent acute exacerbations called the paramedics because of increasing shortness of breath and cough. Her medications included Theo-Dur, (Key Pharmaceuticals, Kenilworth, NJ) 300 mg three times a day, and a tapering course of prednisone, begun on her emergency department (ED) visit 4 days earlier. The family reported the patient was unable to sleep the night prior to presentation.

On arrival, the paramedics found her to be lethargic, but arousable to painful and verbal stimuli. Her best verbal responses were only 3-word sentence fragments. Initial vital signs included blood pressure, 160/100 mm Hg, pulse rate, 120 beats/min; shallow respirations, 40 breaths/min. A presumptive diagnosis of acute asthma exacerbation was made. An albuterol aerosol via nebulized face mask was promptly initiated by the paramedics at the scene. During the 5-minute transport to the receiving facility, the patient's level of consciousness deteriorated and her respiratory rate decreased. On arrival at the ED, the patient was lethargic and responsive only to

painful stimuli. Respirations were shallow and sporadic with a rate of 30 breaths/min. Bilateral wheezing was noted on chest auscultation. Breath sounds were symmetric with no audible rales. Accessory use of abdominal muscles were also visible. Pupils were pinpoint and minimally reactive to light. Neurological examination did not show other localizing signs. Examination of the skin indicated no evidence of old or recent needle marks. Radiographic examination of the chest showed plate-like atelectasis at the left base and the electrocardiogram (ECG) was unremarkable. Complete blood count (CBC) electrolytes, blood urea nitrogen (BUN), creatinine, and glucose levels were all within normal limits. An arterial blood gas on 2 liters nasal canula showed a pH of 7.40, a pCO₂ of 32 mm Hg, and a pO₂ of 88 mm Hg.

Because of her decreased level of consciousness and pupillary miosis, 1 mg of intravenous (iv) naloxone was administered in the ED. After approximately 3 minutes, the patient's level of consciousness was noted to improve. Due to this partial response, an additional 2 mg of naloxone iv was administered, followed by a continued improvement in the patient's mental status. On awakening, the patient denied any recent opioid use. She did report, however, that she had taken frequent doses of Robitussin-DM (A.H. Robins, Richmond, VA) (15 mg dextromethorphan / 1 tsp) the preceding 36 hours, completely ingesting two 120 mL bottles (720 mg of dextromethorphan). Serum samples sent for toxicological analysis from the ED showed a serum dextromethorphan level of 100 ng/mL. Trace levels of phenobarbital (<4.5 µg/mL), phenytoin (<2.2 µg/mL), and carboxyhemoglobin were also detected in the serum. No other narcotic agents were found in the toxicology screen.

The patient remained awake, alert, and oriented after admission to the hospital. No further naloxone was given during her hospital course. Intravenous steroids and aminophylline were both initiated in the ED. The total hospital stay was 4 days without complications. The patient was discharged on oral antibiotic therapy for a presumed bronchitic infection.

DISCUSSION

Although dextromethorphan is a major ingredient in countless nonprescription cough and cold remedies, it has rarely been reported toxic in humans. However, it is important to remember that an overdose of this relatively innocuous medication may result in significant toxicity with signs typical of opioid ingestion, such as pinpoint pupils and CNS depression. Katona and Wason¹ described a 3-year-old boy who had taken 18 Mediquell cough squares (Parke-Davis, Morris-Plains, NJ) (270 mg of dextromethorphan) and presented with lethargy, ataxia, and nystagmus. Dodds and Revai² described a toxic psychosis secondary to dextromethorphan. Two fatal cases were reported by Rammer et al³: an 18-year-old woman and a 27-year-old man each ingested an unknown quantity of the drug. Postmortem examination showed serum dextromethorphan levels of 9.2 and 3.3 ng/g respectively. These high levels were believed to represent the loss of liver metabolism.

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Dextromethorphan is rapidly metabolized by the liver to the active metabolite dextrorphan⁴ generally reaching peak levels in 2 hours. However, 10% to 20% of individuals are "slow" dextromethorphan metabolizers and may show higher serum concentrations of free drug (personal communication, July 1990, S. O'Connell, Bristol-Myers Products). Peak serum-free drug levels after a 20 mg oral dose of dextromethorphan are below 2 ng/mL in normal metabolizers. However, in "slow" metabolizers, levels may be as high as 8 ng/mL.⁵ Using linear kinetics, the oral dose of 720 mg taken by our patient should have resulted in a serum level of 70 to 140 ng/mL if taken as a bolus dose (personal communication, July 1990, S. O'Connell, Bristol-Myers Products). This level might be higher if our patient were a "slow" metabolizer. However, the predicted level does correlate well with actual level of 100 ng/mL. We have been unsuccessful in determining the time from the last dose of dextromethorphan to the blood level in our patient.

Dextromethorphan acts centrally to elevate cough threshold. It has a minimal respiratory depressant effect and little analgesic activity. Overdoses usually result in a moderate degree of sedation. Dextromethorphan's effects on pupillary function are identical to other opioids. They are implemented by diminishing supranuclear inhibitory influences at the pupilloconstrictor resulting in miotic but reactant pupils.⁶

Use of naloxone as an antidote for dextromethorphan has not been well described. We were able to find only one case report by Shaul et al⁷ in which naloxone reversed the toxicity in a 22-month-old girl who had ingested 360 mg of dextromethorphan. The total dose of naloxone given parenterally was 0.005 mg/kg. Current recommendations are to administer 0.4 to 2.0 mg IV and repeat the dose every 2 to 3 minutes as needed to a total dose of 10 mg.⁸ This dose of naloxone is similar to that used in other opioid overdoses. All symptomatic patients who respond to naloxone should be observed for at least 4 to 6 hours. Continuous IV infusion of naloxone may be required in cases in which long-acting preparations of dextromethorphan are involved. Gastric decontamination is also recommended after an acute ingestion of greater than 10 mg/kg.⁸ Activated charcoal and/or gastric lavage may be preferable to syrup of ipecac in drowsy patients or if the time from ingestion is greater than 15 minutes.⁸

The toxicological results were verified despite the patient's denial of additional drug ingestion. Because dextromethorphan was found in the sample, it appears unlikely that the samples were switched with another patient's blood. Therefore, one must consider the history obtained from the patient may have been inaccurate. The majority of the nonfatal ingestions reported have been in children, manifested by ataxia and somnolence. Our patient presented with CNS depression and respiratory failure, without prior evidence of psychosis or ataxia. The only other sign of opioid toxicity was the presence of pinpoint pupils. Initial therapy with naloxone was empiric, and the dramatic response was unexpected. Only in retrospect did we uncover the ingestion of dextromethorphan. This case, however, reminds us of the usefulness of an empiric naloxone trial in the comatose patient particularly with pinpoint pupils and respiratory depression.

CONCLUSION

We conclude that naloxone can antagonize the CNS and respiratory depressive effects of dextromethorphan. We recommend that the dose of naloxone for dextromethorphan-induced CNS depression be liberal, starting at 0.4 to 1.0 mg, IV in the adult with 2 to 3 minute dosing repetition as needed.

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