

Dextromethorphan anaphylaxis

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Dextromethorphan is a widely used, highly effective, and relatively safe nonopioid antitussive drug.^{1,2} It is available without prescription as a single medication or in combination with other common cold remedies used for symptom relief. Adverse reactions are infrequently reported and usually are not severe. Most symptoms are dose-related and can include nausea, constipation, diarrhea, drowsiness, slurred speech, and ataxia. To date, there have been no reports of severe systemic anaphylactic/anaphylactoid reactions associated with therapeutic doses of dextromethorphan.

In this report we describe a patient who had anaphylactic-type symptoms after ingestion of a dextromethorphan-containing compound. Investigation and subsequent management of this patient is also presented.

CASE REPORT

A 40-year-old woman was seen in consultation at the Drug Safety Clinic for recurrent reactions to cough and cold preparations. Although she could not provide the specific names of each of these combination products, she believed that they all contained dextromethorphan as the active cough suppressant. Her reactions consisted of hives, lip swelling, and shortness of breath. None had become severe enough to warrant an emergency department visit, but she had begun to avoid dextromethorphan. As an alternative cough preparation, her physician prescribed hydrocodone (eg, Hycodan or Robidone), and she had no further adverse reactions. There was no past history of asthma, urticaria, or seasonal allergies. She was unaware of any prior exposure to codeine, oxycodone, or hydromorphone (eg, Dilaudid).

Our testing procedure on this patient consisted of a two-dose dextromethorphan oral challenge. After the initial 1 mg of dextromethorphan, the patient noted mild transient pruritus of her eyes. This was followed by hives and nasal and conjunctival congestion 20 minutes after the full-dose oral challenge with 30 mg dextromethorphan. There was no bronchospasm or angioedema, and her vital signs and peak flow remained stable. Oral diphenhydramine quickly reversed her symptoms without need for adrenaline. The patient subsequently tolerated hydrocodone and codeine without any adverse effects. Skin testing to dextromethorphan was refused by the patient.

DISCUSSION

Dextromethorphan is the methylated dextrorotatory analogue of levorphanol, which is a phenanthrene derivative. Dextromethorphan acts centrally in the medulla oblongata by elevating the cough threshold. Unlike other phenanthrene derivatives, such as codeine or morphine, dextromethorphan has no analgesic, euphoriant, or physical dependence-producing properties.² This adds to its popularity and widespread use in various age groups. In a review of spontaneous adverse event reports,² psychiatric (eg, depression or hallucinations) and central nervous system reactions were reported most frequently (29% and 25%, respectively), followed by skin (9%), gastrointestinal (7%), and cardiovascular (5%) disorders. There are no reports of anaphylaxis to dextromethorphan.

Our patient described the development of hives, angioedema, and shortness of breath, consistent with an IgE-mediated reaction, after ingestion of various cough and cold preparations. Cough and cold products commonly contain ingredients such as an antihistamine, expectorant, decongestant, cough suppressant, and/or analgesic/antipyretic. Therefore it can be difficult from history alone to ascertain which ingredient may be responsible when a patient has an adverse event. The decision was made to challenge our patient initially to dextromethorphan, as this was common to a number of cough and cold preparations to which she had reacted.

Because many of the opioids are potent histamine releasers, most reactions are anaphylactoid rather than IgE-mediated. The propensity for various opioids to cause histamine release is not based on structural class.³ Although there are published case reports describing IgE-mediated reactions to opioids,⁴ cross-reactivity among narcotics has not been well studied. In one study⁴ positive skin test results suggested cross-reactivity between fentanyl, alfentanil, sufentanil, and possibly meperidine, all of which are phenylpiperidine derivatives; morphine was well-tolerated. On the basis of similarities in the chemical structures of phenanthrene derivatives, such as codeine, hydrocodone, and oxycodone (Fig. 1), logic would dictate that the safest approach is avoidance of all chemically related compounds in patients who have anaphylactic reactions to any one of them. It is therefore of particular interest to note that our patient was able to tolerate hydrocodone and codeine subsequent to her dextromethorphan reactions. Therefore our recommendation to this patient was to avoid all dextromethorphan- and levorphanol-contain-

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I. Phenanthrene Derivatives

codeine

hydrocodone

hydromorphone

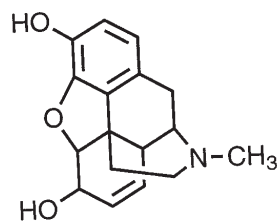
levorphanol

morphine

oxycodone

oxymorphone

opium alkaloids (Pantopon)



morphine

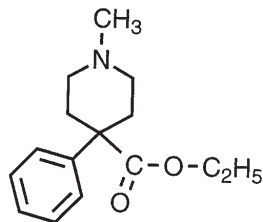
II. Phenylpiperidine Derivatives

anileridine

fentanyl

meperidine

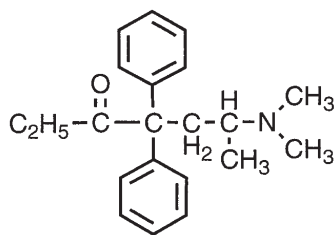
sufentanil



meperidine

III. Diphenylheptane Derivatives

methadone



methadone

FIG. 1. Structural classification of narcotic analgesics.

ing compounds (eg, Levo-Dromoran) but not all other phenanthrene derivatives.

This case illustrates a significant systemic reaction to a commonly used and presumably safe active ingredient in over-the-counter cough and cold preparations. It emphasizes the need to test each active component independently even if it has never previously been implicated in a significant adverse drug reaction. Compounds of similar chemical structure may need to be avoided in patients who have an immunologically mediated reaction, but further testing may allow future use of individual members of chemically similar families.

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