Abuse of Coricidin HBP Cough & Cold tablets: Episodes recorded by a poison center

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Abstract: Cases involving ingestion of a dextromethorphan-containing product recorded at a poison control center were studied.

A retrospective review of all consultations involving the ingestion of Coricidin HBP Cough & Cold tablets recorded by the California Poison Control System was conducted for the period from January 1 to October 1, 2000. Computerized charts on the consultations were reviewed to obtain data on patient age and sex, number of tablets taken, reason for tablet ingestion, symptoms, treatment, disposition, and outcome.

A total of 92 charts (for 92 patients) documenting Coricidin HBP Cough & Cold tablet ingestion were reviewed. The reason for tablet ingestion was classified as abuse in 65 patients (71%), a suicide attempt in 8 (9%), misuse in 1 (1%), malicious administration in 1 (1%), and normal use (but with an adverse drug reaction) in 1 (1%); 16 patients (17%) consumed the tablets for an unknown reason. The 92 patients comprised 42 males and 50 females. Among all patients, 78 (85%) were 13–17 years old, and among those classified as having abusive intent, 58 (89%) were in the same age range. The most commonly reported signs and symptoms associated with ingestion were tachycardia (50 patients), hypertension (29), lethargy (40), mydriasis (20), agitation (15), ataxia or dizziness (20), and vomiting (9). Sixty-one patients (66%) had some alteration in mental status. Fifty-six (61%) were treated in the emergency department; 11 (12%) were admitted. All patients recovered completely.

Information on the ingestion of Coricidin HBP Cough & Cold tablets recorded at a poison control center indicated a high rate of abuse of the product among teenagers.

Index terms: Adolescents; Antihistamines; Antitussives; Chlorpheniramine maleate; Dextromethorphan hydrobromide; Dosage; Drug abuse; Poisoning; Toxicity

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Dextromethorphan is present in many nonprescription cough-and-cold products. At its recommended dosage, dextromethorphan is a safe and effective cough suppressant with minimal adverse effects.[1] However, it can have euphoric effects at high dosages, and recreational abuse has been reported with mail-order dextromethorphan powder[2] and with the dextromethorphan-containing products Robitussin-DM[3] and Vicks Formula 44 D.[4] In February 2000, the Cincinnati Poison Control Center reported a trend among teenagers of ingesting large amounts of Coricidin HBP Cough & Cold tablets (dextromethorphan hydrobromide 30 mg and chlorpheniramine maleate 4 mg per tablet; Schering-Plough, Kenilworth, NJ) to obtain a "high" like that attained with lysergic acid diethylamide.[5] That report prompted us to evaluate cases involving ingestion of Coricidin HBP Cough & Cold tablets recorded at a poison control center.

Methods

A retrospective review of all consultations involving the ingestion of Coricidin HBP Cough & Cold tablets recorded by the California Poison Control System (CPCS) was conducted for the nine-month period from January 1 to October 1, 2000. CPCS is a 24-hour emergency telephone-consultation service providing evaluation of poisonings and treatment advice to health care professionals and the public. CPCS receives approximately 325,000 calls a year. The CPCS staff generates a computerized chart for each consultation, in accordance with the criteria of the American Association of Poison Control Centers.[6] All such charts for calls regarding Coricidin HBP Cough & Cold tablets during the study period were evaluated, and

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information was compiled on patients' age and sex, number of tablets taken, coingestants, reason for tablet ingestion (as defined by the American Association of Poison Control Centers[6]), symptoms, treatment, disposition, and outcome. Charts were excluded if consultations were for drug information only, if patients were younger than five years, or if Coricidin HBP Cough & Cold tablet ingestion was the result of a therapeutic error. Both authors independently reviewed all charts for this information.

Results

A total of 100 charts involving Coricidin HBP Cough & Cold tablet ingestion were identified. Eight charts were excluded from further study—four because the consultations were for drug information only, two because the patients were younger than five years, and two because ingestion resulted from a therapeutic error. The remaining 92 charts (for 92 patients) were included in the study. During the study period, CPCS received approximately 240,000 calls.

The reason for Coricidin HBP Cough & Cold tablet ingestion was classified as abuse (a probable attempt to gain a euphoric or other psychotropic effect) in 65 patients (71%), a suicide attempt (self-destructive or manipulative exposure) in 8 (9%), misuse (intentional improper or incorrect use for reasons other than the pursuit of a psychotropic effect) in 1 (1%), malicious administration (result of another person's intent to inflict harm) in 1 (1%), and normal use (but with an adverse drug reaction) in 1 (1%); 16 patients (17%) consumed the tablets for an unknown reason. Seventy-four patients (80%) were recorded as ingesting Coricidin HBP Cough & Cold tablets only, but 18 (20%) coingested at least one other substance. These substances included ethanol in 9 patients (10%), marijuana in 8 (9%), and cocaine, Drixoral (specific preparation unknown), chlordiazepoxide, pseudoephedrine, acetaminophen, dextromethorphan–guaifenesin, trifluoperazine, or caffeine in 1 patient (1%) each.

The 92 patients comprised 42 males (46%) and 50 females (54%). Ages ranged from 11 to 65 years (mode, 14 years). Among all patients, 78 (85%) were 13–17 years old, and among those classified as having abusive intent, 58 (89%) were in the same age range (Table 1). Patients most frequently ingested 8 or 16 Coricidin HBP Cough & Cold tablets (range, 2–60 tablets). This product is sold in boxes containing two cards of eight tablets each. It appears that a majority of adolescents abusing the product ingested the entire contents of one or two cards.

The most commonly reported signs and symptoms associated with ingestion of the tablets were tachycardia (50 patients), hypertension (29), lethargy (40), mydriasis (20), agitation (5), ataxia or dizziness (20), vomiting (9), confusion (16), elevated temperature (8), dry mouth (6), slurred speech (5), and hallucinations (3); 61 patients (66%) had some alteration in mental status. Fifty-six patients (61%) were treated in a hospital emergency department, usually with activated charcoal; 11 patients (12%) were admitted. Three patients received benzodiazepines for agitation. One patient who had ingested multiple medications—one of which contained acetaminophen—had an elevated serum acetaminophen concentration and was admitted for acetylcysteine treatment. All patients were reported as having a full recovery, with no permanent disability.

Discussion

Dextromethorphan is known among teenagers as a drug of abuse. Slang terms for Coricidin HBP Cough & Cold tablets or dextromethorphan include "CCC," "robo," "red devils," "poor man's PCP," "DXM," and "Dex."[7] Many Web sites advise viewers how to obtain, extract, and use dextromethorphan for euphoria.[8-10] Some Web sites list specific nonprescription dextromethorphan-containing products for abuse purposes.[11,12] Others discuss the abuse of Coricidin HBP Cough & Cold tablets, describe the effects of an excessive dose,[13] or outline the potential dangers arising from the tablets' inclusion of chlorpheniramine.[14-16] It seems that Coricidin HBP Cough & Cold tablets are abused because of their high dextromethorphan content, not because they contain chlorpheniramine.[5,13]

Dextromethorphan is the dextrorotatory isomer of the codeine analogue levorphanol. Dextromethorphan acts as an antitussive by stimulating opiate σ-receptors; it does not produce other typical opi-

Table 1.
Age Distribution of Patients for Whom a Consultation Was Requested for Ingestion of Coricidin HBP Cough & Cold Tablets

Age (yr)	No. (%) Patients in All Consultations (*n* = 92)	No. (%) Patients with Abusive Intent (*n* = 65)
11	2 (2)	1 (2)
12	3 (3)	1 (2)
13	8 (9)	7 (11)
14	30 (33)	23 (35)
15	18 (20)	11 (17)
16	12 (13)	9 (14)
17	10 (11)	8 (12)
18	4 (4)	3 (5)
19	2 (2)	1 (2)
20	1 (1)	1 (2)
30	1 (1)	0 (0)
65	1 (1)	0 (0)

ate effects, like analgesia and respiratory depression, at recommended dosages.[17] Dextromethorphan is converted by hepatic cytochrome P-450 (CYP) isoenzyme 2D6 to dextrorphan, and this metabolite, like phencyclidine, binds to and blocks *N*-methyl-D-aspartate (NMDA) receptors, which can result in euphoria, dysphoria, hallucinations, or hyperactive behavior.[18] Dextromethorphan has also been shown in animal studies to bind to NMDA receptors, but dextromethorphan and dextrorphan differ in their psychopharmacologic profiles. In a study comparing the behavioral effects of the two agents in rats, only dextrorphan had true phencyclidine-like properties.[19] A study in rats and rhesus monkeys found that phencyclidine-like effects were produced more reliably by dextrorphan than dextromethorphan.[20] In acute overdosage in humans, dextromethorphan may cause nausea, vomiting, dizziness, drowsiness, ataxia, lethargy, slurred speech, nystagmus, mydriasis, euphoria, tachycardia, hypertension, urinary retention, stupor, hallucinations, hysteria, agitation, or coma.[21] Classic opiate effects, such as miosis and respiratory depression, are not commonly seen. Cases of dextromethorphan-associated toxic psychosis[4] and mania[22] have been reported.

Dextromethorphan has been used in nonprescription products for over 30 years. It was originally available in Romilar tablets, but that product was withdrawn from the market because of an abrupt upswing in sales resulting from abuse. Dextromethorphan was later combined with other drugs to discourage abuse,[23] and the chlorpheniramine in Coricidin HBP Cough & Cold tablets can be problematic when the tablets are abused. Chlorpheniramine, an alkylamine that antagonizes histamine H_1-receptors,[17] produces anticholinergic effects, and intoxication can cause agitation, hallucinations, confusion, sedation, coma, seizures, hypertension, tachycardia, hyperthermia, mydriasis, dry flushed skin, decreased gut motility, and urine retention.[24] In fact, many of the clinical manifestations of chlorpheniramine and dextromethorphan overdosage are identical, and the signs and symptoms recorded in the CPCS charts most likely resulted from both dextromethorphan and chlorpheniramine.

Because of the genetic polymorphism of CYP 2D6, individuals are either slow or extensive metabolizers of dextromethorphan. Some 7–10% of Caucasians lack CYP 2D6 and are thus unable to metabolize dextromethorphan to dextrorphan.[25,26] Individuals who are extensive metabolizers of dextromethorphan may produce more dextrorphan and have more intense phencyclidine-like effects.

Dextromethorphan is available as the hydrobromide salt. Bromide poisoning may be a concern for patients who chronically abuse large doses of dextromethorphan but is unlikely in periodic recreational abuse. Chronic bromism targets the central nervous system, gastrointestinal tract, and skin (manifested as bromoderma). Standard laboratory tests do not distinguish chloride from bromide ions, so an elevated serum bromide concentration commonly results in what appears to be an elevated chloride concentration. An apparently negative anion gap—the result of an incorrectly reported (high) chloride concentration being used in computing the gap—is a common biochemical marker in patients with bromide toxicity. Bromide intoxication was reported in a man who ingested excessive amounts of a dextromethorphan-containing product for four or five years.[27] The patient reportedly had hyperchloremia and an apparently negative anion gap (–28.5 meq/L). His symptoms included headache, lower-extremity weakness, lethargy, and eventual loss of consciousness. Whether he had pseudohyperchloremia or true hyperchloremia was not reported, but the authors suggested the use of a more specific measure of chloride detection.

Patients manifest signs and symptoms of acute bromide toxicity only rarely, because large ingestions of bromide typically cause vomiting and thus limit gastrointestinal bromide absorption. The acceptable daily intake of bromide is 1 mg/kg.[28] Coricidin HBP Cough & Cold tablets each contain 6.9 mg of bromide, so the 8–16 tablets typically ingested by abusers (55–110 mg of bromide) should produce a serum bromide concentration of 26–52 mg/dL (bromide's volume of distribution is 0.3 L/kg). Serum bromide concentrations may be useful for diagnostic purposes but are not well correlated with toxicity. When bromide is taken therapeutically for long periods, the serum concentration should not be allowed to exceed 50 mg/dL, because higher concentrations may result in bromide toxicity.[29] Periodic ingestion of 8–16 Coricidin HBP Cough & Cold tablets would not be expected to cause bromide toxicity.

Dextromethorphan dependence has rarely been reported but may be a problem among those chronically abusing dextromethorphan. Dextromethorphan purportedly has no addictive properties,[17] although there have been reports of dextromethorphan dependence and craving. Fleming[30] described a man who admitted snorting dextromethorphan powder regularly for two or three months. While hospitalized, the patient consistently craved the drug. Walker and Yatham[22] described a man who had been ingesting a dextromethorphan-containing syrup regularly for eight years. He became manic and was hospitalized. His mania rapidly resolved during the period of abstinence, but he had cravings for the syrup. Later, when he resumed taking the syrup, his manic symptoms returned, but the craving disappeared.

The long-term mental effects of dextromethorphan are unknown. Hinsberger et al.[31] described a man

who, over several months, reportedly ingested as much as 1500 mg of dextromethorphan hydrobromide at a time. Shortly after an ingestion he would develop a mania-like psychosis (lasting 24–48 hours) that was followed by depression, suicidal ideation, and insomnia. The man's abnormal mental state persisted despite periods of abstinence.

The management of acute dextromethorphan poisoning is largely supportive. Activated charcoal should be given in cases of recent ingestion. Naloxone therapy has produced inconsistent results.[21] If the exact product ingested is not known, serum acetaminophen and salicylate concentrations should be determined, since some Coricidin formulations and other dextromethorphan-containing products contain acetaminophen or aspirin. Dextromethorphan does not appear to cross-react with toxicological assays for opiates.[32] Thus, standard urine testing is not useful in detecting dextromethorphan. However, dextromethorphan has been shown to cause false-positive phencyclidine readings in urine drug screening.[33] The treatment of chlorpheniramine overdosage is also supportive. The use of physostigmine to reverse chlorpheniramine's anticholinergic symptoms is not recommended.[24]

Conclusion

Information on the ingestion of Coricidin HBP Cough & Cold tablets recorded by a poison control center indicated a high rate of abuse of the product among teenagers. The dextromethorphan and chlorpheniramine in the tablets may cause adverse effects, and bromide poisoning may result from chronic abuse.

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