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CASE REPORT

TOXICOLOGY

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Dextromethorphan Abuse Leading to Assault, Suicide, or Homicide

ABSTRACT: Dextromethorphan is a commonly encountered antitussive medication which has found additional therapeutic use in the treatment of pseudobulbar disorder and as an adjunct to opiate use in pain management. Dextromethorphan at high doses has phencyclidine-like effects on the NMDA receptor system; recreational use of high doses has been found to cause mania and hallucinations. The toxicology and pharmacology of the drug in abuse are reviewed, and the historical literature of adverse psychiatric outcomes is assessed. Five new cases of dextromethorphan intoxication that resulted in assault, suicide, and homicide are reported, together with the corresponding toxicology results. Blood concentrations ranged from 300 to 19,000 μg/L. These results are compared with typical concentrations reported in therapeutic use and impaired driving cases. Based on these findings, dextromethorphan should be considered as a potential causative agent in subjects presenting with mania, psychosis, or hallucinations, and abusers are at risk for violent and self-destructive acts.

KEYWORDS: forensic science, forensic toxicology, dextromethorphan, psychosis, suicide, intoxication

Dextromethorphan is an over-the-counter antitussive medication present in many brands of cough, cold, and flu preparations, such as Robitussin, Coricidin, Benylin, and others (1). It is also the subject of renewed therapeutic interest as an adjunct to opiate use in pain management (2) and has been proposed as a possible rapidly acting antidepressant (3). The antitussive effects are believed to be mediated through the sigma receptor group, which has affinity for opioid antitussives such as codeine (4). Both dextromethorphan and its major metabolite dextrorphan have agonist activity at the phencyclidine (PCP)-1 receptor in the *N*-methyl-D-aspartate (NMDA) complex. When taken in significant excess, dextromethorphan produces hallucinogenic and dissociative effects similar in nature to PCP and ketamine. In the drug user community, dextromethorphan goes by the names Red devils, Robo, Skittles, Triple C's, Dex, and DXM. Dextromethorphan metabolism is mediated through the isoenzyme group CYP2D6, which is subject to genetic polymorphism, which may result in impaired metabolism and accumulation of the drug, leading to toxicity (5).

There is a significant Internet drug subculture regarding the recreational use of dextromethorphan, discussing and promoting the intoxicating and hallucinogenic effects of the drug, including out-of-body experiences which can be achieved by increasing dose levels through four "plateaus" to achieve the ultimate dissociative high (6). These plateaus, which have been related to dose amounts by user self-reports, correspond to different levels of altered consciousness. The first plateau (1.5–2.5 mg/kg) is described by users as causing mild stimulant and perceptual effects similar to MDMA (Ecstasy) (http://www.dextroverse.org/whatis.html, accessed May 29, 2011). The second plateau (2.5–7.5 mg/kg) may cause effects similar to those experienced with the co-ingestion of marijuana and ethanol including a more profound impairment of perceptual, cognitive, and motor functions than either drug alone (7). Mild hallucinations allegedly begin at this dosing level. In the third plateau (7.5–15 mg/kg), users report experiencing strong hallucinations, described as similar to low doses of ketamine. The fourth and highest plateau (>15 mg/kg) is described as the highest level, and effects are reportedly comparable to high-dose ketamine use. At this level users claim to have experienced complete mind/body dissociation (6). This dissociative state can result in violent behavior causing harm to the user or to bystanders. Diagnosis of the condition may be based on history, self-report, and circumstantial evidence. As demonstrated in the cases reported here, blood toxicological concentrations may also be helpful in assessing the degree of ingestion.

We describe a series of cases in which individuals abusing dextromethorphan became involved in violent or harmful behaviors. In contrast to previous reports, blood concentrations of dextromethorphan were measured to provide context to toxicological measurements made in future cases. Following the case reports, we review and discuss the various adverse psychological effects of the drug including psychosis, dissociation, and mania described in the literature since the 1960s.

Methods

The cases described were submitted in the course of routine criminal or death investigations and submitted for toxicological

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analysis at a laboratory accredited by the American Board of Forensic Toxicology. Samples were tested for the presence of alcohol and other volatiles by gas chromatography, for selected drug classes by enzyme multiplied immunoassay technique, and for acidic and basic drugs by gas chromatography mass spectrometry. Drugs identified by screening were confirmed and quantified by gas chromatography with nitrogen phosphorus detection. Drug concentrations outside the verified calibration range were re-extracted on appropriate dilution and re-analyzed. Procedures are described in detail elsewhere (8,9). Case information and investigative details were provided by the authors from the corresponding coroner or medical examiner's office. Autopsies were performed on all decedents (subjects A, F, M, and N). Samples were peripheral blood in each case. In the case narratives, users frequently talk about ingestion of numbers of dextromethorphan or Coricidin® pills (Merck & Co. Inc., Whitehouse Station, NJ). These come in various formulations and typically contain between 10 and 30 mg of dextromethorphan hydrobromide.

Case Reports

Case 1

Subject A was a 31-year-old man, sporadically employed in the software industry and heavily immersed in dextromethorphan-related drug culture. He lived in a rented apartment with his girlfriend (subject B, woman aged 18). After meeting in Internet chat rooms promoting recreational dextromethorphan culture and use, two other subjects C (man, aged 23) and D (woman, aged 30) relocated from Colorado and Nevada to Washington State where the four shared an apartment.

All four subjects engaged in intensive dextromethorphan use in the apartment over a period of 12 months. Their pattern of use was to ingest pure dextromethorphan purchased over the Internet in gelatin capsules at doses of 600–900 mg. A single gelatin capsule typically contains 200–300 mg of material. They supplemented this with use of over-the-counter dextromethorphan-containing products.

Over time, subject D became less engaged in drug use and moved out, relating that she feared for her life because of the unpredictable behavior of A and B during their periods of intoxication.

Two weeks after D's departure, the following incident occurred. Subjects A, B, and C ingested intoxicating amounts of dextromethorphan and watched videos of "The Matrix" and "The Matrix Reloaded." During the movie, A began hitting his head on the floor, yelling "Let me through," moving around the apartment, punching holes in the drywall, and hitting his head on the wall, damaging the drywall. During this period of agitation, he stated "they're in the walls," or "I've got to get them out" alluding to scenes from the movie. During this time, B and C attempted to calm A, but he became withdrawn and nonresponsive. He moved to the kitchen, picked up a kitchen knife with an eight-inch blade, and began cutting himself on the arms and chest. B followed him to the kitchen where he hugged her, and during the embrace, drove the knife into her neck/shoulder, and then stabbed himself in the chest. C summoned paramedics, who on arrival with police, found A dead and B seriously wounded, although she would later recover. C remained in the apartment, but was completely free from any blood at the time aid arrived, suggesting he had not had any contact with the scene or subjects, who were heavily bloodied.

Blood was collected from subjects A and C and submitted for toxicology testing. A's blood dextromethorphan concentration (postmortem, peripheral) was 4740 μg/L, and C's (living subject, whole blood) was 300 μg/L. C survived the incident and would later say that they had ingested about 950 mg of dextromethorphan.

Autopsy of A showed two penetrating stab wounds to the chest, 1 inch deep and the other 4 inches deep. There were eight superficial incised wounds across the chest and eight superficial puncture wounds to the chest. The cause of death was ruled as multiple stab wounds to the chest and acute dextromethorphan intoxication. The manner of death was suicide. No criminal charges were filed in this case.

A's behavior over the months prior to the incident included statements by A that he was "fighting his internal demons" and communicating with "universe governing entities" while under the influence of the drug.

Case 2

Subject F was an 18-year-old male college student, living in a fifth-floor college dorm room with a male friend. F, his roommate, and another friend ingested large doses of dextromethorphan (Coricidin® Brand) and smoked marijuana with the intent of becoming intoxicated. Each subject is believed to have ingested a "full box" of Coricidin® each. They had all ingested dextromethorphan before without experiencing psychosis.

Once intoxicated, F related that he believed he could fly and attempted to exit the window of the fifth-floor room. He was restrained by his friends and resisted their efforts to calm him, with one of them eventually sitting on his chest. One of his friends then noticed that F was not breathing and called paramedics. F was pronounced dead at the scene.

Toxicology testing revealed dextromethorphan at a concentration of 1050 μg/L, chlorpheniramine 170 μg/L, and carboxy-THC 25 μg/L. Dextrorphan was qualitatively positive. An autopsy was performed, and the manner of death was ruled a homicide. No criminal charges were filed in this case. The other individuals involved were expelled from the college.

Case 3

Subject M was a 15-year-old boy whose drug history included use of dextromethorphan in combination with chlorpheniramine (Coricidin HBP®), LSD, and marijuana. On the day of his death, he had gone to school, but left after his first class. He had reported to a friend and classmate that he had taken 22 Coricidin® pills and was going to smoke marijuana. He had contact with his sister in the afternoon up until about 5:30 PM who reported that he was acting "dumb," "strange," and "spacey," and staring at the wall. She identified this as behavior typically associated with his use of dextromethorphan. When she returned home at about 10:00 PM that evening, she found subject M hanging by the neck from the closet doorknob. A small garbage can inside the closet contained six empty eight-pill Coricidin Cough and Cold blister packs.

Toxicology results on peripheral blood are as follows: pseudoephedrine 170 μg/L; chlorpheniramine 210 μg/L; dextromethorphan 2420 μg/L; and sertraline <50 μg/L. Identified in blood, but not quantitated, were caffeine, cannabinoids, and desmethylsertraline.

M had discussed suicide and "being with his father" who committed suicide 2 years previously. The deceased did not have a regular physician; however, a prescription for sertraline had been filled 23 days before his death.

After the autopsy was completed, the cause of death was listed as asphyxia because of hanging, and the manner of death was listed as suicide.

Case 4

Subject N was a 13-year-old boy who is reported to have used Coricidin® on three occasions during the last week of his life. It is not known whether he had experimented with the drug prior to this, but this occurred shortly after the death of subject M (case 3) who lived about a half mile away and with whom he was acquainted.

On the evening before he was found, he came home at about 5:00 PM reporting that he had been with friends. He stayed in his room most of the evening. He had contact with his mother who brought him his homework. He also had contact with an older sister who questioned him about Coricidin® use that evening which he denied. His last known contact was his mother at about 8:30 PM to say goodnight.

One torn and one intact note were found in his room. In one note, he indicated that he was bored and wanted something new and different. In the other note, he indicated that he took 164 pills. Two empty eight-count blister packs were found in his room.

Toxicology testing on peripheral blood found the presence of chlorpheniramine 2600 μg/L and dextromethorphan 19,500 μg/L.

After the completion of the autopsy, the cause of death was listed as chlorpheniramine and dextromethorphan intoxication, and the manner of death was listed as suicide.

Case 5

Subject R was a 29-year-old man who worked as a manager in a fast-food chain restaurant. He had a distant past history of opiate dependence 10 years in remission and had no prior history of psychiatric illness. He was high functioning and had a fiancé and 2-year-old child. Several months prior to presenting, he began to experiment with taking over-the-counter cold medications containing dextromethorphan. Use was initially limited to weekends when he would engage in dextromethorphan use with friends. For a period of 1–2 weeks, he began using dextromethorphan daily that he had obtained over the weekend. His typical dose was estimated to be 300–500 mg. His family noticed a dramatic change in his behavior. He became socially withdrawn and easily agitated. His speech was quick and pressured. He expressed that he could predict an impending crash of the stock market and that voices would give him information about the government. His family became alarmed when they confronted him about his behaviors, and he became physically aggressive prompting them to call police to assist. When confronted by the police, he again became aggressive, which included a brief physical altercation with the police. He was taken to the hospital by the police, and he was admitted for treatment. After 2 days of symptomatic treatment, his mental state cleared and his behavior returned to baseline. He had no further delusions or auditory hallucinations. No toxicology data were available.

Discussion

There are numerous reports of dissociative, psychotic, or manic episodes associated with excessive ingestion of dextromethorphan or dextromethorphan-containing compounds in the medical literature, going back to the 1960s. Often, the drug is formulated with other psychoactive compounds such as chlorpheniramine and pseudoephedrine, which can contribute to the overall presentation of toxicity (Table 1). The condition is variously characterized as psychosis, toxic psychosis, dextromethorphan-induced mania, and many others. The focus of clinical treatment is typically symptomatic, followed by identification and treatment of any co-occurring psychiatric or medical conditions. Symptomatic treatment has included use of short-acting benzodiazepines such as lorazepam for symptoms of anxiety or agitation, although efforts should be made to limit this use because of the primary substance abuse involvement. Use of typical or atypical antipsychotic medications including risperidone, quetiapine, and haloperidol has also been useful for acute agitation or other acute psychotic symptoms. Many patients benefit from a sleep aide (e.g., trazodone or zolpidem) for acute insomnia or dysregulation of sleep cycle. Most patients, however, require only a few (2–5) days of symptomatic treatment, and symptoms generally resolve fairly quickly.

Co-ingestion of dextromethorphan with other drugs present in cough and cold preparations may add to the general level of impairment and intoxication. Pseudoephedrine has stimulant properties and has specifically been noted as having caused paranoid psychotic states in high overdose (10,11). Chlorpheniramine and diphenhydramine are antihistamines with largely central nervous system depressant activity, which may add to the overall level of sedation. They have been reported to cause delirium and hallucinations, but have not been independently associated with the delusional or psychotic behavior seen in these cases. Logan has reported that the overall presentation of dextromethorphan intoxication in drivers appeared similar either with or without chlorpheniramine present (8).

Table 2 summarizes the case reports described previously, correlating symptoms and levels to dosage. Table 3 summarizes previously published case reports of dextromethorphan-related psychotic and manic reactions. Common factors are consistent with Diagnostic and Statistical Manual, 4th Edition, Text Revision (DSM-IV-TR) diagnostic criteria for psychosis, including hallucinations (including auditory, tactile and visual), delusions (often with lack of insight and paranoia), and disorganized thought (pressured speech and flight of ideas) (12). In some cases, mania was present. These symptoms are similar in presentation to PCP or ketamine intoxication, consistent with the fact that PCP, ketamine, and dextromethorphan and its metabolite dextrorphan all bind to a binding site in the open ion channel of the NMDA receptor, acting as antagonists and reducing neural activation. The symptoms associated with high levels of dextromethorphan ingestion include: pressured thoughts and slurred speech, hallucinations (visual, auditory, olfactory), aggressive and disruptive behavior, delusions (often linked with paranoia and religion), euphoria, irritability, and ataxia. These are the most common symptoms found in the cases in this report as well as in cases described in Table 3. Together, these cases indicate that in amounts higher than recommended, dextromethorphan carries a significant risk with hazardous consequences, both to self and others.

TABLE 1—*Toxic effects of drugs often found in combination with dextromethorphan in cough and cold preparations.*

Drug	Toxic Effects (Behavioral)	Reference
Pseudoephedrine	Irritability, anxiety, paranoid psychotic state, paranoia, auditory hallucinations, pleasant perceptual changes	Hall et al. (27) Leighton (10)
	Mania closely resembling schizophrenia and visual and tactile hallucinations	Sullivan (11)
Guaifenesin	No psychiatric symptoms	Hall et al. (27)
Chlorpheniramine	Agitation, hallucinations, confusion, sedation	Banerji and Anderson (28)
Diphenhydramine	Delirium, inattention, altered consciousness, perceptual disturbances, disorientation	Agostini et al. (29)

TABLE 2—*Summary of dose, blood concentration, and diagnosis from cases reported in narrative.*

Subject	Dose (if Known)	Dextromethorphan Blood Concentration	Diagnosis and Symptoms
A	Not known	4740 μg/L	Psychosis, hit head on floor and wall, punched drywall, cut himself on chest and arms, cut girlfriend in shoulder and neck, ruled a suicide from multiple stab wounds
C	950 mg	300 μg/L	Intoxication, no mania, or psychosis*
F	"Full box" of 30 mg tablets	1050 μg/L	Psychosis, thought he could fly, attempted to jump out a window, homicide by suffocation while being restrained
M	48 missing tablets	2420 μg/L	Intoxicated, acted "spacey," flat affect, suicide by asphyxia
N	Note states ingested 164 pills	19,500 μg/L	No behavioral information, DXM intoxication resulting in suicide
R	300–500 mg (est.)	NA	Delusional, aggressive, agitated, pressured speech*

*Subject survived.

The concentrations of dextromethorphan in the cases reported here were significantly elevated over those associated with therapeutic use. Rates of dextromethorphan metabolism can vary as a result of pharmacogenetic factors with both extensive and poor metabolizers having been identified (13). Super-extensive metabolizers with multiple copies of the CYP2D6 gene most likely also exist (14). Individuals ingesting 30 mg of dextromethorphan four times daily for 7 days achieved peak plasma concentrations of 2.4 μg/L (range 0.5–5.9 μg/L) in rapid metabolizers and 207 μg/L (182–231 μg/L) in poor metabolizers (15). Steinberg et al. (16) administered dextromethorphan doses of up to 400 mg QID to neurosurgery patients in an assessment of the neuroprotective effects of the drug. Subjects receiving 400 mg of dextromethorphan orally achieved serum concentrations of up to 1514 μg/L and dextrorphan (total) concentrations of 502 μg/L. Up to 64% of patients experienced side effects such as nystagmus, dysarthria, visual disturbances, feeling "drunk," euphoria, visual hallucinations, persecutory delusions, nausea and vomiting, gait ataxia, and dizziness. Logan (8) reported whole-blood dextromethorphan concentrations in impaired drivers of 676 μg/L, 300 times the concentration normally seen in plasma samples following therapeutic use in rapid metabolizers and three times the concentrations encountered following therapeutic use in poor metabolizers. Logan et al. have reported dextromethorphan concentrations in five individuals who died accidentally while intoxicated with dextromethorphan with concentrations ranging from 1300 to 3230 μg/L (17). The dextromethorphan concentrations in four of the subjects reported here A, F, M, and N were found to be 4740, 1050, 2420, and 19,500 μg/L, respectively. These levels overlap completely with the range associated with fatal outcomes in Logan's study, and are also consistent with patterns of use that have resulted in psychotic and manic behavior and intoxication in the cases summarized in Table 3, and in driving populations (8,18). Although high concentrations of dextromethorphan tend to indicate illicit use and abuse, drug interactions and metabolic deficiencies may influence the blood concentrations and potentially even toxicity after therapeutic use.

Drug interactions should also be considered, as dextromethorphan is no longer simply an over-the-counter antitussive. The drug has been found to be beneficial in the treatment of pseudobulbar effect (19) (emotional outbursts that cause a significant negative impact on a patient's quality of life), in the co-administration of opioid analgesics, poststroke ischemia, and as a cough suppressant. Dextromethorphan is a substrate for CYP2D6, and drugs that inhibit this metabolic pathway, such as quinidine, sertraline, and diphenhydramine, prolong the pharmacokinetics and effects of the drug without excessive accumulation of its more psychogenic metabolite dextrorphan (20–23). The co-administration of terbinafine or other CYP2D6 inhibitors with dextromethorphan may cause an increase in undesired side effects as a result of increased dextromethorphan levels. Methadone and dextromethorphan have been implicated in a drug interaction delirium (24). As an NMDA receptor antagonist, dextromethorphan has also proven valuable in postoperative pain management in combination with opioid analgesics, where it enhances opioid-induced analgesia (25).

Although it was not performed in these cases with a clear history of abuse, in cases where abuse versus accidental intoxication is in question, genetically determined metabolic capacity should also be considered. Significant genetic polymorphism of cytochrome P4502D6 (CYP2D6) exists (26), and three classes of phenotype, poor metabolizers, extensive metabolizers, and ultra-extensive metabolizers, have been characterized. Approximately 5–10% of the Caucasian population are poor metabolizers, 2% are ultra-extensive metabolizers with the remaining population are considered extensive. In a study showing the difference in metabolite formation rates between extensive and poor metabolizers, dextrorphan and 2-methoxymorphinan formation rates increased as dose increased in extensive metabolizers. The formation rate of 3-methoxymorphinan was similar between poor and extensive metabolizers, whereas the formation of dextrorphan was more than 10 times slower in poor metabolizers (5). This extreme variation in metabolism of dextromethorphan to dextrorphan could cause significant differences in the effects and blood concentrations between extensive and poor metabolizers. Ultra-extensive metabolism of dextromethorphan may result in formation of elevated dextrorphan levels, which may also precipitate adverse effects.

Excessive dextromethorphan consumption either for the purposes of becoming intoxicated or experiencing dissociative effects, or from long-term habituative use are the most common causes of elevated blood drug concentrations and intoxication. Other causes, however, including metabolic drug interaction or genetic metabolic insufficiency coupled with chronic dosing could also result in elevated blood concentrations and associated adverse effects. In cases of adverse effects from apparent therapeutic use of dextromethorphan, consider the patient's dosage history and co-ingested drugs to determine the potential for metabolic interactions with CYP2D6. Potentially, pharmacogenomic testing could be performed to establish the genetic metabolic status of the individual (14).

The most common presentations in the cases presented here, and in previously reported cases, include disturbance in mental equilibrium with the onset of false beliefs regarding external threats, ideas of reference and grandiosity, and superhuman powers such as power of flight or the ability communicate telepathically. Either as a result of abuse as in the cases described here or as a result of variability in metabolism and drug interactions, dextromethorphan accumulation may result in adverse effects with psychosis, mania, hallucinations, or delusions that can turn violent.

Clinicians should be aware that dextromethorphan is not specifically tested for in hospital-based urine drug screens, although false

TABLE 3—*Prior case reports of mania and psychosis associated with dextromethorphan ingestion, including known drug ingestion, symptoms, diagnosis, and citation.*

Dose if Known	Diagnosis and Symptoms	Reference
Dextromethorphan (20 pills)	Toxic psychosis because of dextromethorphan: hyperactive behavior, extreme pressure of thought, visual and auditory hallucinations, synesthesia. Prior psychedelic drug use	Dodds and Revai (30)
Dextromethorphan, "up to two bottles several times a week"	Psychosis—dextromethorphan caused or exacerbated: anxious, aggressive, abusive, irritable, disruptive, psychotic. Diagnosed as schizophrenic. Family history of drug abuse	Orrell and Campbell (31)
Benylin Forte, phenylephrine nasal drops, actifed linctus	Psychosis: complex and frightening hallucinations, including auditory (his own thoughts recorded and played over the public speaker system). Wanted to overthrow the government. Disoriented in time	Lambert (32)
Dextromethorphan 2400 mg, phenylpropanolamine 2000 mg, guaifenesin 16,000 mg, daily	Psychosis: disheveled, frightened, speech tangential, affect labile, delusions regarding whereabouts of hostages in Lebanon	Craig (33)
Chlorpheniramine 72–345 mg, dextromethorphan 360–960 mg, phenylpropanolamine 450–1200 mg	Dextromethorphan mania: drug-induced mania, diagnosed with bipolar disorder, went on expensive shopping sprees, claimed to be an undiscovered musical genius, claimed divine revelations, pressured speech, and flight of ideas. Family history positive for mania	Mendez (34)
Dextromethorphan 1200 mg (est.)	Recurrent dextromethorphan mania: manic symptoms	Walker and Yatham (35)
Robitussin (3–8 oz. bottles/week)	Self destructive behavior: felt "high and drunk," self-mutilation. Was being treated for depression	Murray and Brewerton (36)
Dextromethorphan 1500 mg, guaifensin 5000 mg, frequently	Acute dextromethorphan mania with cognitive deterioration from long-term abuse of dextromethorphan: euphoric mood, aggressive and disruptive behavior, poor attention span, copious note writing, frequent grandiose religious experiences (communication with God; chosen by God for a special purpose), persistence of symptoms for weeks. No family history for mood disorders	Hinsberger et al. (37)
Robitussin DM (three 12 oz. bottles) and several beers	Psychosis: found in a snowbank "agitated and hallucinating," mildly confused, oriented to name and year but not month or location, thick and slurred speech, horizontal and vertical nystagmus, ataxia, floating and flying sensations, visual and auditory hallucinations	Wolfe and Caravati (38)
Dextromethorphan (180 mg est.)	Dextromethorphan-induced mania: delusions (believed his wife was being held captive in their home, tried to free her with a gun), frantic endless energy, euphoric mood, expensive shopping sprees, flights of ideas, auditory hallucinations, paranoid belief that he would be killed if he fell asleep. Family history for alcoholism and affective disorder	Polles and Griffith (39)
Dextromethorphan and pseudoephedrine	Dextromethorphan-induced mania: self-described "manic, crazy mood," racing thoughts, distractibility, restlessness, irritable, and elated. No family information	Polles and Griffith (39)
Dextromethorphan 15 mg, pseudoephedrine 60 mg, carbinoxamine 4 mg (1–2 daily for 7 days)	Psychosis associated with dextromethorphan and pseudoephedrine: personality changes, irritability, psychomotor agitation, auditory hallucinations, fecal/urinary incontinence, agitated, intrusive, disinhibited hypersexual behavior, circumstantial thought processes, paranoia, explosive speech, with sexual and racial themes. Family history of depression and alcohol abuse	Soutullo et al. (40)
Robitussin CF® (three doses of 1.5 tsp 6 h apart)	Acute psychosis: child acting bizarrely, "walking like he's drunk," hyperexcitability, irritability, incoherent babbling, difficulty maintaining balance, dilated pupils. No significant prior medical history	Roberge et al. (41)
Dextromethorphan 711–1422 mg/day	Dextromethorphan-induced psychosis: dissociative beliefs (believed he had died, had become "just his thoughts"), observing himself from afar, visual hallucinations ("360° vision," could "see into people"), delusions (telepathy, mindreading, belief that his employer was trying to kill him, strangers might hurt him). Father had bipolar disorder	Price and Lebel (42)
Dextromethorphan and methadone	Dextromethorphan-induced delirium: lethargic, sadness, intermittent episodes of staring, markedly impaired attention, delirium, hypersomnia, confusion	Lotrich et al. (24)
Dextromethorphan (*c*. 480–720 mg/day, up to 3600 mg/day)	Dextromethorphan psychosis: intoxication, euphoria, paranoia, delusions of communicating with aliens, delusion that her intestines had become loose, profound anxiety, visual hallucinations (flowers) with intact reality testing, tactile hallucinations of "fiber" rolling around under her skin which she interpreted as "evil" and needed to be removed. No family or other history of psychosis	Miller (43)
Dextromethorphan and chlorpheniramine (eight capsules)	Acute psychosis: paranoid thoughts, severe auditory hallucinations, paranoia, hyper-religiosity, delusions (hospital employees were "dogs of darkness," he was possessed by demons). No family history of psychosis	Sharma et al. (44)
Coricidin® Cough and Cold (dozen pills at a time)	Acute psychosis: head would spin, reality would shift, see colors, bright lights, bizarre shapes	DiConsiglio (45)
Dextromethorphan, propoxyphene, hydrocodone–acetaminophen	Psychosis: agitated, psychotic, experienced religious delusions, acted out violently toward paramedics, visual hallucinations, olfactory hallucinations (called landlord complaining of strange smell)	Jamison and Vasudeva (46)
Dextromethorphan	Dextromethorphan-induced psychotic manic bizarre somatic delusions, stated that the medical doctor had injected "Salium" into her anus. Paranoid thought someone was draining her bank account; experienced blackouts; pressured speech. Her family history was not significant for any mental illness	Amaladoss and O'Brien (47)

positives for PCP may be generated by high doses of the drug (1). Confirmatory testing by a mass spectrometric technique should be ordered to differentiate PCP from dextromethorphan.

Frank intoxication has been associated with dextromethorphan concentrations in excess of 150 μg/L (8), and users report increasingly profound intoxicating and dissociating effects in a dose-dependent manner. There is no established concentration threshold for the onset of dissociation. Subjects displaying altered perception in this series had concentrations in the range between 1000 and 5000 μg/L. Deaths have been reported at concentrations in excess of 5000 μg/L (17).

Conclusions

As illustrated in the extensive history of adverse event reports, and in the cases reported here, dextromethorphan intoxication can be profound and can result in dangerous, irrational, unpredictable, and violent behaviors. The dissociative nature of the drug has few parallels (PCP and ketamine are the principal examples), making dextromethorphan abuse one of the few drug intoxication conditions that can cause significant disruption of the normal integration of a person's conscious functioning. This has important consequences for premeditation and intent issues in drug intoxication defenses, or when a person's drug use is raised in mitigation in sentencing. Individuals in a true dissociative state are unlikely to be able to form intent. While blood drug concentrations should be taken into account as indicators of the degree of ingestion, a dissociative condition should not be diagnosed based solely on an elevated blood drug concentration, relying instead on the DSM-IV criteria.

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