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Dextromethorphan Abuse - A Rising Menace In India: Case Review and Its Toxicokinetics

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Abstract

Dextromethorphan is a dissociative antitussive agent which is being sold freely as an over the counter drug in combination or solo in the form of tablets or syrups. The desire to be one of a kind amongst their peers is causing adolescents to experiment with different drugs. The problem is complicated with the free information available on internet regarding the new and the latest use of this drug which this savvy generation has easy access to. The recreational use of DXM is rising at a very fast pace in India and esp. Punjab. The menace needs to be checked on priority if we want to save our youth from the demon of drugs.

Key Words: Dextromethorphan, anti tussive, Adolescents, Recreational use.

Introduction

Dextromethorphan (DXM) is an over-the-counter (OTC) cough suppressant commonly found in cold medications either alone or in combination with other drugs such as analgesics (e.g. acetaminophen), antihistamines (e.g. chlorpheniramine), decongestants (e.g. pseudo- ephedrine) and/or expectorants (e.g. guaifenesin) 1. When taken as directed, side-effects are rarely observed. Recreational use of this drug is gaining popularity as a drug of abuse amongst adolescents for experimentation due to it's over the counter status and legality2, 3. Illicit use of DXM is referred to on the street as "Robo-tripping" or "skittling", Triple C, Poor Man's PCP. To date there is scanty data in the Indian Medical literature pertaining to the abuse, toxicity and potential hazards of using this drug recreationally. We discuss here two cases of dextromethorphan toxicity in two teenagers who reported to the emergency department of Sri Guru Ram Das Institute of Medical Sciences and Research along with a brief review of the toxicokinetics and toxicodynamics of dextromethorphan and its metabolites.

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Case Reports

Case 1:

A 15 year old boy was brought to the emergency department due to alteration of consciousness. His parents gave the history of the boy having consumed 6 bottles of anti tussive syrup formulation. They also told that they were unaware of his addiction but now on searching the room of their son they had found empty bottles of the anti tussive syrup and their son had confirmed of having consumed them. Initially it was half to one bottle daily. Then he increased it to two bottles per day and today he had consumed 6 at one go to get a greater kick. He reported feeling sleepy with nausea, abdominal discomfort and increasing confusion. On physical examination vital signs were B.P- 118/68 mm of Hg, Pulse- 124/min, fast and feeble, Respiratory rate-24/min and Temperature-38.20C. Liver function tests were deranged with S. Bilirubin 1.6, SGOT-106 IU, SGPT-367. The patient appeared drowsy with Glasgow coma scale of 15 (E4V5M6). He was responsive but speech was slow. Pupils were dilated. Fundoscopy was normal. His stomach was washed with normal saline and intravenous fluids were administered to him.

Case 2:

A 17 year old boy was brought to the emergency department after consuming 4 bottles of anti tussive syrup along with cocaine. He had attended a party the night before where the group had experimented freely with the drugs and he was a first timer. He had been brought to the emergency by his parents when he did not respond to their command to wake up and appeared drugged with altered state of consciousness. On Physical examination, B.P -126/70mm of Hg, Pulse -116/min, Temperature -37.4 C, Respiratory Rate-26/min. Pupils were partially dilated. Fundoscopy was normal. Neurological examination was normal with Glasgow Coma Scale (E4V5M6).The patient appeared drowsy and confused and apprehensive. Laboratory tests done were complete blood count, urine examination and ECG. ECG showed slight QRS widening, Liver function tests were abnormal with SGOT = 74 IU and SGPT = 689 IU. The boy was administered IV fluids along with gastric lavage with normal saline and naloxone to reverse the effects of cocaine. He was also managed symptomatically for his withdrawal symptoms. He was also referred to Psychiatry for counseling, psychotherapy and de-addiction.

Discussion

Dextromethorphan is a dextro-rotatory isomer of codeine analog levorphenol. It exerts its anti tussive effect by binding to the opiate delta receptor 4. It is metabolized by the body's hepatic cytochrome p-450 isoenzyme 2D6 to dextrophan, which can potentiate neuronal serotonin release, as well as act as an antagonist of the N-Methyl-D-Aspartate receptor.5 Recent literature suggests that heavy dextromethorphan use may produce phencyclidine (PCP)-like effects from the metabolic conversion of dextromethorphan to its immediate metabolite, dextrorthan, which acts like an NMDA receptor antagonist. These include bizarre and hyperactive behavior, nystagmus, ataxia, hallucinations, CNS depression, and a false-positive urine test for PCP. Dextromethorphan, when consumed in low "recreational doses" (usually around or slightly more than 200 mg, or around 1.5 to 2.5 mg/kg), is described as having a euphoric effect. With middle doses (about 400 mg, or 2.5 to 7.5 mg/kg), intense euphoria (or dysphoria), vivid imagination, and closed eye hallucinations occur. With high doses (600 mg, or 7.5 mg/kg and over), pro-

found alterations in consciousness have been noted, and users often report out-of-body experiences or temporary psychosis. 6, 7

Frequent and long-term usage at very high doses could possibly lead to toxic psychosis and other permanent psychological problems. Most users find such high doses to be extremely uncomfortable and are unwilling to repeat them. Flanging (speeding up or slowing down) of sensory input is also a characteristic effect of recreational use 8. A document entitled "The DXM FAQ," by William E White 9 classifies dextromethorphan's high-dose effects into five or six plateaus, each defined by a dosing range. The dosages are specified in ratios of milligrams (of the drug) per kilogram (of one's body mass). According to the FAQ, the plateaus occur as follows

- First plateau: At a dosage of 1.5 to 2.5 mg/kg, effects include a sensation of alertness, stimulant effects such as restlessness, increased heartbeat, and increased body temperature, intensification of emotions, general euphoria, and euphoria linked to music, alteration of sensations of gravity, loss of balance, and slight intoxication.
- Second plateau: At 2.5 to 7.5 mg/kg, effects include the same effects of the first plateau, with added choppy sensory input, entering a dreamlike state of consciousness, increasing detachment from outside world, a heavier "stoned" feeling than with first plateau, and/or closed-eye hallucinations.
- Third plateau: At 7.5 to 15.0 mg/kg, effects include flanging of visual effects, difficulty recognizing people or objects, chaotic blindness, dreamlike vision, inability to comprehend language, abstract hallucinations, delayed reaction time, decision making impairment, feelings of peace and quiet, near complete loss of motor coordination, short-term memory impairment, and/or feelings of rebirth.
- Fourth plateau: At 15.0 mg/kg or more, an individual may experience a perceived loss of contact and control with their own body, changes in visual perception, out-of-body experiences, perceptions of contact with "superior," supernatural, or other archetypal beings (i.e. Gods, aliens, vampires, etc.), other miscellaneous delusions, lack of movement or desire to move, rapid heart rate, complete blindness, increased hearing, and intensification of third plateau effects.
- Plateau Sigma / Fifth plateau : 2.5-7.5 mg/kg every three hours for 9-12 hours; There are some reports that suggest this fifth plateau occurs by prolonging dosage, rather than increasing it, ingesting small to moderate doses over time. White characterizes Plateau Sigma as bona-fide psychosis, a complete disconnection from reality, with prevalent, realistic, vivid open-eye visual and auditory hallucinations.

Dextromethorphan's euphoric effects have sometimes been attributed to the triggering of an increase in dopamine levels, since such an increase generally correlates to pleasurable response to a drug, as is observed with antidepressants 10. Just like all NMDA receptor antagonists, dextrorphan and dextromethorpan inhibit a neurotransmitter called glutamate from activating receptors in the brain. This can effectively slow or even shut down certain neural pathways, preventing areas of the brain from communicating with each other. This leaves the user feeling dissociated (disconnected) or potentially "out-of-body."11,12 Most risks result from abusing multi-symptom cold medications, rather than using a cough suppressant whose sole active ingredient

is dextromethorphan. Recreational use of medications with multiple active ingredients can produce negative psychological and physiological effects. 13

1. CNS depressants such as ethanol (drinking alcohol) will have a combined depressant effect, which can cause a decreased respiratory rate.
2. Combining dextromethorphan with other CYP2D6 substrates can also cause both drugs to build to dangerous levels in the bloodstream. Multi-symptom cold medicines contain other active ingredients, such as acetaminophen, chlorphenamine, and phenylephrine, any of which can cause permanent bodily damage, or even death, if taken on the generally-accepted recreational dosing scale of Dextromethorphan. 14, 15
3. Guaiphenisen, an expectorant commonly accompanying dextromethorphan in cough preparations, is not generally fatal if taken on dextromethorphan's recreational dosing scale, but can cause unpleasant symptoms including vomiting, nausea, and headache 16, 17.
4. Chlorpheniramine or pseudoephedrine: When such a preparation is ingested for drug abuse, anti cholinergic poisoning with tachycardia, dilated pupils, dry mucus membranes, agitation, QRS widening, sedation, coma and seizures can occur.
5. In addition, bromide content of dextromethorphan preparations can cause bromide toxicity. It manifests as falsely raised chloride levels and a negative anion gap. Chronic bromism targets CNS, GIT and skin. Periodic recreational use of DXM is unlikely to result in such toxicity.18

Management of overdose

It is mainly supportive. Gastric decontamination with gastric lavage should be done if patient presents within one hour of ingestion. Activated charcoal should be administered within 4 hours of ingestion.19 Naloxone therapy has been shown to be effective when used in children and for specific indications of hyperexcitability, altered mental status or respiratory depression. Studies have shown the lethal dose to be between 50 and 500 mg/kg, however doses as high as 15-20 mg/kg have been shown to be taken by some recreational users. It is suggested by a single case study that the antidote to dextromethorphan overdose is naloxone, administered intravenously. 20

Legality:

Since Dextromethorphan's use as a recreational drug usually involves only the ingestion of large quantities of an over-the-counter medication, no legal distinction currently exists between medical and recreational use, sale, or purchase. Dextromethorphan is generally available over the counter in most countries, with three exceptions being Hong Kong, Sweden and Denmark. In India, it is freely available from the chemists even without prescription.21

Conclusion

Recreational drug use and experimentation is a well recognized phenomenon in adolescents. Convenient availability of preparations containing dextromethorphan renders the drug to become a substance of abuse. As a forensic expert, being hyper vigilant on unusual seeking habits among

adolescents is as important as informing friends and parents to recognize the signs and symptoms of drug experimentation and abuse in teenagers .Teens need to be steered through these rough waters with a steel hand in a velvet glove. Professional counseling provided in the family settings along with peer group support can work wonders. Unrestricted sale of this drug should be prohibited by the Government with strict enforcement to curb this rising menace.

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