Case Report

Dextromethorphan Abuse in Thai Adolescents: A Report of Two Cases and Review of Literature

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Introduction: *Dextromethorphan is an opiod-derived, easily available cough remedy that, when used in large quantities, can have stimulatory effects which mimic that of amphetamine and other psychedelic drugs. Due to its easy availability, dextromethorphan is gaining widespread popularity as a recreational drug among Thai youths. Symptoms of overdose are directly related to its pharmacodynamic and pharmacokinetic properties. Dextromethorphan is metabolized by cytochrome p450 2D6, an isoenzyme that exhibit polymorphism in Asians. The drug is also a serotonin-reuptake inhibitor and has significant interactions with other drugs that exert their effects through the serotonin pathway such as the amphetamines, cocaine, and Lysergic Acid (LSD).*

Case Report: *We report here two cases of dextromethorphan overdose that presented to the Pediatric Toxicology Service at Siriraj Hospital, Bangkok, Thailand. Both cases presented with hyper-agitation, confusion, with signs of sympathomimetic overdose. Both patients were treated with supportive care and fully recovered within 24 hours without sequalae.*

Conclusion: *Although the acute toxicity of dextromethorphan is abated within 24 hours, its pharmacological properties still render it a dangerous drug to use alone or in combination with other drugs.*

Keywords: *Dextromethorphan abuse, Antitussis drugs, Recreational drugs*
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Dextromethorphan is an antitussis drug which is an over-the-counter dissociative agent of increasing popularity as a drug abuse among younger adolescents[1,2]. In the United States, dramatic increase in the abuse of dextromethorphan has been observed recently. Data from the Toxic Exposure Surveillance. System suggested abuse or misuse of the drug by adolescents between 13 and 19 has increased more than 300% over a 3-year period, with the abuse being slightly more prevalent in females in early adolescence. Because of its legality and over-the-counter status, it is considered by its users to be a harmless drugs for experimentation[1-3].

In Thailand, dextromethorphan abuse has been noticed to be on the rise, with the first official report of dextromethorphan abuse being among the adolescents in Southern Thailand[4]. To date, there are no report in the Thai medical literature pertaining to the abuse, toxicity, and potential hazards of using this drug recreationally. We report here two cases of dextromethorphan toxicity in two teenage girls who tried this drug for experimentation. A brief review of the toxicokinetic and toxicodynamic of dextromethorphan and their pertinence on the drugs harmful effects is also reviewed.

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Patient 1: A 12-year-old girl was brought to the emergency room due to alteration of consciousness. Her parents gave the history of using an over-the-counter antitussive drug, a small yellow coated tablet, for illicit purposes. Her habit changed from gradual to progressive increase in the dosage of drug use, and from occasional with a few tablets at a time to daily doses in order to gain the desired effect of euphoria and an increased sense of well-being. Six hours prior to

hospitalization, the patient took 26 tablets of dextromethorphan (Romilar). She reported of feeling sleepy, with nausea and abdominal discomfort. Her father noted that she became increasingly confused and brought her to the emergency department (ED).

On physical examination in the ED, vital signs were: blood pressure 117/70 mmHg, pulse 122 / min, respiratory rate 20 / min and a temperature of 38.2° C. The patient appeared drowsy with Glascow coma scale of 15 (E4V5M6). She was responsive and verbalized with notably slow speech. Fundoscopic examination was normal.

Patient 2: A 13-year-old girl was brought by her mother after her ingesting 20 tablets of dextromethorphan 4 hours before arrival to the ED. The patient admitted to using dextromethorphan once before and that she was often asked to purchase the drug for her friends. On physical examination, the vital signs were: blood pressure 130/80 mmHg, pulse 112 / min, respiratory rate 28 / min and a temperature of 36° C. The patient appeared drowsy. Neurological examination was normal except for slight confusion.

Laboratory tests, including complete blood count, urine examination, urine pregnancy test, urine toxicology screening and electrocardiogram were negative on both patients. Both received intravascular fluid during a brief observation period and were discharged after their vital signs have normalized. Psychiatric referral was made for the first patient who was subsequently diagnosed with a coexisting major depressive disorder. The second patient was followed by the Adolescent Health Service and continued to do well with family counseling and periodic follow ups.

Discussion

Dextromethorphan is a dextrorotary isomer of a codeine analog levorphanol. It exerts its antitussive effect by binding to the opiate δ-receptor. Its high selectivity and lack of other opiod effects make it a safe medication for over-the-counter use[5].

It is metabolized by the body's hepatic cytochrome p450 isoenzyme 2D6 to dextrorphan which can potentiate neuronal serotonin release, as well as acting as an antagonist of the N-Methyl-D-Aspartate receptor. Such blockage of the receptor mimics that of phencyclidine (PCP) and may explain the typical euphoria, hyperactivity and hallucination experienced by this drug[6, 7].

Its metabolism by isoenzyme 2D6 may explain differences in symptoms observed during the acute period between our two patients. Only dextrorphan, and not its precursor dextromethorphan, is known to produce PCP-like symptoms in laboratory animals. Since the CYP 2D6 isoenzyme exhibits polymorphism in different individuals, fast metabolizers of dextromethorphan may produce larger quantities of its metabolite, and therefore are more likely to experience the intense PCP-like effects such as that seen in case #2[2, 8-11].

In general, acute overdose of dextromethorphan causes nausea, vomiting, hyperexcitability, restlessness, hallucination, dizziness, drowsiness, lethargy, slurred speech, mydriasis, euphoria, tachycardia, hypertension and urinary retention. The classical opiod effects such as respiratory depression and miosis are not commonly seen[6, 9]. Intense psychosis and various kinds of hallucination, such as auditory, tactile, or visual, have been reported. Management of dextromethorphan overdose is mainly supportive. Gastric decontamination with gastric lavage should be given if patient presents within 60 minutes of ingestion and activated charcoal should be administered within 4 hours of ingestion. Naloxone therapy has been shown to be effective when used in children and for the specific indications of hyperexcitability, altered mental status or respiratory depression[5, 9, 12-14].

There are other less obvious toxicities from dextromethorphan abuse. Its concomitant use with other drugs of abuse can pose significant risk for serious drug interaction. When used with other drugs with serotoninergic effects such as the amphetamines, cocaine, or psychiatric drugs such as monoamine oxidase inhibitor (MAOI) or serotonin-reuptake inhibitors (SSRI), toxicity in the form of serotonin syndrome can ensue. In the United States, available preparations of dextromethorphan are always mixed with other cough and cold ingredients such as chlorpheniramine or pseudoephedrine. When such a preparation is ingested for drug abuse, anticholinergic poisoning with tachycardia, dilated pupils, dry mucous membranes, agitation, QRS widening, sedation, coma and seizure can result. In addition, bromide content of dextromethorphan preparations can cause bromide toxicity, manifested by falsely elevated chloride on serum electrolyte panel and an apparent negative anion gap. Chronic bromism targets the central nervous system, gastrointestinal tract

and skin. Luckily, periodic recreational use of dextromethorphan is unlikely to result in such toxicity[2, 6, 7, 9, 12, 15].

Conclusion

Recreational drug use and experimentation is a well recognized phenomenon in adolescents. Convenient availability of dextromethorphan, over the counter, renders the drug to become a substance abused by adolescents. As health care providers, being hypervigilant on unusual drug-seeking habits among adolescents is as important as informing teachers and parents to recognize the signs and symptoms of drug experimentation and abuse in their teenagers.

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การใช้ยา DEXTROMETHORPHAN เป็นสารเสพติดในวัยรุ่นไทย: รายงานผู้ป่วย 2 ราย และทบทวนบทความ

บุญยิ่ง มานะบริบูรณ์, จุฬธิดา โฉมฉาย

บทนำ: *Dextromethorphan เป็นหนึ่งในอนุพันธุ์ที่สกัดมาจากฝิ่นซึ่งใช้เป็นยารักษาอาการไอ เมื่อใช้ในปริมาณมากมีผลกระตุ้นระบบประสาทคล้ายกับยากลุ่มแอมเฟตตามีน และยาเสพติดกลุ่มที่ทำให้เกิดภาพหลอน เนื่องจากยา Dextromethorphan เป็นยาที่หาซื้อได้ง่าย ดังนั้นจึงถูกใช้อย่างแพร่หลายเพื่อใช้เป็นยาให้ความบันเทิงในวัยรุ่นไทย อาการของการได้รับยาเกินขนาดสัมพันธ์กับคุณสมบัติทางด้านเภสัชพลศาสตร์ และเภสัชจลนศาสตร์ของยา Dextromethorphan ถูกทำให้เปลี่ยนแปลงในร่างกายผ่านทาง cytochrome P450 2D6 ซึ่งเป็นไอโซเอนไซม์ที่แสดงออกได้หลากหลายในชนชาติเอเชีย ยานี้เป็น Serotonin - reuptake inhibitor และมีปฏิสัมพันธ์อย่างชัดเจนกับยาตัวอื่นที่ออกฤทธิ์ผ่านทาง Serotonin pathway เช่น แอมเฟตตามีน, โคเคน และ LSD*

รายงานผู้ป่วย: *รายงานผู้ป่วย 2 รายที่ได้รับยา Dextromethorphan เกินขนาดที่มารับการรักษาที่ศูนย์พิษวิทยา โรงพยาบาลศิริราช ผู้ป่วยทั้ง 2 รายมาด้วยอาการกระวนกระวาย สับสน ร่วมกับอาการของระบบประสาทอัตโนมัติ (Sympathomimetic overdose) ทั้งสองรายได้รับการรักษาตามอาการและอาการกลับคืนเป็นปกติใน 24 ชั่วโมง โดยไม่มีผลแทรกซ้อนใดๆ*

สรุป: *ถึงแม้ว่าพิษอย่างเฉียบพลันของ Dextromethorphan จะลดลงใน 24 ชั่วโมง แต่คุณสมบัติทางด้านเภสัชวิทยาแสดงให้เห็นว่า Dextromethorphan เป็นยาที่อันตรายในการใช้เพื่อเสพติดไม่ว่าจะใช้ยานี้ตัวเดียวหรือร่วมกับยาตัวอื่น*