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Abuse of Dextromethorphan: Review and A Case Report

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Abstract: Dextromethorphan is a nonopioid antitussive drug. It is widely available in over-the-counter. Although it is a licit and safe drug, it can produce a substance dependence syndrome. The case is a 24 year old man who has abused dextromethorphan for 4 years. He abused 1050 mg dextromethorphan over 30 min. After 15 min of DEX consumption, he found gastrointestinal symptoms, dizziness and sweating. After 30 min, his symptoms were alleviated but euphoria, hallucinations and feelings of floating started. He abused dextromethorphan to reach these symptoms. No emergency symptoms which need emergency care was found.

Key words: Dextromethorphan, drug abuse, euphoria

INTRODUCTION

Dextromethorphan (DXM), the d-isomer of the opiate agonist levorphanol, is a highly effective and widely used antitussive drug. This drug has been used from 1960s and it has been in use for more than 40 years. A large body of clinical experiences has been used to formulate a safety profile. The resulting safety profile indicates when dextromethorphan is used in therapeutic dosage, it is a very safe drug and adverse drug reactions are infrequent and usually not severe^[1,2]. Dextromethorphan, alone or in combination with other drugs is widely available in over-the-counter in Iran. Although a few cases of recreational abuse have been reported in the last 3 decades, an increased report of abusing the drug by adolescents and young adults is seen in literature. Dextromethorphan sometimes mixed with heroin, morphine and opiate or other substances abused to increase the pharmacological effects and decrease dependency to the mentioned drugs. Dextromethorphan is not an addictive drug, but it usually produces a substance dependence syndrome, that causes psychological dependency and not physical^[2,3]. The recreational use and abuse of DXM have been increased in recent years and the full extent of the problem is unknown^[4]. Dextromethorphan similar to other synthetics associated with the morphine line of chemistry has an extensive abuse potential. There are a few reports of DXM abuse in literature review, which have identified its serious side effects. Some cases have had a background of psychotic disorders (e.g. schizophrenia^[5] and mania^[6]), but other cases used

higher doses of DXM to get high when other drugs were not available^[3,7]. This is the first case report in the literature of DXM abuse from Iran.

Case report: Mr. D is a 24 year old college student. The whole information in this study has been achieved via interview with the patient after he has abused DXM and was presenting the sign and symptoms after abuse.

He had a history of DXM consumption for chronic cough and he did not have a major psychiatric disorder, but he was a recreational substance abuser. For the first time he had taken one bottle (60 cc vs 180 mg DXM) of cough medication 4 years ago. He has recreationally abused DXM with higher doses at least for 40 times, alone or with his friends. Recently, he abused 70 tablets of DXM (totally 1050 mg DXM), in 30 min (started with 40 tablets and after 30 min 30 more tablets). He did not have any emergency signs and symptoms after DXM consumption and he never referred to clinic or hospital for this consumption. In addition to DXM, he has abused marijuana, cocaine, heroin, opiate, alcohol, ecstasy ((3,4-methylenedioxymethamphetamine (MDMA)) speed (WY) and sedative agents. Sometimes he abused DXM along with marijuana, but he did not use any substance rather than DXM this time.

Symptoms: After 15 min from the first 40 tablets of DXM consumption, he experienced vomiting, nausea, dizziness, sweating, hot flashes, visual disturbances (diplopia and darkness of vision), malaise, dysarthria. These symptoms were alleviated following 30 min after which he had

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feelings of euphoria, photophobia and hallucinations (auditory, visual and tactile), dissociation, feelings of floating, imbalance and ataxia and enteritis that started concurrently, but continued up to 3 h. Auditory hallucination was hearing desirable sounds (to hear the voice of an interested singer) or undesirable sounds. Effects, which occurred within 24 h after use, included altered perceptions, feelings of happiness, relaxation, feeling of presence in desirable places, sleep disorders (insomnia, drowsiness), fatigue, constipation and decrease of libido. Sleep disorders continuing up to 3 days became aggravated by alcohol consumption during the days after DXM abuse; just like thinking of events while consuming DXM which had exacerbated the patient's insomnia. He didn't experience any metabolic disorders, electrolytes and acid-base disturbance and other emergency symptoms which need emergency care after consumption.

DISCUSSION

Dextromethorphan is a highly effective and widely used nonopioid antitussive drug. It is absorbed quickly from the GI tract; (within 30 min, all of DXM might have entered the bloodstream). It has pharmacologically a half-life of about 2-4 h, but its duration of effects is about 3-6 h^[9]. After a single 20 mg oral dose of DXM, its blood level is less than 2 ng L⁻¹, but it can reach up to 8 ng L⁻¹ in patients who are slow metabolizers of drugs. Dextromethorphan is metabolized to dextrorphan by cytochrome P450-2D6 or P450-3A^[9]. In addition to adverse effects of DXM abuse with high doses, there are some people who are at increased risk of side effects of DXM with its normal dosage like those who take it along with MAO inhibitors and serotonin reuptake inhibitor drug use or those with P450 2D6 enzyme polymorphism^[9,10]. Dextromethorphan is a d-isomer of the opiate agonist levorphanol and is approved for over-the-counter use as an antitussive^[3,8]. It is available in various combinations with other medications, in nonprescription cough suppressant and common cold formulations and its availability in Iran is not controlled. For these reasons, DXM abuse is being increased every day. Dextromethorphan similar to N-methyl-d-aspartate (NMDA) receptor antagonist enhances release, prevents reuptake of serotonin and acts at CNS sigma receptors. Besides antitussive effects of dextromethorphan which are well known, there are some studies performed to recognize other therapeutic effects. Its use in treatment led to a significant but modest reduction in opiate substances requirements such as morphine and heroin and reduced withdrawal symptoms^[11,12]. In addition, it attenuates the behavioral or toxic effects of cocaine^[13].

Dextromethorphan suppresses microglial effects in CNS and prevents destruction of dopaminergic cells in cocaine abusers^[12]. It also prevents hyperthermia in amphetamine drug abusers such as Ecstasy^[14]. Although DEX is used to attenuate post surgical pain (e.g. post knee surgery, cesarean and neuropathic pains)^[15,16]. Hallucination states are seen in DXM abusers, similar to LSD and Phencyclidine abusers, it is due to DXM and Phencyclidine receptors like^[17].

Naloxone has been shown to be effective in managing patients with overdose of DXM as a specific antidote^[3,18]

The recommended dosage of DXM in adults is 60-120 mg daily in divided doses. This case abused 1050 mg DXM; it is one of the greatest amounts of drug reported so far. This amount of drug is equilibrated to a concentration of 20-50 times above the recommended dosage. Although DXM is a very safe drug and adverse reactions are infrequent and usually not severe and in doses in excess of 100 times the usual adult dose have not been reported fatal^[1], deaths have been reported to occur as a result of DXM abuse^[19,20]. Despite frequent consumption of DXM by our patient (at least 40 times), he didn't have to refer to emergency care at the time of abuse. It can be due to low half life of DXM. Euphoria, altered time perception, feeling of floating, visual disturbance, tactile, visual and auditory hallucination, disorientation and increased perceptual awareness are primary psychological symptoms that were identified by Wolfe and Miller^[21,22]. Our patient developed most of these symptoms and he abused DXM for these reasons. Based on the studies in animals, psychological symptoms observed in abusers of DXM probably are caused by the active metabolite of dextrorphan, which binds to the same central nervous system receptor as phencyclidine^[17,21,23].

According to Jones *et al.*^[24], drugs abuse can be classified into two categories: licit and illicit psychoactive drugs. Also, there are five forms of abuse including: experimental use (a short term trial), social recreational use (occasional indulgence among friends to share an experience), circumstantial (situational use in specific stressful circumstance), intensified (long term, regular and habitual use) and compulsive use (frequent use of drug; to the point where an individual becomes physiologically and/or psychologically dependent. DEX is a nonaddictive licit drug that doesn't have physiological or psychological dependency, although produces a substance dependence syndrome^[3]. It is probably abused in circumstantial or intensified forms. Our patient said that he abused DXM because his friends used DXM and encouraged him to abuse it. In addition it made him to feel excited and euphoric and he got used to it. Momodou^[25] believes,

DXM is abused because it is more readily available, cheaper and more socially acceptable than other licit substances. It is not associated with any widely known effects and its physiopsychological implications are not fully established or known to the potential abuser population. In addition, it is relatively cheap, convenient, not legally restricted to any age and does not require a prescription^[25].

Dextromethorphan abuse is a potential social problem in the future and availability of DXM over the counter to all age group must be revised.

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