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Adverse Effects of Abuse Potential by Ritalin among Iranian Medical Students

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Abstract: Methylphenidate (Ritalin) is a CNS stimulant that inhibits dopamine and nor-epinephrine reuptake into presynaptic neurons. It has potential for abuse and diversion. This case-series study has been performed in Tehran University of Medical Sciences. Thirty six medical students of 4 medical schools participated in this study in spring 2004. A questionnaire has been designed for this study for collecting data. This questionnaire was certificated by psychiatric professors of Tehran University of Medical Sciences. Thirty three male and three female students participated in this study. The mean age was 25.1 and 94.4% of the students retried Ritalin for more than one time. Two third of the students had history of other illicit drugs abuse (42.5% alcohol, 28.6% Cannabis). The most common adverse effects after the last time of abusing were increasing in concentration (97.2%), tachycardia (61.1%), restlessness (41.7%), decreasing the appetite (38.4%), anxiety (35.7%), diaphoresis (32.5%) this case series shows, unfortunately the average illicit drug abusers was high in participants. Ritalin abuse in medical students is a potentially serious health threat.

Key words: Ritalin, methyphenidate, medical students, drug abuse, side effect, alcohol

Introduction

Methylphenidate (Ritalin) is a Piperidine derivative, structurally related to amphetamine. An extended-release formulation of Methylphenidate (Ritalin) is commonly prescribed for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) (Greenhill *et al.*, 2002). In addition it is used for treatment of narcolepsy and as antidepressant, particularly in the treatment of medically ill withdrawn elderly patients (Challman and Lipsky, 2000). The neuropharmacologic profile of methylphenidate is similar to that of other commonly used or abused stimulants like cocaine (Hoffman and Lefkowitz, 1996) and it blocks the dopamine transporters (DAT) (Ritz *et al.*, 1987).

Because of structural and pharmacological similarity to drugs such as cocaine and D-amphetamine, Methylphenidate could have significant abuse potential (Musser *et al.*, 1998). Diller (1996) reported recent data from the Drug Enforcement Agency (DEA) indicates that methylphenidate use and abuses correspondingly increasing and represents as significant public health concern and the number of cases involving methylphenidate as a single substance increased sevenfold from 1993 to 1999 (Klein-Schwartz and McGrath, 2003). However, it has been suggested that Ritalin abuse is underreported (Kollins, 2001). Babock and Byrne (2000) found that more than 16% of students at a public liberal arts college had tried methylphenidate recreationally. Further 13% of students had taken methylphenidate intranasal. Ritalin has street names such as Vitamin R, Skippy and the smart drug (Llana and Crismon, 1999).

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According to a report by McAuliffe *et al.* (1986), 59% of physicians and 78% of medical students in England had used psychoactive drugs sometimes in their lives, although most of the use was experimental or infrequent. Recent years have brought increasing evidence that university students in Iran are abusing illicit drugs such as Ritalin especially for increasing concentration before exams. A number of case-studies reported abusing of methylphenidate among university students. In this study, we intended to set exploring adverse effects resulting from abuse oral methylphenidate by Iranian medical students without any medical indication as a licit drug.

Materials and Methods

This case-series study was conducted in spring 2004. Forty two volunteers medical students of four medical schools in Tehran, participated in this study.

A self rating questionnaire was designed to collect demographic information, including sex, age, marital status, living arrangements, education level and past medical history. It also required volunteers about alcohol and drug use, prescription drug use, history of methylphenidate use and adverse methylphenidate related consequence after the last consumption. Illicit drug use was assessed by the following question: Have you ever used the following type of drugs during your lifetime? The following substances were listed as possible answers: marijuana, cocaine, LSD, MDMA (Ecstasy), heroin, crystal and other (please specify). Oral Methylphenidate use was consisting of 39 close ended items (25 items during first 6 h after the last use and 14 items during first 72 h after the last use). Volunteers rated each item. All items included symptoms. This questionnaire has been certificated by psychiatric professors of Tehran University of Medical Sciences.

The research office and ethical committee of Tehran University of Medical Sciences approved the protocol of this study.

Statistical analysis was performed using the statistical package for the social science version 11.5 (SPSS 11.5). Demographic values, Methylphenidate dosage and frequencies are given as means ($\pm$ SD). Drug history and adverse complications of Ritalin are given as mean. Correlation between last dosage, frequency of using and adverse complications were calculated with the Pearson correlation coefficient.

Results

The mean age of volunteers was 25.1 ± 3.0 years (19-34). Thirty nine students were male and three were female and 71.4% of subjects were single. Thirty two students (76.2%) were educating at clinical level and 40 students (95.2%) retrieved Ritalin for more than one time (Table 1 shows the reinforcement cause). For the first and last consumption dose, the mean $\pm$ SD was 8.4 ± 3.6 mg and 19.7 ± 17.4 mg, respectively. All of participants had consumed methylphenidate in the past year without physician prescription. They also consumed methylphenidate for increasing concentration at the first time and seventeen (40.5%) of them consumed methylphenidate more than one time for purpose of increasing concentration. Forty one students reported reach to this object after consumption of Ritalin.

Twenty eight of consumers (66.7%) were aware of medical indication of Ritalin. Two third of the students had history of other illicit drugs abuse. Table 2 shows the alcohol and illicit drug abuser behaviors among medical students. The complications during the first 6 h and the first 3 days after the last consumption were shown in Table 3. There was a significant correlation between frequency of usage and last dosage ($p < 0.05$), reinforcement for each euphoria ($p < 0.05$), history of alcohol consuming ($p < 0.05$) and other illicit drug abuses ($p < 0.05$).

Table 1: Reinforcement causes among medical students with Ritalin abuse

Reinforcement cause	Mean
Increase concentration	17 (40.5%)
Decrease appetite	7 (16.7%)
Reaching euphoria	5 (11.9%)
Physical reinforcement	4 (9.5%)
Without reason	1 (2.4%)

Table 2: Illicit drug abuser behaviors among medical students

Substance	Frequency (%)
Alcohol	18 (42.5%)
Cannabis	12 (28.6%)
Sedative tablets	9 (21.4%)
Opium	2 (4.8%)
Dextrometorphan	1 (2.4%)
Ecstasy	1 (2.4%)
Cocaine	0 (0.0%)
Heroin	0 (0.0%)

Table 3: Acute and subacute effects of Ritalin abuse in medical students

Side effects	Percent
Tachycardia	61.1
Restlessness	41.7
Decrease appetite	38.4
Anxiety	35.7
Diaphoresis	32.5
Reinforcement	27.8
Increase appetite	22.2
Feeling love	22.2
Palpitation	20.4
Decrease libido	19.4
Headache	19.4
Nightmare	16.7
Tremor	15.4
Paranoia	14.4
Visual hallucination	11.1
Increase libido	11.1
Increase smell feeling	11.1
Euphoria	10.4
Abdominal pain	5.6
Dizziness	2.8
Auditory hallucination	2.8

Discussion

The goal of this study was evaluation of the pattern and side effect of Ritalin abuse in Iranian medical students. All of participants had consumed methylphenidate in the past year without physician prescription and 66.7% of them knew medical indication of treatment with methylphenidate for ADHD and Narcolepsy.

According to many studies assessing the reinforcing or subjective effects of Ritalin in human (Garland, 1998; Massello and Carpena, 1999), it has abuse potential similar to D-amphetamine and cocaine (Kollins, 2001). Further more, Ritalin and cocaine show similar pharmacokinetic and pharmacodynamic profiles in human brain and have very similar actions at the dopamine transporters (Volkow *et al.*, 1995, 1999).

According to the national institute survey on drug abuse community epidemiology in USA (1995), actual abuse rates for methylphenidate appear to be much less than dose for cocaine and D-amphetamine. However, it has been suggested that Ritalin abuse is underreported (Kollins, 2001).

Increasing concentration has been mentioned the reason of repeat consumption in more than 40% medical students, but the average of illicit drug abuse was high in the participants and we found a significant correlation between frequency of consuming and reaching euphoria.

In this study, the side effect of Ritalin abuse were usually mild and generally well tolerated by subjects. The most common side effects of Ritalin were tachycardia, restlessness and decrease of appetite. Klein-Schwartz and McGrath (2003) also reported tachycardia in 31.7% and agitation/irritability in 25.7% of cases abused methylphenidate. Because our subjects often abused Ritalin concurrent with other substance abuse especially alcohol or cannabis (Table 2), the prevalence of these side effects may be affected from the abuse of additional substance with Ritalin. Polysubstance abuse Ritalin overdoses abuses with other substances suggested that may be associated with increase toxicity. Klein-Schwartz and McGrath (2003) reported symptoms occurred more commonly in exposures involving coingestants (84.3%) than in methylphenidate-only exposures (71.1%). There is a few documented data known about the effects of mixing Ritalin with other substances (Barrett, 2005).

There was a significant correlation between frequency of usage and history of alcohol consuming and other illicit drug, in this study. Barrett and Pihl (2002) reported combined alcohol and Ritalin causes in increased euphoria and a decreased sense of drunkenness. In addition, it is well known that the behavior of the alcohol and/or drug users, cluster together with other problematic behaviors.

In other studies high school students and university students who used Ritalin were more likely to smoke cigarettes, report heavy episodic drinking and use marijuana and cocaine (Klein-Schwartz and McGrath, 2003; McCabe *et al.*, 2004).

Present findings suggested that the factors associated with illicit methylphenidate use are very similar to those previously found to be associated with use of other illicit drugs among medical students.

A review of the literature suggested that serious complications are to be expected from frequent abuse of Ritalin. Death from the recreational intranasal and parenteral abuse of Ritalin have been reported in a few case reports (Farquhar *et al.*, 2002; Massello and Carpenter, 1999).

As we found in our study Ritalin abuse in medical students is a potentially serious health threat, however more investigations are needed to promote understanding and awareness of this problem among clinicians and researchers.

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