

Drug dependence and abuse potential of tramadol¹

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ABSTRACT

AIM: To assess the drug dependence and abuse liability of tramadol. **METHODS:** Subjects of opiate addicts with history of tramadol abuse were 219. Physical dependence of tramadol was assessed using opiate withdrawal scale (OWS), psychic dependence was assessed by association test of Addiction Research Center Inventory-Chinese Version (ARCI-CV); the degrees of craving experienced for tramadol was self-reported on visual analogue scale (VAS). **RESULTS:** The scores of OWS of tramadol were 0.05 - 1.07; 3 scores on scales in particular being used to identify euphoric effects — MBG, sedative effects — PCAG, and psychotomimetic effects — LSD of ARCI were 7.3, 6.1, and 3.4, respectively ($F = 38.1$, $P < 0.01$); 57.1 % of tramadol abuse subjects had craving for tramadol ($\chi^2 = 75.86$, $P < 0.01$). **CONCLUSION:** Tramadol produced high abuse potential among opiate addicts.

INTRODUCTION

Tramadol, a central acting analgesic, was originally marketed in Germany in the late 1970s. Preclinical, clinical, and epidemiological data indicated that the drug dependence

potential of tramadol was low^[1-3]. Tramadol was first marketed in China in the early 1990s as a non-controlled analgesic. In recent years, however, with the advent of drug abuse, non-medical purpose misuse of tramadol was increasing in opiate addicts. To detect and measure the abuse property of tramadol, an investigation was carried out in 6 detoxification centers of different areas assigned by Drug Administration of Ministry of Public Health.

SUBJECTS AND METHODS

Subjects Tramadol misuse cases ($n = 219$, M 182 and F 37) were screened from opiate addicts in 6 detoxification centers of Shanxi, Yunnan, Zhejiang, Heilongjiang, Henan, and Jiangsu provinces. Subjects aged (29 ± 5) a had more than 2-year history of drug addiction before they took tramadol [the age of tramadol initial use was (28 ± 5) a, and the age of drug addiction was (25 ± 5) a].

Methods The physical dependence of tramadol was assessed using opiate withdrawal scale (OWS) which composed of 31 symptoms/signs^[4]. A 4-point scale was used to rate each symptom: nil (0), mild (1), moderate (2), and severe (3). Subjects were asked to rate their symptoms according to severity of previous experienced tramadol withdrawal. The psychic dependence was assessed by association test of Addiction Research Center Inventory short form — Chinese Version (ARCI-CV). ARCI-CV consist of 3 scales in particular being used to identify euphoric effects — Morphine Benzadrine Group (MBG), sedative effects — Pentobarbital-

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Chlorpromazine-Alcohol Group (PCAG), and psychotomimetic effects (disphoric) — LSD-Specific (LSD)^{5,6)}. Craving for tramadol was rated by visual analogue scale (VAS). This is a line of 100 mm in length, which one end represented no craving, while the other end represented maximal craving of tramadol. Subjects made a mark on the line⁷⁾ which was divided into 5 degrees: not at all (I), slightly (II), moderately (III), obviously (IV), and extremely (V) to represent the degree of craving experienced for tramadol. All the assessments were carried out by trained interviewers using the structured questionnaires.

Statistics Original data input and data analysis (factor analysis, Chi-square and ANOVA) were by EPI INFO⁸⁾.

RESULTS

The degree of physical dependence of tramadol was mild in 142 experienced tramadol withdrawal cases according to OWS (the range of scores of withdrawal symptoms were 0.05 - 1.07, Tab 1).

Three scores of MBG, PCAG, and LSD were 7.3 ± 3.5 , 6.1 ± 2.0 , and 3.4 ± 1.9 , respectively. Analysis of variance indicated that this variation in 3 scales was significant ($F = 38.12$, $P < 0.01$). The result of VAS indicated that 57.1% (125/219) of tramadol abusers had different degrees of craving experienced for tramadol effect (Tab 2).

DISCUSSION

Taken together, the findings of the preliminary study indicated that tramadol appeared to produce high abuse liability in this population of opiate addicts although the physical dependence was relatively low. The result did not support the previous study that tramadol had a low abuse liability among opiate addicts⁹⁾. The reasons of tramadol abuse in drug addicts in China were

Tab 1. Score of tramadol withdrawal symptoms/signs. $n = 142$.

Criterion symptoms/signs	OWS factors $\bar{x} \pm s$
Weakness	1.07 ± 1.07
Insomnia	0.97 ± 0.99
Increased sweating	0.87 ± 0.98
Ache and pain	0.95 ± 1.00
Restlessness	0.85 ± 1.09
Poor appetite	0.84 ± 1.00
Yawning	0.83 ± 1.05
Feeling sick	0.79 ± 1.00
Runny eyes	0.77 ± 1.03
Fatigue and tiredness	0.77 ± 0.99
Gooseflesh	0.69 ± 1.01
Hot and cold flushes	0.69 ± 0.97
Dry mouth	0.66 ± 0.89
Depression	0.64 ± 1.02
Runny nose	0.62 ± 0.91
Stiffness of arms or legs	0.53 ± 0.88
Feeling cold	0.52 ± 0.85
Dizziness or giddiness	0.51 ± 0.85
Vomiting	0.50 ± 0.91
Headache	0.42 ± 0.75
Diarrhoea	0.42 ± 0.86
Stomach cramps	0.37 ± 0.81
Heart pounding	0.35 ± 0.71
Drowsiness	0.35 ± 0.78
Trembling hands	0.27 ± 0.66
Spontaneous twitching of muscles	0.27 ± 0.71
Feeling unreal	0.19 ± 0.57
Muscular tension	0.17 ± 0.51
Trouble in starting urination	0.14 ± 0.48
Eyes sensitive to light	0.11 ± 0.45
Others	0.05 ± 0.32

Tab 2. Craving for tramadol. $P < 0.01$.

Degree	n	%	χ^2
I	94	42.9	75.86
II	39	17.8	
III	31	14.2	
IV	34	15.5	
V	21	9.6	

complex and multifactorial. First, opiate addicts try to misuse tramadol for "detoxification" from opiate dependence or ameliorate opiate withdrawal symptoms because get it easy as an un-controlled drug; furthermore, they want to treat "protracted abstinence" with tramadol during rehabilitation after acute opiate withdrawal; finally, some

opiate addicts want to seek psychological effects (euphoria) from tramadol, in specially, produced by interaction of tramadol with other abused drugs (polydrug abuse). In order to prophylactically prevent the abuse of tramadol among opiate addicts, it is necessary to strength the drug administration and surveillance of tramadol.

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曲马朵药物依赖性和滥用潜力¹ R971.2

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关键词 曲马朵; 物质滥用; 药物评价;
麻醉剂依赖性

目的: 在 219 例有曲马朵滥用史的阿片成瘾者中评价曲马朵的药物依赖性和滥用潜力。方法: 采用阿片戒断症状量表(OWS)评价曲马朵身体依赖性; 采用中文成瘾研究中心问卷(ARCI-CV)评价曲马朵精神依赖性; 采用视觉类比量表(VAS)评价曲马朵的渴求程度。结果: 曲马朵 OWS 各项戒断症状分值为 0.05-1.07; ARCI 测量药物欣快效应的 MBC 分量表, 测量镇静效应的 PCAG 分量表和测量拟精神病效应的 LSD 分量表的平均值分别是 7.3, 6.1 和 3.4 ($F=38.12, P<0.01$); 57.1% 的曲马朵滥用者对曲马朵有不同程度的渴求 ($\chi^2=75.86, P<0.01$)。结论: 曲马朵在阿片成瘾者中具有较高滥用潜力。

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