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Psychoactive Substance Use among Methadone Maintenance Therapy Clients in China

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Abstract

A proportion of methadone maintenance therapy (MMT) clients in China shifted their substance use habit from opiate to psychoactive substances. The objective of this study was to examine the pattern and associated factors of psychoactive substance use among MMT clients. The study was conducted among 2,448 clients from 68 MMT clinics of China. The type and frequency of psychoactive substance use were self-reported. About 38.1% (N=933) of the participants reported psychoactive substance use in lifetime, and 6.5% (N=158) in the previous 30 days. The most commonly used psychoactive substances were sedative/hypnotic/antidiarrheal agent and amphetamine. Psychoactive substance use in the past 30 days was correlated with younger age, recent heroin use, having psychoactive substance using friend(s), and depressive symptoms. The finding suggested that urinalysis of psychoactive substances should be routinely administered in the MMT clinics. Young clients, concurrent heroin users, and clients with depressive symptoms deserve more screening and intervention efforts.

Keywords

psychoactive substance use; methadone maintenance therapy; heroin; China

Introduction

Opiate drugs, especially heroin, have been the primary type of illicit drug used in China since the 1980s (Sun et al., 2014). During the recent years, there is a profound change in the profile of drug abuse in China: psychoactive substances, including crystal methamphetamine (also known as ‘ice’), 3,4-Methylenedioxy-N-methylamphetamine (MDMA; also known as

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Conflict of Interest

All authors have no conflict of interest.

Informed Consent

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). Informed consent was obtained from all patients for being included in the study.

‘ecstasy’), as well as ketamine and others, have surpassed heroin and become the most popular drug choice in China (Jia et al., 2015; Office of China National Narcotic Control Commission, 2015; XinhuaNet, 2015). As of 2014, the number of drug users officially documented by the Chinese public security department was 2.955 million, among whom approximately half (1.459 million) were psychoactive substance users (China National Narcotic Control Commission, 2015). Among the 480 thousand drug users newly reported in 2014, psychoactive substance users accounted for near 80% (China National Narcotic Control Commission, 2015). Psychoactive substances are neurotoxic, and long term use may induce cognitive and behavioral implications (Montoya et al., 2002; Parrott, 2006). In addition, its attendant behaviors, including high risk sexual behaviors and injection drug use, place the users at elevated risk for HIV infection (Reback, Shoptaw & Grella, 2008; Shoptaw, Reback & Freese, 2002). Therefore, the increasing trends in psychoactive substance use are of particular public health concern in China.

Methadone maintenance therapy (MMT) could block the effects of opiate withdrawal symptoms and the euphoria produced by opioids, such as heroin, so it could reduce or even eliminate opiate use (Sees et al., 2000; Strain et al., 1999; Vanichseni et al., 1991). However, its impact on psychoactive substance abuse is not as clear (DeMaria, Sterling & Weinstein, 2000). As a matter of fact, psychoactive substance use has been a serious concern among MMT patients in other countries (Kolar et al., 1990; Iguchi et al., 1993; Peirce et al., 2006; Shariatirad, Maarefvand & Ekhtiari, 2013). Reasons for using psychoactive substances during MMT included negative attitudes toward methadone, increased euphoria, enhanced energetic level and sexual performance, and self-medication for depression (Shariatirad, Maarefvand & Ekhtiari, 2013; Shaffer & LaSalvia, 1992).

To combat the substance abuse issue in the country, Chinese government started piloting MMT in 2004 (Wu et al., 2007). During the past decade, China has established the largest MMT program worldwide (Zhao et al., 2013). By August of 2014, 756 methadone maintenance clinics and more than 300 outreach clinics have been established in 28 provinces, autonomous regions and municipalities, cumulatively treating 410 thousand opiate users (WHO Representative office China, 2014). While the program has generally been successful, the issue of psychoactive substance use exists in MMT clinics in China. A pilot study indicated that a proportion of clients who attend MMT shifted their substance use habit from opiate to psychoactive substances (Lin, Ding & Li, 2012). A cross-sectional study conducted in eastern China revealed that 6.8% and 6.2% of the current MMT clients were tested positive for methamphetamine and MDMA, respectively (Bai et al., 2015). Because of the newness of the drug use trend, psychoactive substance use, particularly within MMT settings, has previously received little systematic investigation. Literature has documented factors correlated psychoactive substance use, which included demographic characteristics (such as being male, being married, having primary education, and unemployment), mental health status, alcohol and other illicit drug use (Ardila & Bateman, 1995; Malta et al., 2014; Okpataku et al., 2014), yet these associations have not been confirmed among MMT clients in China. This aim of this study was to examine the prevalence, patterns, and correlates of psychoactive substance use among MMT clients in China. We hypothesized that psychoactive substance use would be associated with a client's demographic characteristics, drug use related factors, and his or her mental health status.

Methods

Study Setting and Participants

The study used baseline data from a randomized controlled intervention trial before any intervention activities were delivered. In order to increase the representativeness of the study sample, MMT clients were recruited from five provinces (Sichuan, Guangdong, Shaanxi, Jiangsu, and Hunan Provinces, China) with varying economic and drug use conditions. Only the MMT clinics with more than 80 current clients were included to ensure enough eligible participants at each clinic. A total of 68 MMT clinics were randomly selected out of 110 clinics that meet our selection criteria in the five provinces. Using a random number table, about 36 clients were randomly selected from each of the 68 participating clinics, rendering a total sample size of 2,448 clients. According to the country's national guidelines, all MMT clients must be at least 20 years of age with opiate dependence, excluding those who are currently convicted of criminal or civil charges, and those who have severe mental disabilities (Ministry of Health of China, Ministry of Public Security of China & State Food and Drug Administration, 2006). This study included only the clients who met these criteria and were receiving MMT from the participating clinics at the time of the study.

Procedure

The data were collected between September 2012 and August 2013. The selected clients were approached by our project outreach staff when they came into the clinic for daily treatment. Using a standard script, our project staff explained the study purpose, procedure, risks, and benefits to the study participants. Each participant was assured of confidentiality and their right to refuse participation without affecting their treatment services. The refusal rate was less than 5%. Written informed consent was obtained from each of the participants. The study was reviewed and approved by the Institutional Review Boards of the participating institutes in the U.S. and China.

The survey questionnaire was administered face-to-face using the Computer Assisted Personal Interview (CAPI) method, with trained interviewers reading questions to the participants and recording their responses on laptop computers. The CAPI database was developed to automatically incorporate skip patterns and logistic check to reduce human errors. The survey took place in a private office within a MMT clinic and lasted about 45 to 60 minutes. The participants received 30 yuan (approximately 5 USD) for their time spent on the assessment.

Measures

The clients' psychoactive substance use was documented using the Addiction Severity Index (ASI) (McLellan et al., 1992). This instrument is widely used in addiction research to quantify the severity of drug using problems (Denis, Cacciola & Alterman, 2013). The Chinese version of ASI has been previously validated in China, and its reliability, validity, and responsiveness were confirmed (Luo, Wu & Wei, 2010; Sun et al., 2012). Using ASI, the consumption of the following seven types of psychoactive substances during lifetime and in the previous 30 days was documented: 1) antipsychotics (Barbiturate and sedative/hypnotic/antidiarrheal agent); 2) cocaine; 3) amphetamine; 4) cannabis; 5) hallucinogen; 6)

inhalance, and 7) others. The main outcome of interests were psychoactive substance use in the last 30 days (defined as having used any of the aforementioned seven types of substances for at least one day in the last 30 days) and psychoactive substance use in lifetime (defined as having used any of the seven types of substances for at least one year in lifetime).

The clients' depressive symptoms were measured using a brief version of the Zung's Self-Rating Depression Scale (Zung 1965). The scale has been validated previously among Chinese population (Li et al., 2011). The participants were asked to evaluate how often they experienced nine different situations (such as "I feel down-hearted and blue," "I get tired for no reason," and "I feel hopeful about the future"). Response categories ranged from (1) "a little of the time" to (4) "most of the time." After the positively-worded items reversely coded, a continuous overall score was constructed by summing all the items. A higher overall score indicated a higher level of depressive symptoms (Cronbach's $\alpha=0.75$).

The study also collected the clients' background characteristics, including demographics (age, gender, marital status, years of education, income earned during the past 30 days) and drug use-related factors (including duration of heroin use, MMT admission date, average daily methadone dosage, heroin use during the past 30 days, and if they had friend(s) who use drugs other than alcohol or heroin). The duration of MMT (in year) was computed by subtracting the reported date of admission in MMT clinic from the date of assessment. Days of heroin use during the past 30 days were self-reported, and the number was later dichotomized (1=used heroin for at least one day; 0=no heroin use).

Data Analysis

The statistical analyses were performed using the SAS 9.4 statistical software package (SAS Institute Inc., Cary, NC, USA). Firstly, descriptive statistics and frequency distribution for demographic and drug use related factors were summarized. These characteristics were compared between psychoactive substance users (both in the past 30 days and in lifetime) and non-users. Due to the study design, the participants were clustered within MMT clinics. Participants within a particular clinic may tend to be more similar to each other than to participants from different clinics, so we used mixed-effect models (*proc glimmix* and *proc mixed* for categorical and continuous variables, respectively) with clinic-level random effects to account for the clustering effect within a clinic (Hedeker, Gibbons, & Flay., 1994). Second, we descriptively analyzed the proportion of each type of psychoactive substance use during the last 30 days and in lifetime. Lastly, in order to examine the factors associated with psychoactive substance use, mixed-effect models were built for the participants' psychoactive substance use during the past 30 days (yes vs. no) and in lifetime (yes vs. no). The factors included in the models were: age (in year), gender (female vs. male), marital status (married/living with partner vs. single/separated/divorced/widowed), education (in year), personal income during the last 30 days (per 1000 yuan, approximately 157 USD), duration of heroin use (in year), duration of MMT use (in year), heroin use in the last 30 days (yes or no), lifetime alcohol use (yes or no), if have friend(s) uses drug other than heroin and alcohol (yes or no), and depressive symptoms (as a continuous score). The selection the covariates was based on our prior understanding of the population and the correlates of psychoactive substance use suggested by literature (Ardila & Bateman, 1995;

Malta et al., 2014; Okpataku et al., 2014). The models included clinic-level random effects to account for correlation within the clinics.

Results

Table 1 summarizes the characteristics of the study population. Among the 2448 participants, the majority (N=1938; 79.2%) were men. The average age was 40.6 years, with about half of the participants (N=1293; 52.8%) being between the ages of 36 to 45. More than half of the participants (N=1370, 56.0%) were married or living with a regular partner at the time of the study. Approximately one third (N=853, 35.0%) had a high school or above education. The average monthly income was 2070.0 yuan (approximately 333 USD), and 763 (31.2%) of the participants had no income during the previous 30 days. At the time of the study, the average duration of heroin use was 14.9 years and the average duration of MMT was 3.6 years. The average daily methadone dose was 54.0 ml. Half (N=1065, 49.7%) of the participants have used alcohol in their lifetime, and 14.2% (N=347) self-reported heroin use in the previous 30 days. About one tenth (N=266, 10.9%) of the participants had friend(s) who used drugs other than heroin and alcohol.

Among the 2448 participants, 158 (6.5%) have used psychoactive substance use during the past 30 days, and 933 (38.1%) did so in lifetime. Among the 158 lifetime users, 148 (15.8%) reported using psychoactive substance during the past 30 days. Table 2 presents the types of psychoactive substance used in the last 30 days and in lifetime. Sedative/hypnotic/antidiarrheal agent was the most commonly used psychoactive substance (29.9% in lifetime; 5.1% in the last 30 days), followed by amphetamine (14.2% in lifetime; 1.4% in the last 30 days) and hallucinogens (8.3% in lifetime; 0.3% in the last 30 days).

The frequency distribution of psychoactive substance use and its cross tabulation with background characteristics are also presented in Table 1. Participants who were 35 years or younger reported more psychoactive substance use in lifetime than older participants ($p<0.001$). Those who were married or living with a regular partner were less likely to report psychoactive substance use than those who were single, divorced, separated or widowed ($p=0.0028$ for last 30-day use; $p=0.0322$ for lifetime use). Lifetime psychoactive substance use was found to be the highest among those who had used heroin for 11–20 years (41%; $p<0.001$). Psychoactive substance users reported more heroin use in the previous 30 days than non-users ($p<0.001$). Having psychoactive substances using friends was positively correlated with psychoactive substance use in lifetime ($p<0.001$) and in the past 30 days ($p<0.001$). Those who had used psychoactive substances in the last 30 days reported significantly higher level of depressive symptoms than those who had not (21.9 vs. 18.0; $p<0.001$); this was also true for lifetime users (19.0 vs. 17.8, $p<0.001$).

Table 3 summarizes the results of mixed model for psychoactive substance use in the last 30 days and in lifetime. When all were held constant, heroin use in the past 30 days was the most important factor in association with psychoactive substance use in the past 30 days (OR=3.339, 95% CI: 2.226, 5.010). Other covariate significantly associated with psychoactive substance use in the last 30 days include younger age (OR=0.952; 95% CI: 0.921, 0.984), having psychoactive substances using friend(s) (OR=1.778; 95% CI: 1.098,

2.880), and having higher level of depressive symptoms (OR=1.130; 95% CI: 1.091, 1.170). Factors associated with lifetime psychoactive substance use included having psychoactive substance using friend(s) (OR=1.855; 95% CI: 1.329, 1.587), heroin use in the last 30 days (OR=1.528; 95% CI: 1.147, 2.036), lifetime alcohol use (OR=1.305; 95% CI: 1.066, 1.598), duration of heroin use (OR=1.074, 95% CI: 1.053, 1.096), depressive symptoms (OR=1.052; 95% CI: 1.031, 1.074), and age (OR=0.940; 95% CI: 0.924, 0.956).

Discussion

The paper reported that a substantial proportion of the MMT clients in China either have initiated or are currently involved in psychoactive substance use. The number indicates a need for increased attention to this issue. As previous studies suggested, after cessation of opioid abuse, MMT clients might seek psychoactive substances as an attempt to achieve alternative rewarding effect (Maremmanni & Shinderman, 1999; Maremmanni et al., 2007). The concomitant use of psychoactive substances may lead to poor MMT adherence and compromise the treatment outcome (DeMaria, Sterling & Weinstein, 2000; Pashaei et al., 2014), so the issue is in an urgent need to be prevented and controlled. The current Chinese national MMT guideline requires MMT clients to receive urine morphine test on both regular and random basis during the maintenance treatment to monitor the use of heroin (Ministry of Health of China, Ministry of Public Security of China & State Food and Drug Administration 2006). However, the guideline did not specify the testing of non-opiate substances, so urine psychoactive substance screening is not consistently performed in MMT clinics (Cai et al., 2011). Given the considerable prevalence of psychoactive substance use among MMT clients, urinalysis of psychoactive substances should be incorporated and routinely administered in the MMT clinics, so that psychoactive substance users could be detected and linked to treatment and care. More importantly, behavioral, psychological, and medical interventions are warranted to be integrated into the current MMT to protect the clients from the negative impacts of psychoactive substance use and to maintain the benefits of MMT (Shariatirad, Maarefvand & Ekhtiari, 2013).

The study revealed several factors associated with psychoactive substance use among MMT clients. More psychoactive substance use was found to be associated with younger age, which was consistent with the literature which indicated that psychoactive substances were primarily popular among young people (Goggin, Gately & Bridle, 2015). The study also found a strong correlation between recent heroin use and recent psychoactive substance use, which suggested that client who was detected to use heroin should simultaneously receive psychoactive substance screening and interventions. In this study, high dose of methadone did not show to have a protective effect against psychoactive substance use, which was supported by previous studies (Grabowski et al., 1993; Hartel et al., 1995). Findings also confirmed that having a psychoactive substances using friend increased the MMT clients' likelihood of psychoactive substance use (Au & Donaldson, 2000; Lau, Tsui & Lam, 2007). As reported by numerous literatures, social network had an impact on psychoactive substance using behaviors by making drugs more available and emitting environmental cues to trigger craving and withdrawal (Li et al., 2012). In order to reduce psychoactive substance use, intervention effort should aim to supplant the harmful friendship with nondrug-using supportive networks (Costenbader, Astone & Latkin, 2006).

Mental health status was also found to be correlated with psychoactive substance use. The interplay between psychoactive substance use and mental illnesses has been documented by numerous studies (McKetin et al., 2011; Wang et al., 2012). In particular, psychoactive substances have direct effect on monoamine regulation within the brain, producing various depressive symptoms including low mood, fatigue, sleeping disorder, appetite changes, irritability, and/or poor concentration (Bamford et al., 2008; London et al., 2004). Conversely, depressive symptoms can reduce adherence to addiction treatment and elevate the risk of psychoactive substance use (Glasner-Edwards et al., 2009). The finding implies that the MMT services providers should closely monitor the clients' mental health status to identify early signs of psychoactive substance use, so that interventions can be delivered in a timely manner.

Findings should be interpreted within the context of the study limitations. First, this study used a cross-sectional design, so that we were unable to make causal inferences. Second, the psychoactive substance use was based on self-reports that might be under-reported due to social-desirability bias. The report of drug-related factors might also be subject to recall bias. Third, the study participants were recruited from only the MMT clinics with more than 80 current clients in five provinces of China, so the results might not be generalizable to clinics with fewer clients or clinics outside of the study areas.

Despite the limitations, the study has implications for the MMT programs in China. The study findings highlight the importance for policy-makers and health administrators to recognize and respond to the issue of psychoactive substance use within MMT clinics. Interventions to help MMT clients maintain abstinence from psychoactive substances are urgently needed. It is recommended that more attention should be paid to a subset of MMT clients who are young, those who concurrently use heroin, and those who demonstrate depressive symptoms.

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Table 1

Sample description

	Overall	Last 30-day use	P	Lifetime use	P
	N=2448 N (%)	N=158 N (%)		N=933 N (%)	
Age			0.091		<0.001
35 or younger	615 (25.1)	50 (8.1)		272 (44.2)	
36–45	1293 (52.8)	83 (6.4)		494 (38.2)	
46 or older	540 (22.1)	25 (4.6)		167 (30.9)	
Gender			0.124		0.654
Male	1938 (79.2)	130 (6.7)		743 (38.3)	
Female	510 (20.8)	28 (5.5)		190 (37.3)	
Marital status			0.003		0.032
Single, divorced, separated or widowed	1077 (44.0)	92 (8.5)		456 (42.3)	
Married or living with a regular partner	1370 (56.0)	66 (4.8)		477 (34.8)	
Education			0.770		0.246
Elementary or lower	362 (14.8)	26 (7.2)		157 (43.4)	
Secondary school	1224 (50.2)	72 (5.9)		452 (36.9)	
High school or higher	853 (35.0)	59 (6.9)		323 (37.9)	
Personal income in the last 30 days			0.178		0.251
No income	763 (31.2)	56 (7.3)		316 (41.4)	
1–1500 yuan	732 (29.9)	48 (6.6)		270 (36.9)	
1501 yuan or more	952 (38.9)	54 (5.7)		347 (36.5)	
Years of heroin use			0.453		<0.001
Less than or equal to 10 years	575 (23.5)	35 (6.1)		179 (31.3)	
11–20 years	1466 (60.0)	100 (6.8)		601 (41.0)	
More than 20 years	403 (16.5)	23 (5.7)		153 (38.0)	
Duration of MMT use			0.551		0.584
Less than one year	341 (14.0)	26 (7.6)		133 (39.0)	
1–5 years	1426 (58.6)	87 (6.1)		533 (37.4)	

	Overall N=2448 N (%)	Last 30-day use N=158 N (%)	P	Lifetime use N=933 N (%)	P
Longer than 5 years	668 (27.4)	45 (6.7)	0.295	264 (39.5)	0.191
Methadone dosage 60 ml					
Yes	987 (40.4)	72 (7.3)		404 (40.9)	
No	1461 (59.6)	86 (5.9)	<0.001	529 (36.2)	<0.001
Heroin use in the last 30 days					
Yes	347 (14.2)	65 (18.7)		182 (52.5)	
No	2101 (85.8)	93 (4.4)	0.256	751 (35.7)	0.004
Lifetime alcohol use					
Yes	1065 (43.5)	80 (7.5)		478 (44.9)	
No	1383 (56.5)	78 (5.6)	<0.001	455 (32.9)	<0.001
Friend(s) uses drugs other than heroin/alcohol					
Yes	266 (10.9)	34 (12.8)		138 (51.9)	
No	2182 (89.1)	124 (5.7)		795 (36.4)	

Table 2

Types of psychoactive substance used by the participants

	Last 30-day use		Lifetime use	
	N	%	N	%
Antipsychotics				
(1) Barbiturate (<i>pentobarbital, secobarbital, calmine, amobarbital, phenobarbital, butalbital, glutethimide and so on</i>)	16	0.7	97	4.0
(2) Sedative/hypnotic/antidiarrheal agent (<i>diazepam, triazolam, alprazolam, clonazepam, chlordiazepoxide, chloralHydrate, methaqualone, clozapine, chlorpromazine, promethazine, diphenoxylate, tramadol and so on</i>)	125	5.1	731	29.9
Cocaine	8	0.3	31	1.3
Amphetamine (<i>such as amphetamine, dexamphetamine, ritalin, phenmetrazine, methamphetamine, MDMA and so on</i>)	35	1.4	348	14.2
Cannabis	8	0.3	108	4.4
Hallucinogens (<i>such as ketamine, LSD, PCP, mescaline, psilocybin, peyote and so on</i>)	6	0.3	202	8.3
Inhalance (<i>such as nitrous oxide, Isoamyl nitrite, glue, organic solvent, gasoline, toluene and so on</i>)	3	0.1	7	0.3
Others	3	0.1	6	0.3

Table 3

Mixed-effect models for psychoactive substance use

	Last 30-day use	Lifetime use
	OR (95% CI)	OR (95% CI)
Age (<i>Per year</i>)	0.952 (0.921, 0.984)	0.940 (0.924, 0.956)
Gender (<i>Female vs. male</i>)	0.686 (0.405, 1.161)	0.803 (0.620, 1.040)
Marital status (<i>Married or living with a regular partner vs. not married</i>)	0.704 (0.476, 1.041)	0.934 (0.760, 1.149)
Education (<i>Per year</i>)	0.991 (0.923, 1.065)	0.979 (0.943, 1.018)
Personal income in the last 30 days (<i>Per 1000 yuan</i>)	1.010 (0.981, 1.040)	0.993 (0.969, 1.017)
Duration of heroin use (<i>Per year</i>)	1.032 (0.993, 1.073)	1.074 (1.053, 1.096)
Duration of MMT use (<i>Per year</i>)	1.057 (0.953, 1.172)	1.007 (0.952, 1.065)
Methadone dosage (<i>60 ml vs. <60 ml</i>)	1.011 (0.680, 1.503)	1.002 (0.810, 1.239)
Heroin use in the last 30 days (<i>Yes vs. No</i>)	3.339 (2.226, 5.010)	1.528 (1.147, 2.036)
Lifetime alcohol use (<i>Yes vs. No</i>)	1.206 (0.820, 1.772)	1.305 (1.066, 1.598)
Friend(s) uses drugs other than heroin and alcohol (<i>Yes vs. No</i>)	1.778 (1.098, 2.880)	1.855 (1.329, 2.587)
Depressive symptoms (<i>Per point</i>)	1.130 (1.091, 1.170)	1.052 (1.031, 1.074)