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Socio-demographic and clinical profile of mixed opioid and amphetamine type stimulant dependent subjects in Malaysia: A preliminary report

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ABSTRACT

Aims: In recent years, the increasing trend of amphetamine type stimulant (ATS) use among opioid dependent subjects was strikingly afflicted worldwide, including Malaysia. To study socio-demographic and clinical characteristics of mixed opioid and ATS dependent subjects undergoing methadone maintenance therapy (MMT) program in order to provide supportive information and enhance the management of mixed drug abuse related to health and social effects.

Methods: A descriptive study was carried out in Methadone Clinic in Kuala Terengganu among mixed opioid and ATS dependent patients (n=36) who fulfilled the inclusion and exclusion criteria, and all of them were interviewed.

Results: The mean standard deviation (SD) age of patients was 40.98 years (SD: 4.64), and the most common age of initiation was 15-20 years (42%). Most of the educational background was up to high school level (44%). Morphine and methamphetamine were the most commonly abused substances. The majority of 83.1% used injections as their method of opioid ingestion, while 65.3% preferred chase to ingest ATS. About 30.6% of drug-dependent subjects in this study were on MMT for a 4-year duration and 63.5% of them were on methadone dosage between 45 and 70 mg/day. Most of them demonstrated no history of arrest and conviction for drug use (63.9%) or other criminal acts nonrelated to drug abuse (94.5%).

Conclusions: This study provides update and supportive information of socio-demographic and clinical characteristics of mixed opioid and ATS dependent subjects undergoing the MMT program that may contribute towards comprehensive management to overcome the significant surge of ATS use among opioid dependents.

Introduction

Drug addiction imposes a major threat to public health and social issue worldwide involving opioids addiction, methamphetamine, amphetamine type stimulant (ATS), cocaine, cannabis and other psychoactive substances (1). Malaysia is facing a serious public health problem associated with drug addiction. Through a historic window, this problem was initiated in Malaysia by hippy culture during the 1970s during

the period of Vietnam War, which introduced cannabis and heroin to local residents (2). A cumulative total of 512,767 drug users were identified as reported by National Anti-Drugs Agency (NADA) between 1988 and 2017, representing 1.6% of the total Malaysian population (NADA, 2017) (3). The actual figure of the total drug users may exceed more than half a million as the national database has only reported individuals who have been arrested and convicted for illicit drug use and sent to mandatory

institutional rehabilitation (4). The annual number of reported drug addicts by the NADA in 2010 to 2017 is approximately 15,000 to 30,000 per annum with a peak of 30,844 in 2016 and the least cases were detected in 2012 with 15,101 cases.

Heroin maintains the first rank of the most frequently used drug from 2010 to 2013 with a peak of 75.07% of total abused drugs in 2013. The percentage of heroin addiction per year shows a steady decline from 2014 to 2017 in which it reduced by half in 2017, which accounts for 39.1% (3).

The scenario is evidenced by the growing problem of usage of ATSs including crystal methamphetamine and various other methamphetamine and/or amphetamine-containing substances/pills in Malaysia and the surrounding countries (5). The rise of methamphetamine use in South East Asia has attracted significant attention as it emerges as the world's fastest-growing methamphetamine market and the report that this drug is the primary drug of concern in Southeast Asia (SEA) countries (6). According to Chawarski et al. (7) (2012), ATS use in Malaysia was insignificant before 1987. Over the next several years, the total ATS use increased gradually before spiking up after 1997. By 2018, the total ATS use was 75% of the participants. Vicknasingam et al. (8) (2010) found that approximately 60% of opioid injection drug users reported lifetime use of ATS and 29% also reported lifetime injection of ATS in many regions in Malaysia. Between 2010 and 2017, it was observed that ATSs addiction ranged around 30-40% of the total drug abuse per year. The percentage started to rise steadily from 2014 and eventually resulted in more than half of the total drug used in 2017, which exceeded the heroin usage by 20.88% (3). The rising of ATSs usage is also evidenced by the increasing number of admissions in recent years for amphetamines use. In 2015, the total number for admission related to drug treatment was 6,032, of which opiates accounted for 71% (4,287), while the amphetamines use-related admission was 1,571, accounting for 26% of the total in 2015, and having an estimated increase of 47% compared to 2014 (839 admissions).

Of this total, methamphetamine (crystalline form) represented 77% (1,213 admissions) of the amphetamines-related treatment admissions in 2015 (9-11). The male population continues to represent the majority (96.4%) of cumulative drug addict cases in Malaysia, with a ratio of 1 female for every 26 males. About 41.7% of reported cases are amongst young people between the ages of 13 and 29 years. In term of ethnicity, 80.6% of Malays, 7.5% of Chinese, and 6.8% of Indians were drug addict with other ethnics contributing 5.1% (3).

Opioids including synthetic or naturally occurring alkaloid (benzylisoquinoline alkaloids) are derived from the opium poppy plant (12). Of all, morphine and heroin are the most known and used opioids, while others include methadone, buprenorphine, codeine, tramadol, oxycodone, and hydrocodone (6). They are prescribed clinically for its analgesic properties and in treating

opioid dependence. Excessive opioid use, in the absence of proper medical supervision, can lead to fatal respiratory depression (13). Opioids are also available in the form of liquid, solid, and powder (14). Apart from its powerful analgesic effects, opioid intake may also induce relaxation, 'high' feeling, as well as other side effects such as physical dependency, tolerance, respiratory depression, sedation, constipation, nausea, and death.

ATS are manufactured composites that consist of two main sub-type substances: amphetamine and ecstasy. Amphetamine group substances include amphetamine, methamphetamine and their derivatives, such as methcathinone, fenethylamine, and methyl-phenidate (9). Methamphetamine (street name is frequently known as "crystal", "glass", "speed", "ice") is being manufactured simply in illicit laboratories from readily accessible, cheap elements. Ephedrine or pseudoephedrine is the most commonly used precursors for methamphetamine synthesis (14). Amphetamine group substances are being prescribed for several clinical conditions under strict rules and regulation (15). Ecstasy group substances are synthesized from amphetamine derivatives, including methylenedioxy-N-methylamphetamine (MDMA) and MDMA-like drugs. They are classified as 'entactogens' with no therapeutic use that has been recognized so far.

Unlike opioid, which is commonly administered by injection, ATS is available in various forms like tablets, crystal, and liquid which are smoked, snorted, injected, or used per rectal (16). ATS administration, particularly the amphetamine-group substances, induce euphoric in users, heighten their confidence level, and increase their alertness, arousal, libido, energy level, and physical strength. Besides, ATS also raises blood pressure, heart and respiratory rates (14). Meanwhile, a wrongful usage of methamphetamine and ATS may lead to a severe complication, including neurological damage to the brain, acute renal failure, and toxic effect to cardiovascular system (17).

Comprehensive management and intervention strategy were launched to overcome the alarming increase of ATS use among opioid dependents. The objective of this study is to provide the socio-demographic and clinical characteristics of mixed opioid and ATS dependent subjects undergoing the methadone maintenance therapy (MMT) program in order to provide supportive information and help in enhancing the management with recent knowledge of drug abuse pattern in relation to health and social effects.

Methods

A descriptive, cross-sectional study was carried out in Methadone Clinic in Kuala Terengganu. The study protocol was approved by the Medical Research and Ethics Committee, Ministry of Health Malaysia [National Medical Research Register-18-1989-41507 (IIR)]. The sample was recruited

among patients undergoing the MMT program in this clinic, who fulfilled the inclusion criteria as follows: (1) Diagnosis for COATS based on The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; (2) male, aged from 18 to 50 years; (3) no previous history or current mental disorder including major depression, psychoses, or bipolar disorder; (4) seronegative for human immunodeficiency virus (HIV); and (5) Malay (third generation). Only 36 out of a total 70 male patients attending the MMT program in this clinic, who fulfilled the criteria, were enrolled in this study. No female patient registered in this MMT clinic. All subjects gave voluntarily signed informed consent after the explanation of the study procedures and objectives. A pre-designed questionnaire form which was based on the Addiction Severity Index criteria was used for data collection and subject's evaluation. The questionnaire contained the subject's personal details, including age, race, religion, relevant family history, and physical assessment [body mass index (BMI) and blood pressure measurement]. Besides, socio-economic status, such as marital status, occupation, educational level, were also included. A detailed history of substances abused was also taken including the age of drug initiation, duration, mode of ingestion, duration on MMT program, frequency of methadone use, methadone dosage, and involvement with criminal arrest or conviction.

Statistical Analysis

Descriptive statistics were applied for demographic data of subject analysis using the GraphPad Prism (GraphPad Prism version 6 for Windows, GraphPad Software, San Diego, CA, USA, www.graphpad.com).

Results

Socio-demographics Characteristics

All subjects recruited in this study were Malay male, and the minimum and maximum ages for the subjects were 31 and 49 years, respectively. Approximately 42% and 14% of them were employed and self-employed, respectively, while 44% were unemployed. About 37.5% of the drug-dependent subjects were married, whereas more than 52.5% were single, and the remaining 10.0% were divorced. As for the educational background, at least 44% of the drug-dependent subjects had studied up to high school. All the subjects had a normal range of BMI and blood pressure measurement. Details of the socio-demographic characteristics were shown in Table 1.

The minimum of opioid and ATS initiation age among the subjects in this study was 15 years, while the maximum was 30 years with the mean and standard deviation of 23.23 and 4.301, respectively, and 58.6% of drug-dependent subjects were on both opioid and ATS addiction for more than 10-year duration. The most commonly used drug for opioids was morphine while that for ATS was methamphetamine. The majority of 83.1% used injections as their method of opioid ingestion while 65.3%

preferred chase to ingest ATS. About 84.2% (n=30) used opioid 1 to 5 times on a daily basis while most of the drug-dependent subjects used ATS 1 to 5 times per week, which accounted for 70.7% (n=25). Most of them demonstrated no history of arrest and conviction for drug use (63.9%) and other crimes which were nonrelated to drugs (94.5%) (Table 2). About 30.6% (n=11) of drug-dependent subjects in this study were on MMT for a 4-year duration while the longest duration on MMT among them was 11 years, accounting for 5.6% (n=2) of all subjects. Majority of the drug-dependent subjects were on methadone dosage between 45 and 70 mg/day, representing approximately 63.5%

Table 1. Socio-demographic characteristics of mixed opioid and amphetamine-type stimulant dependent subjects undergoing methadone maintenance therapy program in Bukit Tunggul Health Clinic

Age group (years)		
31-40	15	41.7
40-50	21	58.3
BMI		
Underweight	1	2.8
Normal range	30	83.3
Overweight	5	13.9
Blood pressure (mm/Hg)		
Systolic blood pressure		
100-110	1	2.8
110-120	8	22.2
120-130	27	75
Diastolic blood pressure		
60-70	3	8.3
71-80	21	58.3
81-90	12	33.4
Gender		
Males	36	100
Females	0	0
Education level		
Primary	4	11
High school	32	89
Employment status		
Unemployed	16	44
Employed	5	14
Self-employed	15	42
Religion		
Muslim	36	100
Non-Muslim	0	0
Marital status		
Married	14	37.5
Single	19	52.5
Divorced	3	10
BMI: Body mass index		

(n=23). The highest methadone dosage among them was 120 mg/day, which accounted for 2.8% (n=1), while 28% (n=10) were on methadone dosage of 40 mg/day and less with the lowest methadone dosage of 2.5 mg/day, representing 2.8% (Table 3).

Discussion

The present study reported a similar demographic pattern with the previous study regarding predominantly male gender among drug-dependent subjects (18). Mohamed et al. (19)

Table 2. Clinical characteristics of the mixed opioid and amphetamine-type stimulant drug-dependent subjects undergoing methadone maintenance therapy program in Bukit Tunggul Health Clinic

Drug addiction initiation age (years)		
15-20	15	42
21-25	13	36
26-30	8	22
Duration on mixed drug addiction		
<10 years	21	41.4
>10 years	15	58.6
Main drug		
Opioid		
Morphine	29	80.6
Heroin	7	19.4
ATS		
Methamphetamine	36	100
Others	0	0
Methods of ingestion		
Opioid		
Injection	30	83.1
Chase	5	14.3
Both	1	2.6
ATS		
Injection	9	24.9
Chase	23	65.3
Both	2	9.8
Patterns of drug use		
Frequency of daily opioid use		
1-5 times	30	84.2
>5 times	6	15.8
Frequency of weekly ATS use		
1-5 times	25	70.7
>5 times	11	29.3
History of drug use arrest and conviction		
Yes	13	36.1
No	23	63.9
History other crime arrest and conviction		
Yes	2	9.8
No	34	90.2

ATS: Amphetamine-type stimulant, MMT: Methadone maintenance therapy

Table 3. Clinical characteristics of methadone usage among mixed opioid and amphetamine-type stimulant drug-dependent subjects undergoing methadone maintenance therapy program in Bukit Tunggul Health Clinic

Duration on MMT (years)		
1-5	24	66.7
5-10	10	27.8
>10	2	5.5
Methadone dosage (mg)		
1-40	10	27.8
41-80	19	52.8
81-120	7	19.4

MMT: Methadone maintenance therapy

(2008) reported the significant association of male gender and drug dependence in which male participants showed a higher tendency for substance and drug dependence. Tuchman (20) (2010) suggested that women faced more obstacles regarding access to substance abuse compared to men. Above all, multiple factors affecting the difference in gender-related drug use disorder include epidemiology, social background, biological responses, underlying psychiatric illness, progressions to drug dependence, difficulty to access treatments, follow-up, and completion. The average age of our subjects was 40.94 (4.64) years, while the drug addiction initiation age was ranging between 15 and 30 years, which is in line with the increasing trend worldwide that substance abuse begins at a young age (21).

Previous studies linked the opioid-dependent patients on methadone maintenance with higher preference and consumptions of sugary foods that lead to weight gain and higher BMI (22,23). However, the mean BMI for the drug-dependent subjects in this study was 21.15 (3.08). The possible explanation is because of the ATS use among drug-dependent subjects. Effects of amphetamines on hypothalamic receptors would lead to a norepinephrine release together with slight dopamine and serotonin release that resulted in central nervous system stimulation and increased activity, decreased appetite - hence, resulting to a weight reduction (24). In addition, previously in the 1940s and 1950s, amphetamine and amphetamine derivatives had become primary drug used in treating obesity in the United States and was approved by US Food and Drug Administration (25).

MMT program is effective and gives numerous benefits for opioid dependence subjects, which includes health benefits as well as markedly improved family stability, social functioning, and well-being (26). Most of our drug-dependent subjects were either employed or self-employed, which represented by 36% and 14%, respectively. Employment involved working as a security guard, a waiter at restaurant, welder, and many more. Approximately 37.5% of them were married and had children while 52.5% remained single.

The current study is confined to Malay subjects which represent the largest ethnicity in Malaysia population. NADA (2017) reported that the majority of drug users involved Malay ethnicity compared to others. Hence, we have selected Malay subjects from three generations of Malay ethnicity (his father, mother, grandfather, and grandmother must be of Malay origin). This is important in preventing ethnicity bias as Malaysia is a multi-racial country.

Besides, despite the increasing trend of drug use among women in recent years, as reported by NADA, (2017), the male population still accounts for the majority of the drug users in Malaysia. Mohamed et al. (19) (2008) reported the significant association of male gender and drug dependence in which male participants showed a higher tendency for substance and drug dependency. Tuchman (20) (2010) suggested that women faced more obstacles regarding access to substance abuse compared to men. Above all, multiple factors affecting the difference in gender-related drug use disorder include epidemiology, social background, biological responses, underlying psychiatric illness, progressions to drug dependence, difficulties in accessing treatment, follow up, and completion.

According to drug report by NADA (2017) and Ibrahim et al. (27) (2012), teenagers represented 2.67% of all those arrested and charged as drug dependents with the majority of them aged between 14 and 15 years, which accounted for 57.5% of all teenagers involved. This report also revealed that crystalline methamphetamine was the drug of choice which was commonly used among both teenagers and youth group. A possible explanation for this might be due to the easy access and the low price of the drug that made it affordable for the students to try this potent drug and subsequently become addicted (28). Besides, this drug can be taken through various routes including smoking, injection, swallowing or snorting. All of these may be the key factors that excite teenagers and youth to get and try them.

Another possible factor contributing to this scenario is due to the locality of Malaysia, which is situated in the SEA and shares a border with Thailand. UNDOC (6) (2019) has reported that the SEA region is recognized as the fastest-growing methamphetamine market worldwide. Apart from being produced in Malaysia on a small scale, ATS and other synthetic drugs are brought in Malaysia through trafficking routes across Thailand (29,30).

Majority of drug-dependent subjects preferred injection as their route of choice in using opioid [59.3% (n=22)]. This finding is consistent with that of Desrosiers et al. (29) (2016) where most of the subjects take opioid through injection. The reason for such preference might be due to the fast effect of the drug even with a small amount. As for ATS, our study reported the chase method ("chase the dragon") as the most preferred route, which accounts for 73.6% (n=26). Through the usage of this method,

the methamphetamine is vaporized by crushing the tablets and then heated on tin foil. The formed fumes are smoked in the same way to the 'chasing the dragon' used in opioid smoking (31). MMT program has been introduced as substitution therapy to opioid addiction in Malaysia since 2005, and currently, this program becomes widely available in almost all health care centres throughout Malaysia (32). In this study, a total of 30.6% (n=11) of drug dependents were on for a 4-year duration while the longest duration on MMT among them was 11 years [5.6% (n=2)]. This result is in line with previous reports stating that MMT program is effective at improving the quality of life of drug-dependent subjects including significantly reducing relapse of opioid use, mortality rates, blood-borne illness such as hepatitis B, hepatitis C, and HIV/AIDS; in addition to improving family stability and increase employment potential (33,34). Being a single-dose therapy on a daily basis at low cost with tolerable side effects are also the contributing factors rendering this MMT program successful and effective for the drug-dependent subjects.

Approximately 63.5% (n=23) of our subjects are on average of 45-70 mg/day of methadone. This finding was supported by a previous review by Faggiano et al. (35) (2003) in which it was suggested that maintaining the patient on higher methadone dosages (60-100 mg/day) was more effective to ensure patient's compliant on MMT program and it helped to reduce the opioids use relapse during the program compared to lower dosages. However, the optimal dosage still subjected to the clinical ability and patient's condition. This finding was further supported by a study of Mohamad et al. (36) (2010), which also recommended that a higher dosage of methadone might reduce the risk of illicit opioid abused.

The present study has several limitations. The relatively small sample size for this study is due to our objectives that aimed only drug dependent subjects who were on both opioid and ATS addiction at the same time, which made it harder to recruit eligible volunteers. Another limitation was the place of recruitment, where we recruited the drug dependent subjects receiving MMT in methadone clinic hosted by Health Clinics in Kuala Terengganu only, instead of involving other possible potential facilities such as drug rehabilitation centre and prison. Besides, our study is also confined to Malay male adult population, which only represents the sub-group population from a general population from specific location in Malaysia. As we excluded other races such as Chinese and Indian population, hence our result only represents the effect of drug dependence to peripheral dopamine systems among Malay male population. It makes these findings less generalisable to represent Malaysian male population as a whole.

Conclusion

This study provides update and supportive information of socio-demographic and clinical characteristics of mixed opioid

and ATS dependent subjects undergoing the MMT program that may contribute towards comprehensive management to overcome the significant surge of ATS use among opioid dependents.

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Ethics

Ethics Committee Approval: The study protocol was approved by the Medical Research and Ethics Committee, Ministry of Health Malaysia [National Medical Research Register-18-1989-41507 (IIR)].

Informed Consent: All subjects gave voluntarily signed informed consent after the explanation of the study procedures and objectives.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: I.A., Concept: R.A.B., I.A., Design: N.K.M.J., A.A.N., R.A.B., I.A., Data Collection or Processing: N.K.M.J., A.A.N., R.A.B., Analysis or Interpretation: N.K.M.J., A.A.N., R.A.B., I.A., S.I., Literature Search: N.K.M.J., Writing: N.K.M.J., I.A.

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