



## **Amphetamine induced psychosis and its related symptoms**

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### **Introduction**

Methamphetamine is the second most popular illicit drug worldwide, whose use is particularly common in Asia, Oceania and North America. The abuse rate of this substance was quite low about eight years ago and no cases of its abuse were indicated in a rapid situation assessment (RSA) performed in 2004, when opium was the main substance of abuse among 52.8% of substance users, followed by heroin (20.7%) and cannabis (9.3%). However, another RSA carried out in 2007 in showed that 3.6% of drug dependents used methamphetamine. In this study, the ranking of the other substances had also changed and opium was the main drug of abuse in 34% of the users. Crack cocaine, a newly introduced drug to the market, was second with 26.6% and heroin was third with 19.2%. RSA 2007 was a cross-sectional national survey performed on 7406 substance users, which were selected from one of the three substance user populations: addiction treatment centers, prisons and homeless addicts. No published evidence exists on the prevalence of different substances in a national level in recent years. Anecdotal reports of psychiatrists and clinicians working in addiction treatment clinics suggest a several fold increase in the number of patients using methamphetamine. Furthermore, the local production of methamphetamine has increased its accessibility and its

price has fallen to less than one-tenth its previous price; as a result, a significant increase in methamphetamine use in the recent years is highly probable. Most of the patients use methamphetamine by smoking and rare cases of other routes, including injection, snorting or eating, have also been reported. Psychosis has long been considered to be a side effect of amphetamine and methamphetamine use in the literature. McKetin et al. (2006) have shown that the prevalence of psychosis is 11 times higher in methamphetamine users than in general population. High doses of methamphetamine or its chronic use can induce symptoms similar to those seen in paranoid schizophrenia, including delusion of persecution and auditory hallucinations. It seems that the development of psychosis in methamphetamine users is dependent on several factors, including dose and duration of use, route of administration (intravenous, smoking and oral) and personal vulnerability to psychosis. Japan is the country with the longest experience with methamphetamine abuse and as a result with methamphetamine-induced psychosis (MIP). At least three epidemics have happened in Japan during the last 60 years; the first epidemic in 1954, the second in 1984 and the third in 1995. Ujike and Sato compared the data of the three epidemics and showed that some clinical features of MIP differ between the three epidemics. For example, the latency between abuse and the development of psychotic

episode was longer in the second epidemic than the first epidemic, or the prevalence of cases with prolonged psychosis was higher in the third epidemic compared with the second. Acute psychosis of methamphetamine often presents with agitation, anxiety and confusion as well as auditory and visual hallucinations and paranoid delusions. In a study on 445 methamphetamine users from a psychiatric hospital and a detention center, Chen et al. found that 174 (39.1%) of subjects who had used the substance more than 20 times a year, had the lifetime diagnosis of MIP. The most common symptoms in these patients were auditory hallucination (84.5%), persecutory delusion (71%) and delusion of reference (62.8%). Although most cases of MIP resolve hours to days after discontinuation of methamphetamine, a significant percentage of cases have been claimed to continue to experience psychotic symptoms for weeks to months and even years after abstinence. Therefore, in cases of chronic psychosis, differentiating amphetamine-induced psychosis from idiopathic schizophrenia can be difficult, especially because symptoms of both disorders could also be indistinguishable. This is especially important because most cases of MIP, unlike the patients with schizophrenia, do not need a long term treatment with antipsychotic medications. Although little evidence exists on how long antipsychotics should be continued in patients with MIP, some authors suggest that several weeks after stabilization of the patients is sufficient for those whose symptoms remit in the first two weeks. Despite the high prevalence of methamphetamine use and the considerable potential for development of MIP, only very limited information is available on the clinical aspects of MIP. To our knowledge, this is the first study from a Middle Eastern country to report the clinical picture of psychosis in a relatively large sample of patients with MIP. The present research was carried out to improve our understanding of

the different aspects of MIP in a sample of psychiatric inpatients, as well as to provide a basis for comparison with research in other locations.

### **Methods**

This was a retrospective descriptive study that was performed on the files of patients who were admitted to the Psychiatric Hospital. In general, all of the patients are thoroughly evaluated by psychiatric residents on admission and then the supervising board certified the psychiatrists visiting the patients and confirm the diagnoses based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, Text Revision (DSM-IVTR). For this study, all of the files of patients admitted to the hospital during the specified period were manually searched for the diagnosis of MIP, substance-induced psychotic disorder and psychotic disorder. These terms were considered by the researchers to be most related with the diagnosis of MIP. The extracted files were scanned for the diagnosis of MIP and those with the diagnosis were examined. One hundred and eleven files with MIP in the two years interval were identified. A checklist was designed to extract data related to psychotic episode (the onset latency, types of symptoms and duration of symptoms), substance use history (age of first drug abuse, route of administration and the frequency of drug abuse) and previous psychiatric history as well as demographic data of the patients on admission (including age, education level, occupation, etc.). The patients remained anonymous; also, all information gathered from the files was considered confidential and are not to be availed to any party or person. Descriptive and frequency statistics were calculated and used to describe the data. SPSS 17 software was used for data analysis.

### **Results**

Demographic data of the cases are explained. The mean age of patients was 30.44 years (SD = 7.54), and the mean

age of first methamphetamine abuse was 28.8 years (SD = 7.74). The lowest age of first abuse was 17 and the highest was 54. All patients used smokable methamphetamine and there was no report of other routes of administration. Twenty patients (18%) used methamphetamine more than once a day, 67 patients (60.4%) reported a daily use and 24 patients (21.6%) used methamphetamine on occasions or "every once in a while". Most of the patients had also a history of abusing other substances. Only eight patients (7.2%) reported that they had not experienced other substances, 25 (22.5%) had used one, 39 (35.1%) two, 27 (24.3%) three, 9 (8.1%) four and 3 (2.7%) five of the substances during their lifetime. Current use of substances other than methamphetamine (excluding alcohol) was also prevalent among the subjects. Seventeen patients (15.3%) reported that they do not currently use other substances, 43 patients (38.7%) used one other substance, 30 patients (27%) two, 16 patients (14.4%) three and 5 patients (4.5%) four of the substances concurrently. Latency from abuse to development of psychotic episode About one-third of the cases had developed psychosis in the first 3 months of methamphetamine use (29%, n = 31), another third had developed psychosis between 3 months to 1 year (34.6%, n = 37) and the latency for the last third was more than 1 year after the beginning of methamphetamine use (36.4%, n = 39). The interval for four cases could not be determined and they were considered as missing data in the analysis. Previous psychiatric history Thirty-three subjects (29.7%) had experienced at least one previous psychotic episode related to methamphetamine use. Four individuals (3.6%) had a history of major depressive disorder, three had a history of bipolar disorder Type I and one individual (0.9%) had a history of schizophrenia. Sixty-five patients (58%) did not have any previous psychiatric history. Psychotic symptoms All patients had experienced more than one psychotic symptom (with a

mean number of four symptoms) in the psychotic episode with the following frequencies: persecutory delusion 82%, auditory hallucination 70.3%, reference delusion 57.7%, visual hallucination 44.1%, grandiosity delusion 39.6%, infidelity delusion 26.1%, bizarre delusion 7.2%, thought broadcasting 6.3%, passivity feelings 4.5%, thought withdrawal 3.6%, tactile hallucination 1.8%, thought insertion 1.8%, olfactory hallucination 0.9% and nihilistic delusion 0.9%. Duration of admission and psychotic episode The mean duration of admission was 21.43 days, with the range of 1–54 days. Determining the duration of psychotic episode was not possible for 31 subjects due to patients' discharge with consent or escape; therefore, the following results are obtained from 80 files. The mean duration of psychotic episode was 17.37 days with the range of 2–42 days. Fourteen (17.5%), 23 (28.75%) and 36 (45%) patients experienced symptom remission in less than 1 week, between 1 and 2 weeks, and 2 weeks to 1 month, respectively; and symptoms had continued for more than 1 month in seven (8.75%) patients. In other words, 91.25% of patients had recovered from psychotic symptoms by the end of the first month of admission, whereas in 8.75% the symptoms had continued for more than one month. Effect of comorbid substance use In order to assess the effect of substance use on the variables related to MIP, we compared the following variables in the patients with and without history of abusing different substances: psychotic symptoms, latency to develop psychotic episode, duration of admission and duration of psychotic episode. We found no significant and meaningful difference in the frequency of psychotic symptoms or latency to develop psychotic episode between users and non-users of other substances. Patients with a history of cannabis abuse had a non-significant higher duration of psychotic episode (16 days vs. 19 days) and admission (20 days vs. 23 days) than non-users.

Heroin users also had a non-significant higher duration of admission (20 days vs. 24 days).

### **Discussion**

The data on MIP in the literature are mostly obtained from Japan; and despite the growing number of methamphetamine users' worldwide, data from other countries are limited. The current study reports the clinical picture and course of disorder of 111 patients with MIP during admission in a psychiatric hospital. Comparing demographic characteristics of the samples of the current study with previous literature drug dependents show no significant difference in gender ratio (current study: 4.5% female vs. RSA: 5.2% female), marital status (current study: 49.6%, 10.8% and 39.6% vs. RSA: 41.7%, 47.9% and 9.4% for single, divorced or separated and married, respectively) and education level (current study: 1.8%, 58.6%, 33.3% and 6.3% vs. RSA: 5.3%, 54.4%, 31.5% and 8.5% for illiterate, below high school, high school and university degree, respectively). However, unemployment rate seems to be higher in the current study than that reported in RSA and in the general population (73.9% in current study vs. 23.5% in RSA and 10.4% (Unemployment rate in 10-year-olds and older, 2010) and 11.9% in 2008 and 2009 in the general population, respectively). Higher functional impairment in MIP compared with other patients with substance dependence could be due to different factors. First, methamphetamine users experience behavioural adverse effects that make interpersonal relationships and keeping a job more problematic. Second, the disabling effects of psychotic symptoms could play an important role in functional disability of patients with MIP. Third, many of the patients with MIP also use or have used other substances, which could increase the functional impairment of the subjects. In our study, 51% of the patients also used opium, 50% used cannabis and 39% used heroin

concurrently. In this study, 58.6% of patients had no past psychiatric history; however, 29.7% had experienced at least one previous episode of MIP. This finding is in line with previous studies showing an increased vulnerability to recurrence of psychosis after MIP, and additionally suggests that methamphetamine abuse is still on the rise and new cases still outnumber the recurrent cases. According to the present study, 21.6% of patients developed psychosis subsequent to the casual use of methamphetamine, which could point either to the high psychosis inducing potential of this substance, or to the possibility that some patients might have underreported their use. McKetin et al have also reported that 21% of their subjects with MIP used the substance less than once a week. Regarding the latency from methamphetamine abuse to the development of a psychotic episode, the subjects of the study could be roughly categorized into three equal groups, with latencies of less than 3 months, 3 months to 1 year and more than 1 year. This finding is not in line with the Japanese studies performed in the first, second and third epidemic. More than 50% of the patients with MIP in the second and third epidemics had a latency of more than one year, which is much higher than our study. Findings of the current study are more compatible with the first epidemic of Japan in the 1950s than the more recent ones. Frequency of positive psychotic symptoms in this study is compared with the study by Chen et al. (2003) on patients with MIP, and two studies on schizophrenic patients. Because psychotic symptoms are affected by the social-cultural background of the patients, the two studies on schizophrenia were selected from two neighboring countries, Turkey and Pakistan. However, grandiosity delusions were more prevalent and control delusions were less frequent in our study. No consistent difference in frequency of delusions could be observed between the studies performed on patients with

schizophrenia and MIP. Concerning hallucinations, auditory and visual hallucinations had similar rates in the studies, but other hallucinations were more frequent in the study by Chen et al. In another study on 168 patients with MIP, auditory hallucinations were the most common symptom (44.6%), followed by strange or unusual beliefs and visual hallucinations. The current knowledge on the type and frequency of psychotic symptoms does not seem to help in distinguishing between schizophrenia and MIP. The mean duration of hospitalization was 21.43 days in the present study. This indicates that methamphetamine abuse is presently imposing a significant burden on the health system, because each patient with the diagnosis of MIP spends a significant number of days in a hospital. This figure will probably rise in the coming years due to the increasing duration of use. Psychotic symptoms were eliminated in only 17.5% of patients in the first week of hospitalization. However, this ratio reached 91.25% by the end of the first month, which is in line with, where 90% of patients had recovered from psychotic symptoms in the first month, but quite different from the rate of persistent type of MIP reported in other Japanese studies, i.e. 23% in the first epidemic (1956), 18% in the second epidemic (1982) and 41% in the third epidemic (2003). The difference could be partly due to the shorter period of methamphetamine abuse in our sample (i.e. less than 2 years) relative to Japanese studies, because it has been suggested that longer and heavier use of methamphetamine could both delay remission of symptoms and worsen the prognosis. Duration of psychosis could not be determined in 31 patients and the present figures are based upon data gathered from 80 files, which might render these results less valid. A more precise assessment of the duration of the psychotic episode in these patients requires a prospective study with follow-up of the patients until full recovery of psychotic

symptoms. The current study faced some limitations mainly due to its method. For example, files of some of the patients were not complete; especially we had problems in determining the duration of psychosis in one-third of the patients. Although the study was performed in an educational centre where patients are thoroughly evaluated in general, symptoms of the patients still might not have been systematically extracted and registered in the files. Additionally, we did not re-evaluate the diagnoses of the patients made by the treating board-certified psychiatrist during admission. Even though this could have been a source of inaccuracy in the diagnosis, it is not very likely given the high level of expertise of the psychiatrists working in the centre. Comorbid substance use was high among the subjects of the study. This, in turn could have affected the symptoms and courses in the patients; and therefore, ascribing all of the observed findings to methamphetamine is difficult. Nevertheless, the fact that we did not find any significant difference between users and non-users of the other substances lessens this concern. Finally, we cannot claim that our sample is representative of all the countries, although the hospital is a referral centre, which receives all. A more accurate evaluation of the duration of psychotic episodes requires designing prospective studies to comprehensively evaluate the related clinical and course variables. Treatment of MIP is still a challenge; and evidence indicating the efficacy of medications and duration of treatment is scant. Furthermore, a precise differential diagnosis between cases of primary psychotic disorders developing in methamphetamine users and cases of persistent MIP is yet to be determined; also, it could not be firmly stated if their treatments should differ from each other. These as well as many other questions still remain unanswered, and await further studies.



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