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Predictors of Methamphetamine-Induced Psychosis: A Comparison of Socio-Demographic Factors, Clinical Factors and Psychopathology with Acute Episode Schizophrenia

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Abstract

Methamphetamine is an illicit psychostimulant that can produce psychotic symptoms similar to those seen in a primary psychotic disorder such as schizophrenia. During an acute episode, the symptoms of methamphetamine-associated psychosis (MAP) can be difficult to distinguish from those of schizophrenia, making a correct diagnosis difficult. This distinction is crucial to understanding the cause of the illness, but very few studies have been conducted to assess these differences. The aim of this study was to determine the differences between the demographic and clinical characteristics and psychopathology of patients diagnosed with methamphetamine-associated psychosis and schizophrenia. A comparative cross-sectional study was conducted with a total of 201 patients who had acute psychosis and were admitted to the psychiatric ward of a general hospital in the Klang Valley. 94 patients were diagnosed with methamphetamine-associated psychosis and 107 with schizophrenia. Significant differences were found in some domains. Multiple logistic regression revealed that patients with methamphetamine-associated psychosis were more likely to be in a younger age group (odds ratio, OR =0.89, 95% confidence interval, CI: 0.80-0.99), have a family history of drug dependence (OR =16.91, 95% CI: 1.02-279.06), have no family history of mental illness (OR =0.04, 95% CI: 0.00-0.55), with a shorter length of stay on the ward (less than 1 week) (OR =0.01, 95% CI: 0.00- 0.06), were more likely to be physically fixated (OR 0.05, 95% CI: 0.01-0.38), exhibited grandiosity (OR: 1.92, 95% CI: 1.04-3.56) and had a good rapport (OR:0.44, 95% CI: 0.25-0.79). There were demographic, clinical and psychopathological differences between acute psychosis in methamphetamine-associated psychosis and schizophrenia. Identifying the most important predictors can help to make the correct diagnosis and plan the most appropriate treatment for the illness.

Keywords: Methamphetamine-associated Psychosis, Psychopathology, Demographic, Acute Setting

Introduction

Psychosis is often defined as a loss of contact with reality and is generally considered a common symptom of a severe mental illness such as schizophrenia. While schizophrenia is generally the cause of psychosis and is classified as functional psychosis, drugs such as cocaine, cannabis, alcohol, hallucinogens, stimulants and sedatives are associated with substance-induced psychosis (Aggarwal et al., 2012).

Amphetamine-type stimulants (ATS) consist mainly of amphetamine and methamphetamine (World Health Organisation, 2000; Gowing et al., 2001). Other drugs in this group include methcathinone, fenethylline, ephedrine, pseudoephedrine, methylphenidate and MDMA or 'ecstasy' (World Health Organisation, 2000). The production and abuse of methamphetamine has increased significantly in Malaysia in recent years (Farid Yusof & Suzaily Wahab, 2015) and is now the second most common reason for admission to a drug treatment programme (Lai & Norliza, 2012; Singh, et al., 2013; Sulaiman, et al., 2014). Their use or abuse can trigger psychotic symptoms in people without severe mental illness, requiring crisis treatment (Caton, et al., 2000; Yusof & Wahab, 2015; Ardani & Nasab, 2015; Griswold, 2015).

Stimulant psychosis is a transient psychiatric condition that usually occurs in some individuals who take and/or abuse stimulants in abnormally high doses (Norsiah & Suzaily, 2016). Methamphetamine is thought to be able to induce psychosis similar to schizophrenia by inhibiting the dopamine transporter, leaving dopamine in the synaptic cleft (Thirthalli & Benegal, 2006).

The psychopathology between schizophrenia and methamphetamine-associated psychosis in acute settings has been found to be almost similar (Bramness et al., 2012; Caton et al., 2005; Grant et al., 2012; Hides et al., 2015; Medhus, 2013; Zarrabi et al., 2016). Several studies have mentioned the absence of negative symptoms in methamphetamine psychosis (Grant et al., 2012; Hsieh et al., 2014). Most studies have found that the delusions and hallucinations seen in methamphetamine users are similar to those seen in patients with schizophrenia (Caton et al., 2005; Grant et al., 2012; Medhus, 2013; Srisurapanont et al., 2003). The use of urine drug testing can help distinguish the diagnosis during the acute admission, but has its limitations, as it is not uncommon for the diagnosis of a substance use disorder to change over time to a primary psychotic disorder (Medhus, 2013). Anamnestic features of significant substance use prior to the onset of psychotic symptoms are helpful in establishing a diagnosis. However, in many clinical settings, the history is less clear and distinguishing between psychosis due to methamphetamine use and that due to acute schizophrenia symptoms can be a diagnostic challenge (Grant et al., 2012; Srisurapanont et al., 2003; McKetin et al., 2016).

Differentiating between schizophrenia and psychosis triggered by methamphetamine use is important for understanding the course of the illness so that appropriate treatment can be effectively delivered, particularly when psychotic symptoms occur during the acute onset (Caton et al., 2005). Often, patients with methamphetamine psychosis require significant interventions due to agitation and aggression (Bramness et al., 2012; Medhus, 2013). There is also the question of whether they should be treated by a psychiatric team or by drug services. Patients with methamphetamine psychosis may need different medication or brief psychotherapy. Knowing the subtle differences in acute treatment is therefore very helpful

for the legal and forensic aspect, reduces the overall budget for treatment and increases the awareness and efficiency of the doctor in dealing with these patients.

As far as we know, this is the first study of its kind conducted in Malaysia. The aim of the study was to determine the differences in the demographic and clinical characteristics and psychopathology of patients with methamphetamine-associated psychosis and schizophrenia in the acute phase, and to identify the key predictors that favour the diagnosis of methamphetamine-associated psychosis.

Methodology

Study participants were recruited from the inpatient psychiatric unit and emergency department of a general hospital in the Klang Valley. Eligible subjects included patients diagnosed with schizophrenia and methamphetamine-associated psychosis, aged between 18 and 65 years, who were randomly selected. 150 patients diagnosed with schizophrenia and 130 patients diagnosed with methamphetamine psychosis on admission were screened. Initial screening was by urine drug test on admission; the group of schizophrenia patients (whose urine test was negative) and the group of patients with methamphetamine-associated psychosis (whose urine test was positive for methamphetamine and amphetamine). The diagnosis of schizophrenia was later confirmed using MINI International Neuropsychiatric Interview Version 6.0. (M.I.N.I ver 6.0) Sheehan et al (2009) with acute psychosis (either as a new case or a relapse) and a negative urine test for methamphetamine and/or amphetamine were included in the study. As for the methamphetamine-associated psychosis group, the inclusion criteria included those whose diagnosis was confirmed using M.I.N.I Version 6.0 Sheehan et al (2009) and who had acute psychosis, a positive urine test for methamphetamine and/or amphetamine and, if the subjects had used other drugs in the past, had to have been drug-free for at least 2 years.

Exclusion criteria for both groups were patients with dual diagnosis/ comorbidity (i.e. schizophrenia with substance abuse/ head injury/ trauma), polysubstance use, history of psychosis not caused by schizophrenia or methamphetamine use, and impaired sensorium/ mental retardation.

This is a cross-sectional comparative study examining the differences in psychopathology between schizophrenia and methamphetamine-associated psychosis, conducted from December 2016 to May 2017. The study was approved by the NMRR (NMRR-16-1209-29431(IIR)) and the Universiti Kebangsaan Malaysia Medical Centre (UKMMC) Medical Ethics Committee (FF -2016-280). Informed consent was obtained from all subjects before the study was conducted. All subjects were tested for drugs in their urine before being assigned to their respective groups. To further clarify the subjects' group membership, MINI was used to determine the diagnosis before further assessment with the PANSS [25]. Almost half of the patients were assessed for psychosis within the first 3 days of admission. About 30% of patients were assessed within a window of 7 days after admission. For those patients who were too psychotic, consent was obtained from family members, which contributed to a delay in assessment. History of previous mental illness was assessed by asking participants if they had ever been told by a doctor that they might have schizophrenia, schizoaffective disorder, schizophreniform, bipolar disorder, brief psychotic disorder or methamphetamine-induced psychosis, as well as information from family, ward staff and clinical records. Each interview lasted between 45 and 60 minutes. Participant confidentiality and anonymity was maintained through the use of a unique identification code (IC) rather than using subjects' names on the research forms. All clinical records were kept in a secure, password-protected

electronic database system. Clinical records were also reviewed after patient discharge before being sent to the records department of the hospital under study.

In this study, M.I.N.I version 6.0 Sheehan et al (2009) was used to diagnose schizophrenia and methamphetamine-associated psychosis. M.I.N.I was developed to help researchers diagnose psychiatric disorders according to DSM-IV or ICD-10. The interview takes about 15 minutes to complete and is designed for epidemiological studies and multicentre clinical trials.

The Positive and Negative Symptoms Scale (PANSS) Kay et al (1987) is a 30-item scale designed to assess the presence, absence and severity of positive, negative and general psychopathological symptoms of schizophrenia. The 30 items are divided into seven positive symptom subscale items, seven negative symptom subscale items and 16 general psychopathology symptom items. Each item has a definition and a scoring basis. All 30 items are scored on a 7-point scale (1 = absent; 7 = extreme). Often the scores for the positive items, the negative items and the general psychopathology are given separately.

A structured questionnaire was used to collect the individual characteristics of the subjects, i.e. demographic data, history of substance use, medical history and history of admissions to the ward.

Complete data were collected from the 201 subjects, 107 of whom were in the schizophrenia group and 94 in the methamphetamine group, all of whom met the inclusion criteria for the study. Subjects with schizophrenia were compared with those with methamphetamine-associated psychosis using the sociodemographic and clinical characteristics described previously. The data were consistent with the assumptions of the test used to analyse them. Depending on whether a variable was measured categorically or continuously, group differences were tested using univariate analysis, namely the independent t-test, the Pearson chi-square test and the Fisher exact test.

Next, we conducted an analysis to predict the extent to which the differences reported between the groups were significant in contrast to the correlated characteristics of the 2 groups. For the significant variables, we proceeded with multivariable analysis using multiple logistic regression with the backward likelihood ratio method (LR) to determine the association between independent and dependent variables. All analyses were conducted using SPSS software (SPSS Inc, Chicago, III). Statistical significance was determined at $p< 0.05$.

Research Findings

The aim of this study was to determine the differences between demographic and clinical characteristics and psychopathology in patients with methamphetamine-associated psychosis and schizophrenia.

i) Demographic Characteristics

The following Table 1 shows social demographic characteristics of patients with acute psychosis, schizophrenia, and methamphetamine-associated psychosis.

Table 1
Social Demographic Characteristics of Patients with Acute Psychosis, Schizophrenia, and Methamphetamine-Associated Psychosis

	Schizophrenia (n=107)	Methamphetamine-associated psychosis (n=94)	Statistical Test (df)	*p*-value
Age in years (Mean/SD)	37.53 (10.47)	32.66 (7.99)	t (199) = 12.41[a]	0.001*
Sex:				
Male	68 (63.6)	79 (84.0)	χ2(1) = 10.69[b]	0.001*
Female	39 (36.4)	15 (16.0)		
Race:				
Malay	65 (60.7)	66 (70.2)	χ2(3) = 6.58[c]	0.089
Chinese	21 (19.6)	13 (13.8)		
Indian	17 (15.9)	7 (7.4)		
Others	4 (3.7)	8 (8.5)		
Marital status:				
Single	77 (72.0)	62 (66.0)	χ2(3) = 3.03[c]	0.412
Married	17 (15.9)	20 (21.3)		
Divorced	9 (8.4)	11 (11.7)		
Widowed	4 (3.7)	1 (1.1)		
Education level:				
Uneducated	2 (1.9)	2 (2.1)	χ2 (4) = 3.45[c]	0.465
Primary school	11 (10.3)	9 (9.6)		
PMR	40 (37.4)	28 (29.8)		
SPM	41 (38.3)	35 (37.2)		
Tertiary education (College/University)	13 (12.2)	20 (21.3)		
Occupation:				
Not working	85 (79.4)	55 (58.5)	χ2(4) = 23.52[c]	<0.001*
Self-employed	6 (5.6)	0 (0.00)		
Full-time working	10 (9.3)	16 (17.0)		
Part-time working	4 (3.7)	19 (20.2)		

Pensioner	2 (1.9)	4 (4.3)		
Self-income:				
No income	85 (79.4)	54 (57.4)	$\chi 2(3) = 18.89^{c}$	<0.001*
Less than RM1000	12 (11.2)	8 (8.5)		
RM1001 - RM2000	7 (6.5)	26 (27.7)		
RM2001 and above	3 (2.8)	6 (6.4)		

*indicates significant *p*-value
[a] Independent t- test
[b] Pearson chi square
[c] Fisher Exact test

In the sociodemographic characteristics listed in Table 1, there were few factors that showed a significant difference between the two groups. Patients with schizophrenia were older [mean, 37.53 (standard deviation, SD, 10.47) years] compared with patients with methamphetamine-associated psychosis [mean, 32.66 (standard deviation, SD, 7.99) years]. The majority of patients in both groups were male, but females predominated less in the group of patients with methamphetamine-associated psychosis. Patients with schizophrenia were mostly unemployed (79.4%) and had no income (79.4%), while more than half of the patients with methamphetamine-associated psychosis were unemployed (58.5%) or had no income (57.4%). The majority of patients in the schizophrenia sample have a history of an underlying mental illness (89.7%), while only half of the patients with methamphetamine psychosis (47.9) have been previously diagnosed with a mental illness. Both groups of patients have a positive family history of mental illness, but in the group of schizophrenia patients the proportion was significantly higher (26.4%).

About 17.8% of patients with schizophrenia had a history of substance dependence. A higher percentage of the methamphetamine psychosis group had a positive family history of substance use (10.6%) compared to schizophrenia (1.9%).

Table 2
Clinical Characteristic of Patients with Acute Psychosis; Schizophrenia and Methamphetamine-Associated Psychosis

	Schizophrenia (n=107)	Methamphetamine-associated psychosis (n=94)	Statistical Test (df)	*p*-value
History of mental illness:				
Yes	96 (89.7)	45 (47.9)	$\chi2(1) = 41.85^{b}$	<0.001*
No	11 (10.3)	49 52.1)		
Family history of mental illness:				
Yes	26 (24.3)	5 (5.4)	$\chi2(1) = 13.60^{b}$	<0.001*
No	81 (75.7)	88 (94.6)		
Other medical illness:				
Yes	21 (19.6)	15 (16.0)	$\chi2(1) = 0.46^{b}$	0.582
No	86 (80.4)	79 (84.0)		
History of substance dependence:				
Yes	19 (17.8)	94 (100.0)	$\chi2(2) = 137.51^{c}$	<0.001*
No	64 (59.8)	0 (0.0)		
Cigarette only	24 (22.4)	0 (0.0)		
Family history of substances dependence:				
Yes	2 (1.9)	10 (10.6)	$\chi2(1) = 6.86^{c}$	0.014*
No	105 (98.1)	84 (89.4)		
Previous history of psychiatric admission:				
Never admitted	1 (0.9)	3 (3.2)	$\chi2(2) = 36.43^{c}$	<0.001*
First time admitted	15 (14.0)	49 (52.1)		
Multiple time admitted	91 (85.0)	42 (44.7)		
Mode of current admission:				
Involuntary	106 (99.1)	94 (100.0)	$\chi2(1) = 0.88^{c}$	1.000
Voluntary	1 (0.9)	0 (0.0)		
Duration of ward stays:				
Less than 1 week	12 (11.2)	82 (87.2)	$\chi2(1) = 116.16^{b}$	<0.001*

More than 1 week	95 (88.8)	12 (12.8)		
Seclusion needed:				
Yes	4 (3.7)	0 (0.0)	$\chi 2(1) = 3.59^{c}$	0.124
No	103 (96.3)	94 (100.0)		
Chemical restraint:				
Yes	76 (71.0)	73 (77.7)	$\chi 2(1) = 1.15^{b}$	0.284
No	31 (29.0)	21 (22.3)		
Physical restraint:				
Yes	37 (34.6)	46 (48.9)	$\chi 2(1) = 4.26^{b}$	0.039*
No	70 (65.4)	48 (51.1)		

*indicates significant *p*-value
[a] Independent t-test
[b] Pearson chi square
[c] Fisher Exact test

In terms of socio-demographic characteristics (Table 1), only a few factors showed a significant difference between the two groups. Patients with schizophrenia were older [mean, 37.53 (standard deviation, SD, 10.47) years] compared with patients with methamphetamine-associated psychosis [mean, 32.66 (standard deviation, SD, 7.99) years]. The majority of patients in both groups were male, but females predominated less in the group of patients with methamphetamine-associated psychosis. Patients with schizophrenia were mostly unemployed (79.4%) and had no income (79.4%), while more than half of the patients with methamphetamine-associated psychosis were unemployed (58.5%) or had no income (57.4%). The majority of patients in the schizophrenia sample have a history of an underlying mental illness (89.7%), while only half of the patients with methamphetamine psychosis (47.9) have been previously diagnosed with a mental illness. Both groups of patients have a positive family history of mental illness, but the proportion was significantly higher in the schizophrenia group (26.4%). About 17.8% of patients with schizophrenia had a history of substance dependence. A higher percentage of the methamphetamine psychosis group had a positive family history of drug use (10.6%) compared to schizophrenia (1.9%).

Table 2 describes the clinical characteristics of the patients. Almost half of the patients diagnosed with methamphetamine-associated psychosis were admitted to the ward for the first time (51%), compared to schizophrenia patients who mostly have a history of repeated admissions (85%). Patients with methamphetamine-associated psychosis also recovered more quickly and stayed on the ward for a shorter time, less than 1 week (87.2%), before being discharged, compared to schizophrenia patients (11.2%). Patients with methamphetamine psychosis had a higher need for physical restraint (48.9%) than schizophrenia patients (34.6%). The two groups did not differ significantly in terms of race, marital status, education level, other medical conditions, type of current admission, need for isolation and use of chemical restraint.

ii) PANSS score

Schizophrenia patients had a significantly higher negative PANSS total score and general score than the methamphetamine-associated psychosis group. No significant difference was found in the positive PANSS total score and PANSS overall score between the two groups, as shown in Table 3.

Table 3
Psychiatric symptomatology: Mean scores on the Positive and Negative Symptom Scale (PANSS) between patients with schizophrenia and methamphetamine-associated psychosis

PANSS	Schizophrenia (n=107)	Methamphetamine-associated psychosis (n=94)	t- test (df)	*p*-value
	mean (sd)	mean (sd)		
Positive	29.36 (5.77)	23.27 (6.10)	1.02 (199)	0.313
Negative	26.39 (7.85)	14.07 (5.90)	4.44 (199)	0.036*
General	39.99 (9.72)	30.34 (7.01)	12.78 (199)	<0.001*
Total	95.74 (18.00)	67.69 (15.44)	2.24 (199)	0.136

* indicates significant *p*-value

iii) Psychiatric Symptomatology

Schizophrenia patients showed significantly higher PANSS total negative score and general score than methamphetamine-associated psychosis group. There was no significant difference noted in PANSS total positive score and total PANSS score between the two groups, as shown in Table 3.

Table 3
Psychiatric symptomatology: Mean scores on the Positive and Negative Symptom Scale (PANSS) between patients with schizophrenia and methamphetamine-associated psychosis

PANSS	Schizophrenia (n=107)	Methamphetamine-associated psychosis (n=94)	t- test (df)	*p*-value
	mean (sd)	mean (sd)		
Positive	29.36 (5.77)	23.27 (6.10)	1.02 (199)	0.313
Negative	26.39 (7.85)	14.07 (5.90)	4.44 (199)	0.036*
General	39.99 (9.72)	30.34 (7.01)	12.78 (199)	<0.001*
Total	95.74 (18.00)	67.69 (15.44)	2.24 (199)	0.136

* indicates significant *p*-value

Table 4
Psychiatric symptomatology: mean scores on the rating of the symptoms of Positive and Negative Symptom Scale (PANSS) between patients with schizophrenia and methamphetamine-associated psychosis

PANSS	Schizophrenia (n=107)	Methamphetamine-associated psychosis (n=94)	Statistical Test (df)	*p*-value
POSITIVE (Mean/SD)	29.36 (5.77)	23.27 (6.10)	1.02 (199)	0.313
PANSS P1 Delusions	4.98 (1.51)	3.10 (1.49)	0.15 (199)	0.699
PANSS P2 Conceptual Disorganization	4.57 (1.51)	2.46 (1.57)	2.11 (199)	0.148
PANSSP3 Hallucinatory Behaviour	5.91 (1.01)	4.29 (1.56)	20.67 (199)	<0.001*
PANSS P4 Excitement	3.22 (1.26)	3.65 (1.11)	1.99 (199)	0.16
PANSS P5 Grandiosity	1.68 (1.09)	1.80 (1.23)	4.18 (199)	0.042*
PANSS P6 suspiciousness	4.59 (1.50)	3.99 (1.34)	5.75 (199)	0.017*
PANSS P7 Hostility	4.41 (1.52)	4.00 (1.44)	1.14 (199)	0.288
NEGATIVE (Mean/SD)	26.39 (7.85)	14.07 (5.90)	4.44 (199)	0.036*
PANSS N1 Blunted affect	4.93 (1.41)	2.10 (1.11)	2.11 (199)	0.148
PANSS N2 Emotional Withdrawal	4.07 (1.34)	2.29 (1.12)	0.03 (199)	0.874
PANSS N3 Poor rapport	3.80 (1.63)	2.06 (1.23)	4.64 (199)	0.032*
PANSS N4 Passive Apathetic Withdrawal	4.11 (1.49)	2.09 (1.26)	0.47 (199)	0.493
PANSS N5 Abstract thinking	4.40 (1.49)	2.45 (1.25)	2.87 (199)	0.092
PANNS N6 Lack of flow and Spontaneity	3.22 (1.84)	1.95 (1.31)	13.97 (199)	<0.001*
PANNS N7 Stereotyped Thinking	1.85 (1.32)	1.15 (0.44)	84.69 (199)	<0.001*
GENERAL (Mean/SD)	39.99 (9.72)	30.34 (7.01)	12.78 (199)	<0.001*
PANNS G1 Somatic	1.78 (1.30)	1.22 (0.88)	33.47 (199)	<0.001*
PANNS G2 Anxiety	1.63 (1.14)	1.50 (1.05)	0.89 (199)	0.347

PANSS G3 Guilt feeling	1.37 (0.94)	1.56 (1.24)	7.17 (199)	0.008*
PANNS G4 Tension	1.54 (1.11)	1.45 (1.07)	0.89 (199)	0.346
PANSS G5 Mannerism and Posturing	1.86 (1.67)	1.01 (0.10)	122.28 (199)	<0.001*
PANSS G6 Depression	1.47 (1.00)	1.77 (1.36)	13.82 (199)	<0.001*
PANSS G7 Motor retardation	1.41 (0.93)	1.09 (0.43)	41.19 (199)	<0.001*
PANSS G8 Uncooperativeness	2.65 (1.61)	2.43 (1.21)	10.11 (199)	0.002*
PANSS G9 Unusual Thought	3.93 (1.58)	1.99 (1.29)	0.88 (199)	0.35
PANSS G10 Disorientation	1.36 (0.97)	1.10 (0.44)	22.29 (199)	<0.001*
PANSS G11 Poor attention	3.23 (1.58)	2.61 (1.25)	2.76 (199)	0.098
PANSS G12 Lack of judgment and Insight	5.23 (1.50)	4.24 (1.27)	3.76 (199)	0.054
PANSS G13 Disturbance of Volition	2.00 (1.35)	1.29 (0.91)	38.51 (199)	<0.001*
PANSS G14 Poor Impulse Control	3.47 (1.45)	3.29 (1.17)	4.70 (199)	0.031*
PANSS G15 Preoccupation	3.65 (1.85)	1.59 (1.21)	27.83 (199)	<0.001*
PANSS G16 Active Social Avoidance	3.40 (1.21)	2.22 (1.07)	0.47 (199)	0.493
TOTAL (Mean/SD)	95.74 (18.00)	67.69 (15.44)	2.24 (199)	0.136

* indicates significant p-value

Table 4 shows the comparison of psychiatric symptomatology in methamphetamine-associated psychosis and schizophrenia. For the profile of positive symptoms, only 3 items show a statistically significant result. Mean scores for hallucinatory behaviour and distrust/persecution were higher in schizophrenia than in methamphetamine-associated psychosis [mean, 5.91 (standard deviation, SD, 1.01) vs. mean, 4.29 (standard deviation, SD, 1.56)] and [4.59(1.50) vs. 3.99 (1.34)], respectively. The mean score for grandiosity was also higher in the methamphetamine-associated psychosis group than in the schizophrenia group [1.80 (1.23) vs. 1.68 (1.09)].

There are also 3 items in the negative symptoms profile that have statistically significant results. The mean scores of all 3 items (poor relationship, lack of spontaneity and flow of conversation, and stereotyped thinking) were higher in the schizophrenia patients than in the

methamphetamine-associated psychosis patients [3.80 (1.63) vs. 2.06 (1.23)], [3.22 (1.84) vs. 1.95 (1.31)] and [1.85 (1.32) vs. 1.15 (0.44)], respectively.

In the general symptom profile, 10 out of 16 items have a statistically significant result. There are 8 items that have higher mean scores in the schizophrenic group than in the methamphetamine-associated psychosis group. The items were somatic preoccupation [1.78 (1.30) vs 1.22 (0.88)], mannerism and posture [1.86 (1.67) vs 1.01 (0.10)], motor retardation [1.41 (0.93) vs 1.09 (0.43)], uncooperativeness [2.65 (1.61) vs 2.43 (1.21)], disorientation [1.36 (0.97) vs 1.10 (0.44)], volitional disturbance [2.00 (1.35) vs 1.29 (0.91)], poor impulse control [3.47 (1.45) vs 3.29 (1.17)] and worry [3.65 (1.85) vs 2.22 (1.07)]. The other 2 items were in favour of methamphetamine-associated psychosis, as higher mean scores were found in this group than in the schizophrenia group. These were guilt and depression [1.56 (1.24) vs 1.37 (0.94) and 1.77 (1.36) vs 1.47 (1.00), respectively].

iv) Multivariable Analyses Using Multiple Logistic Regression

The following Table 4 shows factors associate with methamphetamine-associated psychosis.

Table 5
Factors associate with methamphetamine-associated psychosis.

Factors	**Adjusted OR (95% CI)**	**χ^2 stat (df)[a]**	***p*-value**
Age	0.89 (0.80-0.99)	4.34 (1)	0.037*
Family history of mental illness			
Yes	0.04 (0.00-0.55)	5.82 (1)	0.016*
No	1		
Family history of substance dependence			
Yes	16.91 (1.02-279.06)	3.91 (1)	0.048*
No	1		
Previous history of psychiatric admission			
First time admitted	0.28 (0.10-11.92)	0.45 (1)	0.503
Multiple admitted	0.05 (0.00-1.71)	2.77 (1)	0.096
Never admitted	1		
Duration of ward stays			
More than 1 week	0.01 (0.00-0.06)	21.97 (1)	<0.001*
Less than 1 week	1		
Mechanical constraint			
No	0.05 (0.01-0.38)	8.26 (1)	0.004*
Yes	1		
PANSS Positive			

Hallucinatory behaviour	0.52 (0.26-1.03)	3.49 (1)	0.062
Grandiosity	1.92 (1.04-3.56)	4.31 (1)	0.038*
PANSS Negative			
Poor rapport	0.44 (0.25-0.79)	7.61 (1)	0.006*

***indicates significant *p*-value
[a]Backward Likelihood Ratio (LR) test
Nagelkerke square value: 87.3%

The results in Table 5 show that there are few variables that favour methamphetamine psychosis. Age is a significant predictor in this study, with younger patients more likely to have methamphetamine psychosis. Patients 1 year older are 11% (1-0.89) less likely to develop methamphetamine psychosis compared with schizophrenia (OR =0.89, 95% CI=0.80-0.99). Patients with a family history of mental illness are 96% less likely to develop methamphetamine-associated psychosis compared with schizophrenia (1-0.04) (OR =0.04, 95% CI= 0.00-0.55). Patients with a family history of substance dependence were about 17 times more likely to be in the methamphetamine psychosis group (OR =16.91, 95% CI= 1.02-279.06) than patients with schizophrenia. Patients who have been admitted for more than 1 week are 99% less likely to be in the methamphetamine psychosis group than patients with schizophrenia (1-0.01) (OR =0.01, 95% CI= 0.00- 0.06). Patients without physical limitations have a low risk of being in the methamphetamine-associated psychosis group (95%) compared to patients with schizophrenia (1-0.05) (OR 0.05, 95% CI= 0.01-0.38). A patient with a higher score for grandiosity was about 2 times more likely to be associated with methamphetamine-associated psychosis compared with schizophrenia (OR = 1.92, 95% CI=1.04-3.56). Poor rapport is associated with negative symptoms. A patient with a score 1 higher for poor rapport is 56% less likely to fall into the methamphetamine-associated psychosis group compared with schizophrenia (1-0.44) (OR = 0.44, 95% CI= 0.25-0.79). A history of psychiatric hospitalisation and hallucinatory behaviour are not reliable predictors of methamphetamine-associated psychosis.

Discussion

The results of our study showed that methamphetamine-associated psychosis was more strongly predicted in younger subjects, similar to the results of previous studies by (Vos et al., 2010; Thomas et al., 2016). Younger age of methamphetamine use predicted younger onset of psychosis in stimulant users (Sara, 2014). The prevalence of younger patients abusing methamphetamine tends to increase in Malaysia (Mohamed et al., 2008). Younger methamphetamine users (NCETA, 2017) may be related to the current trend of substance use and the extremely rewarding effects they advertise to their peers, thereby recruiting more new younger users (Wheelahan, 2016). No significant differences were found in terms of gender, race, employment status and education level.

This study also found that methamphetamine psychosis was less predictive in patients with a positive family history of mental illness. The findings reflect the ability of methamphetamine and amphetamine to induce psychosis in healthy people, even in the absence of genetic predisposition, by increasing dopamine levels in the brain through various mechanisms (Bramness et al., 2012). Methamphetamine inhibits the reuptake of dopamine by interacting with the dopamine transporter (DAT), interacts with the vesicular monoamine transporter 2 (VMAT2), leading to an increase in dopamine concentration in the brain, which

is directly linked to the "reward centre", leading to addiction and psychosis (Sara, 2014; Curran et al., 2004; MacKenzie, 2016). Many other studies have shown that family history of mental illness was higher in methamphetamine psychosis (Ardani & Nasab, 2015; Hides et al., 2015; MacKenzie, 2016), which is in contrast to this study. This may need further research.

Interestingly, patients with a family history of drug dependence have a higher risk of developing methamphetamine-associated psychosis. A similar result was found in an earlier study by Thomas et al [27]. Social learning theory provides a good explanation for the higher methamphetamine use among patients with a family history of substance dependence, even at a young age and with easy acquisition. The earlier the substance is used, the greater the risk of neurotoxic brain damage, making the patient vulnerable to developing methamphetamine-associated psychosis with a positive family history of drug dependence (Sara, 2014; Paul, 2011; Semple, 2011).

The length of stay on the ward often depends on the remission of symptoms. It is thought that the transient effects of methamphetamine might lead to early remission of symptoms, so that patients with methamphetamine psychosis would be discharged earlier (Grant et al., 2012), and in this study the same relationship was demonstrated. As defined in the Diagnostic and Statistical Manual (2013), substance-induced psychosis is due to the direct effects of drug withdrawal and intoxication. The symptoms of methamphetamine psychosis usually last only two to three hours, but sometimes the symptoms become more severe and can last for days (Association, 2013).

Our results also show that physical restraints are used more frequently in patients with methamphetamine-associated psychosis. The finding is similar to a study by Hadi (2015), who, in line with several other studies Vos et al (2010); Hadi (2015), pointed out the frequent violent behaviour of this population in the emergency department (McKetin, 2006; Association, 2013). Whether the tendency towards violence is due to certain types of delusions or directly to the aggression-promoting effect of the drug methamphetamine itself requires further investigation in the future.

Only a few studies showed significant differences in the association with positive psychotic symptoms. Positive symptoms were more pronounced in the amphetamine-induced psychosis group than in the negative amphetamine group (Desoky et al., 2011) and individuals with substance-induced psychosis had lower scores on the Positive and Negative Syndrome Scale (PANSS) (Ardani & Nasab, 2015; Caton et al., 2005; Hsieh et al., 2014). In this study, the presence of grandiosity highly predicted the diagnosis of methamphetamine psychosis. This is consistent with the findings of previous studies that found similar mood states such as hypomania and mania during methamphetamine intoxication and depression during methamphetamine withdrawal (Phillips, 2017; Mavrikaki, 2009; Ross, 2006). Patients with methamphetamine psychosis were also less likely to have poor rapport, which may be related to their antisocial personality factors (Sulaiman et al., 2014) and persistent cognitive impairment (Ross, 2006; Sharma, 2016; Green, 2014).

Depression and guilt are estimated to be significant predictors of methamphetamine psychosis in this study, but the relatively low rate of these symptoms is surprising. This is an interesting finding to investigate further, considering that the withdrawal effects of methamphetamine cause depression (Kaneda, 2009; Midin, 2011) and the co-occurrence of depression in substance abusing patients is also quite common (Zweben, 2004; Zorick, 2010).

The stability of the diagnosis of methamphetamine-associated psychosis and schizophrenia is another problem that could indirectly explain the different results of the various studies. There are quite a number of cases where the primary diagnosis was

substance-induced psychosis, but the diagnosis was changed to schizophrenia years later (Bramness et al., 2012; Medhus, 2013). According to Medhus (2013), small differences were found in the baseline characteristics of both groups, with the group that transitioned mainly functioning worse than the stable group in terms of the PANSS score and improving only minimally during hospitalisation. However, this question is not the focus of this study.

Limitations

There were a number of limitations to this study. Since it is a comparative cross-sectional study, it was not possible to determine the cause and effect of the variables studied. The study also focuses on a single tertiary centre, which may have very different patient characteristics than other treatment centres, which could lead to a different outcome. Apart from this, the results should be interpreted with caution due to the relatively small sample size, which limits the power of the study. Due to the small sample size, it was also not possible to run a regression model for each item of the general PANSS score in this study.

Conclusion

Psychosis is a symptom. There are many diagnoses that can be accompanied by psychotic symptoms. Diagnosing schizophrenia or methamphetamine-induced psychosis can be difficult because they usually occur together and the only difference is the presence of methamphetamine use. However, during the acute episode and when a urine drug test is not available or is inconclusive, it can be difficult to differentiate these two diagnoses based on the psychotic symptoms. The correct diagnosis is important for the correct treatment plan. This study attempts to distinguish different psychopathologies in psychosis that can differentiate between the two diagnoses.

Despite some limitations, our study contributes to the current knowledge on the differences in psychopathology and symptomatology during acute psychosis between schizophrenia and methamphetamine-associated psychosis.

Future studies should examine other parameters of substance use prior to the onset of first symptoms, personality factors and socioeconomic status that may contribute to symptom onset. In addition, a prospective study should be conducted to clearly observe the trend of psychosis, its persistence and remission.

Although it is difficult to distinguish between these two types of psychosis, the results of this study may help clinicians to make the most accurate diagnosis by identifying the key distinguishing features, which may also have important implications for treatment. However, this should not go beyond the doctor's judgement and the need for further longitudinal investigation.

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Conflict of interest

None

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