



Research Article

Causative Agents of Substance Induced Psychotic Disorder amongst Inpatients and Outpatients of a South East Asian Tertiary Addictions Management Service

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Abstract

Introduction: There is a paucity of local research on patients with substance induced psychotic disorder and their causative agents in South East Asia including Singapore. This study examines the main substances contributing to substance induced psychosis in patients receiving treatment at a tertiary addictions management service in Singapore. It also identifies factors predictive of subsequent conversion to a primary psychotic disorder.

Methodology: Retrospective case-note analysis of 48 patients referred to the National Addictions Management Service between 01/04/2007-31/03/2012 with a diagnosis of substance induced psychotic disorder and no prior history of a primary psychotic disorder.

Results: Amphetamine, alcohol, benzodiazepines and codeine were most commonly associated with substance induced psychosis. 10 (20.8%) of the patients were re-diagnosed to a primary psychotic disorder. The younger the age of onset of substance induced psychotic disorder, the higher the risk of conversion to a primary psychotic disorder.

Conclusion: Illegal and so-called prescription drugs can cause SIPD or precipitate a primary psychosis in those with an underlying psychotic diathesis, and the risk of the latter is higher the younger the age of onset of the SIPD. This message should be used more often in primary and secondary prevention strategies.

Keywords:

Substance induced psychosis; Primary psychotic disorder; Singapore; National Addictions Management Service

Introduction

Studies on substance induced psychotic disorder (SIPD) are sparse in Singapore. To the authors' knowledge, thus far only one article has pertained to the subject matter locally and that article discussed the abuse of Erimin, a benzodiazepine [1]. Many substances have the potential to cause a drug induced psychotic state, and this

includes cannabis, amphetamines, inhalants, alcohol, hallucinogens, phencyclidine and even caffeine [2,3]. A 13 year retrospective study done in India found that in their setting, only cannabis and alcohol were causative agents for SIPD [4]. In Taiwan, continuous use of methamphetamine was associated with SIPD [5]. An interesting study done in Hong Kong also showed the occurrence of cough mixture induced psychotic disorders [6]. Ketamine, methamphetamine and cough mixtures were the 3 most commonly misused drugs based on the referrals made to a substance abuse clinic of a regional hospital in Hong Kong [7]. A prospective longitudinal study in Australia on 278 participants with a diagnosis of methamphetamine dependence showed a large dose-dependent increase in the occurrence of psychotic symptoms during periods of methamphetamine use [8]. Chronic or usage of high doses of methamphetamine can result in auditory hallucinations and persecutory delusions similar to those in paranoid schizophrenia [9-11]. A recent study on patients who were Methamphetamine dependent showed that 13.0% had co-morbid psychotic disorders [12]. There is also a well-known association between psychoses and cannabis use [13-16]. Cannabis has also been linked to the development of schizophrenia when taken over a long period of time [13]. A recent review article showed that patients with an initial diagnosis of brief and affective psychosis and who use Cannabis are subject to diagnostic instability and a greater likelihood of progression to schizophrenia [17].

It is rational to assume that the causative agents for SIPD in Singapore would depend on the culture of drug use seen locally. Singapore has a zero drug tolerance policy. Notwithstanding its stiff penalties for drug use, it was reported in the Central Narcotics Bureau drug situation report in 2012 that about 93% of all drug abusers arrested abused either heroin or methamphetamine [18]. In the first half of 2013, Heroin and Methamphetamine continued to be the most commonly abused drugs, with 92% of all drug abusers arrested being heroin or methamphetamine abusers. Cannabis was the third most commonly abused drug [19]. International Studies done show that patients with SIPD have a high propensity for transition into the schizophrenia spectrum disorders [20].

The primary objective of this study was to identify the main agents accounting for SIPD in Singapore. Our secondary objective was to evaluate for conversion to a Primary Psychotic Disorder (PPD) at the end of a one year follow up period and to identify factors predictive of conversion. We hypothesize that Methamphetamine would be the most common causative agent of SIPD locally in view of the high percentage of drug abusers using it as well as its propensity to cause psychosis based on international literature. The results of our study can better inform clinicians of the outcome for this group of patients seen locally and be used for our public education efforts.

Methodology

This study used a single site retrospective case-notes analysis design. Ethics approval was obtained from local institutional review board (Ref: 388/2013) and informed consent was waived. The Institute of Mental Health (IMH) is the only tertiary psychiatric hospital in Singapore and the National Addictions Management Service (NAMS), a subsidiary of IMH, is the national provider of addictions management. Further details of NAMS can be found on the IMH website [21].

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Table 1: Demographic Characteristics of 48 SIPD patients (N=48).

Gender	Male (%)		Female (%)	
	43 (89.6)		5 (10.4)	
Ethnicity	Chinese (%)	Malay (%)	Indian (%)	Others (%)
	26 (54.2)	16 (33.3)	4 (8.3)	2 (4.2)
Marital Status	Single (%)		Engaged/Married (%)	Separated/Divorced (%)
	24 (50)		14 (29.2)	10 (20.8)
Employment	Employed (%)		Unemployed (%)	
	20 (41.7)		28 (58.3)	
Education	No education/special school/primary school (%)		Secondary school/ITE (%)	Poly/JC/Deg/masters (%)
	19 (39.6)		23 (47.9)	6 (12.5)
Housing	Destitute home/homeless/hostel (%)		HDB (%)	Private (%)
	4 (8.3)		42 (87.5)	2 (4.2)

The registered database of patients seen at NAMS between 1st April 2007 to 31st March 2012 was reviewed to identify patients who had a diagnosis of Substance Induced Psychotic Disorder, Drug Psychosis or mental/behavioural disturbances due to drug use and their case notes were reviewed to determine if a diagnosis of SIPD was made based on the Diagnostic and Statistical Manual (DSM-IV-TR) [2]. Patients with a diagnosis of a primary psychotic disorder (e.g. Schizophrenia) before the substance induced psychotic episode would be excluded from the study. Importantly, based on DSM-IV criteria, SIPD diagnosis is made only when the psychotic symptoms are above and beyond what would be expected during intoxication or withdrawal and when the psychotic symptoms are severe [2]. For these patients, essential baseline socio-demographic and clinical parameters were taken from their medical records. Any change in diagnosis to a PPD was also noted.

Demographic Characteristics

A total of 115 patients were seen by the National Addictions Management Service between 1st April 2007 to 31st March 2012 with a diagnosis of Substance Induced Psychotic Disorder, Drug Psychosis or mental/behavioural disturbances due to drug use and their medical records were examined. Those patients with a primary psychotic disorder diagnosed before the stated period were excluded from the study. In total, 48 patients remained after the exclusion criteria were applied. The sample was predominantly male, Chinese and mostly unemployed (Table 1).

Statistical Analysis

Statistical analysis was performed with SPSS version 20 for windows. We compared the socio-demographic and clinical characteristics between patients whose diagnosis remained as SIPD versus those who converted to PPD using student's T-test for continuous variables and chi-square test for categorical variables. Logistic regression analysis was then carried out to identify variables predictive of a change in diagnosis to PPD.

Results

Clinical characteristics

The mean age of Diagnosis of SIPD for our 48 patients was 37.4, (SD= 10.0; range 18-54). The mean duration of index hospitalization was 11.2 days (SD= 8.15). The mean number of hospitalizations at the Institute of Mental Health in the subsequent 2 years from the date of diagnosis of SIPD was 2.4 (SD= 1.9). The range for the number of admissions being 0 to 7, with the mode being 2 admissions in the subsequent 2 years.

The diagnosis of SIPD was a clinical one based on DSMIV-TR criteria and on the history that the offending drug had been used prior to and within a month of onset of the psychotic symptoms. Although not ideal, urine drug tests were done on only 44 (91.6%) of the patients at the point of diagnosis. This being a clinical sample, it was likely that the remaining 4 patients did not provide consent for the urine drug tests. Importantly, all 48 patients were clinically well prior to consuming the illicit substances and had no past history of psychotic disorder. In total, 27 patients (56.3%) had negative urine drug tests. This was probably due to the short window of opportunity for detecting such drugs in the urine, amphetamines and opiates for instance only remain positive for 2-4 days after last use.

Of the substance induced psychotic disorders, 14 (29.2%) were amphetamine induced, 13 (27.1%) were alcohol induced, 13 (27.1%) were benzodiazepine induced, 11 (22.9%) were codeine induced, 3 (6.3%) were marijuana induced and 2 (4.2%) were inhalant induced. 2 (4.2%) other patients who denied usage of any substances had the diagnosis made based on the nature of the presenting complaints, past psychiatric history of drug use or collateral information from friends or relatives. 9 (18.8%) had usage of more than 1 class of substances; 8 used 2 classes of substances and 1 used 3 classes. For these 9 patients who had used multiple substances, the SIPD was attributed to each drug that the patient was using as it is impossible to identify the causative agent. Majority of the patients (87.5%) were started on antipsychotics at diagnosis of SIPD.

Conversion to PPD

At the end of the 1 year follow up period or until the latest date of follow up, 10 patients (20.8%) had a change in diagnosis to a PPD. 6 patients (12.5%) were diagnosed as suffering from schizophrenia, 2 patients (4.2%) were diagnosed with psychotic disorder/psychotic disorder NOS and 2 patients (4.2%) were diagnosed with affective psychosis. The change in diagnosis to a PPD was made by the psychiatrist after noting the persistence of psychotic symptoms despite the patients being drug free for more than 1 month in duration and in accordance to DSM-IV criteria for the various psychotic disorders. Of note was that out of the 48 patients, 12 patients (25%) defaulted follow up before 1 year elapsed from the date of diagnosis of SIPD and another 1 patient passed away. For these patients, the diagnosis stated at the most recent follow up was used to determine whether or not they had converted to another primary psychiatric disorder. Out of the 13 patients who defaulted follow up/passed away before the one year follow up period was completed, only 2 (15.4%) had a change in diagnosis at the most recent follow up appointment, one to schizophrenia and the second to psychotic disorder NOS. There were no significant differences in baseline clinical and socio-demographic

Table 2: Logistic Regression.

Variables in the equation	P Value
age_at_diagnosis_of_SIPD*	.031
gender	.657
marital_status	.199
ethnicity	.141
Housing*	.043
education	.931
employment	.233
duration_of_index_hospitalization	.167
number_of_hospitalizations_IMH_2_years	.265
antipsychotic_at_baseline	.999

*P<0.05

characteristics between the group that converted to PPD and the group whose diagnosis remained as SIPD.

Predictor of conversion to PPD

In a multivariate logistic regression model involving 48 patients (38 stable, 10 converted to primary psychotic disorder) considering variables of gender, marital status, ethnicity, housing, education, employment, antipsychotic use, age at diagnosis of SIPD, number of hospitalizations in 2 years and duration of index hospitalization, the age at diagnosis of SIPD was significant in predicting subsequent conversion to a primary psychotic disorder (Wald $\chi^2=4.640$, $p=0.031$, $\text{Exp}(B)=0.839$, 95% C.I.=[0.716, 0.984]) (Table 2). Baseline Housing status was also significant in predicting conversion to a primary psychotic disorder (Wald $\chi^2=4.107$, $p=0.043$, $\text{Exp}(B)=0.006$, 96% C.I.=[0.000, 0.846]) (Table 2). Variables in the model accounted for 46.4% of the outcome variance (Nagelkerke $R^2=0.464$). The results indicate that for every 1 year later that SIPD is diagnosed, there is a $(1 - 0.839) = 16.1\%$ reduced risk that it will convert to PPD (Table 2).

Discussion

Our study showed that the main causative agents for SIPD in the National Addictions Management service were amphetamines, alcohol, benzodiazepines and codeine. Cannabis which has a large association with psychosis in international literature was not featured as much here [13-16]. Interestingly none of the 48 cases of substance induced psychotic disorder (SIPD) was related to heroin use which like codeine, belongs to the opiate family. Furthermore, there were also no cases of cocaine induced psychosis which is highly prevalent in USA and Europe [22-24]. This likely reflects the uncommon occurrence of cocaine use in Singapore. The finding that codeine cough mixture use was represented significantly amongst our patients with substance induced psychotic disorder shows concordance with a study done in Hong Kong which reported that the top psychiatric diagnosis amongst cough mixture abusers was SIPD [6]. Of importance in our study is that many of the cough mixtures were reported to have been obtained from illegal sources and hence likely to contain adulterants as well. Interestingly, about a quarter of the cases with SIPD were attributed to benzodiazepines. A search of MEDLINE only revealed isolated case reports of psychotic phenomena during withdrawal from chronic use of benzodiazepines [25]. It is therefore worthwhile studying this further.

10 of the 48 patients were re-diagnosed as having a PPD. Importantly, the younger the age of onset of SIPD, the higher the risk of conversion to a PPD. The rate of conversion is similar to a study in India which reported that 20% of their subjects had a change in

diagnosis to either schizophrenia or affective psychosis on follow up.⁴ This places caution on the physician to actively look out for risk of conversion in younger patients diagnosed with SIPD as management of PPD would be more complex and would require the patient to be followed up more closely. The results also showed that those who were homeless had a greater risk of conversion to PPD. However this result should be interpreted with caution as out of the 48 patients, only 4 were homeless, of whom 2 converted to PPD. Lastly another significant finding was that 12 patients (25%) defaulted follow up. The proportion who defaulted follow up is in accordance with the high rate of defaulters for this group of patients based on international studies [26]. It is plausible that a significant proportion of those who defaulted follow up would still have required treatment.

Limitations and Strengths of Study

There are several methodological limitations to our study. The clinical sample size of 48 is small; the study is retrospective; diagnosis though made by trained psychiatrists is essentially interview derived based on DSMIV-TR criteria while urine drug tests were performed on only 44 patients; around a quarter of the patients were lost to follow-up before one year. The study also did not differentiate between patients who were dependent versus those who were abusing the drugs.

The strength of the study however lies in its contribution to scant research on the topic in South East Asia including Singapore. It provides invaluable information for public education efforts and better informs us with respect to counselling and management strategies to use with this group of patients. Despite the small number, our study is likely to reflect the situation locally as patients with SIPD are generally referred to our tertiary centre for management, given the lack of substance abuse and addiction management services at other restructured hospitals in Singapore. Although a prospective study is recommended, it would be difficult to recruit adequate numbers of patients given that at a tertiary centre, we are only seeing roughly 10 cases per year. Furthermore it has been shown that these patients have a high tendency to default treatment, reducing the numbers even further in a prospective study.

This study could however lay the groundwork for an improved rigorous prospective evaluation using research diagnostic tools and laboratory tests for the diagnosis of SIPD.

Conclusions

Substance Induced Psychotic Disorder is an understudied field in Singapore and South East Asia. Within the limitations of our retrospective study of a clinical sample of 48 SIPD patients seen in a Singaporean tertiary addictions management facility, we have found the causative agents to be Methamphetamine, alcohol, benzodiazepines and codeine. We have also discovered that a fifth of these patients “converted” to a primary psychotic disorder and that the age of onset predicts the risk of conversion, thus informing physicians about the need to monitor younger patients closely.

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