Profiling the psychotic, depressive and anxiety symptoms in chronic ketamine users

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ABSTRACT

Objective: Although concern about chronic ketamine abuse has grown, the characteristic symptomatology of chronic ketamine users has yet to be examined. This study aims to measure the psychotic, depressive and anxiety symptoms in chronic ketamine users.
Methods: A group of chronic ketamine users in Guangzhou, China were evaluated. The socio-demographic and drug use characteristics of subjects were documented. Symptoms of psychosis, depression, anxiety were evaluated by the Positive and Negative Syndrome Scale (PANSS), Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI). The severity of the symptoms was identified by standard severity cutoffs.
Results: The PANSS total score, positive symptom, negative symptom, general psychopathology subscale score were 45.3 ± 8.4, 8.0 ± 1.7, 13.2 ± 3.9 and 24.2 ± 4.9 respectively. BDI and BAI score was 13.1 ± 6.5 and 15.7 ± 9.6 respectively. 77.5% and 46.0% of the subjects showed moderate to severe depressive symptoms and anxiety symptoms respectively. The BDI score was positively correlated with ketamine use frequency. The BAI score was positively correlated with ketamine use frequency.
Conclusions: Depressive symptoms were commonly presented in chronic ketamine users. The higher ketamine use frequency and dosage were associated with more severe depressive symptoms.

1. Introduction

Ketamine, an N-methyl-D-aspartate (NMDA) receptor antagonist was developed in the 1960s and is widely used in medicine for anesthesia and pain management. Its use as a recreational drug of abuse has become widespread, in recent decades, particularly in Europe and Southern China. Ketamine has also attracted the attention of researchers as a potential model of psychopathology because it provokes distinctive psychological symptoms in humans and rodents (Becker et al., 2003; Aalto et al., 2005; Frohlich and Van Horn, 2014). Krystal et al. (1994) reported that a single intravenous dose of ketamine given to healthy volunteers produced acute psychotic symptoms as well as impairment of memory. Recreational ketamine use has been reported to produce psychotic symptoms similar to those observed in schizophrenia (Morgan et al., 2004b).

In addition to these short-term experimental studies, clinicians have observed a broad array of clinical symptoms in chronic ketamine users, although few systematic studies of symptom patterns associated with chronic ketamine use have been published. It was reported that chronic ketamine users had higher levels of sub-threshold psychotic symptoms (Stone et al., 2013). In one study it was reported that the depression scores increased in a group of chronic ketamine users over a 12 month period (Morgan et al., 2010). But the assessments were done in a relatively small sample size and they did not measure the psychosis or anxiety symptoms which were observed in chronic ketamine users. Tang et al. (2013) reported depressive symptoms were more frequently found in current ketamine users than ex-ketamine users and control. Morgan and Curran (2012) reviewed recent literature and noted that ketamine users sometimes reported psychotic symptoms but concluded that there was little evidence of any link between chronic heavy use of ketamine and a subsequent diagnosis of a psychotic disorder. Since experimental studies have linked ketamine to both psychotic and depressive symptoms, a more systematic study of the symptoms associated with chronic ketamine

abuse may be informative.

In the present study we recruited chronic ketamine users hospitalized at 2 hospitals in Guangzhou, China for detoxification and/or treatment of symptoms related to chronic ketamine use. All subjects were assessed with standard and widely used measures of schizophrenia, depression and anxiety symptomatology: the Positive and Negative Syndrome Scale (PANSS) for psychotic symptoms (Kay et al., 1988) , the Beck Depression Inventory (BDI) (Beck et al., 1961) and the Beck Anxiety Inventory (BAI) (Beck et al., 1988) for depressive and anxiety symptoms, respectively. The severity of these symptoms was identified by standard published severity cutoffs on the PANSS, BDI and BAI. Using these measures we sought to systematically profiling the symptoms associated with chronic ketamine use. We thus seek to better understand the problems faced by chronic ketamine users.

2. Methods

2.1. Sample and data collection

From January 2012 to December 2013, 187 ketamine users who were voluntarily hospitalized for detoxification and/or for treatment of symptoms related to long term ketamine use and who were willing to join the study were recruited at the substance-abuse department of the Guangzhou Brain Hospital and the voluntary drug rehabilitation ward of Guangzhou Baiyun mental hospital.

All the participants underwent a 2-h semi-structured interview to assess sociodemographic characteristics, psychopathological status, and substance use during the first two weeks of their current hospitalization. Current illicit drug use of all participants was validated through urine toxicology as well through self-report data. The interviews were conducted by clinicians with 3 or more years of clinical experience. Inclusion criteria required that participants: 1) be chronic ketamine users admitted to Guangzhou Brain Hospital or Guangzhou Baiyun Mental Health Hospital for detoxification or treatment of ketamine-related symptoms; 2) no other substance dependence other than ketamine and tobacco according to DSM-IV-TR; 3) subjects with ketamine as a drug of choice for longer than 6 months; 4) being capable of providing written informed consent form. Exclusion criteria included: (1) any known organic diseases or (2) history of head trauma with loss of consciousness, (3) any unstable physical illnesses, or (4) impairment of color vision or hearing. The study was approved by the Institutional Ethics Committee and written informed consents were signed prior to enrollment.

2.2. Measures

2.2.1. Socio-demographic characteristics
The subjects' age, gender, marital status, years of education, employment, medical history and family relationships were documented.

2.2.2. Drug use
Information on drug use included age of first ketamine use , lifetime duration of ketamine use, frequency of ketamine use in the past month, recent polydrug use, smoking patterns and history of alcohol use.

2.2.3. Standardized scales
The Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1988), a structured rating scale for the symptoms of schizophrenia was assessed by trained raters. The cutoffs used for PANSS were < 58 less than mildly ill, 58–75 mildly ill, 75–95 moderately ill,

> 95 markedly ill, > 116 severely ill (Leucht et al., 2005).

Ketamine users were asked to complete Beck Depression Inventory (BDI,13-item; Beck and Beamesderfer, 1974) and the Beck Anxiety Inventory (BAI; Beck et al., 1988) which assessed their depressive and anxiety symptoms during the two weeks before they were hospitalized. , The cutoffs used for BDI, a widely used structured rating scale for depression ,were 0–4 for no depression, 5–7 for mild depression, 8–15 for moderate depression, and ≥ 16 severe depression(Beck, Epstein et al. 1974). The cutoffs used for BAI, a structured rating scale for anxiety disorder were 0–7 minimal level of anxiety, 8–15 mild anxiety, 16–25 moderate anxiety, 26–63 severe anxiety (Beck et al., 1988).

Assessment of inter-rater reliability for raters in this study was in the excellent to good range on the PANSS, with intra-class correlations ranging from 0.90 to 0.96.

2.3. Analyses

Symptom levels on the PANSS, BDI and BAI were classified using published, standard severity levels (Beck and Beamesderfer, 1974; Beck et al., 1988; Leucht et al., 2005) to determine whether symptom patterns were more reflective of schizophrenia, depression or anxiety disorder.

Bivariate spearman correlation analysis was used to identify correlations between socio-demographic, substance use characteristics and symptom measures. Further multiple linear regression analysis were done on variables which were significant on bivariate spearman correlation analysis.

All analyses were conducted under SPSS version 13.0.

3. Results

3.1. Participant characteristics

Socio-demographic characteristics, drug use and PANSS, BDI, BAI scores are presented in Table 1. Altogether there were 187 chronic ketamine users enrolled in the study of which 173 were male (92.5%), 14 were female (7.5%). The average age was 26.2 ± 5.0 (Mean ± SD) (range 15-44 years). The average time from first ketamine use to the present was 6.3 ± 3.1 years (Mean ± SD) and the time from becoming dependent to the present was 3.1 ± 2.0 years (Mean ± SD). The average dose of ketamine on a typical day of use in the past 30 days was 3.4 ± 2.7 gram/day (Mean ± SD). 141 (75.4%) patients reported using ketamine daily, 14 patients (7.3%) used ketamine more than 4 times per week, and 32 patients (17.1%) used ketamine less than 4 times per week. There were 158 subjects (84.5%) who had used psychoactive drugs other than ketamine, although all the subjects were with ketamine as a drug of choice for longer than 6 months.

3.2. Evaluation by standardized scales

The average PANSS total score, positive symptom subscore, negative symptom subscore and general psychopathology subscore were 45.3 ± 8.4, 8.0 ± 1.7, 13.2 ± 3.9 and 24.2 ± 4.9 respectively. BDI score was 13.1 ± 6.5. BAI score was 15.7 ± 9.6.The percentages of subjects clarified by the cutoffs on standardized scales are presented in Fig. 1. On the PANSS, 172 (92.0%) had PANSS total scores less than 58, indicating less than mild or minimal illness; 15 (8.0%) had PANSS total scores between 58 and 75, indicating for mild illness. No PANSS total scores were in the moderate or severe range. On the BDI, 21 subjects (11.2%) scored 0–4 (no depression), 21 (11.2%) scored 5–7 (mild depression), 84 (44.9%) scored 8–15 (moderate depression), the most common response range, and 61 (32.6%) scored ≥ 16 (severe depression), the second most common