

CLINICAL STUDY

Traditional Chinese Medicine diagnoses in persons with ketamine abuse

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Abstract

OBJECTIVES: To explore the distribution of TCM patterns in ketamine users and the inter-rater reliability of TCM diagnosis among TCM practitioners.**METHODS:** Eighty-four subjects recruited from substance abuse clinics and non-governmental counseling services catering for ketamine abusers were examined by one or two TCM practitioners. The distribution and inter-rater reliability of the TCM diagnoses between the two TCM practitioners were described and measured.**RESULTS:** Seven TCM patterns were differentiated. The four most common patterns were the Heart *Yin* deficiency (29.8%), Kidney *Yang* deficiency (26.2%), Kidney *Yin* deficiency (19.0%), and Spleen *Yang* defi-ciency (14.3%). The agreement between the two TCM practitioners was 59%; the kappa for the three most common patterns was 0.472 ($P=0.003$). The proportion of men was lower in the Kidney *Yin* deficiency group (18.8%), in comparison to the Heart *Yin* deficiency (60.0%, $P=0.009$) and Kidney *Yang* deficiency group (59.1%, $P=0.013$).**CONCLUSION:** The differences between the TCM groups in terms of the source of referral and number of drug uses other than ketamine were of borderline significance. Further research should focus on validating diagnostic tools and improving inter-rater reliability in TCM to enhance the quality of clinical trials of TCM treatments for ketamine abuse.

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Key words: Ketamine; Abuse; *Yin* deficiency; *Yang* deficiency; Syndrome differentiation; Traditional Chinese Medicine

INTRODUCTION

In recent years a change in the pattern of drug abuse has been observed in Hong Kong. It has been a gradual increase in the use of ketamine and a simultaneous decline in the use of opiates, particularly among younger persons. According to the Central Registry of Drug Abuse (CRDA) of the Narcotics Division, Security Bureau, the recent decline in heroin use has been accompanied by a corresponding increase in ketamine use.¹ Seventy-two percent of drug abusers aged under 21 years reported other substance use, while only about 3% admitted heroin use.²

To date, there is no effective medication for the treatment of ketamine dependence. Acupuncture, one of

the treatment modalities of Traditional Chinese Medicine (TCM), is commonly used for the treatment of substance dependence.³ Several clinical trials of acupuncture for cocaine abuse have used the diagnostic and statistical manual (DSM),⁴ the official psychiatric classification of the American Psychiatric Association (APA), to identify cocaine users,⁵ yet many of these trials designed acupuncture treatment based on the theoretical principles of TCM. As a result, this study recruited subjects following one system of diagnosis, whereas the interventions were based on a principally different diagnostic system. As with all medical systems, the role of diagnosis in TCM is believed to be fundamental to the effective treatment of any disease, including substance abuse or dependence.⁶ Hence, it is crucial to examine the impact of a TCM treatment on various diagnostic subtypes based on TCM diagnoses: that is, to harmonize diagnosis and treatment.

It has been suggested that cocaine abuse may fall in to four patterns of TCM diagnosis, namely, Heart *Yin* deficiency, Kidney *Yin* deficiency, Liver *Yin* deficiency and Spleen *Qi* deficiency.³ A comprehensive study on the distribution of TCM patterns in ketamine use is still lacking. In addition, the reliability of TCM diagnoses in ketamine use has not been examined. A literature review of the reliability of TCM diagnoses concluded that the reliability of TCM diagnoses and treatment was generally low.⁶

It is important to evaluate the distribution and reliability of TCM diagnoses prior to designing and conducting clinical trials of TCM treatments for ketamine abuse. This study aimed to determine the distribution of TCM patterns in a group of ketamine users and to measure the inter-rater reliability of TCM diagnosis between TCM practitioners.

MATERIALS AND METHODS

Subjects

A total of 84 subjects were recruited from substance abuse clinics (SACs) and community counseling services (CCS) for drug abusers in Hong Kong from March to October 2011. The inclusion criteria were: 1) aged between 16 and 65 years; and 2) use of ketamine at least twice per month over 6 months in the past year and the duration of its use is the longest among all abused substances. The exclusion criteria were: 1) predominant use of either heroin or alcohol; 2) concurrent severe medical conditions that required regular treatment; 3) major surgery in the past month; and 4) pregnancy or breastfeeding.

Collection of demographic and clinical variables

A trained research assistant interviewed the subjects and collected basic demographic data (age, sex, education, employment and marital status). The severity of dependence scale (SDS),⁷ the 21-item version of the

Beck Depression Inventory (BDI),⁸ the anxiety subscale of the hospital anxiety depression scale (HADS),⁹ and the brief psychiatric rating scale (BPRS)¹⁰ were also administered by a trained research assistant. The SDS,⁷ BDI,¹¹ HADS¹² and BPRS¹³ measure the degree of drug dependence, and depressive, anxiety and psychotic symptoms, respectively. The Cronbach's α for the SDS, BDI, HADS and BPRS in the current study were 0.59, 0.92, 0.83, and 0.86, respectively.

TCM practitioners

Two TCM practitioners participated in the study. Both had completed 5-year bachelor degrees in TCM and were registered TCM practitioners in Hong Kong. Practitioner 1 and 2 had been in full-time practice for 3 and 4 years, respectively. Practitioner 1 assessed all subjects whereas Practitioner 2 examined only 22 subjects in order to determine the reliability of the TCM diagnoses. Both practitioners received further training on data collection, interpretation of data and approach to diagnosis from a senior TCM practitioner (Waizhu Sun) who had been in full-time practice for over 40 years.

Selection of TCM diagnoses

With reference to the Guiding Principle of Clinical Research of Chinese New Drugs,¹⁴ and based on the clinical experience of Waizhu Sun, the TCM diagnosis of ketamine abuse were first divided into five broad categories: heart, kidney, spleen, liver, and lung deficiency (deficiency). In each category, the diagnosis was further subdivided into *Yang* deficiency and *Yin* deficiency. Hence, there were 10 possible patterns for TCM diagnosis, namely Heart *Yin* deficiency, Heart *Yang* deficiency or Kidney *Yin* deficiency, Kidney *Yang* deficiency, Spleen *Yin* deficiency, Spleen *Yang* deficiency, Liver *Yin* deficiency, Insufficiency of Liver *Qi*, Lung *Yin* deficiency, Lung *Qi* Deficiency.

TCM diagnostic procedure

The TCM practitioners conducted separate questionnaire-based clinical interviews and physical examinations including inspection of the tongue and palpation of the pulse. All of the findings in the history taking and physical examination were recorded in a standard TCM assessment form.

The TCM practitioners prescribed one or more patterns as TCM diagnosis to each subject. If there was more than one patterns, the practitioners also selected the most important (primary) patterns as TCM diagnosis.

The study protocol was approved by the Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee. All subjects signed a consent form.

Statistical analyses

The descriptive statistics on the characteristics of the

Table 1 Distribution of TCM diagnoses in ketamine users

		Rater 2				
		Heart <i>Yin</i> deficiency	Kidney <i>Yang</i> deficiency	Kidney <i>Yin</i> deficiency	Heart <i>Yang</i> deficiency	Spleen <i>Yang</i> deficiency
Rater 1	Heart <i>Yin</i> deficiency	4	1	1	1	0
	Kidney <i>Yang</i> deficiency	1	4	2	0	0
	Kidney <i>Yin</i> deficiency	0	2	5	0	0
	Heart <i>Yang</i> deficiency	0	0	0	0	1

Notes: TCM: Traditional Chinese Medicine. Kappa=0.472, $P=0.003$. Total number of raters=22.

study sample were computed. The inter-rater reliability of the TCM diagnoses was examined by the percentage of agreement and kappa statistics. The distribution of sex and source of recruitment, primary drug use, drug use in the past 30 days, the mean duration of primary drug use, age, and the scores on the BDI, SDS, HADSA, and BPRS were compared between the more common primary TCM diagnoses using analysis of variance and *Chi*-square tests, as the sample sizes were inadequate for the uncommon diagnoses.

RESULTS

Characteristics of the sample

Eighty-four participants were enrolled and completed the study; 18 and 66 were recruited from the SACs and CCS, respectively. The study sample had the following characteristics: 53.6% were men; the mean age and education level were (24.5 ± 4.0) and (8.1 ± 1.4) years, respectively. The mean age of onset of primary ketamine use and the mean (median) duration of its use were (16.3 ± 2.9) and (6.9 ± 3.3) years, respectively. The average time since last ketamine use was (6 ± 11) months; 44% of the subjects had abused ketamine in the past 30 days for (2 ± 9) days. The mean number of substances other than ketamine abused was 1.3 ± 1.4 , with a range of 0 to 5. The average time since last drug use other than ketamine was (35 ± 57) months. The mean SDS, BPRS, HADSA and BDI scores were 8 ± 3 , 4 ± 5 , 7 ± 4 and 18 ± 12 respectively; 36.9% and 59.5% scored above the cutoff on the HADSA and BDI.

Distribution of primary TCM patterns

Seven TCM patterns were identified. The four most common TCM patterns were Heart *Yin* deficiency (29.8%), Kidney *Yang* deficiency (26.2%), Kidney *Yin* deficiency (19.0%), and Spleen *Yang* deficiency (14.3%). The three least common TCM patterns were Heart *Yang* deficiency (8.3%), Liver *Yin* deficiency (1.2%) and Lung *Qi* Deficiency (1.2%). The most frequent organ implicated was the kidney (45.2%), followed by the heart (38.1%), spleen (14.3%), lung

(1.2%) and the liver (1.2%).

Agreement of primary TCM patterns

The distribution of the TCM patterns made by the two TCM practitioners is shown in Table 1. The agreement between the two practitioners was 59%; the kappa for the three most common patterns (Heart *Yin* deficiency, Kidney *Yang* deficiency, and Kidney *Yin* deficiency) was 0.472 ($P=0.003$).

Relationship between primary TCM patterns and clinical characteristics

There was significant difference in the distribution of TCM patterns in men and women (Table 2). Post hoc comparison found that Kidney *Yin* deficiency was less common in men ($P=0.002$). There was no significant difference in the distribution of TCM patterns between short and long duration of substance use. The proportion of men was lower in the Kidney *Yin* deficiency group (18.8%), in comparison to the Heart *Yin* deficiency (60.0%, $P=0.009$) and Kidney *Yang* deficiency group (59.1%, $P=0.013$). The differences between the TCM groups in terms of the source of referral and number of drug uses other than ketamine were of borderline significance (See Table 3).

DISCUSSION

To the best of our knowledge, this was the first study to examine the distribution of TCM patterns in people with ketamine abuse. More than half of the subjects were recruited from the community. In this study, the four most common TCM deficiency pattern accounted for 89% of all TCM diagnosis. This predominance of deficiency pattern has also been reported in cocaine³ and heroin dependence.¹⁵ It is common to see a highly skewed distribution of TCM patterns for a given condition.¹⁶

The level of inter-rater reliability between TCM practitioners for the TCM diagnosis of ketamine abuse was moderate.¹⁷ Low levels of agreement for TCM diagnosis have been reported in other diseases, such as rheumatoid arthritis,¹⁶ headache,¹⁸ hypercholesterolemia,¹⁹

Table 2 Relation of TCM diagnoses to gender and current use of ketamine [n (%)]

TCM diagnose	Male (n=45)	Female (n=39)	Statistics	P value
Heart <i>Yang</i> deficiency	6(13.3)	1(2.6)		
Heart <i>Yin</i> deficiency	15(33.3)	10(25.6)		
Lung <i>Yang</i> deficiency	1(2.2)	0		
Spleen <i>Yang</i> deficiency	6(13.3)	6(15.4)	13.187	0.040
Liver <i>Yin</i> deficiency	1(2.2)	0		
Kidney <i>Yang</i> deficiency	13(28.9)	9(23.1)		
Kidney <i>Yin</i> deficiency	3(6.7)	13(33.3)		

TCM diagnose	Duration of drug use< 7 years	Duration of drug use ≥7 years	Statistics	P value
Heart <i>Yang</i> deficiency	4(10.0)	3(6.8)		
Heart <i>Yin</i> deficiency	16(40.0)	9(20.5)		
Lung <i>Yang</i> deficiency	1(2.5)	0		
Spleen <i>Yang</i> deficiency	5(12.5)	7(15.9)	7.239	0.299
Liver <i>Yin</i> deficiency	0	1(2.3)		
Kidney <i>Yang</i> deficiency	9(22.5)	13(29.5)		
Kidney <i>Yin</i> deficiency	5(12.5)	11(25.0)		

Note: TCM: Traditional Chinese Medicine.

and female infertility.²⁰ One of the reasons for the inconsistency in TCM diagnosis is that the assessment of certain features in the TCM diagnostic system is highly unreliable, such as skin texture, tongue, body color and pulse location.¹⁹ Other reasons may include the interpretation process, from symptoms and signs to diagnostic conclusions.²⁰ The inter-rater reliability of TCM diagnosis could be improved with calibration exercises on the administration of rating scales.⁶

Previous studies on ketamine abusers have indicated that the common clinical symptoms of chronic ketamine abusers include lower urinary tract symptoms, such as frequency, urgency, dysuria, urge incontinence, abdominal pain with associated nausea and vomiting, and impaired memory.²¹⁻²³ From the clinical presentations of ketamine abuse, it could be assumed that ketamine has fast moving ability and may easily damage *Qi*, blood, fluid in human body according to TCM theory; therefore the TCM patterns of chronic substance abusers are mainly of deficiency. We further classified the patterns of deficiency in substance abusers into five categories depend on the affected organs: Heart deficiency, kidney deficiency, spleen deficiency, liver deficiency, and lung deficiency.

Our findings indicate that the pattern of Kidney *Yin* deficiency was less common in man than in women. Because it was a post hoc analysis and the sample size was small, no definitive conclusion could be drawn on the possible difference of patterns between males and females. Other factors such as life style, diet, or ket-

amine abuse combined with other drugs may have possibly contributed to the gender difference in the distribution of TCM patterns. We could not locate any reports on the comparison of clinical characteristics between different patterns of TCM diagnosis in the context of ketamine abuse. Further exploration of this issue is warranted.

This study has several important limitations. First, there is no gold standard for the TCM diagnosis of most medical conditions; that is, which diagnoses are "correct" or "best." Similarly, there is no validated TCM diagnostic instrument available in the field of ketamine abuse.

As none of the primary pattern of TCM diagnosis represented more than 30% of the study sample, the present findings suggest that future clinical trials of TCM treatment in ketamine abuse should not use a predetermined treatment protocol. The treatment should be individualized and based on the particular primary patterns of TCM diagnosis.

In summary, this study described the common TCM patterns in persons with ketamine abuse. Further research should focus on validating diagnostic tools in TCM and improving the inter-rater reliability of TCM diagnosis in ketamine abuse to enhance the quality of clinical trials in TCM.

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Table 3 Relation of TCM diagnoses to demographic and clinical characteristics ($\bar{x} \pm s$)

	Heart <i>Yin</i> deficiency n=25 [n (%)]	Kidney <i>Yang</i> deficiency n=22 [n (%)]	Kidney <i>Yin</i> deficiency n=16 [n (%)]	Statistics ^c	P value
Source of recruitment SACs	8 (32.0)	2 (9.1)	6 (37.5)	4.900 ^d	0.086 ^b
CCS	17 (68.0)	20 (90.9)	10 (62.5)		
Men	15 (60.0)	13 (59.1)	3 (18.8) ^e	7.963 ^d	0.019 ^b
Age	24.0±4.6	25.4±3.0	24.8±5.0	0.586	0.560
Duration of ketamine use	6.1±3.2	7.6±3.4	7.7±2.8	1.878	0.162
Age of onset of ketamine use	16.1±3.0	17.0±2.6	16.3±3.8	0.494	0.613
Ketamine use in past 30 days					
Yes	12 (48.0)	8 (36.4)	7 (43.8)	0.654 ^d	0.721 ^b
No. of days	11.2±13.1	7.0±1.5	9.3±13.1	0.651	0.525
Time lapsed since last ketamine use (month)	7.6±15.1	7.9±11.9	3.0±3.6	0.936	0.398
Number of drug use other than ketamine	0.7±0.9	1.5±1.5	1.3±1.5	2.402	0.099
SDS	7.2±3.2	8.6±3.5	7.8±2.9	1.015	0.368
BRPS	4.0±5.8	4.2±5.4	1.6±1.3	1.622	0.206
HADSA	6.4±3.6	6.3±3.4	7.7±4.0	0.813	0.448
HADSA (≥8)	10 (40.0)	6 (27.3)	7 (43.8)	1.303 ^d	0.521 ^b
BDI	16.7±12.9	20.6±12.3	17.7±10.7	0.635	0.533
BDI (≥14)	11 (44.0)	14 (63.6)	11 (68.8)	3.022 ^d	0.221 ^b

Notes: CCS: community counseling services; SACs: ketamine abuse clinics; TCM: Traditional Chinese Medicine; SDS: Severity of Dependence Scale; BPRS: Brief Psychiatric Rating Scale; HADSA: anxiety subscale of the hospital anxiety depression scale; BDI: beck depression inventory. ^aANOVA unless otherwise specified; ^b*Chi*-square test; ^cFunless otherwise specified; ^d*Chi*-square. ^epost hoc comparison with Heart *Yin* deficiency, $P=0.009$ and kidney *Yang* deficiency, $P=0.013$.

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