

## Research Article

### Psychiatric Profiles and Clinical Manifestations of Cathinone Users: Case Series of Analytically Confirmed Cathinone Use in Taiwan

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#### Abstract

The increasing prevalence of new or Novel Psychoactive Substances (NPS) use has been a global public health issue; however, well-described clinical profiles of NPS users have been lacking, especially in Taiwan. Novel cathinone appear to be one of the most popular emerging NPS in East Asia, with a parallel growth in emergency department visits. However, as cathinone is undetectable by standard immunoassay urine tests in most hospitals, any links with associated clinical manifestations remain unclear. Thus, here we presented six treatment-seeking psychiatric patients whose urine samples were analytically confirmed with cathinone use. We first described their socio-demographics and psychiatric profiles, and then reported their toxicological findings confirmed by Liquid Chromatography Mass Spectrometers (LC-MS). We found these cathinone users were relatively young, with short duration from their first

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use to treatment seeking. Furthermore, the reasons for their treatment-seeking included agitation, aggressive or suicidal behaviors, highlighting the potential danger of cathinone use. Interestingly, all of them reported ingesting cathinone via “coffee sachets”, which mimic ordinary instant coffee and each pack, contained numerous illicit drugs, which accounted for multiple substances detected in their urine. In conclusion, this report calls for an urgent need to educate the health professionals and the public on the danger and the complex face of NPS. A significant amount of research is needed to fully understand both the short and long term effects of these rapidly growing NPS in Taiwan.

#### Introduction

New or Novel Psychoactive Substances (NPS), known as “legal highs”, are defined as psychotropic drugs that are not controlled by the 1961 single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances by United Nations [1]. Emergence of NPS is a worldwide phenomenon, evidenced by the fact that 739 different NPS were reported to the United Nations Office on Drugs and Crime (UNODC) between 2009 and 2016 [2]. Although current surveys have shown relatively lower prevalence of NPS when compared to other illicit drugs, this could be underestimated due to survey design or difficulties in forensic science [3]. A national survey from England and Wales revealed that the lifetime use of NPS was 2.9% in adults (16-59 years old) and 6.1 % in adolescents and young adults (16-24 years old) in 2014-2015 [4]. The report from National Survey on Drug Use and Health (NSDUH) showed that 1.2 % of Americans aged 12-34 reported lifetime use of NPS [5]. Furthermore, a remarkable growth of emergency department visits involving NPS use has been noted. For instance, based on data from the New York City Poison Center, prevalence of NPS exposure rose from 7.1% in 2011 to 12.6% of recorded cases in 2014 [6]. Another study from Europe revealed that NPS represented 5.6 % of all acute emergencies involving illicit drug use during 2013/14 [7].

However, conversely, good clinical information characterizing NPS users is scarce, especially in Asia [8]. In a study done by Lee et al, interesting variations in NPS use between countries and regions were noted. Globally, synthetic cannabinoids (40%) are the most commonly consumed agents, followed by synthetic cathinones (22%) and phenethylamines (17%) [8]. Interestingly, a report from the Global SMART Programme (Synthetics Monitoring: Analyses, Reporting and Trends) revealed a totally different trend in East and South-East Asia [9], with the most common type synthetic cathinones, following by synthetic cannabinoids. The major type of NPS in Taiwan is synthetic cathinones, in Korea synthetic cannabinoids, despite their geographical proximity [10].

Pharmacological mechanisms of synthetic cathinones involve increasing release of monoamines, which contributes to its addictive potential and psychiatric manifestations [11]. While data from the Taiwan Analytical Laboratory Drug Abuse Report System (ALDARS) revealed the proportion of synthetic cathinone in non-urine samples increased from 1.55% to 25.95% between 2013 and 2015

[12], an extremely small number of cases of synthetic cathinone use identified in medical system, accounting for only 0.2% of all illegal drug cases in 2017 [13]. The marked discrepancy from these two reporting systems could be attributed to either lack of forensic capacity to identify these substances or the unawareness of clinical features of NPS by most health professionals [14,15].

There is limited information focusing on the clinical manifestations and psychiatric profiles of NPS users. Furthermore, previous case studies of NPS were based on self-report instead of analytically-confirmation of their use [16]. Here we present 6 treatment-seeking cathinone users in a psychiatric center and described their socio-demographic profiles, clinical manifestations and psychiatric profiles, aiming to fill the knowledge gap of cathinone users' profiles in Asia.

## Method

We retrospectively identified 6 patients with analytically confirmed cathinone use by urine samples who sought treatment in Taipei City Psychiatric Center in 2017. These patients had signed written consent for toxicological analysis of urine samples. We collected information regarding their socio-demographic data, psychiatric profiles, laboratory findings, toxicology results and received treatments through chart review methods.

We used Liquid Chromatography Quadrupole Time-Of-Flight Mass Spectrometry (LC-QTOF-MS) to detect the presence of NPS. More than 120 substances were examined. As for NPS, we examined the presence of cathinones as well as synthetic cannabinoids. The detailed method using LC-QTOF-MS for detecting new psychoactive substances was previously published [17]. We also obtained the patients' consent to report our finding anonymously and the consent from the parent of one underage patient.

## Results

### Demographic characteristics and past psychiatric history

Six cases with analytically confirmed cathinone in urine samples were ascertained (Table 1). Half of them were male, and had a mean age of 20.5 (±4.3) years (ranges between 14-26 years). The average education was 9.8 years. Notably, three of them reported to have had experiences of significant childhood adversities and two patients had a family history of depression or suicide. Two patients had a prior psychiatric history before using cathinones, including one with

major depressive disorder and one with methamphetamine-induced psychotic disorder.

### Clinical manifestations, treatment course and toxicological results

Half of the cases came from the psychiatric outpatient department (n=3) and half from the emergency department (n=3). Their clinical manifestations were shown in table 2. Strikingly, five out of six patients experienced psychotic symptoms such as visual and auditory hallucinations, delusions of reference and persecution within months of their first use of cathinone. Alarmingly, four of them reported suicidal attempts whilst directly under the influence of cathinones. The suicidal methods were of high lethality, including attempted hanging, drug overdose, jumping from a height, and wrist cutting. Three of them reported having violent behaviors under the influence of cathinone.

Three out of six were prescribed antipsychotics (risperidone 2-4mg per day) while one patient refused to take any antipsychotics. Three patients were hospitalized to an acute psychiatric ward due to their suicidal attempts or psychotic symptoms with the average length of stay in hospital 16 days.

The toxicology findings of the cases included a variety of cathinones including mephedrone, N-ethylpentylone, 4-chloromethcathinone, butylone, dibutylone, methcathinone. Strikingly, all of them denied using other illicit drug use; however, they all claimed to ingest "instant coffee sachets" containing mixed psychoactive substances including cathinone and other illicit drugs. They denied concurrent use of methamphetamine, amphetamine or ketamine. Based on their report, they did know the coffee drink contained a mixture of illicit drugs; however, most of them did not know the exact components of the drink.

## Discussion

In this study, we reported six treatment-seeking patients with cathinone use analytically confirmed by LC-QTOF MS examination. Through these cases, we found some striking features which require high clinical and public health attention. First, these patients are relatively young with age ranged from 14 to 26. Second, there was a relatively short period of time from their first use of cathinone to their treatment-seeking behaviors, whether due to psychotic symptoms, suicidal attempts, or aggressive behaviors.

Patient No.	Age (years)	Gender	Childhood Adversity	Family History	Psychiatric History	Past History of Other Substances	Onset of Cathinone Use	Route of Cathinone Use
1	19	Male	Emotional neglect	Depression	No	Ketamine Marijuana	18	Ingesting drugs through "coffee sachets"
2	14	Female	Emotional neglect	No	No	Ketamine Methamphetamine	13	Ingesting drugs through "coffee sachets"
3	18	Female	No	Depression	Major depression	MDMA Methamphetamine	17	Ingesting drugs through "coffee sachets"
4	26	Male	Unknown	No	No	MDMA Ketamine	26	Ingesting drugs through "coffee sachets"
5	20	Male	No	No	Methamphetamine induced psychotic disorder	Ketamine MDMA Methamphetamine Marijuana	20	Ingesting drugs through "coffee sachets"
6	26	Female	Physical abuse	No	No	Ketamine MDMA Methamphetamine	23	Ingesting drugs through "coffee sachets"

**Table 1:** Socio-demographic characteristics, past psychiatric and drug use history of the six analytically-confirmed cathinone users.

Patient No.	DSM-5 Diagnosis	Clinical Setting	Reasons for Treatment Seeking	Clinical Manifestations	Toxicology Finding	Treatment	Hospital Admission
1	Stimulant induced psychotic disorder Stimulant use disorder	ED	Suicidal attempt due to psychotic symptoms	Agitation Visual and auditory hallucinations Delusions of reference and persecution	Mephedrone N-ethylpentylone Amphetamine Methamphetamine	Risperidone 4mg/day	Yes
2	Stimulant induced psychotic disorder Stimulant use disorder	ED	Agitation due to psychotic symptoms	Agitation Sensory distortion Visual and auditory hallucinations	N-ethylpentylone Amphetamine Methamphetamine	Risperidone 2-4mg/day	Yes
3	Major depressive disorder Stimulant use disorder Anorexia Nervosa	OPD	Suicidal attempt due to depressive symptoms	Mood liability Auditory hallucination Persecutory delusion	N-ethylpentylone Nimetazepam	Escitalopram 10mg/day	Yes
4	Stimulant induced psychotic disorder Stimulant use disorder	ED	Suicide attempt due to psychotic symptoms	Agitation Jealous and persecutory delusions	Mephedrone N-ethylpentylone 4-Chloromethcathinone Amphetamine Methamphetamine Nimetazepam	Haloperidol 5mg IM Lorazepam 2mg IM	No
5	Stimulant induced psychotic disorder Stimulant use disorder	OPD	Psychotic symptoms	Auditory hallucination Delusions of reference and persecution	Mephedrone 4-Chloromethcathinone Butylone Dibutylone	Risperidone 4mg/day	No
6	Stimulant use disorder	OPD	Mandatory treatment for illicit scheduled II drug use	Alertness, Excitement, Pending behaviors	Methcathinone	No	No

**Table 2:** Clinical manifestations, toxicology finding and treatment course of the six analytically-confirmed cathinone users.

Note: MDMA: 3,4-Methylenedioxymethamphetamine.

Third, all of them reported a new pattern of substance use-ingesting “instant coffee sachets” which contained a mixture of illicit psychoactive substances including amphetamines, ketamine or cathinone. Lastly, we found a high prevalence of suicidal attempts (3 out of 6) with highly lethal methods in these cases, highlighting the significance of suicidal risk evaluation among cathinone users.

The mean age of these six cases was 20.5 years old, which suggested that adolescents or young adults were particularly vulnerable to cathinone use. These cases developed psychotic symptoms in less than one year, which is shorter than typically seen in methamphetamine users. In a previous study, methamphetamine users were on average 30 years old in Taiwan [18] and 64% of methamphetamine users developed psychosis more than one year after their first methamphetamine use [19]. Another Japanese study also showed methamphetamine users developed psychotic symptoms 1.7 to 4.4 years on average after their first use of methamphetamine [20]. As cathinone users in Taiwan seemed to be younger and to report shorter duration from initiation to severe psychiatric symptoms, public campaign aimed at educating the younger population on the potential danger of these drugs was imperative.

There is also a new pattern of drug use that requires our attention—all these cathinone users claimed to drink a mixture of drugs from an instant coffee sachet. In Europe and the United States, cathinone is commonly manufactured as white powder or capsules. Methods of using cathinone includes snorting, ingestion (either with a moistened finger or wrapped in paper), or less commonly, injection [21]. In the six cases, they denied using cathinone directly through snorting or ingestion but to drink “coffee sachets” which contained of mixture of drugs, confirmed by our toxicological findings that each of their urine showed an average of 3.3 kinds of illicit drugs.

Reports from the Forensic Early Warning System (FEWS) showed most of NPS were sold in a mixture of two to three kinds of

psychoactive components [22], which is consistent with our finding of “coffee sachets culture” in Taiwan. However, mixture of psychoactive substances could potentiate their physical harm as the drug interactions between different psychoactive substances could be complex and life-threatening. For example, synthetic cathinones and amphetamine could both cause sympathomimetic effects and severe complications like seizures, arrhythmias were found in some cases [23]. Mephedrone, one of the most common cathinones, could lead to death especially when concomitant use of other substances [24,25].

Three out of six cases reported suicidal attempt with high lethality under cathinone related psychosis. Previous work has shown that delusions induced by cathinone use can be bizarre and accompanied with repeated suicide attempts [26]. Other studies have shown that cathinone users might have a higher prevalence of suicide (Elliott & Evans, 2014). According to a post-mortem study, the proportion of suicide in all-cause mortalities involving cathinone could be as high as 66% [25]. A previous study showed a higher proportion of cathinone-related deaths used hanging or other mechanical ways to commit suicide [27], while the reasons remain unclear.

The rapid emergence of NPS poses challenges to traditional drug control policy all over the world. Several legal responses have been held to tackle this problem in a national level [28]. The most common one is analogue approach, which controls analogue drugs with chemical similarity to already controlled substances as in the U.S [29]. Another approach is general prohibitions, which prohibit supply, import and export of any psychoactive substance that is not exempted like Canada [30]. The third one is full regulatory approach, which permits and regulate sale of limited NPS that are proven to be of low risk, as done in some European countries [28]. Taiwan seems to be unprepared for this public health challenges as in Taiwan we regulated only 10% of the NPS [8], while this new pattern of drug use have increased drastically. To hold a public forum to discuss the drug policy on regulating the NPS is imperative and necessary.

To our humble knowledge, this is the first case series on the clinical features of analytically confirmed cathinone users in Asia. We first described their clinical features and reported their novel route of ingesting cathinone by using “instant coffee sachets” Taiwan. The high risk of developing psychotic symptoms and suicidality calls for serious clinical and public attention. A major limitation of this study is that in some cases several substances were found in their urine; thus it is hard to attribute their clinical manifestations to cathinone only. However, our finding also highlighted the multiple drug use patterns of NPS users. Also, individuals with severe physical complications will not seek treatment in a psychiatric center. Another limitation is that three of six cases showed positive for methamphetamine in urine tests; thus, the effects of methamphetamine in these cases cannot be fully ruled out. Lastly, all of our cases ingest cathinone orally, therefore we did not observe the effects of cathinone once injected intravenously [16,31] and or for long-term use [32]. As these cathinone users were young and most of them showed highly suicidal or aggressive behaviors, we hope this study could help offering implications for health professionals and law makers to curb the increasing trend of NPS use.

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## Conflicts of Interests

All the authors declared no conflicts of interests.

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