The effects and toxicity of cathinones from the users' perspectives: A qualitative study

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Abstract

Objective To explore the users' perspectives regarding the effects and toxicity of cathinones.

Methods A systematic search of Internet discussion forums yielded 303 threads relevant to the research objectives. The threads were analysed by conventional content analysis where concepts were developed from codes and themes.

Results The study identified three main themes in relation to cathinone use, effects and toxicity. The first theme considered the modalities of intake of cathinones in relation to the derivative taken (mainly mephedrone, 3-methylmethcathinone and methylenedioxypyrovalerone), route of administration (eyeballing, insufflation, smoking, intravenous, oral, rectal and sublingual), multi-drug use and purity of the cathinone derivative. The second theme characterised the main effects of cathinones i.e. increased energy, euphoria and empathogenic. Toxic effects were reported regarding the nervous system (anxiety, hallucinations, nervousness, paranoia), cardiovascular system (angina, myocardial infarction, tachycardia), skin (discolouration, itching, allergy) and renal system (difficulty in urination). Drug-drug interactions were also reported including multiple drug use between cathinones, stimulants, depressants and hallucinogens.

Conclusions The Internet discussion forums provide useful sources of information regarding the effects and toxicity of cathinones which can be taken into account when assessing the safety of drugs.

Keywords Novel psychoactive substances, cathinones, content analysis, effects, toxicity, users' perspectives

Introduction

Novel psychoactive substance (NPS) have emerged over the last decade as legal alternatives to classical drugs of abuse (Gibbons, 2012). Until 2015, the European Monitoring Centre for Drug and Drug Addiction (EMCDDA) identified more than 560 NPS derivatives (EMCDDA, 2016). The Internet played a role in the spread of NPS through marketing, sales and distribution (ACMD, 2011; Corraza et al. 2014) therefore, monitoring the Internet is crucial in order to identify trends in the use amongst the NPS and their effects (Deluca et al., 2012).

Synthetic cathinones are one of top reported groups of NPS in Europe (James et al. 2010; Tsujikawa et al., 2015; UNODC, 2014). Along with synthetic cannabinoids, synthetic cathinones represent two-thirds of the drug market (Cottencin et al., 2013). In 2013 10,657 seizures of synthetic cathinones were reported (EMCDDA, 2016). Amongst synthetic cathinones, mephedrone was the most widely used derivative (Dargan et al. 2011; Stevenson and Richardson, 2014). There is however limited information regarding the effects and toxicity of synthetic cathinones in the scientific literature. Most of the available information is limited to emergency department and/or users' reports (Dargan, Albert and Wood, 2010). E-psychonauts are users who meet over Internet forums and discuss their experience with psychoactive drugs including NPS (Hohmann et al., 2014; Davey et al., 2012). The aim of this work is to determine the users' perspectives regarding the effects and toxicity of cathinones.

Methods

Study design

A qualitative study of Internet discussion forums was undertaken to explore the knowledge regarding the effects and toxicity associated with the use of cathinones.

Data collection

Data was obtained from the Internet by searching for published threads regarding the experiences of synthetic cathinones between January and March 2015. Different combinations of keywords were used mainly in Google, and included: “cathinone(s)”, “report”, “experience”, “use”, “misuse”, “effects”, “adverse reactions”, “toxicity”. The first 20 hits of each search were inspected carefully. After examination, the search yielded seven sites related to the use of cathinones (Table 1). These sites were further examined to explore the experiences described by cathinone-users. Inclusion criteria were threads that communicated a subjective experience of users regarding the use of cathinones. Exclusion criteria were: threads that discussed synthesis or prices of cathinones. Subsequently, 371 discussion threads were recovered from the seven websites. The threads were then assessed in further details where 303 threads (of 2,854 posts) were found relevant to the objectives of the study (Table 1). When the thread was considered as relevant, all information relating to user names and complete URLs were deleted in order to protect the identity of authors.

List of definitions

An adverse drug reaction is defined as “ any noxious, undesired and unintended drug effect that occurs at doses used in human for therapy, diagnosis or prophylaxis” (WHO, 1972). A drug drug interactions is defined as “an action of a drug on the effectiveness or toxicity of another drug” (Vervloet and Durham, 1998). Eyeballing is defined as the direct pouring of the NPS solution on the ocular surface epithelium (Burillo-Putze et al., 2013). Smoking is done either using a joint or a pipe and could involve the intake of a single drug or a mixture. Intravenous intake involves the direct injection of the NPS solution into the vein. Nasal insufflation comprises the snorting of the NPS powder. Oral intake involves the swallowing

of the tablet and/or liquid (mixture of drug in alcohol or juice), or bombing. Bombing (or parachuting) encompasses wrapping the NPS (powder) in cigarette paper and swallowing it. Rectal (or plugging) administration encompasses injecting solution of the NPS via a needless syringe. Sublingual intake involves placing the NPS powder under the tongue for less than five minutes or until the taste becomes unbearable.

Analysis

Qualitative data relating to the use of cathinones were analysed. The data included anything the participant reported in threads. The threads were subjected to conventional content analysis (Hsieh and Shannon, 2005). Data in threads were initially coded independently by two investigators (SA and NG) in order to minimise bias. The threads were read carefully line-by-line in order to identify codes and themes that reflected concepts. After the threads were coded, both investigators met in order to discuss any discrepancies among codes, cluster codes into themes and discuss potential relationships among themes that constituted categories. Three broad themes were achieved relating to the uses, pharmacological effects and toxicity described by users. The inter-rater reliability of the themes was evaluated by providing the threads to a third researcher (DO). Threads and codes were provided to the research without the themes. The inter-rater reliability for the final themes was 93% which indicated the validity of the coding methodology.

Ethical considerations

The study has been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Ethical approval was sought from BU Internal ethics committee. The study involved collecting information that was already available in the public domain. However, anonymity

was applied to participant data. All participants' data that could indicate identities/nicknames were removed from the threads, and each thread was give a number. No posts or contribution to the discussion forum were made and no data was shared outside the remits of the study.

Results

The analysis of the discussions relating to cathinones from Internet sources yielded 303 threads with 2,854 posts. These were combined into three main themes: (1) uses, (2) pharmacological effects and (3) toxicity.

Uses

Three main subthemes emerged under uses: the route of administration, multidrug use and purity.

Route of administration

This subtheme uncovered information relating to the modality of intake of cathinones in relation to the: (1) derivative taken, (2) route of intake, (3) matrix, (4) frequency and (5) purity. A total of 27 cathinones were reported in the discussion threads and included alkyl- (n = 12), halogen- (n = 4), methlenedioxy- (n = 6) and pyrrolidinyl- (n = 5) substituted derivatives (Table 2). The main derivatives among these cathinones were methylone, mephedrone, 3-methylmethcathinone (3MMC) and methylenedioxypyrovalerone (MDPV), and were reported by 286, 240, 199 and 173 users respectively.

Where reported, the intake of the aforementioned cathinones was deployed via single route of administration or combination of two routes of administration at a time. The majority of the

users (n = 220) reported the use of a single route of administration. Single routes reported were: eyeballing (n = 2), smoking (n = 21), intravenous (n = 19), nasal insufflation (n = 90), oral by juicing or direct swallowing (n = 58), oral by bombing (n = 12), rectal (n = 13) and sublingual (n = 4). Nasal insufflation was the most popular route among the users (n = 90). The doses of cathinones insufflated varied massively between 2 mg to 1.5 g. Users had mixed feelings about nasal insufflation. Users in favour of nasal insufflation described it as 'quick', 'intense', 'works well', 'produced more love or empathy', 'very productive, active and focused'. Users who did not like nasal insufflation stated it was 'highly addictive', 'completely changes the drug effects to coke line', 'dirty high', 'produces nose aches', 'burns like hell', 'stung like hell', 'waste of drug', and the 'longest lasting route'. One user reported regarding nasal insufflation:

'Mostly nasal route-despite the nasty sting, there's something about sticking drugs up the nose that makes it more moreish and compulsive, fun even (I'm sure we all know that)' (Thread, 114)

The second major route by users was direct swallowing of the cathinone derivative (n = 58). This was carried out either by swallowing the drug itself or by mixing it with a juice/energy drink. Dosage taken of cathinone varied between 10 mg and 2.5 g over different time intervals and frequencies. Intervals ranged between two hours (assumed as duration of action of cathinones) and up to four hours. The frequency also had wide differences between users from once a week once every six months. Users felt direct swallowing was slow, ineffective but safe. They stated that by direct swallowing they had 'nothing noticed', 'zero effects', 'is usually fine', 'much more mellow', 'less speedy' and 'never had a problem'.

Smoking route was less popular among users (n = 20) due to the unwanted effects reported such as: ‘most insane panic/delirium attack’, ‘harsh’, ‘burns the throat’, ‘does not appear to get any heavier’, ‘lungs felt weird’, ‘disgusting smell’, ‘’high anxiety’ and with ‘little effect’. Only three users reported getting the desired effects using the smoking routes and described the effects as ‘melts right on vaping’, ‘stimulation’ and ‘rushing’. The dose of cathinones used for this route was only reported by five users who smoked 10 mg, 25 mg, 60 mg, 400 mg and 500 mg.

Though only 19 users reported the IV route, it was the preferred route of administration. Users enjoyed the IV route as it was ‘pretty intense’, ‘pretty godly’, ‘gave a noticeable rush’ and ‘induced immediate visual and auditory hallucinations’. Only three users reported the doses of cathinones taken by IV route which were 80-210 mg, 150 mg and 3-4 g.

The rectal route was also popular among users (n = 13) and described as ‘quiet pleasant’, ‘amazing’, of quick onset and long duration but dose-dependent. The ideal dose was specified by one of the users as 50-75 mg. Other reported doses were 140 mg, 150 mg, 500-600 mg and 10 g.

Multi-drug use

Cathinones were often taken in combination with other drugs (n =60) that included both classical drugs of abuse and NPS. The multi-drug abuse was either a binary or ternary mixtures. Classical drugs reported were stimulants (amphetamine derivatives, cannabis, cocaine, coffee, lidocaine and tobacco), depressants (alcohol, herbal sleep aids and benzodiazepines), hallucinogens (LSD, magic mushrooms and ketamine), vitamins and supplements and stimulant/depressant mixtures (mephedrone-cannabis-alcohol, mephedrone-

cocaine-ketamine and mephedrone-cannabis-caffeine). NPS used in mixtures were mainly 3FA, 3FMC, ethylphenidate, mephedrone, methylone, MDPV and MXE.

Purity of cathinones

The purity of cathinone products was reported from 40 threads and varied between derivatives. For all derivatives, indicators of purity were the effects of the NPS (gross, nausea, potent), smell (chemical odour, flowery aroma, pungent, root beer/liquorice odour, semen smell, sharp sour, speedy smell, sweet smell), taste (bitter, chalky, disgusting, slightly bitter, synthetic bitter, unpleasant), colour (beige, browny grey, pure bright white powder, snowwhite, urine-smell, white, yellow) and physical properties (big snowflakes, clumpy, crumbly, crystal rock batches, fine-powder, paste-like, sticky, wet clay). One user compared 3-MMC to impure cocaine:

"*Methcathinone is a stimulant all right,*

But it feels like bad coke cut hard with speed".

Another user adopted colour as indicator and described alpha-PVP as impure despite its white colour:

"*…was the white one…but it definitely contains some impurities*"

Pharmacological effects

Users sought effects that increased mood or mental performance when using cathinones. The main psychological effect (n = 53) reported by users was euphoria. Users took euphoria as a basis for choosing the cathinone derivative and reported effects relating to euphoria as:

blissfulness, body warmth, emotional, confidence, having happy thoughts, mood-lifting. The three derivatives 4MEC, MDPV and mephedrone were encountered as strong euphoric agents. 3MMC, alpha-PHP, alpha-PVP, ethcathinone and methylone were experienced as mild euphoric agents. 3MMC was described as the mildest of the cathinone derivatives:

*"*3*MMC is borderline intense roll...but still mellow just like MDMA.....let's put it this way....if I was given 3mmc and told it was MDMA, I would of believed it completely. You can't tell the difference, or at least I can't*."

Effects of 3MMC were below expectations:

"Pretty good rush, but real euphoria never seems to come."

Users were also interested in the empathogenic effects (n = 78) associated with cathinones, being: active listening, affectionate, appreciation for music, emotional intimacy, feeling drunk, feeling happy and grateful, and loving everyone:

"Methylone…..found it my hold grail! I felt at peace with the world
And loved everything all the way down to very small object!"

Hence 16 users took cathinones as alternative to antidepressants and reported them as more effective than antidepressants. One user reported:

"The antidepressant effects were immediate and I've woken up feeling
like completely changed person. I've been on SSRIs and other meds for years...

I feel like the real me is finally back."

Stimulation and increased energy were also reported for (n = 50) where users felt alert and were able to stay awake and productive for longer hours (up to 34 hours). They were very attentive, smart, creative, highly motivated, organised and able complete their work on time. One user reported regarding MDPV:

"*While less giddy and chatty, I was still working like a freaking machine."*

The aforementioned characteristics increased sociability among users who felt 'talkative', 'with a sense of self-satisfaction', 'low anxiety' and 'having intense conversations'. Nonetheless, the stimulation/alertness was high where five users reported an 'overactive mind' with '200-1000 thoughts per second'. Users (n = 37) also experienced increased sexual activity associated with the use of cathinones. They described mephedrone and MDPV as stronger aphrodisiac than 3MMC and methylone.

Toxicity

Adverse drug reactions

Symptoms of 'adverse drug reactions' and drug-drug interactions were encountered among users. Adverse drug reactions were reported for nervous, cardiovascular, renal, skin and respiratory systems. The nervous system had the highest reports among users (n = 270) where cathinones were described as highly addictive with desire to re-dose, irritable on coming down, dehydrating and causing self-harm. Specific adverse effects associated with the use of cathinones were anxiety, nervousness, irritability, restlessness, headache, insomnia, paranoia, feeling of regret, disturbed sleep, bruxism, extreme mydriasis, cognitive impairment,

forgetfulness, lack of concentration, auditory hallucinations, disorientation, difficulty of speech, numbness of face and extremeties, sweating and involuntary body movement. Cardiovascular adverse effects were the second most reported (n = 246) and included: Angina, arrhythmia, cardiac arrest, damaged veins, heart attack, heartache, hypertension, myocardial infarction, palpitations, tachycardia and vasoconstriction. Often cardiovascular effects were seen dependent on the derivative, dose and duration of intake (acute versus chronic). Cardiovascular adverse effects were less pronounced with 3MMC than other cathinone derivatives:

"*Good thing is that side effects seem to be very acceptable, almost no increase in heartbeat whatsoever and no vasoconstriction*."

Respiratory problems were reported by 13 users who experienced shortness of breath upon intake of 3MMC, alpha-PVP, MDPV, mephedrone and methylone. A chesty cough was reported by one of the users who took mephedrone. Several skin adverse effects were seen (n = 21) including: discolouration of skin, dryness/itchiness, allergy and rash. Discolouration of the knees and joints were reported by eight users who experienced yellow or brown patches. Nine users described bladder pain and difficulty in urination following the intake of 3MMC, methylone and mephedrone.

Drug drug interactions

Drug-drug interactions of cathinones were encountered with combinations of stimulants, depressants, stimulants/depressant mixtures, vitamins/nutrition supplements and hallucinogens. Stimulant mixtures induced euphoria and increased energy as desired effects and caused nervous system and cardiovascular toxicities (Table 3). Depressants (e.g. alcohol,

benzodiazepines and herbal sleep aids) were used in order to counteract the effect of cathinones in relation to inducing sleep and making the come down easier. Vitamins and nutrition supplements were used to combat various side effects such as tooth grinding. Fewer adverse effects were reported upon the mixing of cathinones with hallucinogen and were limited to psychological hallucinations.

Discussion

The study explored discussion threads regarding cathinones' use from Internet forums. Three main themes emerged from the discussion threads in relation to cathinones: (1) use, (2) pharmacological effects and (3) toxicity.

Users on discussion threads supported each other in sharing experiences and knowledge regarding cathinones' use. Many users appeared to be knowledgeable regarding NPS and cathinones in relation to dose, duration of action, effects and toxicity. The information extracted from the forums contributes to the greater body of knowledge surrounding NPS (Corazza et al., 2014). Users related doses, frequency of intake and route of intake to the effectiveness of the drug. Newer routes for intake of drugs emerged which were not repeated in previous studies including sublingual and eyeballing. Sublingual and eyeballing routes were described as giving faster effects (Karila et al., 2015) but with more adverse effects. An interesting finding in this study was user-comments regarding the purity of the drugs and its implications on the effects. Previous studies have reported low and variable purity of NPS products (Assi et al., 2011; Assi et al., 2016; Brandt et al., 2010). Users interpreted physical changes of the powder (colour change and water absorption) as an indication of ineffectiveness. This change could be attributed to degradation of the drug.

Not only the general effects were reported to cathinone derivatives but also the strength of the effects associated with specific cathinone derivatives (such as mild, moderate or sever euphoria). Effects of drugs were discussed in relation to single and multi-drug intake. The main positive effects reported by users were increased energy, confidence, euphoria, increased empathy, intimacy and desire to socialise. These findings were found to be consistent with results from key quantitative studies in the literature that reported improved mood and increased socialising ability associated with the use of cathinone derivatives (Karila & Reynaud, 2011; Schifano et al., 2011; Spiller et al., 2011; Winstock et al., 2011). Users reported that it was easier to start a conversation after taking a cathinone derivative. They described cathinone derivatives as a 'social lubricants' which is a similar characteristic of some classical drugs (e.g. MDMA) (Phillips et al., 2014). The socialising effect justified the users' intentions behind taking cathinones despite their short duration of action and potential negative effects. Additional reported positive effects were desire for alertness, improved concentration and cognitive enhancement (Karila & Reynaud, 2011; Coppola & Mondola, 2012). Nonetheless, many adverse effects associated with the use of cathinones were reported including psychiatric, cardiovascular and neurological complications (Karila et al., 2015; Mas-Morey et al. 2013; Prosser & Nelson, 2012). Cardiovascular adverse effects included: hypertension, hyperthermia, and tachycardia. Neurological and psychotic problems reported were: cognitive degradation, increased anxiety, hallucinations, insomnia, paranoia, depression, psychosis and memory problems. Psychotic problems associated with the use of cathinones could be more severe than psychosis encountered with amphetamine (Borek & Holstege, 2012; Loeffler et al., 2012). Other effects included: appetite suppression, breathing difficulties, muscle tension and hyperthermia (Phillips et al., 2014).

The findings of the study uncovered new information in relation to the use and safety of cathinones which has not been described in the scientific literature. Internet discussion forums supported the scientific literature in providing useful information regarding the dangers associated with the use of NPS (Deluca et al., 2012). This information should be taken into account when monitoring NPS and assessing their safety.

Several limitations were encountered in this study. The study could not explore the motivation of the users for cathinones' over other NPS derivatives. This can be an important aspect in relation to drug prevention. Because of the nature of the discussion forums, it was not possible to access the sociodemographic data of the users. The information accessed from discussion forums was limited for the data available. Missing information in relation to dosage and frequency in some threads could influence the results. There was no method for verifying the subjective experience of the users regarding effects and toxicities. Nonetheless, this information could serve as preliminary data for further research where no other sources are available. The varying effects and toxicities reported among users in this study urges the need for further research into NPS. With limited resources in the literature, assessment of data obtained from emergency department admissions (alongside discussion forums) can be beneficial.

In conclusion, the present study uncovered many information regarding the uses, effects and toxicity of cathinones which were lacking in the scientific literature. Users shared their experiences associated with single and multidrug use. Information provided via Internet discussion forums could be used as an early warning system for NPS.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Table 1 Sites that were considered in this study

Website	Threads found	Threads excluded
www.bluelight.org	106	17
www.chemrus.com	10	6
www.drugs-forum.com	47	7
www.erowid.com	142	6
www.legalhighsforum.com	19	5
www.partyvibe.com	15	8
www.reddit.com	21	8
Total	360	57

Table 2 Cathinone derivatives reported by the users in discussion forums

Substitution			
alkyl (n = 254)	**halogen (n = 153)**	**methylenedioxy (n = 300)**	**pyrrolidinyl (n = 115)**
• 2MMC	• 3FMC	• 3,4-MDPV	• alpha-PBP
• 3MMC	• 4BMC	• 5ME	• alpha-PHP
• 3,4-DMMC	• 4F-apha-PVP	• butylone	• alpha-PVP
• 4MBP	• 4FMC	• ethylone	• NRG-1
• 4EMC		• methylone	• alpha-PHPP
• 4MEC		• pentylone	
• ethcathinone			
• mephedrone			
• methedrone			
• mexedrone			
• pentedrone			

2MMC: 2-methylmethcathinone, 3MMC: 3-methylmethcathinone, 3,4-DMMC: 3,4-dimethylmethcathinone, 4-EMC: 4-ethylmethcathinone, 4MEC: 4-methylethcathinone, 3FMC: 3-fluoromethcathinone, 4BMC: 4-bromomethcathinone, 4F-alpha-PVP: 4-fluoro-α-2-(1-pyrrolidinyl)-valerophenone, 4FMC: 4-fluoromethcathinone, 3,4-MDPV: 3,4-methylenedioxypyrovalerone, 5ME: 5-methylethylone, alpha-PBP: alpha-pyrrolidinobutiophenone, alpha-PHP: alpha-pyrrolidinohexiophenone, alpha-PVP: alpha-pyrrolidinopentiophenone, NRG-1: naphyrone, alpha-PHpP: 1-phenyl-2-(pyrrolidin-1-yl)heptan-1-one.

Table 3 Drug-drug interactions reported by the users

NPS derivative	Drug	Effect
Stimulants mixtures		
2MMC	2MA	myocarditis
Alpha-PHP	Synthetic cannabinoid	intense panic/delirium
MDPV	tobacco	painful urination
MDPV	cocaine	tachycardia
Mephedrone	MDMA	weird light- headed mini waves of energy/rush, overpowering
3MMC	coffee	irregular heart beat
Mephedrone	coffee	increased mood
Mephedrone	coffee	chest and arm pain
Mepherone	cannabis	memory blacked out
Methylone	2CB	2CB lengthens methylone effect
Methylone	2CE	erotic thoughts
Methylone	2CI	
Methylone	MDMA	overpowering
Hallucinogen mixtures		
MDPV	LSD	auditory hallucinations
MDPV	magic mushrooms	wandering, feeling lost
Depressant mixtures		
3MMC	alcohol	increased sociability
3MMC	alcohol	increased sociability
MDPV	alcohol	easier come down
MDPV	phenazepam	induce sleep
MDPV	etizolam	beats insomnia
Mephedrone	alcohol	improving experience but counteract is slow
Mephedrone	alcohol	induce sleep
Mephedrone	alprazolam	sleep aid
Mephedrone	GBL	discolouration of the knees
Mephedrone	milk thistle	induce sleep
Methylone	alcohol	induce sleep
Methylone	aniracetam, piracetam	strong palpitations
Novel psychoactive substances mixtures		
3MMC	3FA	feeling down and depressed
3MMC	methylone	smooth and silk
Alpha-PHP	ethylphenidate	enhanced sexual activity
MDPV	MXE	auditory hallucinations
Mephedrone	methylone	Stronger stimulant effect, panic attack
Methylone	MDAI	nausea and chalky taste in the mouth
Methylone	MDPV	very strong effects
Methylone	2CE	increased erotic thoughts
Vitamins/supplements mixtures		

Methylone	magnesium	magnesium combats tooth grinding
Methylone	calcium	better experience
Mephedrone	multivitamins	blushing, minor circulatory changes
	Other	
3MMC	melatonin	induce sleep
MDPV	diphenhydramine	facilitate come down

2MMC: 2-methylmethcathinone, 2CB: 4-bromo-2,5-dimethoxyphenethylamine, 2CE: 4-ethyl-2,5-dimethoxyphenethylamine, 2CI: 4-iodo-2,5-dimethoxyphenethylamine, 2MA: 2-methylamphetamine,3FA: 3-fluoroamphetamine, 3MMC: 3-methylmethcathinone, alpha-PVP: alpha-pyrrolidinopentiophenone, GBl: gamma-butyrolactone, LSD: lysergic acid diethylamide, MDAI: methylenedioxy-2-aminoindan, MDMA: methylenedioxymethamphetamine, MDPV: methylenedioxypyrovalerone, MXE: methoxetamine.