



ORIGINAL ARTICLE

Patterns of use, harm reduction strategies, and their relation to risk behavior and harm in recreational ketamine users

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ABSTRACT

Background: Recent studies have shown that ketamine use has serious adverse consequences. However, no studies have focused on the strategies that users carry out to protect themselves from such potential harm. **Objectives:** (i) analyze harm reduction strategies, risk behaviors, and harms in nonmedical/recreational ketamine users; (ii) analyze the association of their harm reduction strategies and risk behaviors with harms they report. **Methods:** An anonymous cross-sectional web-based survey of 462 persons who had used ketamine in the past year. We designed a questionnaire to collect information on their risk behaviors, harm, and harm reduction strategies. **Results:** The harms most reported were unexpected confusion (58.2%), memory impairment (57.4%), and abrupt mood/behavior changes (49.6%). The most frequent strategies were spacing out sessions (60.8% always/almost always did this), spacing out doses within a session (54.5%), and limiting the amount and not going over it (41.3%). The use of these three strategies was related to a lower probability of perceiving negative consequences associated with ketamine use, including memory impairment, healthcare assistance, psychological dependence, and risk behaviors related to driving under the influence of ketamine. **Conclusions:** This study provides empirical evidence on strategies related to the lower probability of harm associated with ketamine use as employed by recreational ketamine users. Our findings suggest that efforts to minimize harm from ketamine use should focus on increasing awareness of potential harms and the use of identified harm reduction strategies.

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Introduction

The prevalence of nonmedical/recreational use of ketamine has expanded greatly during the last decade (1–3), especially in Southeast Asia where it has become the second most commonly consumed illegal drug, only after heroin (4). This use has been linked mainly to subpopulations of persons who use drugs recreationally (5–7). Thus the Global Drug Survey found a prevalence of ketamine use of 5.7% last year in a worldwide sample of 78,819 drug users (8). In the United States, Pal et al. surveyed 19,000 participants, and found that 18.7% reported lifetime ketamine use and 5.8% were recent users (9).

A number of studies have shown robust empirical evidence on harms associated with frequent ketamine use, including ulcerative cystitis (1,2,10,11), intense abdominal pain (11,12), neurocognitive impairment (13), educational and professional failure (2,14), psychological dependence (2), impairment of psychological well-being (13,15), and delusional and dissociative symptoms (13). The effects of ketamine on coordination expose users to high risk of injury from falling due to

difficulties in balance and walking (1,10,16), and are also important in complicated tasks such as driving (2), even leading to fatal accidents (3).

Many studies have shown that persons who use drugs recreationally are concerned about their health, and want to manage their pleasures and employ strategies to minimize the risks involved, although these studies have focused mainly on alcohol (17–19), 3,4-methylenedioxy-N-methamphetamine [MDMA] (20–22), rarely cocaine (23), and exceptionally on polysubstance users in the dance/rave culture (24,25). However, there are no studies on harm reduction strategies put into practice by ketamine users. Furthermore, it has been shown that users of other drugs employing harm reduction strategies report fewer health-related problems (19), but not ketamine users, even though some authors stress the need for ketamine users to carry out such strategies (2,12,16). It would be useful for preventive and harm reduction organizations working with recreational ketamine users to know what strategies contribute to the perception of less harm.

The aims of this study were therefore to (i) analyze harm-reduction strategies, risk behaviors, and harms in nonmedical/recreational ketamine users, and (ii) analyze the association of their harm reduction strategies and risk behaviors with harms they report. Our main hypothesis was that those participants who carry out harm reduction strategies more frequently will report lower risk/less harm.

Methods

Participants and data collection

A total of 506 persons who had used ketamine in the last year participated in an anonymous cross-sectional web-based survey promoted by Energy Control, a Spanish harm reduction project of the Well-being and Development Association, a nongovernmental nonprofit organization. The questionnaire was hosted online on Energy Control's website (www.energycontrol.org) during February 2013–January 2014 and announced by online social networks and brochures at clubs, festivals, and underground raves. Other Spanish harm reduction organizations, rave party organizers, and websites/forums focusing on persons who use drugs were asked to spread word of the research. Before they took the survey, participants were informed about its duration (around 20 minutes), that it was anonymous, and were asked for their informed consent. The survey was programmed with automatic processes to avoid non-completion, coding errors, and incongruence in the pattern of drug use (i.e., drug use in lifetime, past year, and past month) that allow one to reduce measurement errors (26,27). Moreover, filter questions were included in order to simplify the process of completing the survey and avoid errors (26).

A total of 44 participants were discarded, 37 because they had not completed the full survey and seven because they were under 18. Thus the final sample comprised 462 ketamine users over 18 years of age. This study was approved by the Ethic committee of the Well-being and Development Association.

Instrument

The questionnaire included items adapted from previous studies on ketamine users (11–16,28). Four experts, two in recreational drug use and two in psychometrics, reviewed the questionnaire, which 10 recreational ketamine users answered in a pilot study. The questionnaire comprised four modules covering: (a) a ketamine-use profile and other drug-use patterns, (b) socio-demographic information, (c) harm reduction

strategies, and (d) negative consequences associated with ketamine use. The questionnaire also contained other modules not within the scope of this article, such as information on ketamine's effects, reasons for taking ketamine, and desired effects.

Module (a) referred to the past 12 months and included questions related to the ketamine-use pattern (quantity, route of administration, use in the past six months, use in the past month, and frequency of ketamine use in the last month); settings, activities, and company when using ketamine, and sources of ketamine supply. Lifetime, last year, and last month prevalence were explored for 16 substances other than ketamine.

Module (b) included socio-demographic information, specifically, age, gender, job status, education, socioeconomic class, main sources of income, and nationality.

Module (c) included six questions on harm reduction strategies derived from previous studies on harm reduction (24,29) and ketamine-related harms (1,2). These questions were: How often... (1) Do you avoid mixing ketamine with other drugs? (2) Do you test the ketamine you're going to take beforehand? (3) Do you set a limit to the amount and not go over it? (4) Do you space out doses within a session? (5) Do you space out use sessions? (6) Is there someone sober in the group in case you need help? Answers were on a scale of never/almost never/sometimes/almost always/always.

Module (d) included 20 negative consequences associated with ketamine use and was divided into five parts:

- d.1. Health-related problems. Eight problems related to ketamine use were included, specifically: cystitis, frequent abdominal pain, memory impairments, abrupt changes in mood or behavior, falling while under the influence of ketamine, state of unexpected confusion, sleeping problems, and flashbacks.
- d.2. Variables related to substance-use disorders. Two variables were assessed, psychological dependence and tolerance. We administered the Severity of Dependence Scale (SDS) (30), which assesses the severity of psychological dependence on ketamine. This screening tool, widely used for ketamine users (11,15,31,32), consists of five items on an ordinal four-point scale ranging from 0 to 3. The maximum score of 15 represents the highest level of dependence. The Cronbach's alpha coefficient for internal consistency of the SDS was 0.787. The following yes/no question was included to assess tolerance to ketamine: During the last 12

months, did you need to increase the quantity of ketamine to get the same effect?

- d.3. This module included the following four yes/no questions: Do you think that your ketamine use has influenced problems with: (1) personal relationships, (2) legal status, (3) economic status, and (4) studies and/or job?
- d.4. Yes/no questions referring to healthcare assistance were also included: (1) Have you received psychological or medical emergency care due to your ketamine use? (2) Have you received treatment to quit or reduce your ketamine use?
- d.5. Finally, four risk behaviors were explored: (1) Have you ever driven a vehicle while under the influence of ketamine? (2) How often have you driven a vehicle while under the influence of ketamine? (3) How often have you been a passenger in a car driven by someone under the influence of ketamine? And (4) How often have you taken more ketamine than you had planned? The first question was answered yes/no. The other three questions were answered on a scale of never/rarely/sometimes/frequently/always.

Data analysis

We conducted descriptive analyses to address aim (i). To contrast our main hypothesis, we classified participants into high harm reduction strategies and low harm reduction strategies for each of the six strategies. Adopting a conservative stand, we only classified participants who “always” or “almost always” carried out a strategy in the high harm reduction strategies group. The rest (never/almost never/sometimes) were in the low harm reduction strategies group. Then to test the association of these strategies with harms/risks of ketamine use, we conducted a Chi-square test or *t*-test according to the variable scales. These analyses were performed using the SPSS 18.0 statistical package.

Logistic or linear regressions were performed, depending on the scale of the variable considered dependent, to analyze the contribution of the six harm reduction strategies to the different negative consequences. The effect of polydrug use (as the number of drugs used in the last 12 months) and frequency of ketamine use in the last month were controlled for in these analyses. To do this, we entered controlled variables in the first block of regression analyses using the Introduce method. In the second block we used the Stepwise method, considering only the variables that had shown statistically significant relationships with each of the six harm reduction strategies ($p < 0.05$).

Two dummy variables were created, considering no use as the reference category, to control for the effect of frequency of ketamine use: use less than once a week during the last month, and use one or more times per week during the last month.

The odds ratio, confidence intervals, and significance of the contribution of each variable to the model were reported. Fit of the models was tested using the Hosmer–Lemeshow test. All the regression models showed fit to the data used for their estimation ($p > 0.05$). These analyses were carried out using STATA 12.

Results

Demographic characteristics

The majority of participants were men (66.2%). The mean age was 26.2 (Standard Deviation [SD] = 6.2, range = 18–59), 62.5% had completed high school or the equivalent, and 28.8% had university studies. Of them, 29% were employed, 24.5% were studying, 21% were both studying and employed, and 17.5% were unemployed. Around 69.4% considered themselves middle class, 29.9% lower class, and 0.6% upper class. The participants' main sources of income were their jobs (49.8%) or family allowance (18.4%). Of the total participants, 81.8% were Spanish, 4.3% Argentinean, 3.7% Colombian, 1.9% Mexican, 2.4% were from other Spanish-speaking countries, and 5.1% were from other European countries. The remaining participants were Russian (0.2%) and Brazilian (0.6%). Most of the participants resided in Spain (84.8%), 10.1% in Spanish-speaking countries, 4.7% in European countries, and 0.4% in Brazil.

Ketamine and other drug-use profile

The mean age ketamine was first used was 21.6 (SD = 5.2), 84.8% of participants had used ketamine in the past six months and 55.8% had used it in the past month. Around 58.1% of those who had used ketamine in the past month had done so less than once a week, 26% once a week, 11.6% two to six times per week, and 4.3% were daily users. The amount of ketamine used by participants in each session during the last 12 months was: 0.25 grams or less by 36.6%, 0.25–0.50 grams by 29.2%, 0.5–1 grams by 18.6%, and more than 1 gram by 15.6%. The main route of administration for most of the sample (94.6%) was snorting, while for 4.5% it was injection. Ketamine was used in a variety of settings: home (67.7%), rave (64.9%), and disco/club (51.1%), while dancing (72.5%), staying at home (61.3%), or

listening to music (49.6%). Almost 95.5% of participants used ketamine with friends, 31% with their partner, and 25.5% used it alone. The most frequent source of supply was friends (72.1%), followed by a trusted dealer (61%). Participants had used an average of 8.9 (SD = 2.4) different drugs (excluding tobacco) in their lifetime, 6.3 (SD = 2.1) in the past year, and 3.8 (SD = 1.7) in the past month. The main drugs used in the last year were alcohol (95.7%), MDMA (90.2%), cannabis (87.2%), amphetamines (77.8%), cocaine (70.8%), Lysergic Acid Diethylamide [LSD] (55.9%), magic mushrooms (31.3%), tranquilizers (29.4%), opium (26.9%), and 2,5-dimethoxy-4-bromophenethylamine [2CB] (24.7%).

Negative consequences and harm reduction strategies associated with ketamine use

The main harms the sample reported (Table 1) were unexpected confusion, memory impairment, abrupt changes in mood/behavior, and falling while under the influence of ketamine. More than a quarter of the sample reported urinary symptoms, flashbacks, or abdominal pain. The mean number of problems reported was 3.3 (SD = 2.1), 40.5% of the sample had increased the ketamine dose in the past 12 months to get the same effect, and 5.5% had received treatment to quit ketamine use. The mean score on the SDS was 1.5 (SD = 2.3).

The harm reduction strategies most employed by the sample (Table 2) were spacing out use sessions and

Table 2. Harm reduction strategies (%).

How frequently...	Never/ almost never	Sometimes	Always/ almost always
You avoid mixing ketamine with other drugs	48.3	25.8	25.9
You test the ketamine you're going to take beforehand	78.8	8.0	13.2
You set a limit to the amount you are going to take and not go over it	38.3	20.3	41.3
You space out doses within a session	19.3	26.2	54.5
You space out use sessions of consumption	17.7	21.4	60.8
There is someone sober in the group in case help is necessary	67.3	20.8	11.9

spacing out doses within a session. The harm reduction strategies employed the least were “someone sober in the group” and testing the ketamine they were going to take beforehand.

Association between harm reduction strategies and negative consequences from ketamine use

Bivariate analyses showed that four out of six harm reduction strategies had statistically significant relations with the majority of 20 negative consequences explored (Table 3): spacing out use sessions, spacing out the doses within a session, setting a limit to the amount and not going over it, and not mixing ketamine with other drugs. In all cases, the high harm reduction strategies group reported fewer harms/risks than the low group. The strategy “There is someone sober” was

Table 1. Negative consequences associated with ketamine use.

Health-related problems (%)					
State of unexpected confusion					58.2
Memory impairments					57.4
Abrupt changes in mood/behavior					49.6
Falling while under the influence of ketamine					39.6
Sleeping problems					40.0
Cystitis					32.0
Flashbacks					27.5
Frequent abdominal pain					25.3
Total number of problems (mean, SD)					3.3 (2.1)
Substance use disorder					
Psychological dependence [SDS score: mean (SD)]					1.5 (2.3)
Tolerance (%)					40.5
Influence of ketamine use on... (%)					
Personal relationships					20.1
Legal status					16.7
Economic status					21.9
Studies and/or job					21.2
Health care assistance (%)					
Emergency care					3.5
Treatment to quit					5.6
Frequency of risk behaviors					
Driving under the influence ^a	Never	Rarely	Sometimes	Frequently	Always
More quantity than planned	16.5	27.9	35.9	14.1	5.7
Passenger	37.0	26.8	23.6	11.9	0.6

^a This item was answered only by those participants who had ever driven while under the influence of ketamine ($n = 140$).

Table 3. Relation between harm reduction strategies and negative consequences of ketamine use.

Problems (%), χ^2	I avoid mixing				I test beforehand				I set a limit to the amount and don't go over it				I space out the doses within a session				I space out sessions				There is someone sober			
	High HRS		Low HRS		High HRS		Low HRS		High HRS		Low HRS		High HRS		Low HRS		High HRS		Low HRS		High HRS		Low HRS	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic
Cystitis	23.3	35.1	5.637*	32.8	31.9	0.018	26.2	36.2	5.130*	28.6	36.2	30.54	28.1	38.1	5.064*	29.1	32.4	5.064*	29.1	32.4	5.064*	29.1	32.4	5.064*
Frequent abdominal pain	18.3	27.8	4.190*	26.2	25.2	0.030	18.8	29.9	7.222**	21.4	30.0	4.450*	22.1	30.4	4.032*	27.3	25.1	4.032*	27.3	25.1	4.032*	27.3	25.1	4.032*
Memory impairments	45.0	61.7	10.124**	54.1	57.9	0.306	47.1	64.6	13.957**	49.2	67.1	15.067**	52.3	65.2	7.467**	61.8	56.8	7.467**	61.8	56.8	7.467**	61.8	56.8	7.467**
Abrupt changes in mood/behavior	36.7	54.1	10.792**	50.8	49.4	0.044	41.4	55.4	8.771**	43.3	57.1	8.839**	45.9	55.2	3.843	49.1	49.6	3.843	49.1	49.6	3.843	49.1	49.6	3.843
Falling under the influence of ketamine	35.8	40.9	0.967	26.2	41.6	5.260*	31.9	45.0	8.015**	34.5	45.7	5.997*	34.9	47.0	6.722*	43.6	39.1	6.722*	43.6	39.1	6.722*	43.6	39.1	6.722*
State of unexpected confusion	45.0	62.9	11.657**	55.7	58.6	0.179	49.2	64.6	10.869**	54.4	62.9	3.396	56.2	61.3	1.176	60.0	58.0	1.176	60.0	58.0	1.176	60.0	58.0	1.176
Sleeping problems	29.2	43.9	7.988**	42.6	39.7	0.195	35.6	43.2	2.675	34.5	46.7	7.035**	34.5	48.6	9.115**	34.5	40.8	9.115**	34.5	40.8	9.115**	34.5	40.8	9.115**
Flashbacks	25.0	28.4	0.504	24.6	27.9	0.296	22.5	31.0	4.045*	23.0	32.9	5.566*	22.4	35.4	9.247**	25.5	27.8	9.247**	25.5	27.8	9.247**	25.5	27.8	9.247**
Number of problems (mean, [SD], t)	2.6 (2.1)	3.5 (2.0)	-4.420**	3.1 (2.2)	3.3 (2.1)	-0.661	2.7 (1.9)	3.7 (2.1)	-5.025**	2.9 (1.9)	3.8 (2.2)	-4.621**	3.0 (2.0)	3.8 (2.2)	-4.325**	3.3 (2.0)	3.3 (2.1)	-4.325**	3.3 (2.0)	3.3 (2.1)	-4.325**	3.3 (2.0)	3.3 (2.1)	-4.325**
Psychological dependence [SDS score: mean (SD), t]	1.4 (2.6)	1.5 (2.2)	-0.508	1.7 (2.2)	1.4 (2.3)	0.977	0.8 (1.3)	2.0 (2.7)	-6.306**	1.0 (1.8)	2.1 (2.7)	-5.083**	0.8 (1.4)	2.5 (3)	-6.832**	1.2 (2.2)	1.5 (2.3)	-6.832**	1.2 (2.2)	1.5 (2.3)	-6.832**	1.2 (2.2)	1.5 (2.3)	-6.832**
Health care (%), χ^2	3.3	3.5	0.008	8.2	2.7	4.710*	1.0	5.2	5.685*	2.4	4.8	1.942	1.1	7.2	12.312**	1.8	3.7	12.312**	1.8	3.7	12.312**	1.8	3.7	12.312**
Emergency care	5.0	5.8	0.120	11.5	4.7	4.525*	2.1	8.1	7.655**	3.6	8.1	4.414*	2.1	11.0	16.473**	0	6.4	16.473**	0	6.4	16.473**	0	6.4	16.473**
Influence of ketamine on... (%), χ^2	14.2	22.2	3.585	29.5	18.7	3.845	12.6	25.5	11.589**	15.1	26.2	8.796**	13.2	30.9	21.627**	18.2	20.4	21.627**	18.2	20.4	21.627**	18.2	20.4	21.627**
Personal relationships	11.7	18.4	2.918	16.4	16.7	0.004	14.7	18.1	0.944	13.1	21.0	5.091*	11.7	24.3	12.515**	7.3	17.9	12.515**	7.3	17.9	12.515**	7.3	17.9	12.515**
Economic status	13.3	24.9	6.902**	23.0	21.7	0.049	9.9	30.3	27.056**	13.1	32.4	24.940**	10.3	39.8	55.928**	18.2	22.4	55.928**	18.2	22.4	55.928**	18.2	22.4	55.928**
Studies and/or job	12.5	24.3	7.362**	16.4	21.9	0.976	9.9	29.2	24.722**	12.7	31.4	24.045**	12.1	35.4	35.637**	16.4	21.9	35.637**	16.4	21.9	35.637**	16.4	21.9	35.637**

(Continued)

Table 3. (Continued).

	I avoid mixing			I test beforehand			I set a limit to the amount and don't go over it			I space out the doses within a session			I space out sessions			There is someone sober		
	High HRS	Low HRS	Statistic	High HRS	Low HRS	Statistic	High HRS	Low HRS	Statistic	High HRS	Low HRS	Statistic	High HRS	Low HRS	Statistic	High HRS	Low HRS	Statistic
Tolerance (% χ^2)	32.5	43.3	4.281*	37.7	40.9	0.224	28.3	49.1	20.129**	29.8	53.3	26.416**	31.7	54.1	23.073**	41.8	40.3	0.047
Risk behaviors																		
Driving under the influence (% χ^2)	15.0	35.7	17.964**	29.5	30.4	0.021	21.5	36.5	12.040**	23.0	39.0	13.939**	24.2	39.8	12.652**	23.6	31.2	1.314
Frequency of driving ^a	50.0	53.3	0.068	61.1	51.6	0.565	65.9	47.5	3.930*	70.7	40.2	12.637**	70.6	36.1	16.682**	61.5	52.0	0.433
Frequency of more quantity than planned ^b	62.5	38	21.581**	44.3	44.4	0.000	67.0	28.4	67.637**	56.0	30.5	30.119**	56.2	26.0	40.842**	50.9	43.5	1.081
Frequency of passengers in cars driven by someone under the influence ^c	76.7	59.4	11.532**	77.0	61.8	5.303*	75.4	55.7	18.787**	73.4	52.4	21.952**	75.1	46.4	39.233**	76.4	62.2	4.234*

HRS, Harm Reduction Strategy.

^a This item was responded only by those who had driven anytime under the influence of ketamine ($n = 140$). It is shown the percentage of those who never or rarely had driven under ketamine influence.^b It is shown the percentage of those who never or rarely had taken more quantity than planned.^c It is shown the percentage of those who never or rarely had been passengers in cars driven by someone under the influence.* $p < 0.05$; ** $p < 0.01$.

related to two risks/harms: the participants in the high harm reduction strategies group were passengers in cars driven by someone under the influence of ketamine less frequently ($\text{Chi}^2 = 4.234$; $p < 0.05$) and reported less influence of ketamine on legal problems more frequently ($\text{Chi}^2 = 3.967$; $p < 0.05$).

Tables 4 and 5 show the contributions of the six harm reduction strategies to the negative consequences when controlling for polydrug use and frequency of use. Table 4 shows the regression analyses between harm reduction strategies and the eight problems analyzed for which statistically significant relationships were found (see Table 3). The last column also shows the relationships between the number of problems perceived and each harm reduction strategy.

Avoiding mixing drugs was a protective factor for five out of eight problems, which were less likely to be perceived by those participants who avoided mixing drugs than those who did not (range of odds ratio between 0.523 and 0.592). Spacing out the doses within a session was related to lower probability of memory impairment ($\text{OR} = 0.548$, $p < 0.01$), abrupt changes in mood/behavior ($\text{OR} = 0.647$, $p < 0.05$), and sleeping problems ($\text{OR} = 0.677$, $p < 0.05$).

Using ketamine one day or less per week was a risk factor for psychological dependence on ketamine ($\text{OR} = 1.574$, $\text{CI} = 1.021\text{--}2.425$, $p < 0.05$) when polydrug use and frequency of ketamine use were controlled for. Among those who used ketamine one or more days per week during the last month, the probability of perceiving stronger dependence was over seven times higher ($\text{OR} = 7.505$, $\text{CI} = 4.486\text{--}12.553$, $p < 0.01$). In contrast, two harm reduction strategies were protective against psychological dependence, setting a limit to the amount and not going over it ($\text{OR} = 0.590$, $\text{CI} = 0.388\text{--}0.896$, $p < 0.05$), and spacing out the use sessions ($\text{OR} = 0.472$, $\text{CI} = 0.299\text{--}0.743$, $p < 0.01$). Increasing the amount of ketamine needed to get the same effect was related to polydrug use ($\text{OR} = 1.157$, $\text{CI} = 1.042\text{--}1.284$, $p < 0.01$), to the use of ketamine one day or less per week during the last month ($\text{OR} = 1.985$, $\text{CI} = 1.235\text{--}3.190$, $p < 0.01$), and to the use of ketamine one or more days per week during the last month ($\text{OR} = 8.771$, $\text{CI} = 5.001\text{--}15.382$, $p < 0.01$). In contrast, spacing out the doses within a session was a protective factor for increasing the amount of ketamine needed to get the same effect ($\text{OR} = 0.487$, $\text{CI} = 0.319\text{--}0.742$, $p < 0.01$).

Table 5 shows the regression analyses between the six harm reduction strategies and the influence of ketamine on personal relationships, legal status, economic status, and studies and/or job, healthcare assistance, and risk behaviors. It is noteworthy that when controlling for polydrug use and frequency of use, spacing out

the doses within a session was a protective strategy for all the risk behaviors explored (range of odds ratios from 0.405 to 0.608). Furthermore, as seen in Table 5, spacing out the sessions was a protective factor for problems related to the influence of ketamine on personal relationships, legal status, economic status, and job and/or studies (range of odds ratios from 0.317 to 0.567). It was also a protective strategy for both consequences related to healthcare, as receiving emergency care due to ketamine use and having to receive treatment to quit or reduce ketamine use.

Discussion

To the best of our knowledge, this is the first study documenting harm reduction strategies employed by recreational ketamine users and their relation to its negative consequences. Our results show that ketamine users report several negative consequences associated with the use of this drug, but these consequences are perceived differently depending on user behaviors. Our study shows that putting into practice certain harm reduction strategies is related to the lower probability of perceiving negative consequences.

Our findings are in agreement with growing evidence of impairments caused by ketamine use. As previous research, we found that participants reported urinary symptoms and abdominal pain (11), memory problems (2,33), poor achievement in studies and/or job (2,14), and perceived that ketamine influenced their personal relationships, and legal and economic status (14). The present study, in which almost half the sample had fallen while under its influence, also reflects the effects of ketamine on physical coordination (3,16). These results reinforce the need to make these potential risks known among ketamine users, even though they may not use it frequently.

The most frequent harm reduction strategies were those related to the pattern of use, specifically, spacing out sessions, spacing the doses, and limiting the amount. Based on ketamine's effects on coordination, the strategy "someone sober in the group" has been highly recommended in the literature (2,3,16,28). However, most of our sample never/almost never followed what should be an important risk reduction message.

An important new finding of our results is the strong association of several harm reduction strategies with a lower probability of reporting negative consequences. Polydrug use must be considered in the interpretation of our findings. Our results showed that participants used many other drugs, which is consistent with previous research on ketamine users (7,11,31).

Table 4. Multivariate regression analyses for harm reduction strategies and problems experienced.^a

	Cystitis	Frequent abdominal pain	Memory impairments	Abrupt changes in mood/behaviors	Falling under influence	Unexpected confusion	Sleeping problems	Flashbacks	Number of problems
Number of drugs used in last year	1.043 (0.948–1.148)	1.045 (0.941–1.160)	1.132 (1.029–1.246)*	1.078 (0.983–1.118)	1.134 (1.030–1.247)*	1.104 (0.923–1.113)	0.994 (0.906–1.091)	1.008 (0.912–1.115)	1.128 (1.031–1.235)**
Frequency of ketamine use (last month)	1.065 (0.668–1.698)	1.676 (1.003–2.801)*	1.102 (0.709–1.713)	0.898 (0.581–1.388)	0.767 (0.490–1.200)	0.888 (0.572–1.380)	1.327 (0.851–2.068)	1.045 (0.644–1.696)	1.114 (0.722–1.718)
1 or more days per week	1.499 (0.907–2.478)	2.485 (1.441–4.286)**	1.347 (0.807–2.249)	1.242 (0.757–2.038)	0.572 (0.334–0.982)*	0.857 (0.519–1.416)	1.702 (1.037–2.794)*	0.949 (0.540–1.665)	1.738 (1.071–2.822)**
Harm reduction strategies									
Avoid mixing	0.592 (0.365–0.961)**	EX	0.564 (0.365–0.872)**	0.523 (0.338–0.811)**	–	0.537 (0.346–0.833)**	0.585 (0.370–0.924)*	–	0.417 (0.271–0.640)**
Test beforehand	–	–	–	–	EX	–	–	–	–
Set a limit to the amount	EX	0.646 (0.404–1.032)	EX	EX	0.691(0.452–1.057)	0.594 (0.397–0.889)*	–	EX	EX
Space out doses within a session	–	NI	0.548 (0.370–0.813)**	0.647 (0.440–0.950)*	0.594 (0.319–1.103)	–	0.677 (0.458–0.999)*	EX	EX
Space out sessions	EX	EX	EX	–	0.643 (0.415–0.997)*	–	EX	0.522 (0.333–0.818)**	EX
There is someone sober	–	–	–	–	–	–	–	–	–

^a Associations are given as odds ratios with 95% confidence intervals in parentheses. * $p < 0.05$; ** $p < 0.01$. —Associations that did not show significant relationships in bivariate analyses and were not considered for regression analyses. EX variables excluded for the regression model with best fit to the data. In bold those statistically significant relationships.

Table 5. Multivariate regression analyses for harm reduction strategies and problems influenced by ketamine, healthcare, and risk behaviors.^a

	Influence of ketamine on...				Healthcare			Risk behaviors		
	Personal relationships	Legal status	Economic status	Studies/job	Emergency	Treatment	Driving under influence	Frequency of driving	More quantity than planned	Passengers with someone under influence
Number of drugs used in last year	1.076 (0.960–1.206)	0.918 (0.811–1.040)	1.013 (0.900–1.140)	1.028 (0.917–1.152)	0.902 (0.698–1.165)	0.853 (0.692–1.051)	1.021 (0.923–1.129)	0.833 (0.695–0.999)*	1.014 (0.912–1.128)	1.014 (0.912–1.128)
Frequency of ketamine use (<1 day per week)	1.279 (0.713–2.294)	1.153 (0.601–2.208)	1.415 (0.752–2.665)	1.552 (0.875–2.754)	0.530 (0.098–3.056)	1.638 (0.532–5.039)	1.191 (0.722–1.964)	0.752 (0.291–1.944)	1.929 (1.208–3.082)**	1.929 (1.208–3.082)**
1 or more days per week	2.194 (1.194–4.031)*	2.964 (1.548–5.672)**	4.102 (2.204–7.636)**	1.292 (0.690–2.418)	2.596 (0.713–9.448)	2.052 (0.680–6.188)	2.701 (1.598–4.566)**	1.503 (0.582–3.881)	7.115 (3.718–13.615)**	7.115 (3.718–13.615)**
Harm reduction strategies										
Avoid mixing	–	–	EX	EX	–	–	0.357 (0.203–0.628)**	–	0.545 (0.332–0.897)*	0.545 (0.332–0.897)*
Test beforehand	–	–	–	–	3.922 (1.205–12.764)*	3.570 (1.321–9.649)*	–	–	–	–
Set a limit to the amount	EX	–	0.466 (0.257–0.848)*	0.436 (0.241–0.789)**	EX	0.345 (0.105–1.134)	EX	EX	0.285 (0.181–0.450)**	0.285 (0.181–0.450)**
Space out doses within a session	EX	EX	EX	0.590 (0.346–1.1008)	–	EX	0.574 (0.375–0.879)*	0.405 (0.183–0.896)*	0.608 (0.389–0.950)*	0.608 (0.389–0.950)*
Space out sessions	0.447 (0.269–0.741)**	0.567 (0.327–0.985)*	0.317 (0.185–0.543)**	0.425 (0.245–0.736)**	0.156 (0.039–0.633)**	0.240 (0.084–0.683)**	0.879)*	0.339 (0.146–0.787)*	EX	–
There is someone sober	–	0.408 (0.140–1.188)	–	–	–	–	–	–	–	–

^a Associations are given as odds ratios with 95% confidence intervals in parentheses. * $p < 0.05$ /** $p < 0.01$ —Associations that did not show significant relationships in bivariate analyses and were not considered for regression analyses. EX variables excluded for the regression model with best fit to the data. In bold those statistically significant relationships.

Thus, the relationship between ketamine use and its negative consequences must take into account the hypothesis that other drugs may be an influence. Polydrug use was therefore controlled for in our study, that is, the results showed the relationship between the harm reduction strategies and negative consequences while keeping polydrug use constant. Similarly, given that frequency of ketamine use is relevant to negative consequences (11), this variable was also controlled for.

The “avoid mixing” strategy was a protective factor for five out of eight problems explored. It was also related to a lower probability of risk behaviors, such as driving under the influence of ketamine, taking more than planned, or riding in a car driven by someone under the influence of ketamine. The “spacing out doses” strategy was also identified as a protective strategy for the four risk behaviors explored and, specifically, the three related to driving when using ketamine. Participants who carried out these two strategies had a lower probability of being involved in risk behaviors associated with driving, which supports the distribution of these strategies for preventing injury in traffic accidents, an important consequence of ketamine use (34,35).

Our study also revealed that spacing out ketamine use sessions is an important strategy associated with perceiving less influence of this drug on personal relationships, legal and economic status, and studies or job. This strategy was also related to a strong decrease in the probability of having received emergency care and treatment for quitting or reducing ketamine use.

Previous research has shown ketamine’s potential for eliciting dependence (10,16), even in recreational users (32). The low score on the SDS, along with the profile and pattern of ketamine use detected, describes participants in our study as recreational ketamine users. The SDS scores in our study contrast with what has been observed in previous research where SDS scores were over seven (15,31,36). Nevertheless, these studies were conducted with ketamine users attending counseling centers for psychotropic substance-use disorders, residential treatment centers, or district youth outreach teams.

As expected, more frequency of ketamine use in our study was related to an increased probability of higher SDS scores. However, when controlling for frequency of ketamine use, two strategies were revealed as protective factors for psychological dependence, setting a limit, and spacing out sessions. On the other hand, tolerance is common in ketamine users (2), with some studies reporting an escalation of 600% and 760% in doses administered (12). Our study showed that perception of tolerance is strongly associated with frequency of use, but also that when frequency of use is controlled for, a spacing doses strategy is a protective factor.

Therefore, according to our results, the strategies related to use pattern (mixing, dose spacing, session spacing, and limits) have a protective role for negative consequences of ketamine use. In contrast, strategies such as testing beforehand and making sure someone in the group stays sober do not seem to impact its negative consequences.

Some limitations must be considered in interpreting our findings. First, the limited representativeness resulting from our non-probabilistic web-based sampling must be taken into account. Nevertheless, web-based surveys are especially appropriate for hidden, hard-to-reach populations, such as recreational drug users, and make larger data collection samples possible (26,27,37), as was the case in our study. Coverage errors and bias from self-selection of respondents should also be considered in web-based surveys. It is possible that some ketamine users, like the most severe, are under-represented because of limited access to the internet. Or, in contrast, as recruiting was done through organizations and at sites that promote harm reduction, the percentage of participants who carry out harm reduction strategies may be overrepresented. Finally, the cross-sectional design of our study did not allow us to establish causal or predictive relations.

Despite these limitations, our results have several implications for prevention and harm reduction organizations working with ketamine users. On the one hand, some types of harm with potentially serious consequences have been identified as highly prevalent, and educational materials such as leaflets should therefore draw attention to them. On the other, efforts should also focus on increasing awareness of strategies associated with less harm such as those empirically demonstrated in our study, and on increasing the frequency with which they are employed. Future studies should analyze these and other harm reduction strategies, providing empirical evidence that contributes to increasing the scarce body of knowledge in this field. Longitudinal designs are necessary to better address the influence of harm reduction strategies on the negative consequences of ketamine use. Through them, a valid sequence of this influence can be analyzed.

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