

Effectiveness of a brief information, motivation and behavioral skills program on stage transitions and lapse for individuals who use ketamine

Chia-Chun Hung^a, Lien-Wen Su^b, Muh-Young Yen^b, Peing Chuang^b, Hao-Jan Yang^{c,1},
Tony Szu-Hsien Lee^{d,1,*}

^a Bali Psychiatric Center, Ministry of Health and Welfare, Taiwan

^b Drug Prevention and Control Center, Taipei City Hospital, Taiwan

^c Department of Public Health, Chung Shan Medical University, Taichung, Taiwan

^d Department of Health Promotion and Health Education, College of Education, National Taiwan Normal University, Taiwan

ARTICLE INFO

Keywords:

Information
Motivation and behavior skills
Ketamine
Stage transition
Young adults

ABSTRACT

Objective: Chronic ketamine use is a significant public health and social problem in East and South East Asia and may lead to impairments in health and cognitive functioning. The study evaluated effects of an information, motivation and behavior skills (IMB) program on changes in motivational stage and ketamine use.

Methods: Ketamine using individuals residing in the City of Taipei were recruited (N = 395): 279 selected an IMB program consisting of a 1-day workshop of six 50-minute interactive sessions provided in small groups. The remaining 116 participants selected an education-as-usual (EAU) program consisting of a 1-day workshop of six 50-minute didactic lectures provided in a large group format. Motivational stage of change and ketamine knowledge were assessed before and after the interventions. Participants were followed one year later to assess their ketamine use status.

Results: No significant difference in knowledge increase between the IMB and EAU groups ($p = .59$). The proportion of participants who transitioned from the contemplation to preparation motivational stages was greater in the IMB group than in the EAU group ($p < .01$). A significant difference in the rates of ketamine lapse during a one-year post intervention follow up was observed between the IMB (50%) and EAU (75%) groups ($p < .01$).

Conclusions: Interventions based on IMB principles may be more effective in supporting motivational stage transition and in prevention of lapses to ketamine use as compared to currently offered standard drug education programs. Policy makers should consider including IMB interventions in their rehabilitation programs addressing ketamine use problems.

1. Introduction

Nonmedical ketamine use has emerged as one of significant public health and social problems in East and South East Asia (Hser et al., 2016). In Hong Kong, ketamine has been the second most common substance of use among teenagers since 2005 (Narcotics Division, Security Bureau, The Government of The Hong Kong Special Administrative Region, 2017) and ketamine-related events accounted for 7.1% of all toxicology consultations in 2010 (Chan et al., 2012). The National Household Survey on Health and Substance Use conducted in Taiwan in 2005 among population ages 12–64 years identified 200 individuals reporting nonmedical use of illicit substances (National

Health Research Institute, 2005). Ketamine was third most commonly reported substance (44/200 22.0%), after amphetamine (98/200 49%) and MDMA (70/200 35%). In a more recent survey, ketamine overtook amphetamine and MDMA as the leading substance among high school students: among those who reported using any illicit drugs, 64.4% reported using ketamine, followed by ecstasy (50%) and methamphetamine (29%) (Chen et al., 2009). This study also found that the mean age of first ketamine use was 14 years of age, right in the middle of a critical period of adolescent brain development.

According to the World Health Organization (2015), there is a growing evidence of ketamine dependence symptoms among recreational users of ketamine. Other studies have also documented that

* Corresponding author at: Department of Health Promotion and Health Education, College of Education, National Taiwan Normal University, No 162 Sec. 1 He-Ping East Road, Taipei, 10610, Taiwan.

E-mail address: tonylee@ntnu.edu.tw (T.S.-H. Lee).

¹ These authors contributed equally to this work

prolonged ketamine use leads to uropathy (Shahani et al., 2007), neurocognitive impairments including deficits in working memory, executive functions, and impulse control (De La Torre, 2010; Morgan et al., 2004, 2009, 2010; van Amsterdam et al., 2012) and other social problems. Moreover, due to impaired cognitive functioning, ketamine using individuals may have a higher risk of dangerous driving and behaviors leading to HIV/HCV infection (Cheng et al., 2007).

Ketamine is regulated in Taiwan as a Schedule III substance in accordance with Article 2 of the Narcotics Hazard Prevention Act (Laws and Regulations, the Republic of China, 2017). It is stated in Article 11-1 that using or possessing less than 20 g of ketamine without a prescription results in a fine of 10,000–50,000 New Taiwan Dollars (approximately 330 to 1650 US dollars) and requires participation in four to eight hours in drug education programs. Possession of more than 20 g of ketamine is prosecuted as a crime of drug trafficking with penalties of 7 years or more in prison. To enforce these laws, the police conducts ongoing surveillance of places known for frequent use of ketamine and responds to information about suspicious drug use activities by conducting urine tests among patrons in taverns, bars, karaoke bars, and at parties in various hotels/motels, or other events and venues throughout Taiwan. Individuals testing positive for ketamine and/or who are found to possess less than 20 g of ketamine are required to pay a fine and are given notices requiring them to participate in drug education programs offered by the government. The drug education programs offered to ketamine users in Taiwan consist of lectures held in a large-group format several times per year. Individuals who do not register and do not participate in the drug education programs receive repeated visits by the police at their residences reminding them that they need to complete the drug education program. The visits and reminders continue until they are compliant with the education requirement.

In the City of Taipei, drug education programs offered to individuals with ketamine use are didactic and aimed to increase knowledge and awareness of the laws concerning drug use and dangers and risks associated with ketamine use. Published reports indicate that interventions combining educational or didactic approaches with behavioral, cognitive, and motivational enhancement principles may be more effective in helping individuals who use illicit substances to manage drug-taking behaviors and may result in more successful reductions in drug use (Huang et al., 2011; Lee and Rawson, 2008; Nosyk et al., 2010). However, no extensive research has been carried out to evaluate the effectiveness of cognitive-behavioral or motivational enhancement interventions on individuals with ketamine use.

Motivational interviewing and cognitive-behavioral interventions aim to reduce and/or prevent substance use by increasing knowledge about harmful consequences of substance use, increasing motivation to cease substance use, correcting cognitive misconceptions that contribute to substance use, and providing opportunities to learn coping skills to reduce the likelihood of using drugs. Studies and reviews published to date demonstrated that psychosocial interventions are effective for individuals with cocaine and amphetamine use (Knapp et al., 2007; Lee and Rawson, 2008; Shearer, 2007). In Australia, a brief cognitive behavioral intervention was provided to 214 regular amphetamine users and the results were favorable (Baker et al., 2005). However, no studies have specifically examined results of cognitive-behavioral or motivational enhancement interventions for individuals with ketamine use.

The City of Taipei Taiwan agreed to offer and evaluate an information, motivation and behavioral (IMB) skills program for ketamine-using individuals. Consequently, two types of drug education programs were offered and evaluated in 2016, hypothesizing that the IMB program would result in greater increases in motivation to cease ketamine use, as compared to the education as usual program (EAU).

2. Materials and methods

2.1. Participants

Between August and December 2015, the police in Taipei identified a total of 4105 individuals using ketamine via urine testing of patrons in taverns, bars, karaoke bars, and at parties in various hotels/motels. Because 279 of the 4105 did not reside in the City of Taipei they were required to participate in drug education programs at their places of residence. Consequently, 3826 ketamine using individuals living in the City of Taipei were sent a notice to complete a four- to eight-hour drug education program. A telephone number of the program registration office was listed in the notice. Of the 3826 individuals who received notices, 1051 called the registration office; 211 of those who called provided various reasons for their unavailability to participate, primarily timing conflicts, and 840 individuals registered for one of available time slots in one of two offered drug education programs based on their own preference and choice. Consequently, 415 individuals registered for the information, motivation, and behavioral skills program (IMB) and 425 individuals registered for the education as usual (EAU) program.

All 840 participants in the IMB and EAU were also invited to participate in a program evaluation component. In the IMB group, 285 participants agreed to participate in the evaluation component, in the EAU 124 participants agreed to participate in the evaluation. Participation in the evaluation component was voluntary. Those who agreed to participate provided a written informed consent and filled out a 5-minute study questionnaire immediately before and immediately after the completion of either IMB or EAU programs. Those who refused to take part in the evaluation component (130 in the IMB and 301 in the EAU groups) participated in the programs without providing any additional information, data, or study related feedback. IMB was provided in small group settings while the EAU in large group settings. Consequently, the study procedures and potential participation was probably better explained to IMB participants potentially leading to an increased interest or willingness to participate. Of all participants who initially consented and provided the baseline data, 6 in the IMB and 8 in the EAU group subsequently withdrew their consent or did not provide post-intervention evaluations. This led to 279 participants in the IMB condition and 116 in the EAU condition with complete study data (see Fig. 1).

No compensation was offered for participation in the programs or the evaluation component. The study protocol was reviewed and approved by the Institute of Review Board at the Tri-Service General Hospital, Taiwan.

2.2. Drug education programs

2.2.1. Information, motivation, and behavior skills training (IMB)

The IMB was provided in groups of 8–12 participants over a one-day course of six 50-minute sessions with 10-minute breaks between each session. Between January and June of 2016 42 IMB courses were offered. Each course was given by the same team (one MD psychiatrist and one PhD psychologist, authors CCH and TSHL). The aim of IMB was to instill or increase motivation for change by determining participants' predisposing factors for using ketamine, discussing effective refusal skills, providing examples of effective stimulus control and relapse prevention skills, and addressing concerns about short- and long-term negative consequences of ketamine use. The course instructors primarily applied motivational interviewing techniques, general counseling skills, and moderated group discussions. The transtheoretical model of behavior change postulates that before someone can change his or her behavior, that person must recognize which specific behaviors needed changing, know how to change them, and consider this changing to be a worthwhile expenditure of effort: effort and motivation are both critical components of behavior change (DiClemente

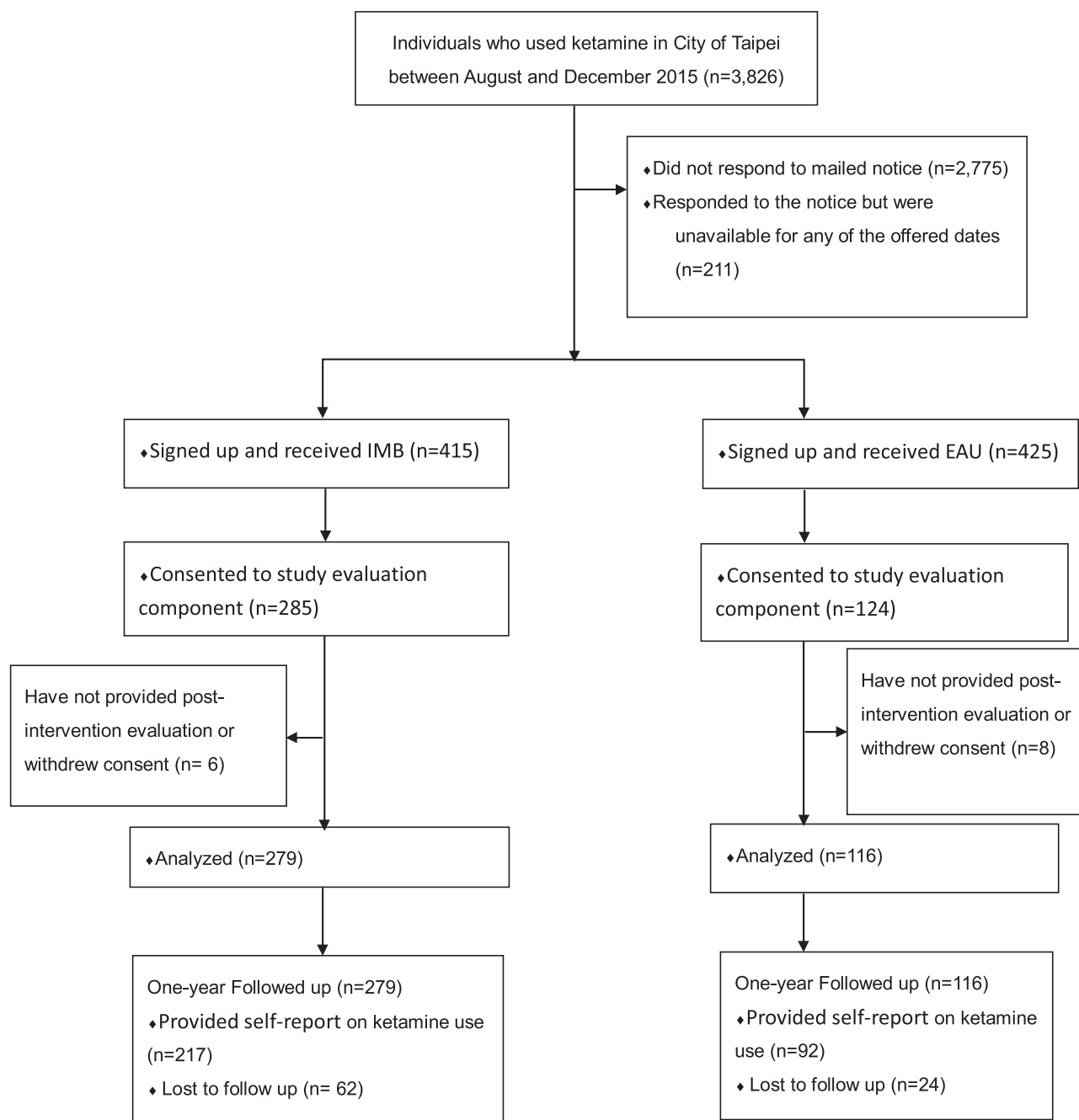


Fig. 1. Participants Flowchart.

et al., 2004).

2.2.2. Education as usual (EAU)

The EAU intervention was provided in groups of 42–112 participants over a one-day course of six 50-minute lecture sets with 10-minute breaks between each lecture. Between January and June of 2016 6 EAU lecture sets were offered. The lectures were given by one lawyer, two MD psychiatrists, one infectious disease MD physician and one PhD counselor/therapist. The EAU provided information about ketamine, its effects on the brain, relevant regulations and laws, and the risks and modes of transmission of infectious diseases, including HIV and hepatitis C.

2.3. Program evaluation component

Program evaluation questionnaire included demographics (e.g., age, gender, and education level), knowledge about ketamine and questions to assess the stage of ketamine cessation that were adopted from previous studies (Brick et al., 2017). Based on answers to these questions, participants were classified to be in the maintenance stage if they reported not using ketamine for more than six months; if they reported not using ketamine for less than six months, they were classified as in the action stage; if they were thinking about or planning to stop ketamine use within the next 30 days, they were classified as in the preparation stage; if they were thinking about or planning to stop within the next six months, they were classified as in the contemplation stage; and if they reported that they were not thinking of stopping ketamine use within the next six months, they were classified as in the

precontemplation stage.

Participants' knowledge about ketamine was assessed by the following questions: Ketamine (1) may cause ulcerative cystitis, (2) may impair memory, (3) may slow movements, (4) may distort perception, and (5) is regulated as an illicit drug in Taiwan. The response options were "yes," "no," and "do not know." Correct answers received one point, and incorrect answers or "do not know" received zero points. The higher the total score, the greater the ketamine knowledge. The Kuder-Richardson reliability for these five items in the study sample was .78.

To evaluate long-term effects of the drug education programs on ketamine use, at one year after program completion all participants were interviewed over the phone with one follow-up question: 'Have you used ketamine in the past year?'

2.4. Statistical analysis

Data were analyzed using SPSS statistical software, version 22.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics, Chi-square and t-tests were performed to examine between group differences on categorical and continuous variables. Repeated measures ANOVAs with demographics as controls were performed to compare the effects of the IMB and EAU programs in increasing ketamine knowledge. Because the stage measure is not an interval scale and not normally distributed, Wilcoxon signed rank sum tests were performed to examine any changes in the stage classifications during the IMB or EAU. Generalized estimating equations were used to examine whether IMB was more likely to motivate ketamine users to enter a new stage than EAU. Lapse to ketamine use was compared using a Chi-square test.

3. Results

3.1. Demographics

As shown in Table 1, 51/395 (12.9%) were female, 111/395 (28.1%) had less than nine years of education, 179/395 (45.3%) had a high school education, and 105/395 (26.6%) had a college degree. Results from the chi-square analyses revealed no significant differences in gender and education level between the two groups. The mean (SD) age was 28 (5.5) in the IMB and 26 (5.8) in the EAU groups ($t(393) = 2.7, p < .05$).

3.2. Effects of interventions

A Fisher's exact test showed that there were no significant differences in proportions of participants across the motivational stages and knowledge scores between the IMB and EAU groups at pretest, $p = .33$.

3.2.1. Knowledge

The means (SD) of scores on ketamine knowledge before and after IMB and EAU increased significantly, from 3.95 (0.98) to 4.09 (0.87)

Table 1
Means (standard deviations) for demographics of participating individuals who used ketamine.

Variables	IMB (n = 279)	EAU (n = 116)	
Age	28 (5.5)	26 (5.8)	$t(393) = 2.7^*$
Gender			$\chi^2(1) = 0.44$
Male	245(87.8%)	99(86.3%)	
Female	34(12.2%)	17(13.7%)	
Education			$\chi^2(2) = 1.09$
Elementary/junior high	80(28.7%)	31(26.7%)	
Senior high	129(46.2%)	50(43.1%)	
College/ university	70(25.1%)	35(30.2%)	

* $p < .05$.

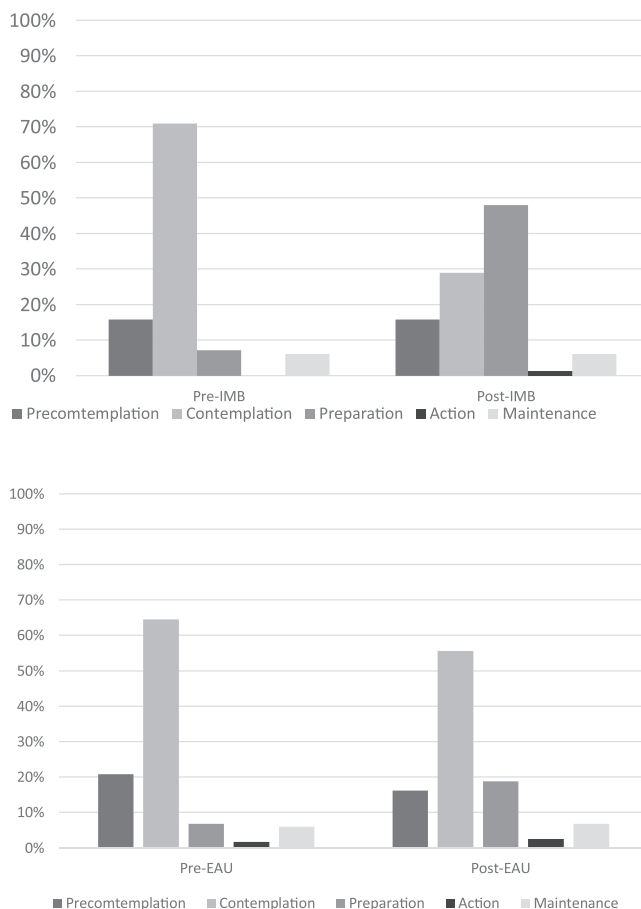


Fig. 2. Distribution of individuals across different motivational stages during pre- and post-intervention assessment for the two study groups.

for IMB ($F(1,249) = 5.55, p < .05$), and from 3.96 (0.78) to 4.12 (0.74) for EAU ($F(1,106) = 4.35, p < .05$). Repeated-measures ANOVAs controlling for age, gender, and educational level showed that there was no significant difference in knowledge increase between the IMB and EAU groups, $F(1,353) = 0.07, p = .59$.

3.2.2. Stages

Before participating in IMB or EAU, most study participants were in the contemplation stage: 198/279 (71.0%) in the IMB group and 75/116 (64.6%) in the EAU group. After the IMB program, the proportion of participants in the contemplation stage dropped to 29%, and the proportion of participants in the preparation stage rose from 7.2% to 48.0% ($Z = 9.20, p < .01$). After the EAU program, the proportion of participants in the contemplation stage decreased from 64.6% to 55.6%, and the proportion of participants in the preparation stage increased from 6.8% to 18.8% ($Z = 4.59, p < .01$). There were no substantial changes in proportions of participants across the pre-contemplation, action, and maintenance stages between pre and post interventions. See Fig. 2 for complete results.

After adjustment for age, gender, education level, and knowledge about ketamine, the results from the analysis of generalized estimating equation showed a significant interaction between group and pretest-posttest on stage transition, $Wald\chi^2 = 4.22, p < .05$.

3.2.3. Lapse at one-year

At one-year after participation in the programs, 217/279 (78%) and 92/116 (79%) were followed in the IMB and EAU groups respectively. A significantly smaller proportion of participants in the IMB group who were followed reported ketamine use in the past year: 109/217 (50%) and 69/92 (75%) in the IMB and EAU groups respectively ($\chi^2 = 19.05,$

$p < .01$).

4. Discussion

In our study, participants in both the IMB and EAU groups increased their knowledge about ketamine, and provision of IMB resulted significantly greater motivation to reduce or cease ketamine use, and in self-reported rates of ketamine use during one year post-intervention.

Previously published studies have demonstrated that motivation affects the success of treatment for smoking (Baker et al., 2004; Jardin and Carpenter, 2012), opioid dependence (Nosyk et al., 2010), amphetamine use (Baker et al., 2005), and MDMA use (Huang et al., 2011) and have shown that an increased level of readiness to change is associated with a longer duration of abstinence from drug use, and a lower frequency/intensity of drug use (DiClemente et al., 2004). The results of the current study indicate that IMB may be effective in improving motivation to change ketamine use, especially for individuals who are in the contemplation stage.

It is noteworthy that participants who begun training in the precontemplation stage have not changed their motivational stage as a result of participation in IMB or EAU. In line with our findings, an earlier study showed that substance-using adolescents in the precontemplation stage manifested significantly higher rates of treatment attrition than individuals in the contemplation or preparation/action stages (Callaghan et al., 2005) indicating that the stage of change should be taken into consideration when tailoring interventions of individuals with addictive disorders (DiClemente et al., 2004). Ketamine using individuals who are in the precontemplation stage may not benefit from brief IMB but may need more intensive interventions.

The study participants had good levels of knowledge about ketamine before their participation in the study interventions potentially due to extensive public health educational programs and campaigns about adverse consequences of ketamine use provided by the Government of Taiwan. Hence, although there was a statistically significant improvement in ketamine knowledge by the end of training in both the EAU and IMB groups, this increase may be trivial. However, a small but significant increase in knowledge may also indicate that a small proportion of participants knew more after the programs, and knowledge itself may or may not help ketamine users to engage efforts to reduce their substance use or achieve abstinence. Further investigation of the relationship between knowledge and motivation to change is needed.

The finding that brief IMB was more effective in improving motivation among ketamine using individuals is clinically significant. People who use ketamine typically initiate their use of this substance at a young age by being introduced to it by their peers (Dillon et al., 2003). They report that ketamine use made it easier for them to communicate with friends, find a group identity, and cope with stress. It has been previously reported that IMB interventions including cognitive, personal self-management, and social skills had positive effects on reduced drug use among adolescents (Botvin et al., 2000; Griffin et al., 2004). The IMB program offered in the current study gave participants an opportunity to reframe their thinking and decisions, learn how to refuse or manage peer pressure, resolve conflicts, and communicate effectively about interpersonal relations and the study results support findings from previous studies on the effectiveness of IMB in reducing drug use behaviors (Moshki et al., 2014).

4.1. Limitations

The study has several limitations. Only individuals who were required by the law to take part in a mandatory drug education program were invited to participate in the study. Consequently, the legal status may have influenced their self-rated motivational stage at the study entry. Selecting the type of drug education program was based on self-selection process potentially introducing self-selection biases. The

differential refusal rates of participation between the two groups may be due to program settings that IMB was provided in small group settings while the EAU in large group settings. Another limitation was that no data on the level of ketamine use and related problems were collected. Additionally, the lapse to ketamine use was assessed through a one question self-report which may be biased due to social desirability and recall inaccuracy. The IMB program was compared to a control condition (EAU) which likely has a very low overall effectiveness. Future studies should compare the effectiveness of IMB against a broader range of interventions.

5. Conclusions

Drug education programs based on IMB principles may be more effective in supporting motivational stage transition and in prevention of lapses to ketamine use during one-year post intervention as compared to currently offered standard drug education programs. Policy makers in Taiwan and elsewhere should consider including IMB type interventions in their prevention and rehabilitation programs addressing ketamine use problems.

6. Authors' contributions

CCH, HJY and TSHL draft the manuscript. LWS, MYY and PC participated in the design of the study and collected the data. HJY and TSHL conceptualized and carried out the study. All authors contributed to analysis of the data. CCH and TSHL draft the discussion.

Role of the funding source

Funding for this study was provided by Taiwan Ministry of Science and Technology (MOST) Grants 104-2410-H-003-012 and 105-2410-H-003-013. The funding organization had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication. This article was subsidized by the National Taiwan Normal University (NTNU), Taiwan, ROC. This work was financially supported by the Higher Education Sprout Project by the Ministry of Education (MOE) in Taiwan.

Declaration of Competing Interest

The authors declared no conflict of interest.

Acknowledgement

The authors wish to thank the participation of patients with ketamine use.

References

- Baker, A., Lee, N.K., Claire, M., Lewin, T.J., Grant, T., Pohlman, S., Saunders, J.B., Kay-Lambkin, F., Constable, P., Jenner, L., Carr, V.J., 2005. Brief cognitive behavioural interventions for regular amphetamine users: a step in the right direction. *Addiction* 100 (3), 367–378. <https://doi.org/10.1111/j.1360-0443.2005.01002.x>.
- Baker, T.B., Brandon, T.H., Chassin, L., 2004. Motivational influences on cigarette smoking. *Annu. Rev. Psychol.* 55, 463–491. <https://doi.org/10.1146/annurev.psych.55.090902.142054>.
- Botvin, G.J., Griffin, K.W., Diaz, T., Scheier, L.M., Williams, C., Epstein, J.A., 2000. Preventing illicit drug use in adolescents: long-term follow-up data from a randomized control trial of a school population. *Addict. Behav.* 25, 769–774.
- Brick, L.A., Redding, C.A., Paiva, A.L., Velicer, W.F., 2017. Intervention effects on stage transitions for adolescent smoking and alcohol use acquisition. *Psychol. Addict. Behav.* 31, 614–624. <https://doi.org/10.1037/adb0000302>.
- Callaghan, R.C., Hathaway, A., Cunningham, J.A., Vettese, L.C., Wyatt, S., Taylor, L., 2005. Does stage-of-change predict dropout in a culturally diverse sample of adolescents admitted to inpatient substance-abuse treatment? A test of the Transtheoretical Model. *Addict. Behav.* 30, 1834–1847. <https://doi.org/10.1016/j.addbeh.2005.07.015>.
- Chan, Y.C., Tse, M.L., Lau, F.L., 2012. *Hong Kong Poison Information Centre: annual*

- report. *Hong Kong J. Emerg. Med.* 19, 110–120.
- Chen, W.J., Fu, T.C., Ting, T.T., Huang, W.L., Tang, G.M., Hsiao, C.K., Chen, C.Y., 2009. Use of ecstasy and other psychoactive substances among school-attending adolescents in Taiwan: national surveys 2004–2006. *BMC Public Health* 9, 27. <https://doi.org/10.1186/1471-2458-9-27>.
- Cheng, W.C., Ng, K.M., Chan, K.K., Mok, V.K., Cheung, B.K., 2007. Roadside detection of impairment under the influence of ketamine—evaluation of ketamine impairment symptoms with reference to its concentration in oral fluid and urine. *Forensic Sci. Int.* 170, 51–58. <https://doi.org/10.1016/j.forsciint.2006.09.001>.
- De La Torre, R., 2010. Commentary on Morgan et al. (2010): ketamine abuse: first medical evidence of harms we should confront. *Addiction* 105, 134–135. <https://doi.org/10.1111/j.1360-0443.2009.02824.x>.
- DiClemente, C.C., Schlundt, D., Gemmell, L., 2004. Readiness and stages of change in addiction treatment. *Am. J. Addict.* 13, 103–119. <https://doi.org/10.1080/10550490490435777>.
- Dillon, P., Copeland, J., Jansen, K., 2003. Patterns of use and harms associated with non-medical ketamine use. *Drug Alcohol Depend.* 69, 23–28.
- Griffin, K.W., Botvin, G.J., Nichols, T.R., 2004. Long-term follow-up effects of a school-based drug abuse prevention program on adolescent risky driving. *Prev. Sci.* 5, 207–212.
- Hser, Y.I., Liang, D., Lan, Y.C., Vicknasingam, B.K., Chakrabarti, A., 2016. Drug abuse, HIV, and HCV in Asian countries. *J. Neuroimmune Pharmacol.* 11, 383–393. <https://doi.org/10.1007/s11481-016-9665-x>.
- Huang, Y.S., Tang, T.C., Lin, C.H., Yen, C.F., 2011. Effects of motivational enhancement therapy on readiness to change MDMA and methamphetamine use behaviors in Taiwanese adolescents. *Subst. Use Misuse* 46, 411–416. <https://doi.org/10.3109/10826084.2010.501664>.
- Jardin, B.F., Carpenter, M.J., 2012. Predictors of quit attempts and abstinence among smokers not currently interested in quitting. *Nicotine Tob. Res.* 14, 1197–1204. <https://doi.org/10.1093/ntr/nts015>.
- Knapp, W.P., Soares, B.G., Farrel, M., Lima, M.S., 2007. Psychosocial interventions for cocaine and psychostimulant amphetamines related disorders. *Cochrane Database Syst. Rev.* 3, CD003023. <https://doi.org/10.1002/14651858.CD003023.pub2>.
- Laws and Regulations, the Republic of China, 2017. Narcotics Hazard Prevention Act. Retrieved at May 1 2019 from <https://law.moj.gov.tw/LawClass/LawAll.aspx?PCode=C0000008> [In Chinese].
- Lee, N.K., Rawson, R.A., 2008. A systematic review of cognitive and behavioural therapies for methamphetamine dependence. *Drug Alcohol Rev.* 27, 309–317. <https://doi.org/10.1080/09595230801919494>.
- Morgan, C.J., Monaghan, L., Curran, H.V., 2004. Beyond the K-hole: a 3-year longitudinal investigation of the cognitive and subjective effects of ketamine in recreational users who have substantially reduced their use of the drug. *Addiction* 99, 1450–1461. <https://doi.org/10.1111/j.1360-0443.2004.00879.x>.
- Morgan, C.J., Muetzelfeldt, L., Curran, H.V., 2009. Ketamine use, cognition and psychological wellbeing: a comparison of frequent, infrequent and ex-users with poly-drug and non-using controls. *Addiction* 104, 77–87. <https://doi.org/10.1111/j.1360-0443.2008.02394.x>.
- Morgan, C.J., Muetzelfeldt, L., Curran, H.V., 2010. Consequences of chronic ketamine self-administration upon neurocognitive function and psychological wellbeing: a 1-year longitudinal study. *Addiction* 105, 121–133. <https://doi.org/10.1111/j.1360-0443.2009.02761.x>.
- Moshki, M., Hassanzade, T., Taymoori, P., 2014. Effect of life skills training on drug abuse preventive behaviors among university students. *Int. J. Prev. Med.* 5, 577–583.
- Narcotics Division, Security Bureau, The Government of The Hong Kong Special Administrative Region, 2017. Central Registry of Drug Abuse Sixty-fifth Report. Retrieved at May 1, 2019 Retrieved from. . https://www.nd.gov.hk/en/crda_66th_report.htm.
- National Health Research Institute, 2005. Outcome Report from the National Household Health and Substance Abuse Survey. Retrieved at March 25 2019 from http://nhis.nhri.org.tw/files/2005NHIS_Final%20Report_2.pdf [In Chinese].
- Nosyk, B., Geller, J., Guh, D.P., Oviedo-Joekes, E., Brissette, S., Marsh, D.C., Schechter, M.T., Anis, A.H., 2010. The effect of motivational status on treatment outcome in the North American Opiate Medication Initiative (NAOMI) study. *Drug Alcohol Depend.* 111, 161–165. <https://doi.org/10.1016/j.drugalcdep.2010.03.019>.
- Shahani, R., Streutker, C., Dickson, B., Stewart, R.J., 2007. Ketamine-associated ulcerative cystitis: a new clinical entity. *Urology* 69, 810–812. <https://doi.org/10.1016/j.urology.2007.01.038>.
- Shearer, J., 2007. Psychosocial approaches to psychostimulant dependence: a systematic review. *J. Subst. Abuse Treat.* 32, 41–52. <https://doi.org/10.1016/j.jsat.2006.06.012>.
- van Amsterdam, J.G., Brunt, T.M., McMaster, M.T., Niesink, R.J., 2012. Possible long-term effects of gamma-hydroxybutyric acid (GHB) due to neurotoxicity and overdose. *Neurosci. Biobehav. Rev.* 36, 1217–1227. <https://doi.org/10.1016/j.neubiorev.2012.02.002>.
- World Health Organization, 2015. Ketamine (INN) Update Review Report. Retrieved at May 1, 2019 from. . https://www.who.int/medicines/access/controlled-substances/6_1_Ketamine_Update_Review.pdf.