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A Survey of Synthetic Cannabinoid Consumption by Current Cannabis Users

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Abstract

Background—Despite growing concern about the increased rates of synthetic cannabinoid (SC) use and their effects, only limited data are available that addresses these issues. This study assessed the extent of SC product use and reported effects among a cohort of adult marijuana and tobacco users.

Methods—A brief telephone interview was conducted with individuals who had given permission to be contacted for future research while screening for a cannabis/nicotine dependence medication development study (NCT01204723).

Results—Respondents (N= 42: 88% participation rate) were primarily young adults, male, racially diverse, and high school graduates. Nearly all currently smoked tobacco and cannabis, with 86% smoking cannabis on 5 or more days per week. Nearly all (91%) were familiar with SC products, half (50%) reported smoking SC products previously, and a substantial minority (24%) reported current use (i.e., past month). Despite a federal ban on five common SCs, which went into effect on March 1, 2011, a number of respondents reported continued SC product use. Common reasons reported for use included, but were not limited to, seeking a new “high” similar to that produced by marijuana and avoiding drug use detection via a positive urine screen. The primary side effects were trouble thinking clearly, headache, dry mouth, and anxiety. No significant differences were found between synthetic cannabinoid product users (ever or current) and non-users by demographics or other characteristics.

Conclusions—Among current marijuana and tobacco users, SC product consumption was common and persisted despite a Federal ban. The primary reasons for the use of SC-containing products seem to be to evade drug detection and to experience a marijuana-like high. (Support: DA027131)

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Keywords

Cannabinoid Receptor Agonists; Designer Drugs; Cannabinoids; Tetrahydrocannabinol; synthetic cannabinoid; cannabinoid K2; Spice; JWH-018

Introduction

During the past several years, concern has been raised about increasing use of synthetic cannabinoid-containing products. Typically the products have been marketed as herbal mixtures and sold via the Internet or at specialty shops under various brand names, such as “Spice” and “K2.” They contain non-psychoactive plant material sprayed with synthetic cannabinoid (SC) compounds (e.g., JWH-018, JWH-073, CP 47,497) that exert psychoactive effects when smoked (1). Initial evidence for rising prevalence of SC product use in the United States was indirect, such as through calls to poison control centers (2). In response to concerns about toxicity associated with the use of these compounds, the Drug Enforcement Agency (DEA) banned five common SCs on March 1, 2011 (3). Despite the federal ban, data from the national Monitoring the Future Survey indicate that product consumption has persisted. In 2012, 11 percent of high school seniors reported past year use of SC products; the prevalence of use was unchanged from that reported during the previous year (4). Furthermore, SC products remained the third most widely used illicit drug by high school seniors (alcohol and marijuana were the most used drugs, respectively (4)). Together, these data suggest that the 2011 federal ban had no effect on SC product use in young people.

Continued SC product use and consequences led to more recent control efforts, including passage of the Synthetic Drug Abuse Prevention Act in July 2012, which provides broad restriction of SCs, and a recent DEA ban on three more specific SCs in May 2013 (5). The prevalence impact of these efforts remains to be determined. However, SC products continue to be available, and the effectiveness of control efforts alone to decrease SC product availability and consumption appears limited (6). Public health concern persists about continued SC use and potential adverse effects.

Anecdotal reports from SC product users suggest that the psychoactive and other effects of SCs overlap with those of cannabis (1, 7-10). The SC-containing products are sometimes referred to as “synthetic marijuana” (2, 4). Despite potential similarities with cannabis, little is known about SC drug product effects relative to marijuana, and the pharmacologic properties of SCs are speculated to pose a potential increased risk of harm. In contrast to delta-9 tetrahydrocannabinol (THC), a partial agonist and primary psychoactive constituent of cannabis (11), some SCs exert full agonism at central nervous system cannabinoid type 1 receptors (CB1), and many are much more potent (1). In addition, substantial variation may exist in content and concentration of SC compounds in the many available SC products, even within the same brand or batch (1, 12). Such variability coupled with potential bioactivity at low doses may complicate titration and increase toxicity risk (1,12). An Internet survey found that negative side effects occurred at least intermittently in 40% SC product users (9). In addition, severe health consequences such as extreme agitation,

anxiety, psychosis, seizures, and renal failure were attributed to SC product use based on information from published case reports, emergency department admissions, and calls to poison control centers, (2, 10, 13-16).

The available evidence about SC product use patterns and potential consequences is limited. In an effort to learn more about the epidemiology and effects of SC product consumption, we conducted a phone survey that examined the prevalence and correlates of SC product consumption among a cohort of adult cannabis and tobacco users. In addition, we also sought to assess factors associated with SC product use and self-reported SC product effects.

Methods

Study Population

Participants were recruited from a sample of individuals who had called to participate in an inpatient residential laboratory study examining the utility of medications to treat cannabis and nicotine dependence. Potential participants had to be age 18 years or older, report regular cannabis use (at least 5 days in the past week) and tobacco use (>10 cigarettes/day), and be non-treatment seeking. However, neither inpatient laboratory criteria nor enrollment impacted eligibility for the current survey project. The only eligibility requirement was that potential laboratory participants had given permission to be contacted for future research projects. All individuals who gave such permission were eligible for the current study, regardless of current smoking status or other factors at the time of cross-sectional phone survey administration. One individual was excluded who exhibited inappropriate behavior toward staff when previously participating in the laboratory study.

Recruitment

Research staff created an Excel spreadsheet Call Log with eligible participant name and telephone number(s). The Call Log was stored on a password-protected computer only accessible to study personnel who were investigators on the laboratory study (and thus had permission to access personally identifiable information). Recruitment took place by phone from January 2011 – May 2011. After an attempt to contact a participant was made, the date of the call and outcome was recorded (e.g., left a voice message, phone is disconnected, or no answer). Study personnel left no more than three messages during a three-month period of time attempting to reach participants. After 3 months elapsed or 3 messages were left, the individual's name and telephone numbers were deleted from the file and s/he was deemed "unreachable." Once a participant was reached and outcome ascertained (verbal consent for study (Y/N), survey completed (Y/N)), the name/number was deleted from the record. Keeping de-identified rows in the Excel Call Log document enabled tracking of participation rate. After study recruitment was completed, all rows were de-identified. The Call Log was kept separately from survey data at all times to avoid identifiable linkage between the completed survey and respondent. The Call Log did not include any information about prior or current substance use.

Informed Consent

After contact was made with a potential participant, verbal informed consent took place by phone following a standard script. The participant was informed that survey completion was voluntary, confidential, that no personally identifiable information would be collected, and that no compensation would be provided for participation. Study personnel assessed participant understanding about the study by asking whether s/he understood the nature of the study, the consent process, and if there were any questions prior to survey administration. Following verbal consent for participation, the survey was administered. The University of Virginia Institutional Review Board for Health Sciences Research approved the study with a waiver of documentation of informed consent under 45CFR46.117(c).

Survey Instrument

The brief 2-page phone survey took approximately 5–10 minutes to administer. Items included questions about demographics, current substance use (tobacco, alcohol, marijuana, and other drugs) in addition to “Spice/K2” product use, the latter of which was used broadly during survey administration to refer to herbal SC-containing products. Specific questions quantified recent marijuana and SC product consumption. The survey also inquired about 1) subjective effects of SC products, 2) presence of irritability during marijuana and SC product abstinence as an indicator of withdrawal (17, 18), 3) adverse effects mentioned in calls to national poison control centers and case reports (2, 19–21), 4) possible reasons for SC product usage (8), and 5) where SC products were obtained. The survey included the Severity of Dependence Scale (SDS), a brief 4-question instrument to screen for DSM-IV dependence (22) on cannabis (23). In addition, SDS instrument questions were adapted to screen for SC product dependence. Data were collected without personally identifiable information. Completed surveys were stored in a locked file cabinet in a private office with data entered into Excel/SPSS on a password-protected computer.

Data Analysis

Descriptive statistics examined respondent characteristics, drug use patterns, and drug effects. To identify factors associated with SC consumption, a Chi-square/Fischer's Exact Test was used for categorical variables and *t* test for continuous variables. Analyses were performed with SPSS 19.0 (SPSS, Inc., Chicago, IL).

Results

Of 48 potential participants reached by study investigators, 42 (88%) agreed to complete the survey. As depicted in Table 1, the sample was comprised primarily of young adult males who were ethnically diverse, high school educated, and underemployed. Nearly all (95%) were daily tobacco users. Approximately two thirds reported current, past month alcohol use, and half screened positive for risky per occasion alcohol consumption using a single item screening question (24), reporting alcohol consumption above recommended cut off levels (>4 drinks for men or > 3 drinks for women) at least once in the past year (25). Past 30-day illicit substance use (non-cannabinoid) was reported by 21% of respondents, primarily cocaine (19%).

Cannabis Use History

Forty-one individuals (98%) reported current, past month cannabis use. Most were regular users, with 86% smoking cannabis on 5 or more days per week. Thirty-one (74%) reported irritability after a day or more of cannabis abstinence, one of the most common symptoms of cannabis withdrawal (18). A majority (52%) screened positive for DSM-IV dependence (22) on cannabis scoring 4 or more on the Severity of Dependence Scale (23).

Synthetic Cannabinoid Product Use

The 38 (91%) respondents familiar with SC products learned about them through a friend (95%), the Internet (18%), or at a store selling the products (13%). SC use details are provided in Table 2. Twenty-one (50%) smoked SC products previously with 10 (24%) reporting past month use. The median age of first use was 23 years and ranged from 16 to 44 years (mean $\pm$ SD, 26 $\pm$ 8 years). In contrast to cannabis, SC product use was less frequent, yet nearly a quarter who had ever tried the products reported current use 3 or more days per week. The median amount spent on SC products per week was \$17.50 (range 0 - \$40). Of 27 surveyed after Federal SC ban on five SCs was implemented 3/1/11, 22% smoked SC products after ban enactment. No significant differences existed between SC product users (ever or current) and non-users by demographics or other characteristics.

Respondents who had previously smoked SC products reported obtaining them from a friend (76%), convenience store (57%), gas station (43%), drug dealer (19%), smoke/head shop (5%), and/or the Internet (5%). Methods of use included smoking a blunt (76%), joint (33%), bong (19%), pipe (19%), or using a vaporizer (14%). Reasons for use reported in Table 2 included primarily seeking a new high (67%), followed by avoiding a positive drug test (57%), because a friend was using the products (52%), they could not get marijuana (48%), or because of a similar marijuana high (33%). Four (19%) individuals, all of whom reported irritability with a day or more of marijuana abstinence, reported use of SC products to decrease irritability when lacking marijuana.

Synthetic Cannabinoid Adverse Effects

Reported adverse effects are listed in Table 3, including: trouble thinking clearly (38%), headache (24%), dry mouth (19%), anxiety (14%), palpitations (14%), diaphoresis (14%), panic attack (10%), cough (5%) and fatigue (5%). Unlike other studies, no participants reported irritability, paranoia, depressed mood, nausea, or tolerance with SC product use. Only 1/10 (10%) with current SC product use screened positive for a syndrome of DSM-IV dependence on the products using an adapted version of the SDS.

Discussion

Synthetic cannabinoid product consumption was common with half of respondents reporting prior SC product use. Nearly a quarter reported using the drug in the past month, including among those surveyed after Federal synthetic cannabinoid ban enactment March 1, 2011. To our knowledge, these are the first prevalence data to be reported in adults. The high prevalence of use raises concern given potential adverse effects associated with SC use. Widespread national use despite the initial federal ban was also found by the Monitoring the

Future Survey, in which 11% of 12th graders reported past year SC product use in 2011 and 2012 (4). Continued SC product use following the initial ban illustrates the regulatory challenges of restricting SC product availability and consumption (6).

Several factors appear to contribute to the high prevalence of SC use in the current participants. They smoked cannabis on a near-daily basis and half screened positive for DSM cannabis dependence. These factors may have contributed to participants' greater inclination to initiate and then continue smoking SC products. Although no significant cannabis-related factors were associated with SC product use, most participants sought a novel high and half reported SC product use when unable to obtain marijuana. SC product substitution for cannabis may relate to overlapping psychopharmacology; both SCs and delta-9 THC exert cannabimimetic effects at central nervous system cannabinoid type 1 (CB1) receptors (1, 11). Experienced users report that SC products elicit similar subjective effects as cannabis (8-10). In addition, approximately 20% smoked SC products to alleviate irritability associated with cannabis abstinence. SC product mitigation of cannabis withdrawal could indicate cross-tolerance between SCs and delta-9 THC, the later of which has been shown to alleviate cannabis withdrawal in human laboratory research (17). Given the pharmacological specificity of CB1 agonism for cannabis withdrawal relief, our findings provide *in vivo* suggestion of SC bioactivity via CB1 receptor agonism in humans, which has also been suggested in other anecdotal cases (10). However, controlled human laboratory studies remain needed to more precisely compare the psychopharmacologic properties of SC compounds, delta-9 THC, and cannabis.

In addition to cannabimimetic effects, over half reported smoking SC products to avoid positive urine drug testing. Similar rationale for SC product use has been reported among other populations in the U.S. (19) and Europe (1). The SCs are not detected by routine urine drug tests identifying metabolites of delta-9 THC, the principal psychoactive component of cannabis. Assays for SCs are being developed and becoming commercially available. However, routine SC testing may not be readily available at many laboratories, and broad screening implementation could be cost prohibitive. SC product usage to evade drug-testing detection is potentially occurring in any situation where regular drug use monitoring is implemented, and thus might be anticipated by the individual undergoing testing (e.g., substance use treatment programs, criminal justice settings, or school-based mandatory urine drug testing programs).

The finding that SC products are used for dual purposes as a cannabis substitute and for drug testing evasion has implications regarding clinical practice and public policy. Clinicians treating patients with regular cannabis use or a cannabis use disorder should consider direct inquiry about SC product use and confirmatory SC testing if ordering urine drug tests. From a policy perspective, cannabis prohibition indirectly could be moving some individuals toward SC product use, such as among those seeking a cannabis high but wanting to evade urine drug detection. Although not specifically related to SC consumption, Monitoring the Future Survey data during 1998 to 2011 indicate that some high school students may have transitioned from cannabis to other illicit drugs based on promulgation of random student drug testing (26). The authors posited that the transition to non-cannabis illicit drugs might have been driven by student awareness about greater detectability of cannabis due to persistent

THC metabolites, as well as a desire to avoid substance use recognition during urine drug testing (26). The findings illustrate the need to continually re-evaluate the risk-benefit ratio of drug policy. In our attempt to monitor and detect illicit drug use, we need to be mindful of potential unintended consequences, such as encouraging use of lesser-known and possibly dangerous drugs, including the SC products.

Adverse effects were common among SC product-using respondents. Side effects included trouble thinking clearly, headache, dry mouth and anxiety, similar to other survey projects (8, 9). One respondent screened positive for DSM-IV dependence on SC products. Screening was conducted with the SDS (23), which has not been validated for SC products and should be considered exploratory. However, other cases of SC product dependence are reported (9, 27). Lastly, although no individuals reported paranoia, such effects are reported in other surveys (8) and there are numerous cases of psychosis, which may be of particular concern in those with biologic vulnerability (28, 29). Extensive use of cannabis among the study participants may have led to cannabinoid tolerance that protected them from the most severe negative effects. However, controlled data are needed for confirmation.

The current study has several limitations. The survey design precludes confirmation of SC compound exposure in the “Spice/K2” products consumed by respondents, limiting conclusions about SC effects. In addition, product use estimates and subjective effects may be limited by recall bias and concomitant use of other substances. The study recruited primarily regular cannabis users from central Virginia, limiting ability to generalize the findings to other populations and regions. In addition, survey items did not include items on effects experienced with marijuana, limiting assessment of comparative effects with SC products. Sample size limitation potentially precludes detection of factors associated with SC product consumption.

Conclusion

Overall, the study extends the anecdotal literature on self-reported SC consumption, effects, and reasons for use. The study population consisted primarily of young adults who regularly smoked cannabis and tobacco. Half had previously tried SC products and 25% were current users of such products, the highest current prevalence yet reported. Many used SC products following a Federal ban, indicating the challenges of regulatory efforts alone to decrease consumption and mitigate potential harm. Cannabis is the most widely used illicit drug in the world (30), and individuals will continue to seek a cannabis-like high. Despite adverse effects, SC products appear to serve as a sufficient marijuana substitute especially when marijuana is unavailable or there is a desire to evade urine drug detection. Although SCs may produce cannabis-like subjective effects and alleviate cannabis withdrawal, carefully controlled studies remain needed to characterize the psychopharmacologic and other health effects of SC product consumption. SC product use trends and correlates require further characterization as well. Such studies are urgently needed to guide clinical practice and public health policy, as well as inform the general public.

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Table 1
Demographic and Clinical Characteristics of Respondents (N=42)

Characteristic	
Age, mean years $\pm$ SD (range)	28.9 $\pm$ 8.5 (18-45)
Sex, male, n (%)	34 (81)
Race/Ethnicity, n (%)	
White	20 (48)
Black	19 (45)
Hispanic	2 (5)
Asian	1 (2)
Education	
Did not complete high school, n (%)	12 (29)
Completed high school, n (%)	18 (42)
Any college classes, n (%)	12 (29)
Employment, n (%)	
Unemployed	23 (55)
Part-time	11 (26)
Full-time	8 (19)
Current tobacco use, n (%)	40 (95)
Cigarettes/day, mean cig/d $\pm$ SD (n=40)	13 $\pm$ 6
Current alcohol use, n (%)	27 (64)
Past year risky per occasion alcohol consumption ^a , n (%)	22 (52)
Current illicit substance use (non-cannabinoid), n (%)	9 (21)
Cocaine	8 (19.0)
Salvia	2 (4.8)
MDMA	1 (2.4)
Cannabinoid Use History	
Current cannabis use, n (%)	41 (98)
Cannabis use pattern	
Daily	25 (60)
5-6 days/week	11 (26)
3-4 days/week	4 (10)
1-2 days/week	1 (2)
None	1 (2)
Irritable or moody with cannabis abstinence, n (%)	31 (74)
Screen positive ^b for cannabis dependence, n (%)	22 (52)
Synthetic cannabinoids, ever smoked, n (%)	21 (50)
Current (past month) synthetic cannabinoid use, n (%)	10 (24)

^a Risky alcohol consumption defined as one or more time in the past year: >5 drinks/occasion (men) or >4 drinks per drinking occasion (women) (25)

^b SDS for cannabis scored as screen positive with 4 or more (23)

Table 2
Synthetic Cannabinoid Product Use (N=21)

Use pattern by current users (n=10), n (%)	
Daily	1
5-6 days/week	0
3-4 days/week	4
1-2 days/week	0
1-3 days/month	5
Amount spent per week by current users (n=10)	
Mean	\$16.00 (SD 13.1)
Median	\$17.50
Range	\$0 - 40
Age of first use, median years (range)	23 (16-44)
Reasons for use, n (%):	
Try new high	14 (67)
Avoid positive drug test	12 (57)
Friend using it	11 (52)
Couldn't get MJ	10 (48)
Easy to obtain	10 (48)
Cheaper than MJ	8 (38)
Similar MJ high	7 (33)
Decrease irritability if no cannabis	4 (19)
Other: "accidental"	1 (4)

Table 3
Consequences of with Synthetic Cannabinoid Product Use (n=21)

Adverse effect	n (%)
Trouble thinking clearly	8 (38)
Headache	5 (24)
Dry mouth	4 (19)
Anxiety	3 (14)
Palpitations	3 (14)
Diaphoresis	3 (14)
Panic attack	2 (10)
Cough	1 (5)
Fatigue	1 (5)
Screen positive for SC dependence ^a	1 (5)

^aScreen adapted from the Severity of Dependence Scale (SDS)(23)