Frequency of Synthetic Cannabinoid Use and Its Relationship with Socio-Demographic Characteristics and Treatment Outcomes in Alcohol- and Substance-Dependent Inpatients: A retrospective study

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ABSTRACT:
Frequency of synthetic cannabinoid use and its relationship with socio-demographic characteristics and treatment outcomes in alcohol- and substance-dependent inpatients: a retrospective study

Objective: The recent emergence of Synthetic Cannabinoids (SCs) has become a serious public health problem. Here we aimed to analyze the frequency of SC use and its relationship with sociodemographic characteristics and treatment outcomes in alcohol- and substance-dependent inpatients retrospectively.

Methods: We retrospectively analyzed medical records of 323 inpatients that were treated at the alcohol and substance dependence treatment center between January 2012 and December 2013. The data were extracted from patient records.

Results: The mean age of SC users was lower than for patients without a history of SC use. The mean duration of education was shorter for SC users. Age at first drug use of SC users was lower, numbers of hospitalizations were lower and duration of substance use was shorter in SC users compared with the other substance user groups. The rate of legal issues was higher in the SC-use group. The rate of lapse and the rate of dropout was higher in patients with SC use than in other substance users (for all p< 0.05). Age, age at first substance use, duration of use (years) and criminal records were predicted as determining variables for SC use in inpatients.

Conclusions: In conclusion, the socio-demographic characteristics can be included as predictive factors for SC use.

Keywords: synthetic cannabinoids, frequency, treatment, outcome

INTRODUCTION
In recent years, novel psychoactive substances (also named legal highs, designer drugs, and herbal highs) have become easily available and prominent. Often misunderstood as being legal or safer alternatives to illicit drugs, these substances have been sold via the Internet and in coffee shops under various names (e.g., Spice in Europe, K2 in United States and Bonsai or Jamaica in Turkey). The recent emergence of synthetic cannabinoids (SCs) has become a serious public health problem.

Although SCs bind to the cannabinoid receptors (as cannabis does), they are well known to be much...
more potent than cannabis. Despite similarities in structure to cannabis, SC compounds include other chemicals that have different physiological effects

While Δ9-tetrahydrocannabinol (THC), the main psychoactive component of cannabis, acts as a partial agonist for both cannabinoid receptors, CB1 and CB2, SCs act as full agonists for both receptors.

According to the available data from case reports, toxicology centers, and clinical follow-up, using SCs can result in various side effects including nausea, vomiting, hypertension, hallucinations, tachycardia, seizures, renal disturbances, and cognitive deficits. Compared to cannabis, SCs are more likely to cause serious clinical adversities and toxicity. Although the duration and severity of unfavorable effects may depend on the SC type and method of use, even a single ingestion of some SCs may cause a withdrawal effect

There is as yet only limited information about SCs in the literature, and according to Papanti et al., most of the available data concerning SC use have been limited to retrospective toxicity surveys, case reports/case series, human laboratory studies assessing potential acute toxicological effects of SCs, and interviews/surveys focusing on self-reported harm/unwanted effects identified in SC users. In 2011, research conducted among 852 college students in the United States found that 8% of the participants had used SCs at least once. Most of these users were younger male students. In a group of 168 people who reported using SC at least once in their lifetime, 37% of the participants met the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV TR) criteria for substance abuse and 12% met criteria for substance dependence.

Here we aimed to analyze retrospectively the frequency of SC use and its relationship with sociodemographic characteristics and treatment outcomes among inpatients who met the DSM-IV TR criteria for alcohol and substance dependence.

METHODS

We retrospectively analyzed medical records of inpatients that had been treated at the alcohol and substance dependence treatment center of a specialized psychiatry inpatient clinic in Istanbul between January 2012 and December 2013. Medical records of 403 inpatients were evaluated; 78 patients were excluded due to lack of sufficient data or the presence of another Axis I psychiatric disorder. All participants were diagnosed by two separate psychiatrists as having substance use disorder (SUD), based on DSM-IV TR. The data extracted from the patient records included sociodemographic data such as gender (male/female), age, marital status, duration of education (years), age at first substance use, duration of substance use (years), type of substances used, number of hospitalizations, presence of SC use, Axis II comorbidity, time to lapse (days), time to relapse (days), presence of criminal records, family history of any drug abuse, any mental disorders, and rate of dropout. The study was approved by the Ethics Committee of Uskudar University on March 26, 2014. In this study, lapse is defined as first substance use after treatment, relapse is determined as a return to previous pattern of substance use. Relapse and lapse were assessed by semi-structured face-to-face or phone interviews with the patients or with a family member of the patient.

Statistical Analysis

Statistical analyses were performed using SPSS 16 (SPSS Inc., Chicago, IL, USA) for Windows. Categorical variables in the study were compared by means of chi-square statistics. One-way ANOVA was used for the comparison of the groups for continuous variables. Values were stated as median with 25%-75% values and mean ± standard deviation (SD). Descriptive statistics were also calculated as frequency or percent. Binary logistic regression analyses were conducted when SC use was the dependent variable, while age, gender, marital status, and duration of education were independent variables. Also, age of first substance use, duration of use, total number of hospitalization and legal issues were examined as independent variables while SC use was accepted as the dependent variable. For all analyses, p<0.05 was
regarded as statistically significant. For multivariate analysis, possible factors associated with prognosis of SC-dependence were entered into the logistic regression analysis to determine independent predictors of patients’ outcome. Hosmer-Lemeshow goodness-of-fit statistics were used to assess model fit. A 5% type-I error level was used to infer statistical significance.

RESULTS

In this study, medical records of 323 alcohol- and substance-dependent patients were included retrospectively. Of the 323 patients, 139 (43%) were determined as SC users. The mean age of SC users was lower than that of patients without a history of SC use (t=-10.06, p<0.001). Men had a greater tendency to use SCs than women (χ²= 6.51, p=0.01) and the mean duration of education was shorter for SC users than other substance users (t=-3.853, p<0.001). The socio-demographic data of all patients is presented in Table 1. The relation of SC use with the diagnosis is presented in Table 2. The presence of Axis-II comorbidity in patients with and without SC use is presented in Table 3. Age at first drug use of SC users was lower (t=-3.95,
p<0.001), numbers of hospitalization were lower (t=-2.54, p=0.01) and duration of substance use was shorter (t=-4.31, p<0.001) compared with the other substance-user groups. The rate of legal issues was higher in the SC-use group ($\chi^2=50.07$, p<0.001). The rate of lapse ($\chi^2=5.073$, p=0.02) and the rate of dropout were higher in patients with SC use than in other substance users ($\chi^2=8.56$, p<0.001). The clinical features and their level of significance in the prognosis of treatment, both in SC users and other substance users, are presented in Table 4.

When age, gender, marital status and duration of education were independent variables, younger age discriminated SC users from other substance users (Table 5). Risk of using SCs considering sociodemographic variables in multivariate logistic regression analyses

### Table 5: Risk of using SCs considering sociodemographic variables in multivariate logistic regression analyses

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>B</th>
<th>S.E.</th>
<th>Wald</th>
<th>df</th>
<th>p</th>
<th>Odds Ratio</th>
<th>95% C.I.for Exp (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.137</td>
<td>0.022</td>
<td>37.952</td>
<td>1</td>
<td>&lt;0.001*</td>
<td>1.146</td>
<td>(1.098-1.197)</td>
</tr>
<tr>
<td>Gender (male vs female)</td>
<td>-1.191</td>
<td>0.524</td>
<td>5.168</td>
<td>-1.191</td>
<td>0.023</td>
<td>0.304</td>
<td>(0.109-0.849)</td>
</tr>
<tr>
<td>Marital status (separated vs others)</td>
<td>0.067</td>
<td>0.251</td>
<td>0.072</td>
<td>1</td>
<td>0.789</td>
<td>1.07</td>
<td>(0.654-1.749)</td>
</tr>
<tr>
<td>Duration of education (years)</td>
<td>0.137</td>
<td>0.054</td>
<td>6.475</td>
<td>1</td>
<td>0.031</td>
<td>1.147</td>
<td>(1.032-1.274)</td>
</tr>
</tbody>
</table>

*Statistically significant

Risk of using SCs considering clinical characteristics in multivariate logistic regression analyses

### Table 6: Risk of using SCs considering clinical characteristics in multivariate logistic regression analyses

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>B</th>
<th>S.E.</th>
<th>Wald</th>
<th>df</th>
<th>p</th>
<th>Odds Ratio</th>
<th>95% C.I.for Exp (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at first substance use</td>
<td>0.127</td>
<td>0.035</td>
<td>13.406</td>
<td>1</td>
<td>&lt;0.001*</td>
<td>1.135</td>
<td>(1.061-1.215)</td>
</tr>
<tr>
<td>Duration of use (years)</td>
<td>0.076</td>
<td>0.018</td>
<td>5.168</td>
<td>1</td>
<td>&lt;0.001*</td>
<td>1.079</td>
<td>(1.041-1.118)</td>
</tr>
<tr>
<td>Total number of hospitalizations</td>
<td>0.252</td>
<td>0.1</td>
<td>6.927</td>
<td>1</td>
<td>0.008*</td>
<td>1.3</td>
<td>(1.069-1.580)</td>
</tr>
<tr>
<td>Legal issues (major crime vs others)</td>
<td>-0.62</td>
<td>0.148</td>
<td>17.468</td>
<td>1</td>
<td>&lt;0.001*</td>
<td>0.538</td>
<td>(0.402-0.719)</td>
</tr>
</tbody>
</table>

*Statistically significant
regression analyses is shown in Table 5. When age of first substance use, duration of substance usage, total number of hospitalizations and legal issues were independent variables; lower age at first drug use, shorter duration of substance use and high legal issues of SC users discriminated these from other substance users (Table 6). Risk of using SCs considering clinical characteristics in multivariate logistic regression analyses is shown in Table 6.

**DISCUSSION**

Although few data about SC use are available, this phenomenon has already become a public health problem. To date, most of the available data focusing on SC use have been limited to toxicology reports, identifying the chemical constituents of commercial products, and reviews or case reports about individuals who have been admitted to hospitals following adverse effects\textsuperscript{12-14}, whereas frequency studies have been mostly population-based and carried out online, with variable findings\textsuperscript{15}.

To our knowledge, no study has yet evaluated the relationship between frequency of SC use, socio-demographic data and treatment progress among inpatients with alcohol and substance dependence in Turkey, and there are only few studies available taking an approach similar to the one used in this present study. In research carried out in 2014 by Bonara et al., 150 of 396 inpatients with substance use disorders reported SC use at least once in their lifetime. In our study, among the 323 patient records examined, 139 reported SC use together with their preferred substance; which is in line with previous findings\textsuperscript{16}. In terms of gender variation, we found that men are more likely to use SCs than women, which is consistent with the literature\textsuperscript{5}. Moreover, it is well known that substance addiction and abuse are generally more frequent in men than in women. Thus, the gender findings reported here are believed not to be specific to SCs.

According to our study, participants using SCs are younger than other substance users and age of first substance use is lower in SC users than in other substance users. These findings are found to be consistent with the literature\textsuperscript{17}. More frequent use of SCs at younger ages may be associated with higher risk-taking behaviors in adolescence. The misperception that SCs are natural and less harmful and the fact that they are easily available and cheap and believed to be undetectable by toxicology screening makes SCs an appealing choice for substance users, especially to those who are on probation. This is supported by our finding that 33.8% of SC-using patients were on probation at the time of hospital referral, whereas this value was 6.5% for other substance users.

In terms of sociodemographic evaluation, 74.8% of participants using SCs were single or widowed. Moreover, we found that the proportion of unemployed or irregular workers were higher among participants using SCs than among participants with other substance use. Low socioeconomic and sociocultural status is known to be related to substance addiction. This finding is not surprising, given that teenagers and young adults without occupation and short education periods are more subjected to street culture. This exposure can therefore be considered a risk factor for teenagers making use of ‘popular’ narcotic/psychostimulant substances. As a consequence, SC use has been emergent in Turkey since 2009, and SCs are now very frequently encountered in this population. In addition, SC use may cause more common intoxication symptoms, more intense withdrawal and craving symptoms, might result in greater functional impairment, and is more likely to have a negative impact on education and employment\textsuperscript{9}. Depending on similar causes, patients using SCs are at risk to apply for treatment sooner. In our study, we also observed that SCs users seek treatment sooner than other substance users.

Regarding the range of diagnoses, only 1% of hospitalized patients with a diagnosis of alcohol use disorder was found to take SCs with alcohol. Various studies have shown that the frequency of other substance use is greater among those with substance use disorder rather than with alcohol use disorder\textsuperscript{18,19}. However, it should be noted that few data are available about SC and alcohol use
concordance. In addition, in a study by Bonara et al., patients tended to report the use of SCs together with heroin, inhalants, methadone, amphetamine, ecstasy, cannabis, and hallucinogens, but not concurrent with alcohol, benzodiazepines, barbiturates, or PCP. Despite these data, patients' onset age for alcohol use, sociocultural and socioeconomic status, accompanying SC use, and the impacts on treatment results remain uncertain and require further investigation. Having been able to conduct only a retrospective survey, no observation of clinical qualities, scaling of substance use severity, or scanning of accompanying psychological illnesses could be made. In addition, very few female patients were included in the study, thus limiting the generalizability of our data; our study is one of only a limited number of studies to have been conducted in this area of Turkey. It provides significant data about SCs, one of the most preferred substances among young people in recent years, which have been relatively understudied in Turkey.

Future prospective studies evaluating the severity of SC use and accompanying psychological complaints and medical conditions will be necessary.

In conclusion, mean age, onset age of substance use, duration of use, and presence of legal problems can be included as risk factors for SC use and can therefore indicate the potential usefulness of preventive mental health in substance use disorder patients.

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