Original article / *Araştırma*

Differences in sociodemographic characteristics, clinical features and serum liver function tests of male cannabis and synthetic cannabinoid users

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ABSTRACT

Objective: *Synthetic cannabinoid (SC) use has recently become a growing substance abuse problem, with serious harmful clinical effects. Young males, especially cannabis (C) users, are at great risk of SC use. The aim of this study is to determine sociodemographic characteristics, clinical features and serum liver function tests of SC users and compare with those of C users.* ***Methods:*** *Out of 118 SC users applied to outpatient clinic of Ankara Numune Training and Research Hospital Alcohol and Substance Addiction Treatment Center, 74 males included in this cross-sectional study. Patients with a concurrent use of any medication or substance other than C/SCs or patients with any physical illness which could affect serum liver function tests were excluded. 44.6% (n=33) of 74 patients were only SC users at least for last three months and 55.4% (n=41) were combined C and SC (C&SC) users. SC users were compared with 34 age and BMI-matched only C using males.* ***Results:*** *Rates of being single and divorced; rates of living with friends and alone were found to be higher in SC users. Adverse effects and withdrawal sypmtoms were found to be similar in C users and SC users. According to serum liver function test results, levels of gama-glutamil transpeptidase, alkaline phosphatase, total/direct bilirubin, albumin, prothrombin time and international normalized ratio were similar. Serum aspartate aminotransferase levels (31.2±22.0 IU/L and 41.5±21.5 IU/L respectively, p=0.026) and serum alanine aminotransferase levels (28.4±18.9 IU/L and 44.3±25.9 IU/L respectively, p=0.015) differed between C users and C&SC users. Results in this study revealed that increased serum levels of aminotransferases were especially associated with combined use of C and SCs.* ***Conclusions:*** *C abuse seems to be a precursor of SCs abuse, and risk of starting SCs use could be bigger for C users, who live alone or with friends, whereas living together with a family could be preventative. Combined use of C and SCs seem to increase the risk of hepatocellular injury compared to either C or SCs alone.* ***Anatolian Journal of Psychiatry 2017; 18(6):543-551)***

Keywords: *cannabis, synthetic cannabinoid, serum liver function tests*

Kannabis ve sentetik kannabinoid kullanan erkeklerde sosyodemografik özellikler, klinik özellikler ve serum karaciğer işlev testleri

ÖZET

Amaç: *Sentetik kannabinoidler (SK), ciddi zararlı klinik etkileriyle, önemli bir madde kullanım sorunu haline gelmiş-*

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tir. Özellikle kannabis (K) kullanan genç erkekler, SK kullanma riskine sahiptir. Bu çalışmanın amacı SK kullanıcılarının sosyodemografik özellikleri, klinik özellikleri ve serum karaciğer işlev testlerinin araştırılması ve bu verilerin K kullanıcılarınınkilerle karşılaştırılmasıdır. ***Yöntem:*** *Ankara Numune Eğitim ve Araştırma Hastanesi AMATEM Polikliniği'nde değerlendirilen 118 SK kullanıcısı arasından 74 erkek hastanın katıldığı kesitsel bir çalışmadır. K ve SK dışında madde veya ilaç kullanımı olan ve serum karaciğer işlev testlerini etkileyebilecek herhangi bir fiziksel hastalığı olan hastalar çalışma dışı tutulmuştur. Yetmiş dört hastanın %44.6'sı (s=33) son üç aydır yalnız SK kullanmaktayken, %55.4'ü (s=41) K ve SK aynı anda kullanmaktaydı. Kontrol grubunu yaş ve beden kitle indeksi açısından eşleştirilmiş 34 yalnız K kullanıcısı erkek oluşturdu.* ***Bulgular:*** *K kullanıcılarında eş-çocukla, anne-babayla birlikte yaşama oranı SK kullanıcılarından daha yüksek, SK kullanıcılarında ise arkadaşlarıyla yaşama ve yalnız yaşama oranı K kullanıcılarından daha yüksek saptandı. Advers etkiler ve kesilme belirtileri K ve SK kullanıcılarında benzerdi. Serum karaciğer işlev testleri karşılaştırıldığında gama-glutamil transpeptidaz, alkalin fosfataz, total/ direkt bilirubin, albumin, protrombin zamanı ve INR (International Normalized Ratio) düzeyleri benzerdi. Kannabis kullanıcıları ile K ve SK kullanıcıları arasında serum aspartat aminotransferaz düzeyleri (sırasıyla 31.2±22.0 IU/L ve 41.5±21.5 IU/L, p=0.026) ve serum alanin aminotransferaz düzeyleri (sırasıyla 28.4±18.9 IU/L and 44.3±25.9 IU/L, p=0.015) anlamlı olarak farklı saptandı. Çalışmamızın sonuçları serum aminotransferaz düzeylerindeki artışın özellikle kombine K ile SK kullanıcılarında olduğunu gösterdi.* ***Sonuçlar:*** *K kullanımı SK kullanımı için bir öncü olabilir ve arkadaşlarıyla veya yalnız yaşayan K kullanıcıları için SK kullanımı riski daha fazlayken, aileyle yaşama koruyucu bir etken olabilir. K ev SK kombine kullanımının hepatoselüler hasara yol açma riski, K veya SK tek başına kullanımından daha yüksek görünmektedir.* ***(Anadolu Psikiyatri Derg 2017; 18(6):543-551)***

Anahtar sözcükler: *Kannabis, sentetik kannabinoid, serum karaciğer işlev testleri*

INTRODUCTION

Cannabis (C), Δ-tetrahydrocannabinol, with a history of abuse since old civilisations, is still the most prevalent illicit substance in the world.[1,2] The World Health Organization estimating in 2013 that 181.8 million people aged 15–64 years used C for nonmedical purposes.[3] On the other hand, the medical use of C products to treat disease or improve symptoms remains debated, even if the benefits and risks of such medications have been investigated in a number of clinical trials on multiple sclerosis, pain, neurodegenerative disorders, and appetite suppression.[3]

Synthetic cannabinoids (SCs) were first created in the 1980s as laboratory research ligands for studying human endocannabinoid receptor systems. Synthetic cannabinoid (SC) containing products supplied by illicit manufacturers were then marketed as herbal incense.[4,5] And the vast explosion of SCs aims to actually create compounds that will be used abusively, to avoid legal restrictions, and to make large profits for underground laboratories.[3] SC users are frequently C users and may experience psychotropic effects such as euphoria and alteration in mood and sensorium similar to C users.[6] The largest group of users is males in their 20s who participate in polydrug use, but prevalence of SCs abuse is yet unclear.[3,7]

SCs have full agonistic effect on both central nervous system cannabinoid type 1 (CB_1) and type 2 (CB_2) receptors, whereas C is a partial agonist of these receptors.[5,8] As a result, SCs potentially pose a greater risk to users' health than natural forms of C.[9,10] Abuse of SCs has been shown to produce serious adverse health effects, including but not limited to hyperactive delirium, psychotic episodes, acute kidney injury, seizures, stroke, myocardial infarctions, and even occasional deaths.[5,11,12] In addition to adverse effects, withdrawal symptoms such as agitation, irritability, anxiety, mood swings, nausea, loss of appetite, sweating and headache were reported by SC abusers.[6,13]

Relationship between C use and hepatotoxicity, including a range from asymptomatic derangement of liver function tests to progression of fibrosis and steatosis, was shown in the literature;[14-17] but there is limited data about the relationship between SC use and hepatotoxicity.[18]

Although SC abuse has recently become a rapidly growing problem, damages of SCs on human health are not as clear as C and studies on use of SCs in Turkey are rare. The aim of this study is to determine sociodemographic characteristics, clinical features and serum liver function tests of SC users and compare with those of C users.

METHODS

Participants

From a total of 118 SC using patients who were examined in the outpatient clinic of Alcohol and Substance Addiction Treatment Center (ASATC) of Ankara Numune Training and Research Hospital between May and November 2014, 74 male users participated in the study. 22 patients refused to participate. 19 patients who did not meet the inclusion criteria were excluded. The

only 3 female SC users who met the inclusion criteria were excluded owing to possible effects of gender difference. The study group consisted of 74 SC using males, who were divided into two groups: 44.6% (n=33) used only SCs at least for the last three months (mean age±standard deviation 24.7±6.8; mean body mass index (BMI): 21.3±2.3) and 55.4% (n=41) used both C and SCs (C&SC) (mean age: 25.7±7.6; mean BMI: 21.6±2.5). Thirty-four age and BMI-matched only C users who applied to ASATC in the same six-month period (mean age: 25.4±6.3; mean BMI: 21.4±2.3) were also included in the study (Table 1).

Table 1. Sociodemographic attributes of cannabis and synthetic cannabinoids users

Variables	CU (n=34) n	%	SCU (n=33) n	%	C&SCU (n=41) n	%	p
Age (Mean±SD)	25.4±6.3		24.7±6.8		25.7±7.6		0.831*
Body mass index	21.6±2.3		21.3±2.3		21.4±2.5		0.820*
Nicotine smoking (pack year)	7.3±5.7		6.7±6.4		8.1±8.0		0.936*
Education							0.869**
Primary school	20	58.8	16	48.5	22	53.7	
High sschool	10	29.4	14	42.4	15	36.6	
College/university	4	11.8	3	9.1	4	9.8	
Occupation							0.355**
Employee	25	73.5	19	57.6	22	53.7	
Unemployed	3	8.8	8	24.2	9	22.0	
Student	6	17.6	6	18.2	10	24.4	
Monthly income (Turkish Liras)							0.943**
Less than 1000	14	41.2	15	45.5	20	48.8	
Between 1000 and 2000	15	44.1	12	36.4	15	36.6	
More than 2000	5	14.7	6	18.2	6	14.6	
Marital status							0.015**
Single	21	61.8	25	75.8	30	73.2	
Married	12	35.3	3	9.1	4	9.8	
Divorced	1	2.9	5	5.2	7	17.1	
Living style							0.002**
With parent(s)	19	55.9	14	42.4	17	41.5	
With spouse (and child)	12	35.3	3	9.1	4	9.8	
With friend(s)	2	5.9	10	30.3	11	26.8	
Alone	1	2.9	6	18.2	9	22.0	
Living region							0.501**
Urban	29	85.3	31	93.9	37	90.2	
Rural	5	14.7	2	6.1	4	9.8	

CU: Cannabis users, SCU: Synthetic cannabinoid users, C&SCU: Both cannabis & synthetic cannabinoid
** Kruskal Wallis test, ** Pearson Chi-Square test.*

All patients were interviewed by two independent clinicians. The subjects were selected based on the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5).[19] According to the DSM-5 criteria, substance use disorder in participants were diagnosed as mild or moderate, and none of them had severe C use disorder. To be included in the study, the participants had to meet the following criteria: (a) aged 18 or above, (b) had BMI between 18.5 and 30, (c) continuous consumption of SCs and/or C for at least last three months. The exclusion criteria were as follows: (a) concurrent use of any medication or substance other than C/SCs, (b) history of intravenous substance abuse, (c) history of alcohol use disorder according to DSM-5 criteria; (d) comorbid DSM-5 axis 1 psychiatric disorder (e.g., psychotic disorder, affective disorder); (e) mental retardation; and (f) physical illness (e.g., endocrinological disorders, hepatic/renal diseases, infectious diseases). All participants recruited in this study provided written informed consent. The study was approved by the ethical committee of Ankara Numune Training and Research Hospital.

Measures

After psychiatric examination, urine samples and

fasting venous blood samples of participants were obtained in following morning. Blood samples were taken for complete blood count, serum electrolytes, viral hepatitis tests and liver function tests including serum levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), gama-glutamil transpeptidase (GGT), alkaline phosphatase (AP), total and direct bilirubin, albumin, prothrombin time (PT) and international normalized ratio (INR). PT and INR were evaluated by coagulometric method and all other liver function tests were evaluated by spectrophotometric method.
Levels of cocaine metabolite, opioid, amphetamines, benzodiazepines, C and SCs were checked in urine samples. Cocaine metabolite, opioid, amphetamines, benzodiazepines and C were evaluated by Cedia Method and SCs were evaluated by N-Pentanoic Acid Method. In urinanalysis of SCs, Randox kits were used; JWH-018 and OH-12 were evaluated. 15 ng/mL was the cut-off limit for SCs and 50ng/mL for C.

Amount and duration of C use and SCs use were stated by the patients. Most of the patients stated the amount of C and SCs in weekly use such as '…grams twice a week'; so weekly amounts were calculated for each patient and used in the study.

Statistics

All statistical analyses were performed with IBM SPSS ver. 23.0. Shapiro Wilk test was used as normality test. Continuous variables were compared using Mann-Whitney U test and Kruskal Wallis test when the data were not normally distributed. Dunn's test was used as multiple comparison test. Categorical variables were compared using Pearson's chi-squared test and Fisher-Freeman-Halton test. Correlations between variables were tested using Spearman correlation coefficients. A p-value <0.05 was considered as significant.

RESULTS

Sociodemographic characteristics including education, occupation, monthly income, living region (urban/rural), nicotine smoking (pack year) and tattooing rates were all similar among three groups. According to marital status and living style characteristics, only C users showed significant differences from SC users (both only SC and C&SC users) (Table 1).

Marital status differed significantly between C users, SC users and C&SC users (p=0.015). According to pairwise comprisons, C users were significantly different from others. There is no significant difference between SC users and C&SC users. Ratio of married users (35.3%) was higher, ratios of single users (61.8%) and divorced users (2.9%) were lower in C users compared with SC using groups. C users were more likely to live together with parent(s) (55.9%) and with a spouse (35.3%) compared with SC using groups (p=0.002) (Table 1).

According to urine analysis results, mean C amount in urine was 166.3±80.7 ng/mL for only C users and 156.1±87.5 ng/mL for C&SC users; whereas it was 18.3±17.9 ng/mL (<50 ng/mL) for only SC users (p<0.001). Mean SCs amount in urine was 19.5±7.5 ng/mL for only SC users and 20.1±7.7 ng/mL for C&SC users; whereas it was 0.7±0.9 ng/mL (<15 ng/mL) for only C users (p<0.001). Urine analysis results revealed no significant difference between C amounts of only C users and C&SC users; and no significant difference between SCs amounts of only SC users and C&SC users.

There was no SC using patient without a history of C abuse. Age at first C use was similar in all three groups (Table 2). Mean ages at first SC use were similar in both only SC users and C&SC users groups. Mean duration of SC use was 5.8±3.3 months for only SC users, whereas 8.8(±6.2) months for C&SC users (p=0.036). Mean amount of SC use was 5.1±2.5 grams/ week for only SC users, whereas 6.9±2.8 grams/ week for C&SC users (p=0.003). When we com pared weekly amount and durations of C use history, no significant difference appeared be tween groups of C users and SC users (Table 2).

Adverse effects reported by the patients were loss of motivation, distractibility, reduced sexual capacity, thirst/hunger, coughing, tachycardia, hallucination, irritability/nervousness, dizziness/ vertigo, drowsiness/lethargy, skin lesions/ itch ing, anxiety, delusion and hair loss. Withdrawal symptoms reported by the patients were irritability/nervousness, anxiety, insomnia, restlessness, loss of appetite, depressed mood, headache, nightmares, sweating, nausea/vomiting and fever. Reported adverse effects and withdrawal symptoms were similar in C&SC users.

Serum GGT, AP, total and direct bilirubin, albumin, PT and INR levels were similar in all three groups (Table 3). Serum AST levels differed significantly between C users and C&SC users (31.2±22.0 IU/L and 41.5±21.5 IU/L respectively, p=0.026) (Figure 1). Serum ALT levels also differed significantly between C users and C&SC

Table 2. Cannabis and synthetic cannabinoid use characteristics of participants

	CU (n=34) Mean±SD	SCU (n=33) Mean±SD	C&SCU (n=41) Mean±SD	p
Age at first C use (years)	21.8±5.0	21.9±5.7	22.5±6.3	0.569*
Age at first SC use (years)	-	24.3±6.7	25.1±7.7	0.870**
Duration between first C use and first SC use (months)	-	27.3±24.7	25.9±23.9	0.309**
Duration of C use (months)	30.5±31.8	32.9±25.1 (till 2 months ago)	31.9±29.4	0.731*
Weekly amount of C use (g)	8.1±4.8	8.9±4.9	8.7±5.2	0.745*
Duration of SC use (months)	-	5.8±3.3	8.8±6.2	0.036**
Weekly amount of SC use (g)	-	5.1±2.5	6.9±2.8	0.003**

*CU: Cannabis users; SCU: Synthetic cannabinoid users; C&SCU: Both cannabis & synthetic cannabinoid users; g: Grams, * Kruskal Wallis test, ** Mann-Whitney U test.*

Table 3. Serum liver function tests of participants

Laboratory results	CU (n=34) Mean±SD	SCU (n=33) Mean±SD	C&SCU (n=41) Mean±SD	p
AST (<37 IU/L)	31.2±22.0	35.2±24.1	41.5±21.5	0.030*
ALT (<45 IU/L)	28.4±18.9	35.7±23.7	44.3±25.9	0.019*
GGT (<55 U/L)	24.6±13.1	27.7±16.1	30.6±18.3	0.408*
AP (<136 U/L)	73.4±30.0	75.3±36.8	82.8±38.5	0.566*
Total bilirubin (0.3-1.2 mg/dL)	0.87±0.27	0.88±0.24	0.91±0.33	0.497*
Direct bilirubin (0-0.2 mg/dL)	0.14±0.11	0.13±0.11	0.16±0.14	0.911*
Albumin (3.5-5.2 g/dL)	4.20±0.6	4.20±0.5	4.10±0.7	0.894*
PT (10-12.7 second)	11.1±0.8	11.2±0.9	11.3±1.0	0.847*
INR (0.9-1.17)	1.04±0.08	1.06±0.09	1.07±0.09	0.099*

*CU: Cannabis users; SCU: Synthetic cannabinoid users; C&SCU: Both cannabis & synthetic cannabinoid users; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase, GGT: Gama-glutamil transpeptidase; AP:Alkaline phosphatase; PT: Prothrombin time, INR:International normalized ratio; * Kruskal Wallis test.*

users (28.4±18.9 IU/L and 44.3±25.9 IU/L respectively, p=0.015) (Figure 2). There was no significant difference between only SC users and other two groups in terms of serum AST and ALT levels (Table 3). Using Spearman correlation coefficients, a weak positive correlation was determined between duration of SC use and serum ALT levels (r=0.230, p=0.049), but no correlation was found between other parameters.

DISCUSSION

This study results revealed that abuse of SCs was associated with existing C abuse, and living without family could increase the risk of SCs use. Besides, combined use of C&SCs could cause hepatocellular injury, which was demonstrated by significant increase in serum aminotransferase levels in this study. Addition of SC abuse to C abuse seems to become not only a more widespread problem, but also increase more serious health problems.

C is one the most commonly used illicit drugs among young people.[20] C use is associated with a variety of potential health risks and harms, including: memory and psychomotor impairment, accidental injury, mental health disorders, dependence, bronchial or pulmonary illnesses, and other illicit drug use.[21] This study is focused on SCs use as the other illcit drug use, and supports the association of SCs use with the C use.

SCs cause changes in mood, perception, thinking, memory and attention as well as changes in neurological, cardiovascular and gastrointestinal function. These effects are similar to those caused by natural C, but they vary

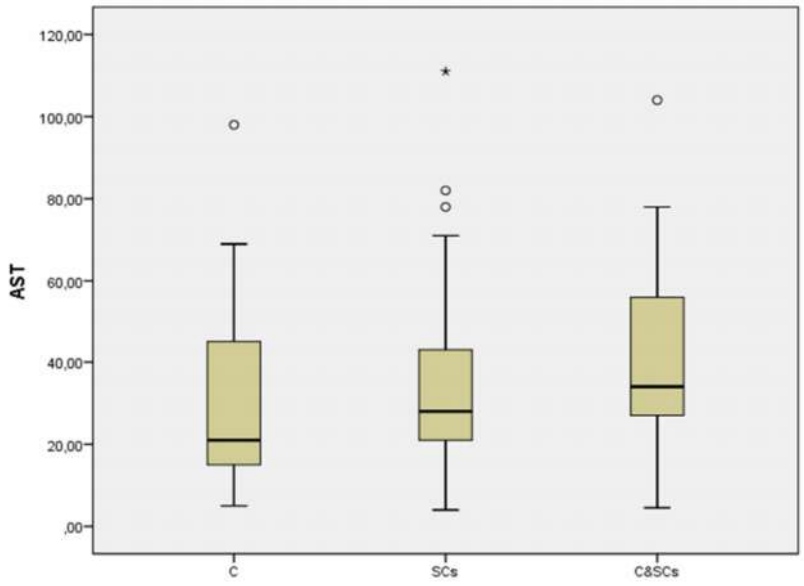

Figure 1. Serum aspartate aminotransferase (AST) levels in participant groups

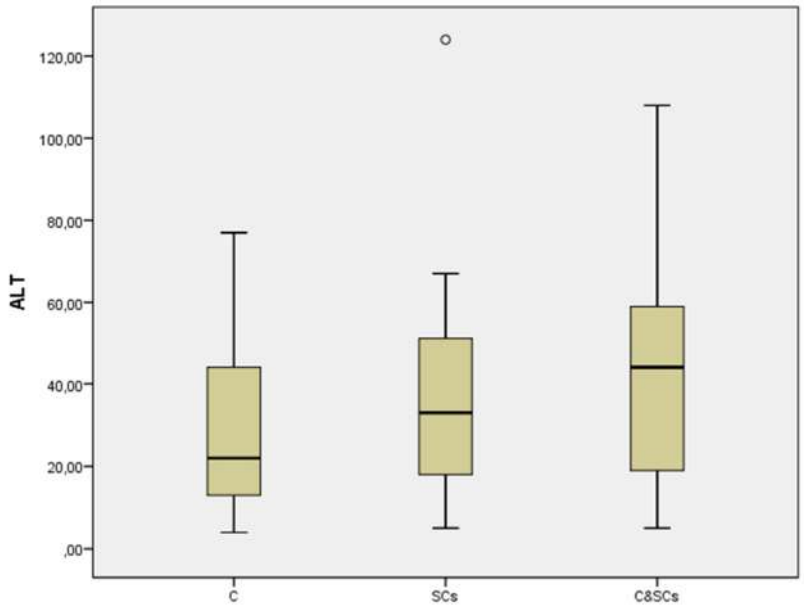

Figure 2. Serum alanine aminotransferase (ALT) levels in participant groups

in both spectrum and intensity.[18,22] Users are primarily male adolescents and young adults and almost all recent SC users have a history of natural C use.[23] All of SC using patients in this study were C users before, similarly.

Winstock et al.[10] reported that median age of C users and SC users were 27 and 25 respectively; and 70.6% and 76.5% were males respectively in a large global sample of drug abusers, who needed emergency medical treatment in 2015. Median age of 316 SC users was found to be 27 in an Australian research in 2013.[24] 77% of SC users were men and 96% were C abusers before using SCs.[23] A Turkish research about clinical features of 158 SC users in 2014 revealed that 94.9% of SC users were men, 67.1% were single, 86% were previous C abusers. Mean age of SC users was 26.1±7.1, mean amount of SCs

used was 2.7±2.2 grams/day and duration of SC use was 17.2±12 months in the same research.[25] The sample group of this study has a lesser mean duration and a lesser amount of use. Along similar lines with other illicit drugs, amount of SC use could increase as time passes by. Out of 118 SCs abusers examined in ASATC during the study duration, only three (2.5%) of them were women. Data about the reasons of gender difference is very limited. Almost half (48.6%) of 74 participants (n=36) mentioned that they started to use SCs when they were soldiers. This could be one of the reasons of male predominance at SCs use, but probable reasons of this gender difference deserves to be searched. Both duration and amount of SCs use reported in the study are less (Table 2). As a limitation of the study, these data were declared by the patients themselves and could be less than real duration and amount of use.

This research revealed that both marital status and living style were significant sociodemographic characteristics considering use of SCs. Being single or divorced, and living alone or with friend(s) seem to increase risk for SC use. Whereas living with parent(s) or being married could be preventative. Living in a family provides social support which is an important protective factor against substance use as reported in the literature.[26,27] Being married, living with parent(s) could limit negative attitudes of an individual by increasing responsibilities and/or guilt feelings. Living with family, independently of living with spouse or parent(s), also means not being alone and feeling more secure. Being single/divorced and living alone could enhance feeling of loneliness and/or getting bored. It could be stated as intimate relations are especially important for substance abusers. Nevertheless, living with friend(s) seem to have opposite effect of living with family. Living with friend(s) could enable, even encourage, risky behaviors. Having substance using friend(s) is reported to be a risk factor for beginning substance abuse in the literature.[28,29] Probable correlations of these sociodemographic characteristics with SC use deserve to be investigated further.

All of the participants reported to have a psychological need for using C/SCs and most of them complained of adverse effects and/or withdrawal symptoms. Most prevalent adverse effects were loss of motivation, distractibility and reduced sexual capacity; and most prevalant withdrawal symptoms were irritability/nervousness, anxiety and insomnia, all of which were reported by more than half. No significant difference was found between groups of C users, SC users and C&SC users, basing on the rates of both adverse effects and withdrawal symptoms.

In the research of Forrester evaluating 305 adolescent SCs exposures, the most frequently reported adverse clinical effects were tachycardia, drowsiness/lethargy, agitation/irritability, vomiting, hallucinations/delusions, nausea, confusion, hypertension, chest pain and dizziness/vertigo.[30] These reported adverse effects are mostly similar to the adverse effects reported by the patients of this study. Gunderson et al. conducted a systematic review of published reports on clinical effects of SCs, highlighting potential toxicity such as acute anxiety and psychosis.[2] Adverse clinical effects and withdrawal symptoms reported by C users and SC users were similar in this study. Nevertheless, this similarity does not mean C and SCs have similar risks, regarding that clinical cases with serious adverse effects and deaths related with SCs reported in the literature.[4,5,9,10,12,18] The relative risk associated with the use of SCs was found to be 30 times higher than that associated with C; and significantly more symptoms were reported by respondents seeking treatment for SCs than for C.[10]

Although both Δ-tetrahydrocannabinol and SCs stimulate the same receptors (CB_1 and CB_2); studies have shown that SCs are associated with higher rates of toxicity and hospital admissions than natural C.[6] This is likely due to SCs being direct agonists of the cannabinoid receptors, whereas C is a partial agonist. Furthermore, the different chemical structures of SCs may interact in unpredictable ways to elicit previously unknown effects, also the commercial products may have unknown contaminants.[7]

SCs are extensively metabolized, but the knowledge about involved enzymes is limited.[31] All investigated SCs are metabolized in human liver microsomes and are predominantly excreted as metabolites in urine.[11,22] Among cytochrome P450 (CYP) enzymes, CYP3A4 was found to be the major CYP enzyme responsible for the oxidative metabolism of SCs; and CYP2C9, CYP2C19 and CYP1A2 seem to have contributions.[31-33] Besides, SCs and their basic molecules were shown to be capable of inhibiting CYP1A.[34]

Research of Borini et al.[14] on C use revealed that serum AST, ALT and AP levels were increased without any correlation with the amount or duration of marijuana consumption. A deleterious role of daily C use, was shown to demonstrate

clearly a rapid progression of fibrosis and steatosis, leading to a major severity in patients with chronic hepatitis C.[17] In serum liver function test results of this study, the only significant difference was that levels of serum aminotransferases were higher in C&SC users than only C users (Table 3, figures 1 and 2). Mean serum AST level was found 41.5±21.5 IU/L in C&SC group, which was the only liver function test result higher than the upper normal limit of 37 IU/L. Serum liver function test results in this study revealed that increased serum levels of aminotransferases were especially associated with combined use of C and SCs; and serum ALT level is positively correlated with the duration of SC use. Increase in serum levels of aminotransferases, indicating hepatocellular injury, is especially related with combined use of C and SCs.

CONCLUSION

C abuse seems to be a precursor of SC abuse, and most of SC abusers continue using both substances simultaneously, leading to increased risk of health problems. Combined use of C and SCs increases the risk of hepatocellular injury compared to either C or SCs alone. Risk of starting SCs use could be bigger for single or divorced C users, whereas living together with a family could be preventative. Sociodemographic risk factors for SC use and their potential to cause hepatocellular injury deserve to be investigated further with larger sample sizes. As a conclusion, SC abuse causes hepatotoxicity especially in C users and C users should also be tackled from this aspect by healthcare professionals.

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