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Research Article

Assessment of Patients Admitted to Emergency Rooms with Synthetic Cannabinoid Intoxication: A Prospective Study

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Abstract

Intoxicants are important causes of morbidity and mortality in emergency rooms. Patients presented due to synthetic cannabinoid (SC) use have become increasingly more common among intoxicated patients. Thus, we intend to contribute to the literature by screening UR-144, XLR-11, AB-PINACA, AB-FUNICA, ADB-FUNICA and their major metabolites through the enzyme-immunoassay technique and providing diagnostic test results in patients with a history of SC use. We aim to contribute to the literature by presenting data regarding patients with SC use, which has become a significant public health issue and may be associated with dose-dependent fatal complications as these patients represent a challenging group due to their complaints upon presentation, tendency to mask the substance used, and diverse symptoms. This is a prospective, cross-sectional study and includes 28 patients with a history of SC use who have been admitted intoxicated to the emergency rooms of the Health Sciences University, Kayseri Research and Training Hospital between January 2017 and January 2018 and who have accepted participating in the study. We have evaluated demographic data, symptoms, clinical findings, biochemical markers, Glasgow Coma Scale (GCS) scores, poisoning severity scores (PSS), and the results from the employed diagnostic tests. The symptoms and presented findings have been found to include anxiety in 17 (60.7%), vomiting in 17 (60.7%), altered states of consciousness in 12 (42.9%), speech disorders in 11 (39.3%), loss of consciousness in 10 (35.7%), convulsions in eight (28.6%), chest pains in eight (28.6%), hallucinations in seven (25.0%), palpitations in five (17.9%), and nystagmuses in three patients (10.7%). Twenty-four patients (86%) were discharged following treatment in the emergency room. Three patients (10.7%) were admitted to the intensive care unit. In 6 patients (21.4%), SCs had been used in combination with alcohol. Three SCs (10.7%) were detected in initial urinalyses while 15 SCs (53.6%) were detected in screening tests. The study revealed 4 major findings. Firstly, patients suspected of consuming new-generation SCs are frequently admitted to emergency rooms. Secondly, patients with suspected SC intake are often found to use SCs in combination with another psychoactive substance. Thirdly, urinary drug testing used for rapid emergency-room diagnosis is misleading. Finally, clinicians should be aware of the various symptoms and clinical findings based on the combined use of SCs with other psychoactive substances.

Keywords

Synthetic cannabinoids • Emergency room • Intoxication • Cannabinoid metabolites • Laboratory • Enzyme immunoassay

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Synthetic cannabinoids (SCs) were first developed for therapeutic purposes without psychotropic effects in the 1960s (Adams & Martin, 1996). All rights resreved. Objectives: To determine the laboratory based drug abuse prevalence of persons who have illicit and/or addictive substance test requests instead of alcohol in a city in Middle Anatolia in Turkey. Methods: Laboratory information system's data of urine samples, submitted to Biochemistry Laboratory from various clinics, between January 2014 and June 2016 were retrospectively investigated. In comprehension of illicit drug use amphetamin, cannabis, opiate, cocaine and benzodiazepin group tests were screened with Cloned Enzyme Donor Immunoassay method. Positivity-negativity rates according to years, age-gender distribution and number of multiple substance usage were investigated. Results: Totally 79873 illicit drugs were screened in 19763 urine samples. 18080 males (% 91.5. SCs are psychoactive substances that are inexpensive, readily available, and commonly abused worldwide. These agents are known as *Bonzai* or *Jamaika* in Turkey, or *Spice* in Europe and *K2* in the USA (Ozer, Ceri, & Evren, 2016). These substances have emerged as a result of the search for legal alternatives to classical, controlled narcotic/sedative substances; they are marketed as legal/herbal highs and have become an important problem worldwide (Adams & Martin, 1996). These substances are collectively termed as psychoactive substances (PASs). Legal oversight is challenging due to the increasing number of PAS types and the difficulty in detecting these produced substances as they are very similar to each other in chemical structure that use simple steps for synthesis. SCs are the most commonly used PASs, whose frequency and diversity are increasing.

Cannabinoid receptors are comprised of the complex endocannabinoid system, and two cannabinoid receptors, CB1 and CB2, have been identified so far. CB1 receptors are responsible for psychoactive effects such as elevated mood, anxiety, and panic responses (Ashton, Wright, McPartland, & Tyndall, 2008). CB2 receptors are predominantly expressed at the marginal zones of the spleen, tonsils, and immune cells, particularly in the macrophages, B lymphocytes, natural killer cells, monocytes, T lymphocytes, polymorphonuclear neutrophils, and astrocytes (Ashton et al., 2008). These receptors are thought to cause immunosuppression by inducing apoptosis and inhibiting proliferation as well as cytokine and chemokine production (Ashton et al., 2008).

Impaired perception, visual problems, hallucination, agitation, diminished motor coordination, dissociation, dizziness, and psychiatric changes such as paranoia or psychosis can be seen reported following SC use (Karakükcü et al., 2018). Cukurova University, Faculty of Medicine. All rights resreved. Objectives: To determine the laboratory based drug abuse prevalence of persons who have illicit and/or addictive substance test requests instead of alcohol in a city in Middle Anatolia in Turkey. Methods: Laboratory information system's data of urine samples, submitted to Biochemistry Laboratory from various clinics, between January 2014 and June 2016

were retrospectively investigated. In comprehension of illicit drug use amphetamin, cannabis, opiate, cocaine and benzodiazepin group tests were screened with Cloned Enzyme Donor Immunoassay method. Positivity-negativity rates according to years, age-gender distribution and number of multiple substance usage were investigated. Results: Totally 79873 illicit drugs were screened in 19763 urine samples. 18080 males (91.5%). In addition, withdrawal symptoms also occur in the case of usage stoppage. Seizures, hemodynamic alterations, electrolyte derangement, renal failure, respiratory depression, and cardiac arrest have been reported to possibly develop in individuals subjected to SCs (Liakoni et al., 2017; Rech, Donahey, Cappiello Dziedzic, Oh, & Greenhalgh, 2015). The literature has many reports of death attributed to SC use (Liakoni et al., 2017). Clinical features may vary considerably depending on type and amount of substance used. The patients often present perceptive impairments, sedation, anxiety, paranoia, hallucinations, psychosis, and seizures (Courts, Maskill, Gray, & Glue, 2016; Rech et al., 2015). Sweating, nausea, vomiting, chills, mydriasis, tachycardia, and hypertension can appear in physical examinations (Courts et al., 2016; Rech et al., 2015).

Determining the presence of SCs in laboratory evaluations is currently difficult as more and more generations of SCs are being produced. In recent years, second-and third-generation test kits have been developed to determine novel PASs (Odoardi, Romolo, & Strano-Rossi, 2016; Qian, Jia, Li, Liu, & Hua, 2017). Of these, second-generation UR-144 kits can detect XLR-11 and its major metabolites, whereas third-generation AB-PINACA can detect AB-FUNICA, ADB-FUBINACA, and their major metabolites through analytical methods (Lam et al., 2017).

The literature has limited numbers of studies on patient samples who have been presented to emergency rooms reporting adverse effects from SCs. This study plans to contribute to the diagnosis and treatment of such patients in Turkey and worldwide by reporting the results we have obtained using the standard immunoassay method from patients suspected of using SCs.

Method

This prospective cross-sectional study includes patients diagnosed under SC intoxication. The study has been approved by the local ethics committee. Clinical presentation, hemodynamic parameters, laboratory tests, clinical courses, and demographic characteristics have been recorded for all patients. The laboratory tests include complete blood counts (CBC), hepatic function tests (AST, ALT), blood urea nitrogen (BUN), creatinine (Cre) serum electrolytes (sodium, potassium, chlorine, calcium). During the emergency-room follow-ups, the time of recovery of consciousness (hour), psychiatric consultations ordered, admissions to ICU, and

outcomes have been assessed. The poisoning severity score (PSS, developed by Persson, Sjöberg, Haines, and de Garbino, 1998) was used to grade the severity of intoxication upon admittance. The study includes patients 16 years and older. Overall, 63 patients admitted to the ER with suspected SC use and who accepted participating were enrolled in the study (see Table 1). The patients with incomplete data (n = 7), patients admitted with traffic accident (n = 8), patients who did not accept participation (n = 4), and patients with inadequate sampling (n = 5) were excluded. Thus, the final study population includes 28 patients. The flow chart is shown in Figure 1. The PSS and GCS scores were estimated for all the included patients.

Table 1
Distribution of Patient Characteristics

Variables	*n* (%) or mean ± SD
Sex (Male : Female)	3:25 (10.7% : 89.3%)
Age (y)	27.35 ± 9.93
By ambulance	21 (75%)
By walk-in	7 (25%)
Poisoning severity score	
Minor	15 (53.6%)
Moderate	9 (32.1%)
Severe	4 (14.3%)
GCS	
14 or under	19 (67.9%)
15	9 (32.1%)
Vital signs	
SBP (mm Hg)	111.67 ± 9.26
DBP (mm Hg)	72.57 ± 8.06
Heart rate (beats/min)	89.46 ± 9.84
Temperature (°C)	36.4 ± 0.5
Respiratory rate (breaths/min)	23.2 ± 6.1
SATO2	95.39 ± 3.87
Number of addicts	17 (60.7%)
Combined intake with alcohol	6(21.4%)
Laboratory results	
Glucose mg/dL	119.80 ± 51.42
BUN mg/dL	13.70 ± 4.69
Creatinine mg/dL	0.96 ± 0.47
Na mmol/L	139.90 ± 2.88
K mmol/L	3.89 ± 0.38
Cl mmol/L	105.10 ± 2.92
AST (U/L)	28.90 ± 12.04
ALT (U/L)	28.90 ± 22.35
Ca mg/dL	9.18 ± 0.72
WBC (/mm3)	10.79 ± 5.19
pH	7.37 ± 0.21
Psychiatric consultation	15 (53.6%)
Time to recovery of consciousness	14.98 ± 15.31
Patients intubated and admitted to ICU	3 (10.7%)
Death	1 (3.6%)

The data are expressed as arithmetic means with standard deviations.
GCS: Glasgow Coma Score.

Abbreviations: Systolic blood pressure (SBP); diastolic blood pressure (DBP); aspartate aminotransferase(AST); alanine aminotransferase (ALT). white blood cells (WBCs). creatine kinase-MB fraction (CK-MB).Year (y). Hour (h).

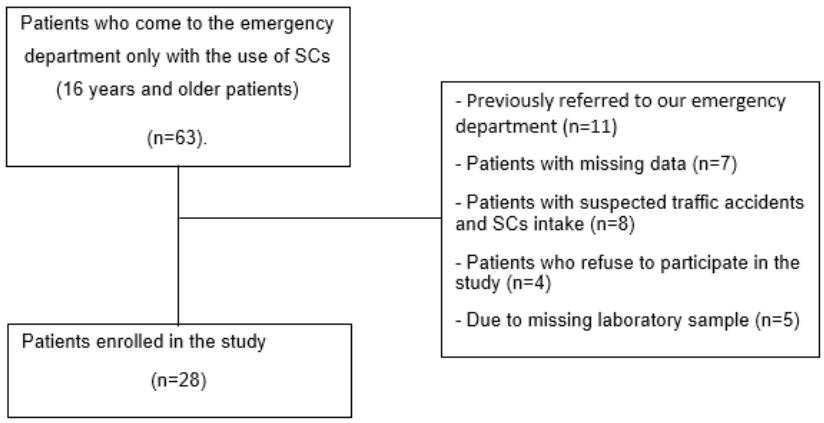

Figure 1. Flow chart of patients included and excluded from the study.

All cases in which a urine sample had been collected were seen in the ER and they were given informed consent. Urine samples were obtained under the surveillance of personnel and analyzed immediately in the laboratory. The temperature of urine samples was measured within 4 minutes after collection; those whose temperature was 32-37°C were accepted while the others were rejected and the sample collection repeated. Before analysis, the integrity of the urine specimens were tested; samples for further tests were determined based on pH values and the presence or absence of antioxidant substances. For all the patients who underwent urine drug testing (UDT), substances in the 5 panel drug test or those ordered from the 5 panel drug test and their metabolites were studied through an automated chemical analyzer using the Cloned Enzyme Donor Immunoassay (CEDIA; Microgenics Corporation, USA) and ThermoScientific (Indiko plus; Thermo Fisher Scientific, Finland) drug screening kits. CEDIA amphetamine/methamphetamine reactives detect MDA, MDMA (ecstasy), MDEA and its metabolites, cannabis, tetrahydrocannabinol and its metabolites, opiates, morphine, codeine, 6-monoacetylmorphine (6-MAM), cocaine and its metabolites, and benzoylecgonine, while benzodiazepine kits detect benzodiazepines and their metabolites. Values above the threshold concentration levels were defined as positive reactions while those the below threshold concentration levels were defined as negative reactions (threshold concentrations: 500 ng/ml for amphetamine, 50 ng/ml for cannabis, 300 ng/ml for opiate, 300 ng/ml for cocaine, and 50 ng/ml for benzodiazepine). All positive samples that were sent for screening and accepted in the laboratory with a toxic substance detected in the screening were divided into aliquots in 2 tubes and stored at -20°C for over a year. In case of exception and/or

clinical suspicion, the stored aliquot was used for confirmation analysis (CA). For CA, solid phase extraction was performed on the urine samples which were spiked by deuterium-labeled internal standards following alkaline hydrolysis. Afterward, confirmation analysis was performed at the Selective Ion Monitoring mode using the gas chromatography-mass spectrometry (GM-CS) technique. Results exceeding the limit of quantitation (LOQ) were considered positive.

Urinary Drug Screening Test

In this study, toxicological substances and analyte measurements in human urine were performed on patient samples according to cut-off levels through lateral flow chromatographic immunoassay.

Statistical Analysis

All data were analyzed using SPSS version 22.0 and MedCalc version 15. For descriptive statistics, quantitative variables are expressed as the mean ± standard deviation while numeric variables are expressed as counts and percentages (%).

Results

During the study period (January, 2017-January, 2018), 63 cases that had been admitted to the ER with suspected SC use were detected. Eleven patients who had previously been admitted to the ER (within the prior month) were excluded. Initially, 52 patients were enrolled in the study. However, the study was completed with 28 patients. The mean age in years is 27.35 ± 9.93 (range = 17 to 63). The mode of arrival to the ER was by walk-in for 7 patients (25%) and by ambulance for 21 patients (75%). Table 1 presents the patients' characteristics.

The poisoning severity score (PSS) was found to be minor in 15 (53.6%), moderate in nine (32.1%), and severe in four patients (14.3%). The GCS score was less than or equal to 14 for 19 patients (67.9%) and 15 for 9 patients (32.1%). The mean systolic pressure is 111.67 ± 9.26 mmHg, whereas the mean diastolic pressure is 72.57 ± 8.06 mmHg. The mean heart rate is 89.46 ± 9.84 bpm while the mean SO_2 is 89.46 ± 9.84%.

When retrospectively reviewing patients' files, 17 (60.7%) of the 28 patients were found to be drug-addicts, and SCs were found to have been used in combination with alcohol in six patients (21.4%). The lab results are as follows: mean glucose level = 119.80 ± 51.42; mean BUN value = 13.70 ± 4.69; mean creatinine level = 0.96 ± 0.47 mg/dL; mean WBC = 10.7 ± 95.19/mm^3; and pH = 7.37 ± 0.21. Psychiatric consultations were ordered for 15 patients (53.6%). Of these, three (10.7%) were admitted to the ICU while the remaining patients were discharged from the ER. One patient died in the ER (3.6%). Table 2 presents the results of the confirmatory analysis.

Table 2
Distribution of Narcotic and Stimulant Substances in Confirmation Analysis

Agents used for narcotic and stimulant features	***n***	**%**
Methamphetamine	6	21.4
Amphetamine	4	14.3
Quetiapine	4	14.3
Gabapentin	2	7.1
Diazepam	2	7.1
Ketamine	2	7.1
Citolapram	1	3.6
Sertraline	1	3.6
Morphine	1	3.6
Codeine	1	3.6
Risperidone	1	3.6
Fentanyl	1	3.6

Drugs with narcotic or stimulant effects including methamphetamine, amphetamine, quetiapine, gabapentin, citalopram, sertraline, codeine, diazepam, fentanyl, and ketamine were detected in confirmation analysis. Table 3 presents these drugs with narcotic or stimulant effects, as well as drugs with false-positive and false-negative results according to confirmation analysis.

Table 3
Drugs with False-Positive and False-Negative Results in Tests

Drugs with false-positive and false-negative results	***n***	**%**
Chlorpheniramine	3	10.7
Ketoprofen	2	7.1
Metformin	1	3.6
Colchicine	1	3.6
Ephedrine	1	3.6
Remitidin	1	3.6

The findings and symptoms when admitted to the ER include: anxiety in 17 (60.7%), vomiting in 17 (60.7%), altered states of consciousness in 12 (42.9%), speech disorders in 11 (39.3%), loss of consciousness in 10 (35.7%), convulsion in eight (28.6%), chest pains in eight (28.6%), hallucinations in seven (25.0%), palpitations in five (17.9%), and nystagmus in three patients (10.7%). Table 4 shows the complaints upon admittance.

Table 4
Complaints upon Admittance

Symptom	*n* (%)
Anxiety/Agitation	17 (60.7)
Vomiting	17 (60.7)
Altered consciousness	12 (42.9)
Speech disorder	11 (39.3)
Loss of consciousness	10 (35.7)
Convulsions	8 (28.6)
Chest pains	8 (28.6)
Hallucinations	7 (25.0)
Palpitations	5 (17.9)
Nystagmus	3 (10.7)

Cannabinoids were detected in three (10.7%), benzodiazepine in seven (25.0%), and amphetamines in six patients (21.4%) through routine UDT, while these were respectively detected in 15 (53.6%), two (7.1%), and 10 (35.7%) through confirmation analysis (see Table 5).

Table 5
Agents Testing Positive in both Urinary Drug Testing (UDT) and Confirmation Analysis

Variable	Urinary drug testing	Confirmation analysis
Cannabinoid	3 (10.7%)	15 (53.6%)
Benzodiazepine	7 (25%)	2 (7.1%)
Amphetamine	6 (21.4%)	10 (35.7%)
Other	6 (21.4%)	4 (14.3%)

Table 6 presents the GCS scores for patients in terms of SC detection. The GCS score was 15 for seven patients (32.1%) with SC use. Figure 2 presents the distribution of patients irrespective of SC use according to their GCS scores.

Table 6
Assessment of GCS and PSS in Patients in Terms of SC Detection based on Confirmation Analysis

	SC use		
	Positive (*n*)	Negative (*n*)	*n* (%)
PSS			
Minor	5	10	15 (53.6%)
Moderate	6	3	9 (32.1%)
Severe	2	2	4 (14.3%)
GCS			
10 points	1	0	1 (3.6%)
11 points	2	0	2 (7.1%)
12 points	0	1	1 (3.6%)
13 points	2	1	3 (10.7%)
14 points	6	6	12 (42.9%)
15 points	2	7	9 (32.1%)

Abbreviations: Glasgow Coma Score (GCS); Poisoning Severity Score (PSS).

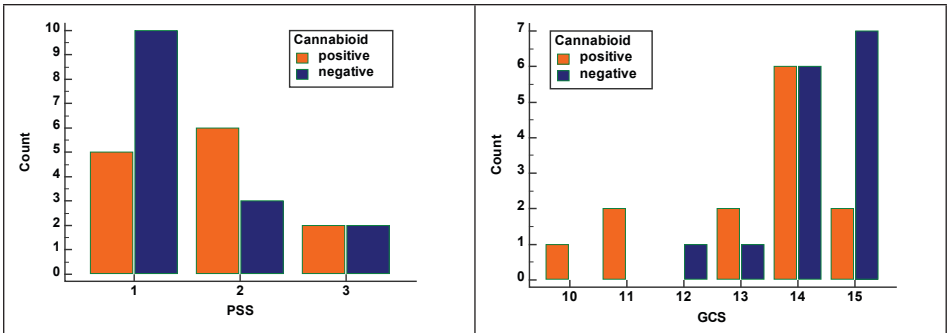

Figure 2A

Figure 2B

Figure 2. Distribution graphic of patients according to PSS (Figure 2A) and GCS (Figure 2B) scores according to positive/negative cannabinoid use irrespective of SC use.

Table 7 presents the PSS scores for patients in terms of cannabinoid detection. PSS scores have been calculated in accordance with the study of Persson et al. (1998). Figure 2A presents the distribution of patients according to PSS scores irrespective of SC use. In addition, Figure 2B presents a box plot graph for the presence or absence of SC use according to PSS and GCS scores based on the results from the confirmation analysis.

Table 7
Distribution of Multiple PAS Use According to Confirmation Analysis

Variable	***n* (%)**
Cannabinoid plus drugs with narcotic effect	6 (21.4)
Cannabinoid plus false-positive and false-negative agent	6 (21.4)
Cannabinoid plus amphetamine	7 (25.0)
Amphetamine plus non-cannabinoid narcotic drug	3 (10.7)
Other	6 (21.4)

Time to recovery of consciousness was calculated for all patients; the average time was found to be 14.98 ± 15.31 hours. Figure 3 presents the time to recovery of consciousness.

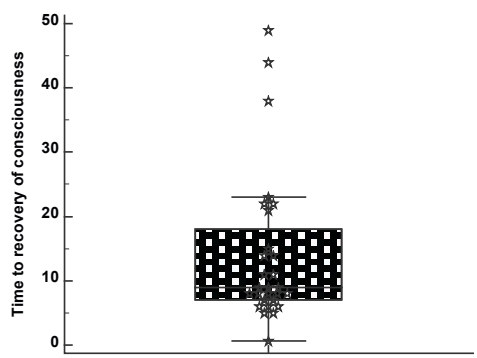

Figure 3. Box plot graph for time to recovery of consciousness.

Our study has found that six patients (21.4%) have used cannabinoids plus additional narcotics, while six patients (21.4%) had used cannabinoids plus a false-positive or false-negative drug, three patients (10.7%) had used cannabinoids plus amphetamine, and three patients (10.7%) had used a non-cannabinoid drug (Table 7).

Discussion

In Turkey and across the world, drug abuse remains an important health issue with increasing incidence among young adults (Castellanos & Gralnik, 2016). Its incidence isn't known precisely as SCs are partially prohibited in Turkey and teenagers tend to hide substance abuse. When compared to other narcotics, the potential complications and harms caused by SCs are unknown as the majority of the population believe SCs to be harmless agents of herbal origin (Castellanos & Gralnik, 2016). This study was conducted over patients admitted to a tertiary emergency room over the course of a year (January 2017 through January 2018). Our study is consistent with previous studies documenting the adverse effects of SC intoxication and reflecting the clinical conditions seen in SC intoxication (Springer, 2016). Barratt, Cakic, and Lenton's (2013) study reported the mean age for SC use to be 27 years in Australia and 77% of SC users to be male. Hoyte et al. (2012) reported the mean age for SC use to be 22.5 years and 74.3% of users to be male. Liakoni et al.'s (2017) study found the mean age for SC use to be 33 years (range = 16 to 74). Our study has found the majority of patients to be male (25 out of 28 [89.3%]) with a mean age of 27.35 ± 9.93 years and a median of 25 years (range = 17 to 63). A marked male preponderance exists in our study. SC users have generally been young male adults in several studies worldwide (Klein, Bangh, & Cole, 2017; Rech et al., 2015; Trecki, Gerona, & Schwartz, 2015; Zaurova, Hoffman, Vlahov, & Manini, 2016). SCs cannot be detected in routine urinary drug testing. SC use increases as younger adults are able to reach marijuana-like addiction through these inexpensive and readily available drugs (Johnson, Johnson, & Alfonzo, 2011). The American Association of Poison Control Centers (AAPCC) has reported the number of SC exposures to have increased from 53 in 2009 to 13,000 in 2011 (Barratt et al., 2013). In a study by Wood et al., the number of SC exposures was found to be 14 in 2009, 2,821 in 2011, and 6,255 in 2011. The authors suggest that the number of cases in 2012 is higher than that for 2011 (Wood, 2013). Our study has found SC use to have increased over time.

Synthetic cannabinoids account for psychoactive effects such as anxiety and panic reactions through the CB1 receptors where they exert a partial or complete agonist effect. Synthetic cannabinoids cause analgesia, decrease motor function, impair memory and time orientations, and influence visual and auditory perceptions through the CB2 receptors (Ashton et al., 2008). Patients presented with symptoms related to SC use may show varying clinical presentations in the ER. In the literature,

psychosis symptoms are the most commonly seen symptoms following SC use. In a study by Forrester et al., the most common symptoms were palpitations and chest pains (48.5%) followed by dizziness and lightheadedness (24.3%; Zaurova et al., 2016). Wiegand et al.'s (2012) study found that consultations had been ordered for 53% of the patients admitted to the ER for intoxication. Our study found agitation and anxiety symptoms to have been detected in 17 patients (60.7%). McKeever et al. (2015) found synthetic cannabinoid intoxication to cause myocardial infarction in 16-year-old patients. Riederer et al.'s (2016) study, conducted between 2010 and 2015, examined intoxication due to synthetic cannabinoids and show it to frequently have neuropsychiatric, cardiovascular, and renal effects.

The clinical variation in SC patients can be related to many factors, including the amount of substance intake, combined use with other psychoactive substances, its distinct chemical composition, individual variations in the effect of the chemicals used, and interactions with other legal drugs used. Admitted patients hiding their history after the onset of withdrawal symptoms and false-positive/false-negative results from urinary drug testing can explain the complexity in diagnosis and treatment. The patients usually are admitted with altered mental states including euphoria and anxiety, loss of consciousness, red eyes, and marked tachycardia, along with a lack of specific symptoms and findings (Rech et al., 2015; Trecki et al., 2015; Westin et al., 2015). The symptoms observed in our study are consistent with past studies in the literature. These findings should be suggested as acceptable as the screening test provides for the wide use of SCs, the legal process, and the unavailability of advanced tests or analysis methods as well as SC screening tests in all facilities.

When assessing standard laboratory data, borderline values are one of the major challenges in diagnosis. SCs and their metabolites cannot be detected in routine drug testing for cannabinoids (Gandhi et al., 2014; Hess, Schoeder, Pillaiyar, Madea, & Müller, 2016; Qian et al., 2017). Our study detected SCs in three patients (10.7%) using UDT and 15 patients (53.6%) using confirmation analysis. Amphetamines were detected in six patients (21.4%) using UDT and 10 patients (35.7%) through confirmation analysis. Despite these tests, non-SC substances were detected in the majority of patients. Gurdal et al.'s (2013) study detected JWH-018 (65.9%), JWH-081 (1%), JWH-250 (0.2%), and CP-47,497 (1%) as SCs. The marked increase in popularity of SCs has resulted in an increased number of patients admitted to ERs with severe adverse effects from SCs. Further studies with larger sample sizes are needed to elucidate the epidemiological pharmacology. Given the introduction of novel SCs into the market, choosing tests that are able to screen multiple SCs will provide significant advantages in clinics and ERs.

In a study on psychoactive substances, Helander, Bäckberg, Hultén, Al-Saffar, and Beck (2014) found the PSS score to be helpful in evaluating psychoactive substance

use. Our study has used PSS scores, which were found to be minor in 15 (53.6%), moderate in nine (32.1%), and severe in four patients (14.3%). PSS scores can be used upon SC cases being admitted. GCS scores are routinely used in ERs. In a case report by Adams et al. (2017), a GCS score of 13 was found in a patient with SC use (AMB-FUBINACA). The literature has suggested that altered states of consciousness are recovered from within 24 hours. Association with another substance or disease should be sought in patients with altered consciousness lasting beyond 24 hours. In our study, the time to recovery of consciousness was found as 14.98 ± 15.31 hours.

Currently, the immunoassay methods commonly used as drug screening tests provide effective evaluations due to their availability, simplicity, and ease of use in practice (Karakükcü et al., 2018) In addition, screening tests inherently have high sensitivity and low specificity. Thus, despite having a low likelihood, false-positive and less frequently false-negative results may be found in some tests or specimens. Drug screening tests are for preliminary analytical results (Karakükcü et al., 2018)in other words, these tests provide positive or negative results but not the quantity amount of a substance. The results can be available within 5-10 minutes. Alternative methods with high specificity should be used to confirm preliminary results in screening tests (Liakoni et al., 2017). Confirmatory analyses are second-line tests with diagnostic superiority; however, they are expensive and require trained staff. In this study, SC use based on positive or negative results were higher in confirmation analysis when compared to urinary drug testing. Our study shows cannabinoid plus amphetamine to be the most common of multiple substance use among patients, followed by SC plus an illicit drug (n = 6; 21.4%) and SC plus other drugs (n = 6; 21.4%). Our study has found amphetamine plus psychoactive substance in three patients (10.7%). Karakükcü et al.'s (2018) Study found similar results. In psychoactive substance users, the tendency to use or combine other substances leads to clinical variations in these patients. In our study, psychiatric consultations were ordered for 15 patients (53.6%). Psychiatric consultation should be ordered, particularly for those admitted with psychotic symptoms.

This study has certain limitations, including a limited sample size due to the tendency to hide SC use and decline providing a sample for testing. The patients generally avoid mentioning the type of psychoactive substance used even when they report psychoactive substance use. However, these challenges represent the clinical problems and challenges in ER treatments worldwide.

Conclusion

The study has revealed four major findings. Firstly, patients suspected of consuming new-generation SCs are frequently admitted to the emergency room. Secondly, patients suspected of SC intake are found to often use SCs in combination

with another psychoactive substance. Thirdly, urinary drug testing used for rapid diagnosis in emergency rooms is misleading. Finally, clinicians should be aware of variations in symptoms and clinical findings due to the combined use of SCs with several psychoactive substances.

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