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Effect of Laboratory Confirmation of Synthetic Cannabinoid Use on Emergency Department Management and Outcomes

Sentetik Kannabinoid Kullanımının Laboratuvar Tanısının Acil Servis Yönetimi ve Sonuçları Üzerindeki Etkisi

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Abstract

Background: Synthetic cannabinoids (SCs) are a structurally diverse class of synthetic substances frequently misused as recreational drugs. The aim of this study is to evaluate the impact of laboratory-confirmed SC use on the treatment process, length of stay in the emergency department (ED), and patient prognosis in individuals presenting to the ED with a reported history of SC use.

Materials and Methods: This prospective observational study included ED patients aged 18–75 years with self-reported synthetic cannabinoid use. All enrolled patients underwent routine laboratory testing, and synthetic cannabinoid screening was performed universally using urine samples analyzed via enzyme immunoassay. SC-positive and SC-negative patients were compared in terms of lab findings, treatment, ED stay, and prognosis.

Results: The study included 101 patients (95% male, mean age 25.8 years). Most presented with symptoms (55.4%) or for addiction treatment (44.6%), commonly reporting fatigue, nausea, agitation, and palpitations. SC was detected in 6.9% of urine samples. No significant lab differences were found between SC-positive and negative patients, except for slightly lower SpO_2 levels in SC-positives. ED stay duration and patient outcomes were similar across groups, with 97% discharged and 3% monitored in the ICU.

Conclusions: The laboratory diagnosis of synthetic cannabinoids in patients presenting to the ED did not significantly affect treatment outcomes, ED length of stay, or prognosis.

Keywords: Synthetic Cannabinoid, Emergency Medicine, Substance-Related Disorders, Diagnosis, Laboratory, Prognosis

ÖZ

Amaç: Sentetik kannabinoidler (SC'ler), yapısal olarak çeşitli sentetik maddelerden oluşan ve sıklıkla eğlence amaçlı kötüye kullanılan bir madde grubudur. Bu çalışmanın amacı, acil servise (AS) SC kullanımı öyküsüyle başvuran bireylerde, laboratuvarla doğrulanmış SC kullanımının tedavi süreci, acil serviste kalış süresi ve hasta prognozu üzerindeki etkisini değerlendirmektir.

Gereç ve Yöntem: Bu prospektif gözlemsel çalışmaya, SC kullanımı bildiren ve yaşları 18–75 arasında olan AS hastaları dahil edilmiştir. Çalışmaya katılan tüm hastalara rutin laboratuvar testleri ve enzim immünoassay ile analiz edilen idrar örneklerinden sentetik kannabinoid taraması yapılmış olup; SC-pozitif ve SC-negatif hastalar, laboratuvar bulguları, tedavi süreci, AS kalış süresi ve prognoz açısından karşılaştırılmıştır.

Bulgular: Çalışmaya 101 hasta dahil edilmiştir (hastaların %95'i erkek, yaş ortalaması 25,8 yıl). Hastaların çoğu semptom (%55,4) ya da bağımlılık tedavisi talebi (%44,6) ile başvurmuş; en sık bildirilen şikayetler yorgunluk, bulantı, ajitasyon ve çarpıntı olmuştur. İdrar örneklerinin %6,9'unda SC saptanmıştır. SC-pozitif ve negatif hastalar arasında laboratuvar parametrelerinde anlamlı fark bulunmazken, SC-pozitif grupta SpO_2 düzeyleri istatistiksel olarak daha düşük bulunmuştur. AS kalış süresi ve hasta prognozu gruplar arasında benzer olup; hastaların %97'si taburcu edilmiş, %3'ü yoğun bakım izlemi gerektirmiştir.

Sonuç: AS'e başvuran hastalarda sentetik kannabinoidlerin laboratuvar tanısının, tedavi sonuçları, AS kalış süresi veya prognoz üzerinde anlamlı bir etkisi bulunmamıştır.

Anahtar kelimeler: Sentetik Kannabinoid, Acil Tıp, Madde Bağımlılığı, Laboratuvar, Prognoz

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Highlights

- This study investigated the clinical significance of laboratory-confirmed synthetic cannabinoid (SC) use in the emergency department and found that only 6.9% of self-reported SC users had laboratory-confirmed positivity, highlighting limitations in current diagnostic testing.
- No significant differences in clinical management, emergency department length of stay, or outcomes were found between SC-positive and SC-negative patients.
- Results support symptom-based clinical decision-making over laboratory confirmation for SC intoxication management in emergency settings.

Introduction

Synthetic cannabinoids (SCs) are a structurally diverse group of novel psychoactive substances (NPS) designed to target the endocannabinoid system. These substances exhibit higher affinity for cannabinoid receptors (CBRs) compared to Δ9-tetrahydrocannabinol (Δ9-THC), the primary psychoactive compound in the cannabis plant (1, 2). As a result, they induce effects similar to those of Δ9-THC but are often more intense and shorter in duration (3).

The first SC, a synthetic version of Δ9-THC, was developed in 1964 by Gaoni and Mechoulam (4). Subsequent SCs were synthesized during research aimed at understanding the regulatory roles of the endocannabinoid system in critical biological processes, culminating in the discovery of CBRs in the 1980s (5).

SCs played a prominent role in the NPS market from 2009 to 2019, though the number of new SCs introduced decreased between 2014 and 2018 (6). Nonetheless, since 2008, a total of 209 different SCs have been identified in European Union member states, and together with synthetic cathinones, they accounted for approximately 60% of all NPS seizures in 2019 (7).

Hospital presentations of individuals using SCs are often due to life-threatening conditions, with acute complications frequently affecting the cardiovascular, central nervous, and respiratory systems (8, 9). Common symptoms leading to hospital visits include altered consciousness, agitation, seizures, hypertension, or hypotension. However, the rapidly evolving chemical structures of SCs present significant challenges in diagnosing and managing these cases. The complexity of such presentations in emergency departments necessitates prompt interventions and a multidisciplinary approach. Due to their high lipophilicity and rapid hepatic metabolism, synthetic cannabinoids exhibit short plasma half-lives, often between 1 to 6 hours, and are typically detectable in urine for no more than 72 hours after use, which complicates timely laboratory confirmation of exposure (10).

This study aims to investigate the impact of laboratory confirmation of synthetic cannabinoid (SC) use on treatment processes, length of stay in the emergency department, and prognosis in patients presenting with a history of SC use.

Material and Methods

Study design

This study was conducted in the Emergency Medicine and Toxicology Clinic of a Tertiary Care Training and Research Hospital. Patients aged 18–75 years who presented with self-reported use of synthetic cannabinoids (SCs) were included in the study. Sociodemographic characteristics of the participants were analyzed using a structured data collection form.

Laboratory evaluations, including complete blood cell count, biochemistry, coagulation tests, troponin levels, and blood gas analyses, were performed for all patients. Additionally, SC levels in urine and blood samples were analyzed. Patients under the age of 18 (n=5) and those who refused to participate in the study (n=7) were excluded. A total of 101 patients were included in the study. All patients gave and signed informed consent **(Figure 1).**

Patients were also asked to report the time elapsed since their last synthetic cannabinoid use.

SC levels were determined using the enzyme immunoassay method (Immunoanalytical K2 enzyme immunoassay) on an Olympus AU 400 device. This testing was conducted on urine samples from all 101 participants, regardless of presenting symptoms or clinical suspicion, ensuring a consistent diagnostic approach across the cohort. The assay was capable of detecting JWH-018, JWH-073, and AM-2201 metabolites with a positive threshold value of 20 ng/ml. Results were reported as either positive or negative based on this cutoff. Urine samples were sent to the laboratory immediately after collection for SC level analysis.

Statistical analysis

The statistical analysis of the data was performed using SPSS (Statistical Package for the Social Sciences) version 16 software. The normality of data distribution was assessed using Kolmogorov-Smirnov and Shapiro-Wilk tests. Descriptive statistics were presented as means and standard deviations.

For comparisons of mean differences between two groups, Student's t-test was used if parametric assumptions were met, while the Mann-Whitney U test was applied if these assumptions were not met. The chi-square test or Fisher's exact test (when appropriate) was used for categorical variables. The relationships between continuous variables were evaluated using Pearson's correlation test. A p-value of <0.05 was considered statistically significant.

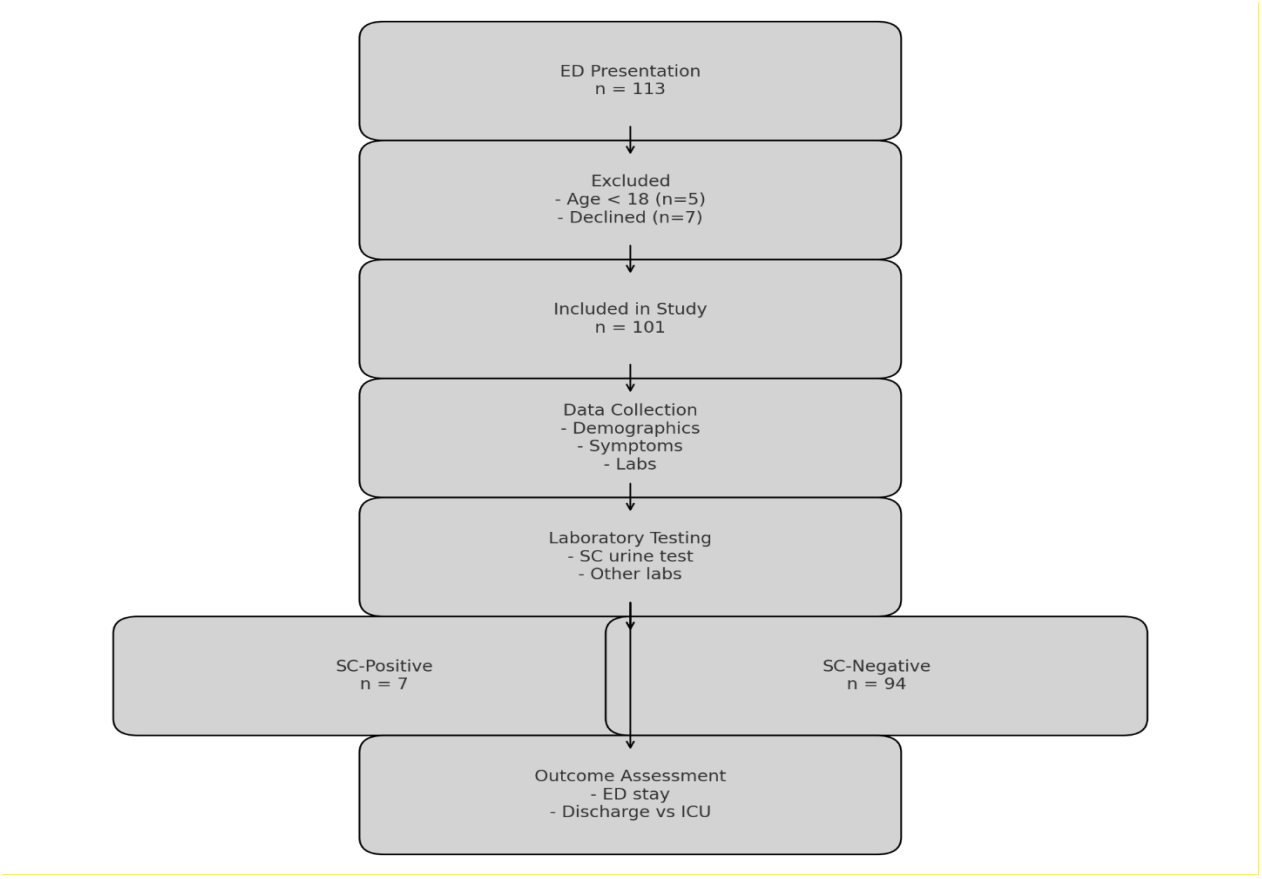

Figure 1. Study Flow Chart

Ethical Approval

This study was conducted in accordance with the Declaration of Helsinki and institutional ethical guidelines. The study approved by the Bakirkoy Dr. Sadi Konuk Training and Research Hospital's Local Ethical Board (number: IRB2015.119, date: 15.06.2015). All participants provided written informed consent prior to data collection, and their confidentiality was strictly maintained throughout the study. Data was anonymized, and access was restricted to authorized personnel only to ensure compliance with ethical standards.

Results

A total of 101 patients were included in the study, 95% of whom were male (n=96), with a mean age of 25.77±6.61 years (min: 18, max: 49). Among the patients, 48.5% (n=49) were unemployed, and only 3% (n=3) had a university degree. Additionally, 71.3% were single, and 48.5% reported having no source of income.

The primary reasons for emergency department (ED) visits were symptoms in 55.4% (n=56) of patients and seeking treatment for addiction in 44.6% (n=45). The most frequently reported symptoms included fatigue (18.8%, n=19), nausea and vomiting (17.8%, n=18), agitation (13.9%, n=14), and palpitations (6.9%, n=7). A notable 22.8% (n=23) of patients presented with no complaints **(Table 1)**.

Table 1. Presenting Complaints of Patients in the Emergency Department

Presenting Complaint	Count (n)	Percentage (%)
No Complaints	23	22.8
Fatigue	19	18.8
Agitation	14	13.9
Palpitations	7	6.9
Headache	3	3.0
Chest Pain	3	3.0
Convulsions	4	4.0
Burning Sensation on Skin	1	1.0
Nausea and Vomiting	18	17.8
Abdominal Pain	2	2.0
Syncope	4	4.0
Fear of Death	3	3.0
Dizziness	2	2.0
Seizures	2	2.0
Altered Consciousness	4	4.0
Hallucinations	2	2.0
Body Pain	1	1.0
Shortness of Breath	1	1.0

Among the 101 respondents, the median self-reported time since last use was 6 hours (range: 1–168 hours). Urine samples from patients who reported SC use revealed SC positivity in only 6.9% (n=7) of cases. No significant differences were observed in Glasgow Coma Scale (GCS) scores between SC-positive and SC-negative patients (p=0.950). Among the patients, 5.9% (n=6) had hypertension (systolic blood pressure >140 mmHg), 2% (n=2) had hypotension (systolic blood pressure <90 mmHg), and 13.9% (n=14) showed tachycardia. The fingertip oxygen saturation (SpO_2) levels were significantly lower in SC-positive patients (95.6±2.4%) compared to SC-negative patients (97.3±1.7%) (p=0.011) **(Table 2)**.

No statistically significant differences were found between SC-positive and SC-negative patients in terms of blood gas parameters (pH, pCO_2, lactate, HCO_3), complete blood count (WBC, HGB, HCT, PLT), biochemical parameters (urea, creatinine, CK, AST, ALT, LDH, amylase), coagulation parameters (INR, PT, aPTT), and electrolytes (sodium, potassium, calcium) (p>0.05). However, lipase levels were significantly higher in SC-positive patients (43.1 ± 67.6) compared to SC-negative patients (26.2±14.1) (p=0.031) **(Table 3).**

Electrocardiographic (ECG) evaluations revealed normal sinus rhythm in 69.3% (n=70) of patients, sinus tachycardia in 11.8% (n=12), and sinus bradycardia in 5.9% (n=6).

Substance use history revealed that 50.5% of patients reported alcohol use, and 96% reported tobacco use.

The average length of stay in the ED was 237.9±172.1 minutes (min: 49, max: 1140), with no statistically significant difference between SC-positive and SC-negative patients (p=0.96). Among the patients, 97% (n=98) were discharged from the ED, while 3% (n=3) required monitoring in the intensive care unit. None of the patients required inpatient ward admission.

Table 2. Patient distribution based on diagnoses.

Vital Parameters	Total	SC Negative	SC Positive	p
Systolic Blood Pressure (mmHg)	119.4 ± 14.1	119.7 ± 14.1	115.0 ± 16.1	0.398
Diastolic Blood Pressure (mmHg)	70.3 ± 12.6	70.3 ± 12.5	69.0 ± 13.6	0.779
Heart Rate (beats/min)	82.7 ± 16.8	82.8 ± 17.1	80.7 ± 12.5	0.749
Respiratory Rate (breaths/min)	18.3 ± 2.7	18.2 ± 2.6	20.1 ± 2.7	0.063
Temperature (°C)	36.6 ± 0.3	36.6 ± 2.9	36.8 ± 3.1	0.060
Saturation (%)	97.2 ± 1.8	97.3 ± 1.6	95.5 ± 2.3	0.011

Abbreviations: SC– Synthetic Cannabinoid

Table 3. Comparison of Laboratory Parameters Between Cannabinoid-Positive and -Negative Patients

Laboratory Parameters	Total	SC Negative Group	SC Positive Group	p	95% CI (Negative Group)	95% CI (Positive Group)
pH	7.38 ± 0.06	7.39 ± 0.06	7.41 ± 0.05	0.416	7.38 – 7.40	7.37 – 7.45
pCO_2 (mmHg)	43.42 ± 7.66	43.63 ± 7.64	40.74 ± 8.11	0.339	42.09 – 45.17	34.73 – 46.75
Lactate (mmol/L)	2.15 ± 1.43	2.17 ± 1.43	1.99 ± 1.57	0.751	1.88 – 2.46	0.83 – 3.15
HCO_3 (mmol/L)	24.40 ± 2.47	24.44 ± 2.51	24.01 ± 2.04	0.664	23.93 – 24.95	22.50 – 25.52
WBC ($10^3/mm^3$)	11.23 ± 3.60	11.14 ± 3.55	12.49 ± 4.28	0.344	10.42 – 11.86	9.32 – 15.66
HGB (g/dL)	14.6 ± 1.09	14.58 ± 1.11	14.94 ± 0.85	0.394	14.36 – 14.80	14.31 – 15.57
HCT (%)	41.95 ± 3.19	41.91 ± 3.25	42.49 ± 2.42	0.649	41.25 – 42.57	40.70 – 44.28
PLT ($10^3/mm^3$)	242.85 ± 56.04	242.57 ± 55.11	246.71 ± 72.45	0.851	231.43 – 253.71	193.04 – 00.38
Glucose (mg/dL)	109.45 ± 28.57	107.66 ± 29.96	119.43 ± 33.77	0.322	101.60 – 113.72	94.41 – 144.45
Urea (mg/dL)	28.55 ± 9.01	28.62 ± 9.24	27.71 ± 5.47	0.8	26.75 – 30.49	23.66 – 31.76
Creatinine (mg/dL)	0.90 ± 0.31	0.91 ± 0.32	0.90 ± 0.14	0.936	0.85 – 0.97	0.80 – 1.00
AST (U/L)	28.65 ± 21.27	29.10 ± 21.95	22.71 ± 5.59	0.447	24.66 – 33.54	18.57 – 26.85
ALT (U/L)	24.28 ± 30.31	24.72 ± 31.36	18.43 ± 5.65	0.599	18.38 – 31.06	14.24 – 22.62
Amylase (U/L)	65.39 ± 35.11	64.29 ± 31.75	80.29 ± 68.16	0.247	57.87 – 70.71	29.80 – 130.78
Lipase (U/L)	27.39 ± 21.82	26.22 ± 14.04	43.14 ± 67.63	0.047*	23.38 – 29.06	6.96 – 93.24
LDH (U/L)	246.82 ± 91.73	248.73 ± 94.50	221.14 ± 31.72	0.445	229.63 – 267.83	197.64 – 244.64
Calcium (mg/dL)	9.53 ± 0.62	9.51 ± 0.63	9.94 ± 0.45	0.076	9.38 – 9.64	9.61 – 10.27
Sodium (mmol/L)	139.83 ± 2.47	139.85 ± 2.43	139.57 ± 3.21	0.774	139.36 – 140.34	137.19 – 141.95
Potassium	4.30 ± 0.40	4.31 ± 0.41	4.27 ± 0.32	0.815	4.23 – 4.39	4.03 – 4.51
INR	1.07 ± 0.12	1.08 ± 0.12	1.05 ± 0.10	0.609	1.06 – 1.10	0.98 – 1.12
PT (sec)	13.63± 1.2	13.65 ± 1.23	13.40 ± 0.96	0.596	13.40 – 13.90	12.69 – 14.11
aPTT (sec)	26.42 ± 2.93	26.49 ± 2.92	25.49 ± 3.07	0.384	25.90 – 27.08	23.22 – 27.76
Troponin (ng/mL)	0.022 ± 0.17	0.023 ± 0.18	0.006 ± 0.01	0.804	0.01 – 0.06	0.00 – 0.01
CK (U/L)	454.33 ± 1094.88	446.88 ± 1099.28	554.43 ± 1112.06	0.803	224.65 – 669.11	269.40 – 1378.26
CK-MB (U/L)	29.12 ± 12.87	29.51 ± 13.20	24.00 ± 5.54	0.277	26.84 – 32.18	19.90 – 28.10

Abbreviations: pCO_2 – Partial pressure of carbon dioxide, HCO_3 – Bicarbonate, WBC – White blood cell count, HGB – Hemoglobin, HCT – Hematocrit, PLT – Platelet count, AST – Aspartate aminotransferase, ALT – Alanine aminotransferase, LDH – Lactate dehydrogenase, INR – International normalized ratio, PT – Prothrombin time, aPTT – Activated partial thromboplastin time, CK – Creatine kinase, CK-MB – Creatine kinase myocardial band, SC – Synthetic cannabinoid, CI – Confidence interval, SC– Synthetic Cannabinoid

Discussion

This study evaluated the demographic, clinical, and laboratory characteristics of individuals presenting to the emergency department (ED) with self-reported synthetic cannabinoid (SC) use, comparing the findings with those reported in the literature. We detected positivity rate of SC usage as %6.9. The short detection window of synthetic cannabinoids, generally up to 72 hours in urine, may explain the low positivity rate despite self-reported use, especially in cases where presentation occurred after the metabolite clearance period.

The results indicated that 95% of the patients were male, with a mean age of 25.77±6.61 years. These findings are consistent with prior studies, such as those by Hu et al. (95% male, mean age 20.6±5.1) and Bozkurt et al. (94.9% male, mean age 26.1±7.1) (11, 12). In Europe, SCs are predominantly used by individuals aged 15–34, with prevalence rates ranging from 0.1% to 1.5% (3). The predominance of young adult males among SC users underscores the susceptibility of this demographic to substance use disorders.

Regarding marital status, 71.3% of the patients were single, a finding in alignment with 67.1% reported by Bozkurt et al. (11). Additionally, the majority of patients had low educational attainment, with only 3% being university graduates. This suggests that low education levels may constitute a significant risk factor for SC use. Furthermore, 48.5% of the patients were unemployed, a rate notably higher than those reported in previous studies. The interplay between low socioeconomic status and SC use may create a self-perpetuating cycle, wherein SC use impairs the capacity for employment, further exacerbating socioeconomic challenges (12).

The primary reasons for ED visits included symptomatic complaints (55.4%) and requests for addiction treatment (44.6%). The most frequently reported symptoms were fatigue (18.8%), nausea and vomiting (17.8%), and agitation (13.9%). These findings are congruent with prior reports highlighting tachycardia and altered mental status as common clinical presentations; however, the broad spectrum of symptoms remains noteworthy (13, 14). SCs, due to

their substantially greater potency compared to natural cannabis, exhibit an elevated risk for inducing severe neuropsychiatric manifestations such as delirium, agitation, and psychosis (15, 16).

A significant finding in this study was the lower oxygen saturation (SpO_2) levels in SC-positive patients (95.6 ± 2.4%) compared to SC-negative patients (97.3 ± 1.7%) (p=0.011). Although the SC-positive group had statistically lower SpO_2 levels compared to the SC-negative group (95.6% vs. 97.3%, p = 0.011), this difference is not likely to be clinically significant, as all values remained within the normal physiological range. The small reduction may reflect mild transient hypoventilation or peripheral vasoconstriction, but it did not result in clinical hypoxia or require intervention. SCs' binding to CB1R receptors may result in deleterious effects on pulmonary function, potentially leading to alveolar damage, hemorrhage, and increased incidence of acute respiratory failure through CB1R-mediated inflammation and immune cell infiltration (17). Although data on the respiratory effects of SCs are limited, these findings provide valuable insights, suggesting the need for careful evaluation of hypoxia in SC users. The elevation in lipase among SC-positive patients was modest and remained within non-diagnostic ranges for pancreatitis. While some case reports suggest SCs may affect pancreatic function, the observed increase was not clinically meaningful in our cohort and did not correlate with abdominal pain or pancreatic pathology.

Consistent with the existing literature, no significant differences were observed in laboratory parameters, including blood gas analyses, biochemical markers, hematological indices, and coagulation profiles, between SC-positive and SC-negative patients (10).

The mean ED length of stay was 237.9 ± 172.1 minutes, aligning with the durations reported in the literature (5–6 hours) (18). A positive correlation was seen between the time elapsed since SC use and ED length of stay, suggesting that patients presenting with withdrawal symptoms require more prolonged treatment than those with acute intoxication.

In terms of outcomes, 97% of patients were discharged from the ED, while 3% required intensive care unit monitoring. No fatalities were observed. Although deaths related to SC use are rare, complications such as myocardial infarction, ischemic stroke, and acute kidney injury have been reported in the literature (19, 20). This underscores the importance of long-term follow-up and monitoring for potential complications in SC users. Because no specific antidote is currently available for synthetic cannabinoid intoxication, patient care hinges on optimized supportive measures; encouragingly, studies in other toxidromes have shown that well-designed adjunctive therapies alone can improve clinical outcomes (21).

Study limitations

Our study has a few important limitations. The number of patients who tested positive for synthetic cannabinoids was small, which makes it harder to draw strong conclusions from the comparisons. The relatively low detection rate of SCs may be attributed to the short detection window in urine. Although the median self-reported time since last use was 6 hours, some patients reported up to 168 hours, possibly exceeding the detectable period for many SC compounds. Furthermore, the SC test panel used in this study was limited to detecting only JWH-018, JWH-073, and AM-2201 metabolites. Given the rapid emergence of newer synthetic cannabinoid compounds, many of which fall outside the detection scope of this panel. The small number of SC-positive patients limits the study's statistical power and may have prevented the detection of meaningful differences between groups. This low detection rate may be due to the rapid breakdown of these substances in the body, delays in testing, or limitations in laboratory used.

Relying on patients to self-report their SC use also introduces the risk of inaccurate or incomplete information, especially given the unpredictable contents of these substances. As our study was conducted in a single emergency department, the findings may not generalize. Lastly, we only looked at short-term outcomes and there is lack of long-term follow-up after discharge, so we can't comment on longer-term effects. This study was conducted in a single-center ED with a predominantly male population (95%), which limits the generalizability of findings to other settings, particularly to female patients or different geographic regions. Future studies should consider broader testing methods, including more diverse patient populations, and explore long-term outcomes.

Conclusion

Laboratory-based diagnostic methods for SC use were not found to significantly impact the treatment process, ED length of stay, or prognosis in patients presenting to the ED. These findings suggest that clinical management should prioritize symptom-based evaluation over laboratory confirmation. Furthermore, there is a pressing need to develop and implement comprehensive public health strategies and awareness campaigns aimed at reducing the individual and societal burden associated with SC use.

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Abbreviations: ALT – Alanine aminotransferase, AM-2201 – Synthetic cannabinoid compound AM-2201, AST – Aspartate aminotransferase, aPTT – Activated partial thromboplastin time, CB_1R – Cannabinoid receptor type 1, CBR – Cannabinoid receptor, CK – Creatine kinase, CK-MB – Creatine kinase myocardial band, CI – Confidence interval, ED – Emergency department, ECG – Electrocardiogram, GCS – Glasgow Coma Scale, HCO_3^- – Bicarbonate, HCT – Hematocrit, HGB – Hemoglobin, INR – International normalized ratio, JWH-018 / JWH-073 – Synthetic cannabinoid compounds, LDH – Lactate dehydrogenase, NPS – Novel psychoactive substances, PLT – Platelet count, pCO_2 – Partial pressure of carbon dioxide, PT – Prothrombin time, SC – Synthetic cannabinoid, SpO_2 – Peripheral oxygen saturation, THC (Δ9-THC) – Delta-9-tetrahydrocannabinol, WBC – White blood cell count

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