Pattern of Acute Synthetic Cannabinoids Toxicity in Patients Presented to the Poison Control Center of Ain Shams University Hospitals

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Abstract	
	Background: Toxicity by synthetic cannabinoids (SCs) is increasing steadily with limited data concerning their use. Serious adverse effects after acute exposure to SCs include myocardial ischemia, stroke, seizures, coma, and acute kidney injury.
	Aim: Characterization of the epidemiological pattern of acute toxicity by SCs in patients presented to Poison Control Center of Ain Shams University hospitals (PCC-ASUH), Cairo, Egypt; from January 2018 to June 2019, and severity assessment using poisoning severity score (PSS).
	Methods: A cross-sectional study included adult patients presented to emergency department of PCC-ASUH from January 2018 to June 2019, with history of acute exposure to SCs.
	Results: About 541 patients attended the PCC-ASUH with history of acute SCs toxicity and only 448 patients were enrolled to our study. Males outnumbered females (96.43 versus 3.57%, respectively). Strox predominated (72.54%) followed by voodoo (27.45%). Recorded PSS was minor in 42.63% of patients, moderate in 18.97% and severe in 5.36%. Two patients (0.45%) died. Metabolic abnormalities predominated (60%), followed by gastrointestinal manifestations (46.2%).
	Conclusion: Incidence of SCs toxicity has recently increased. Several variables could worsen PSS in acute SCs poisoning like age, sex, type of SCs, co-ingestion, medical comorbidities, and respiratory acidosis.
	Recommendations: Early combination of PSS and arterial blood gas analysis could help in identifying patients at risk for acute SCs toxicity.
Key words	Pattern; Poisoning severity score; Synthetic cannabinoids; Toxicity

Introduction

Synthetic cannabinoids (SCs) are a heterogeneous group of compounds developed as research tools to explore the endocannabinoid system and as potential therapeutics. The first synthetic cannabinoids, cyclohexylphenols (CP), were synthesized in 1960s by modulating the chemical structure of Δ9-THC to localize cannabinoid receptors *(Johnson and Melvin, 1986)* and to study the potential medical benefits of marijuana in immunomodulation, regulation of appetite, addiction, analgesia, and inflammatory regulation *(Pertwee, 2006; Vardakou et al., 2010)*.

In the early 2000s, SCs were synthesized by clandestine laboratories, sprayed on dried plant materials and then marketed as alternatives to traditional cannabis *(Crime, 2011)*. As a result, not only a small community of experimental drug users tried these products, but also a wide proportion of habitual cannabis users as well as a lot of curious people abused them as legal alternatives to cannabis due to their hard detection in standard drug-screening assays of human body fluids *(Auwärter et al., 2009; Zanda and Fattore, 2018)*.

Synthetic cannabinoids (SCs) demonstrate higher binding affinities to G protein–coupled cannabinoid receptors CB1 and CB2 when compared to tetrahydrocannabinol (THC) which acts as partial agonist at CB1 and CB2 receptors, while SCs act as full agonists. Additionally, their metabolites have stronger affinities for the previously mentioned receptors resulting in greater potency and longer duration of pharmacologic effects and toxicity *(Noble et al., 2019)*.

Serious cardiac and neurological adverse effects have been reported after acute exposure to SCs as tachycardia, myocardial ischemia, electrocardiographic abnormalities, anxiety, agitation, stroke, seizures, coma, and psychosis. In addition, acute kidney injury (AKI) in the form of acute tubular necrosis or acute interstitial nephritis has been observed *(Thornton et al., 2013; Buser et al., 2014)*. Unpredictable toxic effects due to unregulated manufacturing processes and variability of ingredients were also declared *(Traynor, 2018)*.

In the United States, Emergency Department visits due to SCs use were tripled in two years, from 11,406 in 2010 to 28,531 in 2011. Their prevalence levels in Europe reached 0.9% in 2015 compared to 0.2% in 2012 *(Sud et al., 2018)*. In addition, Centers for Disease Control and Prevention (CDC) found that the number of deaths related to SCs use tripled between 2014 and 2015 where cardiovascular complications were reported as the commonest cause of death *(Adamowicz, 2016)*.

In Europe, SCs are sold under various names as "Spice" by its three subtypes (Silver/ Gold/ Diamond), Yucatan Makes, Yucatan Fire, Sence, Chill X, Smoke, Genie and Shunk. While K2 and K3 are the most popular SCs brands in the USA, Kronic and Bonzai are the commonest brands in Australia. Regarding Egypt, Voodoo and Strox are the commonly used SCs *(Solimini et al., 2017)*.

In contrast to developed countries, there are limited statistical data concerning SCs use in most of the developing Asian and African countries. Up till now, articles that describe acute poisoning with SCs are still insufficient and may focus on one aspect rather than others *(Lee et al., 2017)*.

Aim of the Study:

We conducted this study to characterize the epidemiological pattern of acute toxicity by SCs in patients presented to Poison Control Center of Ain Shams University hospitals (PCC-ASUH), Cairo, Egypt; during the period starting from January 2018 to June 2019, and to assess severity of intoxication in studied patients using poisoning severity score (PSS).

Patients and Methods

Study Design:

This hospital-based cross-sectional study was performed from January 2018 to June 2019 in PCC-ASUH.

Study population:

All adult patients, of both sex, presented to emergency department (ED) of PCC-ASUH with history of acute exposure to any type of synthetic cannabinoid product were included, even when the patient was considered asymptomatic and directly discharged from the ED. Diagnosis was established by history, physical examination, and routine laboratory evaluation following PCC-ASUH protocols. The study period from January 2018 to December 2018 was considered retrospective using electronic database and medical records while the period from January 2019 to June 2019 was considered prospective.

Study variables:

Collected data included demographics (age, sex, residence); type of SC agent(s); mode of poisoning; route of exposure; co-ingestion of other agents; pre-hospital management before presentation to PCC-ASUH; medical comorbidities; clinical assessment (neurological, respiratory, cardiovascular, gastrointestinal, and genitourinary); electrocardiogram (ECG) and arterial blood gas findings. We excluded patients below 18 years and above 60 years; and those giving history of having cardiovascular, renal, hepatic or chronic lung diseases.

Criteria of severity and outcome measures:

- Poisoning Severity Score (PSS) of European Association of Poisons Centers and Clinical Toxicologists (EAPCCT) was used to grade severity of poisoning at the time of initial inquiry as indicated by the patient's clinical features *(Persson et al., 1998 and Junk et al., 2005)*. It was intended to be an overall evaluation of the case, taking into account the most severe clinical features. The score has five grades: [None (0): no symptoms or signs related to poisoning; Minor (1): mild, transient, and spontaneously resolving symptoms or signs; Moderate (2): pronounced or prolonged symptoms or signs; Severe (3): severe or life-threatening symptoms or signs; and Fatal (4): death]. Duration of admission in inpatient ward, ICU and patients' outcome were also recorded.

Ethical considerations:

Administrative approval was obtained from PCC-ASUH. The Institutional Review Boards of Faculty of Medicine, Ain Shams University approved the protocol (Approval number: FMASU MS 119/2019). An informed consent was obtained from the patients themselves or their legal relatives during the last six months of the study only. Confidentiality of data was maintained by code numbers, and used only for the purpose of epidemiological analysis.

Statistical analysis:

Data were tabulated and statistically analyzed using SPSS, version 20 (SPSS Inc., Chicago, IL). Qualitative variables were expressed as frequencies (n) and percentages (%). Continuous variables were presented as mean (SD) and range. Chi-square test was used to test the association between qualitative variables while ANOVA test was used for comparing quantitative variables. P-value ≤ 0.05 was considered significant. Spearman Rank-Order Correlation was used to assess the strength of association between two quantitative variables. The correlation coefficient denoted symbolically by "r" defined the strength and direction of the linear relationship between the two variables.

Results

Monthly variations in the presentation of studied patients: During the study period, a total of 36,439 patients of acute poisoning attended the ED of PCC-ASUH, out of which 541 (1.5%) patients gave history of acute exposure to SCs. Only 448 patients were enrolled to our study and 93 patients were excluded as they were below 18 years or gave history of having chronic liver disease. The majority of studied patients attended the PCC-ASUH in June 2018 followed by May 2018 while the least number of patients were presented in June 2019 as shown in Table 1 and Figure 1.

Demographic characteristics and general health status: All patients were between 18 and 57 years old with mean value 25.8 ± 7.38 years. Nearly all patients were males (96.43%). Demographic characteristics are summarized in Table 2.

Pattern of poisoning: Inhalation was the only route of exposure to SCs (100%) mainly via cigarette or shisha smoking. Overdose due to SCs abuse represented the commonest mode of poisoning (85.4%) followed by accidental poisoning (14.6%). Strox predominated (72.54%) followed by voodoo (27.45%) as presented in Table 3.

Co-ingestion, pre-hospital management and admission status: About 83.48% of patients were poisoned with single SC agent and only 16.52% ingested other drugs or agents in addition to SCs. Tramadol topped the list accounting for 44.59% of co-ingested substances followed by antipsychotics, mainly clozapine (14.86%). Thirty six (8.03%) patients were hospitalized for further

treatment, of which 27 (75%) patients required ICU admission as presented in Table 4.

Clinical manifestations: Metabolic abnormalities due to acid-base disturbances predominated 269 (60%), followed by gastrointestinal manifestations 207 (46.2%). Vomiting and epigastric pain were the only GIT symptoms in the studied patients where vomiting occurred in 164 (36.61%) patients followed by epigastric pain in 108 (24.11%) patients. Moderate neurological manifestations were observed in 17.41% of cases in the form of confusion and hallucinations with only 5.81% of cases experienced severe manifestations as deep coma, extreme agitation or generalized convulsions. Respiratory symptoms affected only 16.3% of patients. Minor affection (mainly breathlessness) was found in 12.95% of the total number of studied patients while respiratory insufficiency denoting severe affection developed in 3.35% of patients. About 2.46% of patients showed minor cardiovascular symptoms as isolated extrasystole while 3.13% of patients had moderate cardiovascular symptoms in the form of sinus bradycardia (HR~40-50 beats/min) and only one patient developed severe symptoms manifested as severe sinus bradycardia (HR~ <40 beats/min). (Table 5). All studied patients did not show any genitourinary manifestations.

Poisoning severity score and outcome: Poisoning severity score was minor in 191 (42.63%) patients, moderate in 85 (18.97%) patients, and severe in 24 (5.36%) patients; while 146 patients (32.59%) were asymptomatic. Two patients (0.45%) died showing PSS (4) where the causative agent was strox.

Factors affecting PSS: Increasing age, male sex, presence of medical comorbidities and overdose due to SCs abuse were associated with PSS increase. Patients intoxicated by strox showed higher PSS compared to voodoo poisoned patients. Residence and pre-hospital management had no effect on PSS as displayed in Table 6. Respiratory acidosis was the main acid-base disturbance that directly affected PSS. In addition, length of hospital stay did not affect PSS as shown in Table 7.

Causes of ICU admission: Coma was the commonest cause of ICU admission (n = 22). Only three patients developed isolated cardiovascular complications, mainly sinus bradycardia. (Table 8)

Both delay time and length of stay showed negative correlation with PSS. On the other hand, a positive correlation was observed between length of stay in ICU and PSS. However, these correlations seemed to be statistically non-significant. (Table 9)

Table (1): Monthly variations in the presentation of acutely poisoned patients with synthetic cannabinoids under the study (N = 541)

Year	Month	N	Percentage %
2018	January	45	8.32
	February	29	5.36
	March	25	4.62
	April	52	9.61
	May	67	12.38
	June	68	12.57
	July	56	10.35
	August	37	6.84
	September	36	6.65
	October	19	3.51
	November	20	3.70
	December	18	3.33
2019	January	16	2.96
	February	12	2.22
	March	14	2.59
	April	12	2.22
	May	10	1.85
	June	5	0.92
	Total	541	100.00

Table (2): Demographic characteristics and medical comorbidities among synthetic cannabinoids intoxicated patients under the study (N = 448)

	N	%
Mean age (SD) (years)	448	25.8 (7.38)
Sex		
Male	432	96.43
Female	16	3.57
Residence		
Urban	370	82.59
Rural	78	17.41
Presence of medical comorbidities		
Negative	446	99.55
Positive	2*	0.45

(*): Diabetes mellitus / Familial Mediterranean Fever

Table (3): Types of synthetic cannabinoid agents in relation to mode of intoxication in synthetic cannabinoids intoxicated patients under the study (N = 448)

SC agent	Mode of intoxication					
	Overdose due to SCs abuse		Accidental		Total	
	N	%	N	%	N	%
Strox	280	72.72	45	71.43	325	72.54
Voodoo	105	27.27	18	28.57	123	27.45
Total	385	85.4	63	14.6	448	100.00

%: Percentage.   N: Number of patients   SCs: Synthetic cannabinoids

Table (4): Delay time, co-ingestion, pre-hospital management, admission rate and length of hospital stay in the studied patients (N = 448)

	N	%
Delay time (Hours)		7.723 ±7.398
Co-ingestion		
Negative	374	83.48
Positive	74	16.52
Types of co-ingested agents		
Tramadol	33	44.59
Antipsychotics (clozapine)	11	14.86
Oral hypoglycemic	9	12.16
Pregabalin	8	10.81
Carbamazepine	8	10.81
Organophosphates	5	6.75
Pre-hospital Management		
Negative	414	92.41
Proper	34	7.59
Patients admitted in inpatient ward	9	2.01
Length of stay in inpatient (Days)		1.61±0.97
Patients admitted in ICU	27	6.02
Length of stay in ICU (Days)		1.59±0.69
Total patients admitted to hospital	36	8.03
Total length of stay (Days)		2.0 ± 1.41

Table (5): The frequency of poisoning severity score according to the body system involved (N = 448)

	None		Minor		Moderate		Severe	
	N	%	N	%	N	%	N	%
Metabolic	179	39.96%	182	40.63%	67	14.96%	20	4.46%
Gastrointestinal	241	53.79%	148	33.04%	59	13.17%	0	0.0%
Neurological	344	76.79%	0	0.0%	78	17.41%	26	5.8%
Respiratory	375	83.71%	58	12.95%	0	0.0%	15	3.35%
Cardiovascular	422	94.2%	11	2.46%	14	3.13%	1	0.22%

Table (6): Poisoning severity score in relation to demographics, type of synthetic cannabinoids, and pattern of intoxication (N = 448)

	PSS					P value
	Asymptomatic (0)	Minor (1)	Moderate (2)	Severe (3)	Fatal (4)	
	N (%)	N (%)	N (%)	N (%)	N (%)	
Age (Years) [!]	25.38±7.4	26.0±7.4	25.4±6.1	28.3±8.8	42.0±14.1	0.009*
Sex						
Male	144 (33.33)	181(41.9)	84(19.4)	22(5.1)	1(0.23)	0.001*
Female	2(12.5)	10(62.5)	1(6.25)	2(12.5)	1(6.25)	
Residence						
Urban	116(31.3)	160(43.2)	70(19)	22(6)	2(0.5)	0.56
Rural	30(38.5)	31(39.7)	15(19.2)	2(2.6)	0(0)	
Presence of medical comorbidities						
Negative	146(32.7)	191(42.8)	84(18.8)	24(5.4)	1(0.2)	<0.001*
Positive	0(0)	0(0)	1(50)	0(0)	1(50)	
Type of SC agent						
Strox	115(35.4)	128(39.4)	61(18.8)	19(5.8)	2(0.6)	<0.001*
Voodoo	31(25.2)	63(51.2)	24(19.5)	5(4.06)	0(0)	
Co-ingestion						
Negative	136(36.36)	163(43.6)	66(17.6)	9(2.4)	0(0)	<0.001*
Positive	10(13.5)	28(37.8)	19(25.7)	15(20.3)	2(2.7)	
Pre-hospital management						
Negative	141(34)	173(41.8)	76(18.35)	22(5.3)	2(0.5)	0.215
Proper	5(14.7)	18(52.9)	9(26.5)	2(5.9)	0(0)	
Mode of poisoning						
Overdose due to abuse	133(34.5)	159(41.3)	68(17.7)	23(5.97)	2(0.5)	0.038*
Accidental	13(20.6)	32(50.8)	17(26.98)	1(1.6)	0(0)	

Chi square test was used   *PSS: Poisoning severity score*   *(*): statistically significant difference*

Table (7): Poisoning severity score in relation to arterial blood gas analysis and length of stay (N = 448)

	PSS					P value
	Asymptomatic (0)	Minor (1)	Moderate (2)	Severe (3)	Fatal (4)	
	N (%)	N (%)	N (%)	N (%)	N (%)	
ABG findings						
Normal	120(67)	49(27.4)	10(5.6)	0(0)	0(0)	
Respiratory acidosis	18(9.9)	99(54.4)	41(22.5)	22(12.1)	2(1.1)	<0.001*
Respiratory alkalosis	8(9.2)	43(49.4)	34(39.1)	2(2.3)	0(0)	
Length of stay in inpatient (Days) [!]	--	1.75 ± .5	1.71 ± 1.1	1.4 ± 1.1	--	0.84
Length of stay in ICU (Days) [!]	--	--	1.56 ± 0.7	1.56 ± 0.6	2.0 ± 1.4	0.7
Total length of stay (Days) [!]	--	1.75 ± .5	1.86 ± 1.6	2.2 ± 1.4	2.0 ± 1.4	0.9

Chi square test was used, (!) ANOVA test was used, PSS: Poisoning severity score, (*): statistically significant difference

Table (8): Causes of ICU admission in acutely intoxicated patients by synthetic cannabinoids (N=27)

Causes of ICU admission		
	N	%
Coma with agitation	13	48.15
Coma	6	22.22
Coma + CVS	3	11.11
CVS	3	11.11
Agitation	2	7.40
Total	27	100.00

N: Number of patients, ICU: Intensive care unit, CVS: Cardiovascular complications

Table (9): Spearman correlation analysis between delay time, length of stay in inpatient/ICU and poisoning severity score in patients under the study (N = 448)

Spearman's rho Correlations	PSS	
	R	P-value
Delay time (Hours)	-0.067	0.160
Length of stay in the inpatient ward (Days)	-0.372	0.129
Length of stay in ICU (Days)	0.078	0.700
Total length of stay (Days)	0.166	0.334

PSS: Poisoning severity score, P>0.05: Non significant difference, r: Correlation coefficient
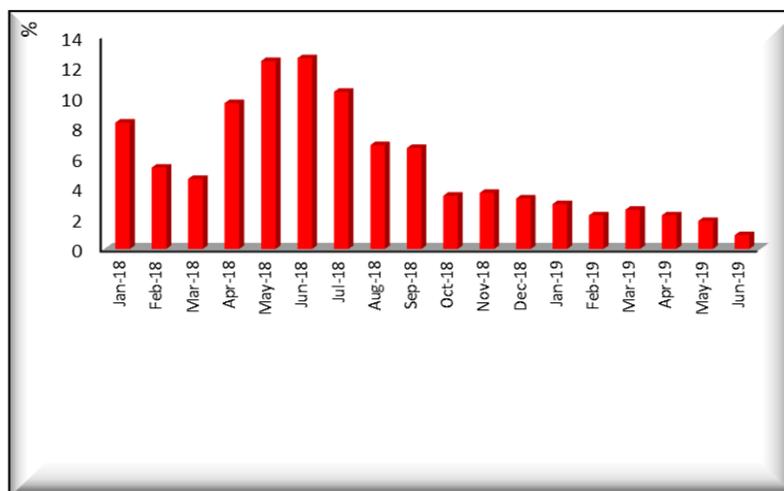
Figure (1): Monthly variations in the presentation of acutely synthetic cannabinoids poisoned patients in our study.

Discussion

The present study characterizes pattern of acute intoxication by SCs in patients presented to PCC-ASUH. The mean age value for all patients was 25.8 ± 7.38 years. Nearly similar results were obtained in an Australian study done by Barratt et al. (2013). The possible reasons for increased incidence of drug abuse in this age may be attributed to psychological family problems, studying, marriage, life costs and un-employment which make them stressed with probable involvement in drug abuse (Jesslin et al., 2010). On the other hand, different mean age values were reported in USA and Turkey by Bonar et al. (2014) and Besli et al.

(2015) who recorded mean age of 34.8 ± 10.7 and 15.4 ± 1.7 years respectively.

In the current study, male intoxicated patients were represented at a higher rate than females (96.4% and 3.6% respectively), and showed higher PSS compared to females. This agreed with Winstock & Barratt (2013) and Jones (2020) where males were more affected than females in United Kingdom. Males generally show aggressive (externalizing) behaviors during personal problems compared to females who often show auto-aggressive (internalizing) symptomatology. So self-poisoning is the main manner of intoxication in females; whereas drug abuse and addiction are more common in males (Foto-Özdemir et al., 2016). Moreover,

women with encountered substance abuse problems mostly show unique barriers to seeking medical help owing to greater stigma, limited access to insurance coverage for addiction treatment and less family support for seeking medical advice (Alvanzo et al., 2014). The reverse was observed by Maxwell et al. (2017) who found that females were highly represented in their American study.

In the present study, overdose due SCs abuse represented the main mode of intoxication (85.4%). In addition, SCs abusers showed higher PSS compared to accidentally intoxicated patients. This was in accordance with Maxwell (2018) who reported that overdose due to SCs abuse was the main mode of intoxication in patients presented to Texas Poison Center Network in 2014 and 2015. On the contrary, Darke et al. (2020) declared that accidental SCs toxicity had been strongly associated with severity and implicated in some fatal cases in Australia.

Strox was the commonest synthetic cannabinoid compound mostly involved in acute intoxication (72.54%) and was associated with significantly higher PSS when compared to voodoo in the studied patients. To date, some reports considered voodoo and strox as pure SCs, while others reported presence of hallucinogens such as atropine, hyoscine and hyoscyamine. As a result, little is actually known regarding their exact composition, toxicity profile and their effects on severity scores (Hussien et al., 2020). Waugh et al. (2016) noticed significant difference in PSS regarding intoxication by different SCs where ''Pandora's Box'' was associated with significantly higher PSS compared to ''Clockwork Orange''. No significant difference in PSS was observed when ''Pandora's Box'' was compared with ''Black Mamba'' in the same study.

In the current study, inhalation was the only route of intoxication by different types of SCs. Similarly, Bonar et al. (2014) and Law et al. (2015) reported that inhalation via smoking was the commonest route of SCs administration, representing 91% and 80.3% of all routes respectively, using cigarettes, vaporizers, water pipes or bongs while SCs ingestion occurred in only 3% and 19.5% respectively. Synthetic cannabinoid users mostly prefer inhalational products than oral ones as oral consumption has delayed onset of action. In addition, oral forms are easily ingested without any pleasure during preparation (Huestis and Smith, 2018).

It was clear that co-ingestion of other drugs or agents significantly affect the PSS of the studied patients. This result was extremely logic as the co-ingested drugs were mostly tramadol accounting for 44.59% of co-ingested substances followed by antipsychotics, mainly clozapine (14.86%), which are well-known to be unsafe medications and greatly affect the clinical course of poisoning owing to tramadol-induced respiratory depression and antipsychotics-induced cardiotoxicity (Lagard et al., 2018; Li et al., 2019). In studies done by Bonar et al. (2014) and Law et al. (2015), alcohol topped the list of co-ingested agents (96%), followed by cannabis and prescriptive opioids in USA.

Despite the small number of our studied patients who reported history of having medical illnesses, they showed the highest PSS. This could be explained by the impacts of underlying medical diseases which could probably worsen the clinical course of acute intoxication, influence the route of metabolism or elimination of various drugs and thus predispose to increased drug toxicity (Rehm et al., 2017).

About 207 (46.2%) patients complained of gastrointestinal manifestations in our study, where vomiting and epigastric pain were the only symptoms. Similar results were reported by Trecki et al. (2015). Gastrointestinal manifestations owed to SCs could be explained by their inhibitory effect on electrically-induced contractions of small intestine causing delayed solid-phase gastric emptying. Thus, repetitive vomiting and abdominal pain are the most prominent gastrointestinal symptoms among SCs abusers (Robinson et al., 2013).

In the current study, moderate neurological manifestations were observed in 17.41% of cases in the form of confusion and hallucinations with only 5.81% of cases experienced severe manifestations as deep coma, extreme agitation or generalized convulsions. These results agreed with Riederer et al. (2016) who found that agitation, hallucinations and perceptual changes were the main neurological findings among their studied SCs abusers followed by CNS depression. Inhibition of gamma-aminobutyric acid neurotransmission in the brain may play a role in the development of anxiety, agitation and convulsions in most SCs abusers. In addition, absence of phytocannabinoids (e.g. cannabinol and cannabidiol) in synthetic cannabinoid preparations with subsequent loss of their anticonvulsant properties increases the risk for developing agitation and convulsions (Harris and Brown, 2013).

To the best of our knowledge, few toxicological case reports were found to show a link between SCs and respiratory dysfunction (Herbst and Musgrave, 2020). The effect of SCs on chemoreceptors and baroreceptors can increase bronchial airway resistance. In addition, CB1 receptor stimulation by SCs induces respiratory depression, and lastly numerous chemical gases released after SCs inhalation may cause damage to the bronchiolar epithelium and disrupt the protective surfactant layer in the alveoli, resulting in interference with effective gas exchange with subsequent hypoxia and acidosis (Alon and Saint-Fleur, 2017).

Cardiovascular manifestations, either extrasystole or bradycardia, occurred in only 5.8% of studied patients. Several theories suggested that SCs were found to elicit dose-dependent bradycardia mediated by CB1 receptors (Ozturk et al., 2019). Cardiac abnormalities could be also justified by the prolonged or potent effects of SCs on cardiac conduction system and myocytes, leading to decreased stroke volume and dysrhythmias in

comparison with traditional cannabis (Von Der Haar et al., 2016). On the contrary, tachycardia and hypertension have been mostly observed among SCs abusers in similar studies (Trecki et al., 2015; Monte et al., 2017).

Respiratory acidosis was the most prominent acid-base disturbance affecting 40.63% of the total number of studied patients. These results were in agreement with Besli et al. (2015) who reported that respiratory acidosis predominated in 40% of their Turkish studied patients. Respiratory acidosis induced by SCs could be attributed to decreased sensitivity of central and peripheral chemoreceptors to carbon dioxide (Ridgway and Pountney, 2007). Additionally, SCs may cause pulmonary edema due to diffusion impairment and ventilation-perfusion mismatch leading to hypoxia and hypercapnea with subsequent respiratory acidosis (Wilkins et al., 2013). It was clear that respiratory acidosis was the main acid-base disturbance that directly affected the PSS in the present study. This was explained by Romito et al. (2018) who stated that respiratory acidosis causes cerebral vasodilation with increased cerebral blood flow and raised intracranial tension; finally central depression may occur at very high levels of PCO2, manifested by dyspnea, disorientation, acute confusion or headache leading to high PSS. On the other hand, Yasar-Durmus et al. (2015) did not record any acid-base disturbance among their Turkish SCs abusers.

Nearly 8.02% of our patients required hospital admission for further management. Wide variations regarding hospital stay were reported where Barratt et al. (2013) found that only 1.8% of their studied patients need hospital admission following SCs exposure while Riederer et al. (2016) reported hospital admission in 58.6% of SCs intoxicated patients.

It was observed that PSS (1) was recorded in the majority of patients (42.63%) followed by PSS (0) in 32.59% of cases while death occurred in two (0.45%) patients with PSS (4). Nearly similar results were reported by Maxwell (2018) where PSS (0) was recorded in 30% of patients and only 3% showed PSS (3). On the other hand, Hermanns-Clausen et al. (2013) recorded PSS (2) in the majority of their patients (58%) followed by PSS (1) in 37% of patients.

In the current study, the mortality rate was 0.45% and strox was responsible for death in the two deceased patients. The first case was a 32-year old male, presented with history of strox inhalation 24 hours before presentation and coma grade IV (by Reed's classification of level of consciousness). Arterial blood gas analysis revealed severe respiratory acidosis and his ECG showed sinus bradycardia. The patient was admitted in the ICU and mechanically ventilated for two days then he developed cardiac arrest.

The second case was a 52-year old female, who developed agitation and coma grade IV two hours after strox inhalation. Arterial blood gas analysis revealed severe respiratory acidosis and her ECG was normal. The patient was admitted in the ICU and mechanically ventilated for three days then she developed repetitive seizures and cardiac arrest. Riederer et al. (2016) recorded mortality rate of 1.2% in a similar study where K2/Spice was the only causative agent. Their study documented cardiac arrest, respiratory depression and acute kidney injury as the major causes of death due to acute SCs intoxication.

Conclusion

Incidence of SCs toxicity has recently increased in Egypt and strox was the commonest brand of SCs abused by patients. To date, little is known about the pattern of acute poisoning by SCs. However, several variables could worsen the PSS in acute SCs poisoning like age, sex, type of SCs, overdose due to SCs abuse, presence of co-ingestion, medical comorbidities, and presence of respiratory acidosis while other variables seem to have no effect on PSS as residence, delay time and pre-hospital management.

Recommendations

Early combination of PSS and arterial blood gas analysis could help in identifying patients at risk for acute SCs toxicity and even those who might progress to severe fatal poisoning. After recovery, patients should be referred for psychiatric consultation, as many have history of poly-substance abuse. Public education by raising awareness among youth about the potential harms of SCs could help in reducing addiction and its related poisoning episodes in this age group. Further multicenter-based studies are needed to provide a more comprehensive picture of acute SCs poisoning, including larger number of patients for more extended time period than 18 months. Further studies are needed to portray and compare the pattern of acute SCs poisoning in different age groups.

Strengths and limitations:

Although the sample size of the present study was enough to reach conclusion, an important limitation is that it included patients who were presented to PCC-ASUH, which is a single Egyptian toxicological center and might not globally represent the pattern of acute SCs intoxication in the whole country. We could expect a greater number of SCs intoxicated patients who were managed at other hospitals or health care centers. Due to exclusion of patients less than 18 years and more than 60 years from the study, the burden of pediatric intoxication and the effect of age in elderly could not be assessed.

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نمط التسمم الحاد بشبائه القُنَّب الإصطناعية لدى المرضى الذين تم استقبالهم بمركز علاج التسمم بمستشفيات جامعة عين شمس

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الملخص العربي

المقدمة: يتزايد التسمم الناتج عن استخدام شبائه القُنَّب الإصطناعية بشكل مطرد مع توافر بيانات محدودة تتعلق باستخدامه. تشمل الآثار الضارة الخطيرة بعد التعرض الحاد لشبائه القُنَّب الإصطناعية نقص تروية عضلة القلب والسكتة الدماغية والتشنجات والغيبوبة وإصابة الكلى الحادة.

الهدف من الدراسة: توصيف النمط الوبائي للتسمم الحاد بشبائه القُنَّب الاصطناعية لدى المرضى الذين تم استقبالهم بمركز علاج التسمم بمستشفيات جامعة عين شمس بدايةً من شهر ينايرعام ٢٠١٨ حتي نهاية شهر يونيو عام ٢٠١٩ وتقييم شدة التسمم الحاد باستخدام "مقياس شدة التسمم" (Poisoning Severity Score).

طريقة البحث: دراسة مستعرضة، أُجريت على جميع المرضى البالغين من كلا الجنسين الذين تم استقبالهم بمركز علاج التسمم بمستشفيات جامعة عين شمس بعد التعرض لأحد شبائه القُنَّب الإصطناعية بدايةً من شهر ينايرعام ٢٠١٨ حتي نهاية شهر يونيو عام ٢٠١٩.

نتائج البحث: بلغ إجمالي عدد المرضى المصابين بالتسمم بشبائه القُنَّب الإصطناعية الذين تم استقبالهم بمركز علاج التسمم بمستشفيات جامعة عين شمس ٥٤١ مريضاً، وقد شملت الدراسة ٤٤٨ مريضا. وكانت إصابة المرضى الذكور أكثر من الإناث، وغالبية الحالات كانت تسمم بالاستروكس (٧٢،٥٤٪) يليه الفودو (٢٧،٤٥٪). وكان "مقياس شدة التسمم" بسيطاً في غالبية المرضى (٤٢،٦٣٪) ومتوسطاً في ١٨،٩٧٪ وشديداً في ٥،٣٦٪. حدثت الوفاة في مريضين فقط (٠،٤٥٪). وكانت الاضطرابات الأيضية هي السائدة (٦٠٪) ، تليها أعراض الجهاز الهضمي (٤٦.٢٪).

الخلاصة: يتزايد معدل التسمم بشبائه القُنَّب الصطناعية في الأونة الأخيرة ويمكن أن تؤدي العديد من المتغيرات إلى ارتفاع "مقياس شدة التسمم" مثل تقدم العمر والجنس، وكذلك النوع الذي تم تناوله من شبائه القنب، وتناول مواداً أخرى إلى جانب الشبائه، والأمراض المصاحبة، ووجود حماض تنفسي.

التوصيات: يمكن أن يساعد الجمع المبكر بين "مقياس شدة التسمم" وتحليل غازات الدم الشرياني في تحديد المرضى المعرضين لخطر الإصابة بالتسمم الحاد بشبائه القُنَّب الصطناعية.

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