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Evaluation of Acute Cannabis Intoxication in Pre- School Children Admitted to Poison Control Center –Ain Shams University Hospitals

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Abstract

Background: In Egypt, cannabis is on the top list of the substances abused according to statistics of Fund for Drug Control and Treatment of Addiction. Its widespread use translates to greater access for children. Cannabis intoxication in young children can cause encephalopathy and coma. **Aim:** to evaluate the prevalence of acute cannabis intoxication in pre-school children (less than 6yrs) in Egypt; analysis of different factors related to the problem, clinical picture, management, assessment of severity and outcome of the problem by poison severity score (PSS). **Method:** prospective observational cross sectional study carried on all pre-school children (less than 6yrs) of both sex who admitted to PCC-ASUH, during the period from first of March 2019 to the end of December 2019, with history of acute cannabis intoxication and confirmed by cannabis positive screen. **Results:** The prevalence of acute cannabis intoxicated pre-school children (less than 6yrs) was 89.9%.The mean age was (17.38 month ±8.75). Fifty four percentages were males. As regard PSS, the majority of patients (55.1%) were of group II, while (31.4%) were of group I & (13.5%) were of group III. Regarding clinical manifestations; tachycardia observed in (5.8%), hypertension in (13.5%), tachypnea (18%), drowsiness (31.4%), muscle rigidity (21.5%), extra-pyramidal manifestations presented in (21.5%), coma grade I in (67.7%), coma grade II in (0.9%), respiratory distress in (1.8%), vomiting in (17.9%), mydriasis in (13%), miosis in (18.8%), flushed skin (12.1%) and respiratory acidosis (26.5%) of patients .ICU admission occurred in (68,7%) of patients and the majority were admitted ≥24 hours (65.9%). **Conclusions:** The prevalence of acute cannabis toxicity in pre-school children (less than 6yrs) has dramatically increased. Severity of acute cannabis intoxication in pre-school children(less than 6yrs) can be evaluated simply by using PSS. **Recommendation**: Public education is very necessary to decrease the problem. Early arterial blood gas analysis with careful neurological examination could help in identifying patients at risk.

Key words Poisoning severity score; cannabis; pre-school, encephalopathy

Introduction

Cannabis use has increased sharply all around the world. According to the World Health Organization, 2.5% of the world population, use cannabis (marijuana), making it the world's most abused illicit substance (Anthony et al., 2017). In Egypt, cannabis is on the top list of the substances abused according to statistics of Fund for Drug Control and Treatment of Addiction. Widespread use of cannabis translates to greater access for children (Odejide and Morakinyo, 2016). Natural compounds of the cannabis plant are referred to as phytocannabinoids (Hamdi et al., 2016). Bango is the stimulating flower containing tetra hydro cannabinol (THC) levels up to 28%. Hashish is the detached trichomes and fine material that falls off cannabis fruits, flowers and leaves or from scraping the resin from the surface of the plants (Fasinu et al., 2016).

The first compound that was isolated from the cannabis plant was cannabinol (Mechoulam and Shvo, 1963). Δ 9 - tetra hydro cannabinol (Δ9-THC) is the major active principle in all cannabis products (Dowd, 2018). The pharmacokinetics of cannabis depends on the route of administration (Newmeyer et al., 2016). Following inhalation, 9 -THC is detectable in plasma within seconds after the first puff and the peak plasma concentration is attained within 3-10 minutes (Russo and Marcu, 2017). Oral 9 -THC formulations exhibit variable absorption and undergo extensive hepatic first-pass metabolism (Eichler et al., 2012). This results in lower peak plasma concentration relative to inhalation and a longer delay (120 minutes) to reach peak concentration (McPartland and Guy, 2017).

CB1 and CB2 are the main cannabinoid receptors. They are distributed in the central nervous system and many peripheral tissues (De Meijer, 2014). Both receptor types are G-protein linked receptors that inhibit adenyl cyclase and thus, inhibiting the conversion of ATP to cAMP (Kaur et al., 2016). Activation of the CB1 receptor produces marijuana like effects, while activation of the CB2 receptor does not produce this psychological effect, so selective CB2 receptor agonists have become an increasingly investigated target for therapeutic uses of cannabinoids,

among them analgesic, anti-inflammatory and anti-neoplastic actions (Abrams, 2018).

Manifestations of acute cannabis intoxication vary and are influenced by patient's age, cannabis potency, method of use and presence of other psychoactive substances. Acute marijuana intoxication in children typically occurs after exploratory ingestion of marijuana (Wang et al., 2019). Cannabis toxicity in young children can result in encephalopathy and coma (Carstairs et al., 2011). The acute encephalopathy has few systemic clinical signs including hyporeflexia, hypotonia and dilated pupils. It is known that large quantities of ingested cannabis can have a delayed and prolonged effect that may last up to twelve hours after the exposure (Murti et al., 2018).

Aim of the Study

The aim of the study was to evaluate the prevalence of acute cannabis intoxication in pre-school children in Egypt, analysis of different factors related to the problem, clinical picture, management & assessment of severity and outcome of the problem by poison severity score (PSS).

Patients and Methods

This work was a prospective observational cross sectional study, carried out on all pre-school children (less than six years) of both sex with history of acute cannabis toxicity. They were admitted to Poison Control Center of Ain Shams University Hospitals (PCC-ASUH) during the period from the first of March 2019 to the end of December 2019. This study was conducted on previously mentally healthy pre-school children Presented with proven cannabis intoxication (compatible clinical symptoms and positive urine toxicological screening). Exclusion criteria included patients with history of neurological, cardiac or mental illness and those with history of co -ingestion of mixed substances.

Collected clinical data included demographics (age, sex, residence, family history of addiction of any family member & family social or psychological problems), place and source of exposure, type and amount of cannabis; mode of poisoning; route of exposure, pre-hospital management, delay time (time elapsed between the exposure and arrival to the PCC-ASUH), clinical assessment (neurological, respiratory, cardiovascular, gastrointestinal, and ocular examination) and investigations included; electrocardiogram (ECG), arterial blood gas findings and cannabinoid toxicological screening.

Evaluation of severity of poisoning was assessed at the time of peak manifestations using PSS of European Association of Poisons Centers and Clinical Toxicologists (EAPCCT). 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 (Persson et al., 1998).

Ethical considerations:

An official approval was taken from the general director of the PCC-ASUH. The approval of the Local Research Ethics Committee was obtained. An informed valid consent was taken from the legal guardians of children. All personal data were kept anonymous to ensure confidentiality of records.

Statistical analysis:

The obtained clinical data and results of investigations (quantitative data) were recorded and organized. Data were collected, tabulated and graphically represented using standard SPSS (Standard Package for Social Science) software package, version 20 (Chicago. IL).

Results

The study period was from the first of March 2019 to the end of December 2019 at (PCC-ASUH). The number of acutely intoxicated cannabis pre-school children admitted to PCC-ASUH during the study period was 227 patients. Four children were excluded from the study, two of them had history of co-ingestion of mixed drugs with cannabis and the other two patients had past history of cardiovascular and/or neurological diseases, so the number of acutely intoxicated cannabis cases in this study was 223 patients. All the studied patients were proven cannabis intoxication by compatible clinical symptoms & positive urine toxicological screening.

Prevalence of acute cannabis intoxication in pre-school children (less than 6 years): The percentage of acute cannabis intoxicated children (less than 18 years) was 92.5%, while the percentage of acute cannabis intoxicated adult was 7.5% during the period as shown in (Table 1). The percentage of acute cannabis intoxicated pre-school children (less than 6 years) was 223 (89.9%) out of 248 acute cannabis intoxicated children (less than 18 years) admitted to PCC-ASUH during the studied period as shown in (Table 2). The percentage of acute cannabis intoxicated pre-school children (less than 6 years) was 223 (24%) from total number of 930 acutely intoxicated pre-school children (less than 6 years) admitted to PCC-ASUH during the studied period as shown in (Table 3).

Severity of cases: The number of acutely intoxicated cannabis cases in this study was 223 patients who classified into three groups according to PSS, the majority of patients (55.1%) were of group II (moderate group), while (31.4%) were of group I (minor group) & (13.5%) were of group III (severe group) (Table 4).

Demographics & exposure characteristics: The mean age of the studied acute cannabis intoxicated pre-school children was (17.38 months ± 8.75). Mostly were male and the majority of cases came from urban areas as presented in (Table 5).

Intoxication data: Most of cannabis intoxicated pre-school children were accidental exposed mainly via ingestion route. The main source of exposure was father in (18.4%) of patients who is a cannabis addict and the majority of exposure of cannabis intoxicated

pre-school children occurred at their home (91.5%). The mean delay time was (6.2±3.3 hours). Activated charcoal was given in (1.3%) as a pre-consultation management. There was a significant difference as regard of the place of exposure between group I & II of PSS being higher in group II than group I as shown in (Table 6).

General examination: Tachycardia was observed in (5.8%) of the studied group. Hypertension was observed in only (13.5%) of patients. Tachypnea was found in (18%) of patients & two patients needed mechanical ventilation in the present study. Minor percentage (31.8%) of the studied patients had hyperthermia. There was a highly significant difference as regards respiratory rate among three groups being higher in group III than I & II as shown in (Table 7).

Clinical manifestations: Neurological symptoms predominated in the studied cannabis intoxicated patients. The most common CNS manifestations in the present study were drowsiness (31.4%), muscle rigidity (21.5%) & extra-pyramidal manifestations (21.5%). According to REED's coma scale, (67.7%) of the patients were in coma grade I, only (0.9%) were in coma grade II, however ataxia observed in (2.7%) of patients. There was a highly significant difference among three groups (group I, II & III) of PSS as regard of (conscious level-seizures-muscle rigidity & ataxia). Coma grades I/II & other neurological findings showed high significant increase in group III than groups I & II. Furthermore, coma grade I showed high significant increase in group II compared to group I as shown in (Table 8).

Regarding respiratory symptoms, respiratory distress was observed in (1.8%) of patients, while respiratory failure was found in (0.9%). Vomiting and abdominal distension were the only GIT symptoms in the studied patients where vomiting occurred in 17.9% of patients & 18.4% of patients had abdominal distension. As regard the eye findings, mydriasis was observed in (13%) of patients, while miosis was observed in (18.8%) & eye redness was observed in (9.9%). Minor percentage (12.1%) of patients had flushed skin .There was a highly significant differences among three groups (group I, II & III of PSS as regards respiratory findings (wheezes / crepitation - respiratory distress & failure), gastrointestinal findings (abdominal distension- vomiting), eye findings (eye miosis - mydrasis & redness) and skin findings, showing high significant increase in group III when compared with groups I & II as presented in (Table 9).

Laboratory findings: Respiratory acidosis was the most prominent acid-base disturbance affecting 26.5% of the total number of studied acute cannabis intoxicated pre-school children. The majority of cases had normal random blood sugar, normal sodium and potassium levels. Regarding ECG findings, the majority of cases had normal ECG findings. There was a highly significant difference among three groups (group I, II & III of PSS) in ABG & PH. Percentages of patients presented with respiratory and metabolic acidosis show high significant increase in group III & group II when compared with group I. pH shows high significant decrease in group III when compare with groups I & II, in addition to, there was a significant difference regarding mean levels of random blood sugar being a significant increase in group III when compare with groups I & II as summarized in (Table 10).

Treatment and outcome: ICU admission occurred in (68 .7%) of patients. Coma was the commonest cause of ICU admission either alone or in combination with extra-pyramidal manifestations or respiratory complications. There was a highly significant difference regarding place of admission and duration of hospital stay among three groups (groups I, II & III) of PSS in acute cannabis intoxicated pre-school children. ICU admission percentage was significantly high in group III and group II when compared with group I as presented in (table 11). Most of patients recovered without any complication during hospital stay (99.6%) while only one patient recovered with visual impairment due to prolonged hypoxia with need of pediatric follow up with no recorded dead case as shown in (Table 12)

Table (1): The percentage of acute cannabis intoxicated children in comparison to percentage of acute cannabis intoxicated adult admitted to (PCC-ASUH) from March 2019 to December 2019.

	Number	%
Admitted adult	20	7.5%
Admitted children	248	92.5%
Total admitted adult and children	268	100%

Table (2): The percentage of acute cannabis intoxicated pre-school children among total acute cannabis intoxicated children admitted to (PCC-ASUH) in the current study.

	N	%
Total admitted acute cannabis intoxicated pre-school children (<6 years)	223	89.9%
Total admitted acute cannabis intoxicated children	248	100 %

N=number

Table (3): The percentage of acute cannabis intoxicated pre-school children in comparison to total acute intoxicated pre-school children admitted to (PCC-ASUH) during study peroid.

	N	%
▪ Total admitted acute ***cannabis*** intoxicated pre-school children	223	24%
▪ Total admitted acute ***intoxicated*** pre-school children	930	100%

N=number

Table (4): The severity of acute cannabis intoxicated pre-school children according to PSS:

Final group	Number	%
Minor group	70	31.4%
Moderate group	123	55.1%
Severe group	30	13.5%

Table (5): The demographics data (Age-Sex-Residence) of acute cannabis intoxicated pre-school children:

		Number = 223
1. Sex	▪ Female ▪ Male	102 (45.7%) 121 (54.3%)
2. Residence (Urban/Rural)	▪ Urban	197 (88.3%)
	▪ Rural	26 (11.7%)
3. Age (month)	▪ Mean±SD ▪ Range	17.38±8.75 6-60

Table (6): Chi-Square statistical analysis & One Way ANOVA test of intoxication data (Route - Manner - Delay time - Child problems- -Place - Family addiction & Source) among three groups (group I, II & III) of PSS in acute cannabis intoxicated pre-school children.

		Group I	***Group II***	***Group III***	***P-value***	***Sig.***
		N = 70	***N = 123***	***N = 30***		
Delay time	**Mean± SD**	4.71±3.55	4.94±3.56	3.97±2.68	0.381•	NS
Route of exposure	**Ingestion (hashish)**	70 (100%)	123 (100%)	30 (100%)	0.41*	NS
No Child social / psychological problems		70 (100%)	123 (100%)	30 (100%)	0.41*	NS
Manner	**Accidental**	70 (100%)	123 (100%)	30 (100%)	0.41*	NS
Family member addiction/Source	**No addiction**	51 (72.9%)	101 (82.1%)	21 (70.0%)	0.307*	NS
	Father	14 (20.0%)	19 (15.4%)	8 (26.7%)		
	Family member	5 (7.1%)	3 (2.4%)	1 (3.3%)		
Place of exposure	**At home**	58 (82.9%)	117® (95.1%)	29(96.7%)	0.048*	S
	At family member home	5 (7.1%)	3 (2.4%)	1 (3.3%)		
	At wedding	7 (10.0%)	3 (2.4%)	0 (0.0%)		

*N= number, SD= standard deviation, P-value >0.05 NS= Non significant, P-value <0.05, S = Significant, *:Chi-square test, •: One Way ANOVA test, ®: comparison between group I & II.*

Table (7): One way ANOVA test of the vital signs (Pulse - blood pressure - temperature & respiratory rate) among three groups (group I, II & III) of PSS in acute cannabis intoxicated pre-school children.

		Group I	**Group II**	**Group III**	**Test value**	**P-value**	**Sig.**
		N= 70	**N = 123**	**N= 30**			
Pulse	**Mean±SD**	109.83±15.09	110.42±13.28	114.40±14.62	1.196	0.304	NS
SBP	**Mean±SD**	99.29±10.40	98.41±9.92	97.00±9.52	0.555	0.575	NS
DBP	**Mean±SD**	72.86±5.68	72.11±4.83	71.33±4.34	1.042	0.355	NS
Respiratory rate	**Mean±SD**	25.83±2.52	26.15±3.51	35.80±1.99 € #	132.757	0.01	**HS**
Temperature	**Mean±SD**	37.37±0.52	37.30±0.46	37.33±0.48	0.484	0.617	NS

N= number, SD= standard deviation, P-value >0.05 NS= Non significant, P-value <0.05, S = Significant, P-value <0.01: highly significant (HS), #: comparison between groups I& III, €: comparison between group II& III.

Table (8): Chi-Square statistical analysis of neurological manifestations among three groups (group I, II & III) of PSS in acute cannabis intoxicated pre-school children.

		Group *I*		**Group *II***		**Group *III***		***Test value****	***P-value***	***Sig.***
		N	***%***	***N***	***%***	***N***	***%***			
Conscious level	**Grade 0**	70	100%	0	0%	0	0%	230.1	0.01	**HS**
	Grade I	0	0%	123	100%®	28	90%#			
	Grade II	0	0%	0	0%	2	6.7%€#			
Seizures		3	4.3%	15	12.2%	30	100%€#	128	0.01	**HS**
Muscle rigidity		3	4.3%	15	12.2%	30	100%€#	128	0.01	**HS**
Ataxia		0	0%	2	1.6%	4	13.3%€ #	15.45	0.01	**HS**

N: number, P-value< 0.01= highly significant (HS), ®: comparison between group I & II, #: comparison between groups I& III, €: comparison between group II& III.

Table (9): Chi-Square statistical analysis of respiratory findings, gastrointestinal findings, eye examination and skin examination among three groups (groups I, II & III) of PSS in acute cannabis intoxicated pre-school children:

		Group I N = 70	Group II N = 123	Group III N= 30	Test value*	P value	Sig.
Respiratory finding:	**1. Chest Wheezes / crepitation**	10(14.3%)	40 (32.5%)®	30(100%)#			
	2. Respiratory distress	0 (0.0%)	0 (0.0%)	4(13.3%€ #)	90.506	0.01	**HS**
	3. Respiratory failure	0 (0.0%)	0 (0.0%)	2(6.7%)€ #			
Gastrointestinal finding:	**1. Abdominal Distension**	1(1.4%)	9(15.4%®)	21(70.0%€ #)	67.384	0.0001	**HS**
	2. Vomiting	6(8.6%)	15(12.2%)	19(63.3%€ #)	46.813	0.0001	**HS**
Eye finding:	**1. Miosis**	5(7.1%)	17(13.8%)	20(66.7%€ #)	53.181	0.01	**HS**
	2. Mydrasis	8(11.4%)	11(8.9%)	10(33.3%€ #)	12.906	0.02	**HS**
	3. Red eye	4(5.7%)	8(6.5%)	10(33.3%€ #)	21.500	0.01	**HS**
Skin finding:	**Flushed skin**	2(2.9%)	10(8.1%)	15(50%**€ #**)	47.935	0.0001	**HS**

N: number, P-value< 0.01: highly significant (HS), ®: comparison between groups I & II, #: comparison between groups I & III, €: comparison between groups II & III.

Table (10): Chi-Square statistical analysis & One Way ANOVA test show metabolic changes, random blood sugar & electrolytes changes among three groups (groups I, II & III) of PSS in acute cannabis intoxicated pre-school children

		Group I N= 70	Group II N= 123	Group III N = 30	Test value	P-value	Sig.
Arterial blood Gas	**Respiratory alkalosis**	2(2.9%)	6 (4.9%) ®	0(0%)	78.20*	0.001	**HS**
	Respiratory acidosis	5(7.1%)	29 (23.6%) ®	25(83.3%)#			
	Metabolic acidosis	4(5.7%)	13 (10.6%) ®	5(16.7%)#			
	Metabolic alkalosis	0(0%)	2 (1.6%)®	0(0%)			
PH	**Mean±SD**	7.37±0.04	7.36±0.05	7.30±0.03#	29.52•	0.001	**HS**
PCO2 (mmHg)	**Mean±SD**	38.51±5.54	39.99±6.21	41.96±12.76	2.47•	0.08	NS
HCO3 (mEq/L)	**Mean±SD**	21.74±2.08	21.80±2.61	20.13±5.05#	4.16•	0.01	**S**
Random blood sugar (mg/dl) (RBG)	**Mean±SD**	96.56±18.34	99.24±19.66	107.90±22.57# €	3.527	0.03	**S**
Na (mEq/L)	**Mean±SD**	138.39±2.88	138.25±2.88	137.87±3.32	0.329	0.72	NS
K (mEq/L)	**Mean±SD**	4.13±0.52	4.10±0.50	4.04±0.41	0.392	0.67	NS

N: number, SD= standard deviation, S = Significant, P-value< 0.01: highly significant (HS), ®: comparison between groups I & II, #: comparison between groups I & III, €: comparison between groups II & III.

Table (11): Chi-Square statistical analysis & One Way ANOVA test show place of admission and duration of hospital stay among three groups (group I, II & III) of PSS in acute cannabis intoxicated preschool children:

	Groups				Test value	P-value	Sig.
		Group I N=70	Group II N=123	Group III N=30			
Place of admission	**Inpatient**	70(100%)	0(0%)	0(0%)	218.38	0.01	**HS**
	ICU	0(0%)	123(100%®)	30(100%#)			
Duration of hospital stay (hours)	**Mean±SD**	22.04±6.25	26.57±5.70®	39.87±2.94€#	106.879•	0.00	**HS**
	<24hr	32(45.7%)	44(35.8%)	0(0.0%)	19.88	0.00	**HS**
	>=24hr	38(54.3%)	79(64.2%®)	30(100.0%€#)	19.88	0.00	**HS**

N: number, SD= standard deviation, P-value< 0.01: highly significant (HS), ®: comparison between groups I & II, #: comparison between groups I & III, €: comparison between groups II & III

Table (12): Chi-Square statistical analysis shows survival rate among three groups (group I, II & III) of PSS in acute cannabis intoxicated preschool children:

		Final group			Test value	P-value	Sig.
		Group I	Group II	Group III			
		N = 70	N = 123	N = 30			
Survival rate %	Recovery	70(100.0%)	123(100.0%)	29(96.7%)	6.462*	0.04	**S**
	Recovery with complications	0(0.0%)	0(0.0%)	1(3.3%)			

N= number, P-value <0.05: Significant (S)

Discussion

The present study is a prospective observational cross sectional study that was carried on all pre-school children of both sex admitted to Poison Control Center of Ain Shams University Hospitals (PCC-ASUH) with history of acute cannabis toxicity during the period from March 2019 to December 2019. All the studied patients were proven cannabis intoxication by compatible clinical symptoms & positive urine toxicological screening.

In the present study, according to PSS, the majority of patients (55.1%) were of group II (moderate group), while (31.4%) were of group I (minor group) & (13.5%) were of group III (severe group). In a previous study in France of Pélissier et al. (2014) they recorded that their studied groups were classified into two groups (minor & moderate) according to PSS with no severe group. The PSS is a standardized system for scoring clinical signs and symptoms due to poisoning. And it is considered as a standardized and generally applicable scheme for grading the severity of poisoning (Oh et al., 2017).

The percentage of acute cannabis intoxicated children in the present study, was 92.5%, while the percentage of acute cannabis intoxicated adult was 7.5% during the period from March 2019 to December 2019. The number of acute cannabis intoxicated pre-school children was 223 (89.9%) out of 248 acute cannabis intoxicated children admitted to PCCASUH during the studied period. The number of acute cannabis intoxicated pre-school children was 223 (24%) from total number of 930 acutely intoxicated pre-school children admitted to PCC-ASUH during the studied period. This was in agreement with Mory et al. (2019) retrospective observational study on admissions from 2010 to 2018 in the pediatric department at the University Hospital of Rouen. They reported that cannabis intoxication in young children was becoming a more common problem as they found more than 70% of their studied groups were younger than 2 years old. Also, this was similar to previous study done by (Noble & Kusin ,2019) who reported that 253 individuals were acutely exposed to cannabis, 28.1% were children in the United States, so this raises a real issue of public health.

In the present study, the mean age of the studied acute cannabis intoxicated pre-school children was (17.38 month ± 8.75) and age did not affect the severity of poisoning as clarified by non-significant difference between groups. This was in accordance to a previous study in France done by Claudet et al. (2017) who found that the mean age was (18 months old or younger) at 71% of the participated patients. On the other hand, Onders et al. (2016) reported a higher mean age of (1.81 years) among the studied acute cannabis intoxicated children in the United States. The patients were mostly males 54.3% (121 patients). The male predominance among patients was also observed by Onders et al. (2016) who reported that male children accounted for (50.7%) of exposure to cannabis in his

study in the United States.. On the other hand, female predominance among patients was observed by Pélissier et al. (2014) in France. In the present study, the majority of the patients (88.3%) were from urban areas. (Masry &Tawfik, 2013) attributed urban–rural differences to the proximity of these areas to PCC-ASUH and not to higher magnitude of poisoning problem.

This study showed that the mean delay time was (6.2±3.3) hours and there was no significant statistical difference between the delay time and severity of poisoning & this was similar to study of Claudet et al. (2017) who reported a lower mean delay which was (4.24 ± 3.6) hours in the patients who presented with acute cannabis toxicity in France . Ingestion was the main route of exposure in the current study. This is could be explained by that children of this age easily grasp small fragments of cannabis resin and then chew or swallow them (Pélissier et al., 2014). In a previous study in the United States done by Eike et al. (2019), they found that ingestion was also the main route of exposure to cannabis in children and this high percentage of ingestion exposures could be associated with the increasing popularity of marijuana food products, such as candy.

Accidental exposure was the only manner of exposure (100%) in this study. This was approximately similar to study done in the United States by (Boadu et al., 2020) who explained that the increase in these accidental exposures is related to the increased availability of marijuana. The main source of exposure was father in (18.4%) of patients who is a cannabis addict, while other family members were the main source in (4%) of patients. This was in agreement with (Noble & Kusin, 2019) who reported that most children (91.9%) were exposed to cannabis products belonging to a family member in the United States. The majority of exposure of cannabis intoxicated pre-school children (91.5%) occurred at their home, while (4.5%) at wedding parties, (4%) at family member home. In addition, there was a significant difference among three groups of PSS regarding place of exposure. This was in agreement with Onders et al. (2016) who reported that most exposures occurred at the child's own residence (83.0%).

In the present study, normal sinus rhythm was observed in the majority of patients (93.3%), while tachycardia was observed in (5.8%) of the studied group. This was consistent with the study in France of Pélissier et al. (2014) who reported that three out of twelve acute cannabis intoxicated patients presented with tachycardia. On the other hand, (Noble & Kusin , 2019) reported a higher percentage of patients (51.2%) presented with sinus tachycardia in the United States. Some studies reported that sinus tachycardia was the most common arrhythmia with acute cannabis toxicity, and was attributed to anti-cholinergic activity and do not usually require any specific treatment (Franz & Frishman, 2016).

Normal blood pressure was observed in most of cases (86%), while hypertension was observed in only (13.5%). This was consistent with Richards et al. (2017) who reported that normal blood pressure was observed in most of his studied group on cannabis toxicity (90%) and hypotension was recorded in a minor percentage in the United States. Increased blood pressure was attributed to the anti-cholinergic activity. Furthermore, the cardiovascular manifestations are a result of the stimulation of CB1 receptors located in the heart. This stimulation leads to potential blockage of the parasympathetic system and activation of the sympathetic system (Chinello et al., 2017).

In the present study, there was a highly significant increase of respiratory rate in group III compared to group I &II. This was in accordance with the previous retrospective study of Spadari et al. (2009), who found increased percentage of mechanically ventilated patients so they recommended that these clinical effects of such toxicity can be potentially life threatening requiring admission to the pediatric intensive care unit. This could be explained by the smaller body mass in children, cannabis ingestion results in high serum 9THC levels, despite a small amount ingested (Lavi et al., 2015) which leads to more disturbance of conscious level, leading to respiratory center depression & hypoventilation that may need airway support and ICU admission (Santander et al., 2011).

In the present study, most of patients (68%) had normal body temperature, while minor percentage (31.8%). had hyperthermia. This was consistent with the case report at Israel of Zarfin et al. (2012), who recorded hyperthermia in an infant exposed to cannabis and attributed it to the anti- cholinergic effect of cannabis as heat dissipation is reduced by impaired sweating.

The most common CNS manifestations in the present study were drowsiness (31.4%), muscle rigidity (21.5%) & extra-pyramidal manifestations (21.5%). This was in accordance with Lavi et al. (2015) who reported that the neurological manifestations were the predominant signs manifested in their studied children at Israel. According to REED's coma scale, 70 patients had drowsiness (31.4%), (67.7%) were in coma grade I. Previously in the United States in 2016, Onders et al. study reported 17 patients (0,9%) were in coma grade I, while 580 patients had drowsiness (29.5%), however Richards et al. (2017) study reported that 45 of children (age 12 years or less) had drowsiness(57.7%). The neurological effects occurred as 9-THC is lipid soluble which leads to rapid distribution into well-vascularized organs such as brain leading to sudden disturbance in conscious level (Dinis Oliveira, 2016).

Respiratory distress was observed in (1.8%) of patients, while respiratory failure was found in two patients (0.9%). This was in accordance with (Noble & Kusin, 2019) study who found that respiratory failure presented in one patient (1.5%), who was successfully extubated on the following day, in his study on clinical effects following acute cannabis exposure to children in the United States. The present study also showed that respiratory findings affected by the severity of poisoning on comparing the three groups of PSS, and this was in accordance with (Spadari et al., 2009 & Le Garrec et al., 2014) who explained that these

respiratory changes due to associated acute respiratory center depression following central nervous system depression.

In the present study, 17.9% of patients complained of vomiting & 18.4% of patients had abdominal distension. This was in accordance with (Noble and Kusin, 2019) who reported that vomiting presented in (11.9%) of his studied patients in the United States. Mydriasis was observed in (13%) of patients, while miosis was observed in (18.8%) & eye redness was observed in (9.9%). Richards et al. (2017) reported that mydriasis was found in a higher percentage (54%) of his studied group on cannabis toxicity in the United States, while miosis in (37.5%), while Pélissier et al. (2014) recorded that red eye presented in a higher percentage (16.7%) of his studied group in France and they explained its occurrence due to conjunctival blood vessels vasodilation. Flushed skin was observed in (12.1%) of patients. Onders et al. (2016) recorded that flushed skin occurred in a lower percentage (0.3%) of their studied group in the United States, and they explained its occurrence due to skin blood vessels vasodilatation.

Most of patients (59%) in this study had normal ABG. That was similar to Claudet et al. (2017) study on cannabis toxicity in France, who reported that (76%) of his studied group had also no ABG abnormality. Respiratory acidosis observed in this study in (26.5%) and this was in accordance with Richards et al. (2017) who reported that respiratory acidosis appeared in (31%) of his studied group in the United States and they explained it by impaired ventilation following central nervous system depression, as 9-THC is lipid soluble which leads to rapidly distribution into well- vascularized organs such as brain (Dinis Oliveira, 2016). The present study showed that the severity of poisoning affected the ABG findings as clarified by presence of a highly statistical significant difference on comparing three groups under study. This was in accordance with previous study in the United States of Richards et al. (2017), who analyzed published reports of unintentional cannabis ingestions in children and reported that 15 children who unintentional ingested cannabis (19.2%), had respiratory acidosis due to associated hypoventilation following central nervous system depression.

In the current study, the severity of poisoning affected random blood sugar being significantly higher in group III when compared with group II. Previously in France, Claudet et al. (2017) reported a higher percentage of patients (6%) having elevated random blood glucose level, especially in patients with excessive agitation. This could be explained due to associated sympathetic system activation that lead to elevation of random blood glucose level in the agitated children.

In the present study, ICU admission occurred in (68,7%) of patients. That was in accordance with the previous observational study in the United States of Noble and Kusin (2019) who reported that inpatient admission occurred in a lower percentage than ICU admission and they explained that could be related to resin type as subjects who used concentrated cannabis products (liquids, resins, extracts) had a higher incidence of intubation and ICU admitted than those who used non-concentrated products. Also children who were exposed to a concentrated cannabis product also had a higher incidence of intubation than those exposed to non-concentrated products. There was a highly significant difference regarding duration of hospital stay among three groups of PSS in acute cannabis intoxicated pre-school children. These findings were similar to study in France of Le Garrec et al. (2014) .Oral 9-THC formulations exhibit variable absorption and undergo extensive hepatic first-pass metabolism (Eichler et al., 2012) and this resulting in lower peak plasma 9-THC concentration relative to inhalation and a longer delay (120 minutes) to reach peak concentration. The elimination half-life of 9-THC vary from approximately 6 minutes to 22 hours, so that most of acute cannabis intoxicated children should better observed for 24 hours (McPartland and Guy, 2017).

In the present study, most of patients recovered without any complication during hospital stay (99.6%) while only one patient recovered with visual impairment due to prolonged hypoxia with need of pediatric follow up (0.4%) and there were no recorded dead cases. These results were similar to review article in the United States of Eike et al. (2019) who concluded that all young children admitted to the hospital after exposure to high concentration edible cannabis products, had a full recovery.

Conclusion

Incidence of acute cannabis intoxicated pre-school children in Egypt has dramatically increased due to their widespread use by the general population as recorded by increasing number of studied cases, representing about 24% from total number of 930 acutely intoxicated pre- school children admitted to PCC-ASUH during the studied period. The clinical course of acute cannabis toxicity in children may vary widely from mild self-limiting to severe life-threatening requiring ICU admission. Severity of acute cannabis intoxication in pre-school children can be evaluated simply by using PSS. Coma grades I/II & other neurological findings in acute cannabis intoxicated pre-school children were associated with higher grade of severity after acute cannabis intoxication in pre-school children, so clinicians should consider cannabis toxicity in any child with sudden-onset encephalopathy in healthy infants and toddlers. In addition, tachypnea and eye findings including red eye were associated with higher grade of severity after acute cannabis intoxication in pre-school children. Furthermore, respiratory and metabolic acidosis can be used as predictors of severity of acute cannabis intoxicated pre- school children. These parameters which are easily available could be used as simple tool to help the prediction of the severity in acute cannabis intoxicated pre-school children.

Recommendations

Early combination of PSS and arterial blood gas analysis could help in identifying patients at risk and

even those who might progress to severe toxicity after acute cannabis intoxication in pre-school children. Careful neurological examination and conscious level assessment should be done after acute cannabis intoxication in pre-school children and can be used as predictor for severity of these patients. As well, presence of tachypnea and red eye could be considered as early predictors of severity of acute cannabis intoxication in pre-school children. Public education by raising the awareness among parents about the potential harms related to cannabis exposure through organizing awareness campaigns at schools and universities and publication of books, brochures, flyers that address the problem of addiction.

An important limitation to the present study is that it only included patients who were presented to PCC- ASUH, which is a single toxicological center and might not globally represent the pattern of acute cannabis toxicity in the whole country. In addition, it was expected that there was a greater number of cannabis intoxicated patients who were managed at other hospitals or health care centers. Moreover, patients less than 6 years who only included in this study, so further studies are needed to portray and compare the pattern of acute cannabis toxicity in different age groups mainly the teenagers. Severity of acute cannabis intoxication in pre-school children can be evaluated simply by using PSS.

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تقييم تسمم القنّب الحاد لدى الاطفال في سن ما قبل المدرسة الذين تم حجزهم بمركزعلاج التسمم بمستشفيات جامعة عين شمس

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الملخص العربي

المقدمه: في مصر، يأتي القنب على رأس قائمة المواد المتعاطه وفقًا لإحصاءات صندوق مكافحة المخدرات وعلاج الإدمان. أدي استخدام القنب على نطاق واسع إلى سهوله وصوله للأطفال. تسمم القنب عند الأطفال يمكن أن يسبب اعتلال دماغي وغيبوبة. **الهدف من الدراسة:** هو تقييم معدل انتشار التسمم الحاد بالقنب لدى الأطفال في سن ما قبل المدرسة في مصر؛ تحليل العوامل المختلفة المتعلقة بالمشكلة والصورة السريرية وتقييم نتائج المشكلة وشدتها من خلال مقياس شدة التسمم. **طريقه البحث:** الدراسة الحالية عبارة عن دراسة مقطعية أجريت على أطفال في سن ما قبل المدرسة من كلا الجنسين الذين تم حجزهم في مركز علاج التسمم في مستشفيات جامعة عين شمس نتيجه وجود سمية حادة بالقنب خلال الفترة من مارس ٢٠١٩ إلى ديسمبر ٢٠١٩. **نتائج الدراسه:** خلال فترة الدراسة، كانت النسبة المئوية للأطفال الذين اعمارهم في سن ما قبل المدرسة ويعانون من تسمم القنب الحاد كان (٨٩.٩٪) وكان متوسط عمر الأطفال اعمارهم في سن ما قبل المدرسة ويعانون من تسمم القنب الحاد هو (١٧.٣٨ شهرًا ± ٨.٧٥) مع اغلبيتهم من الذكور وقد تم تصنيف الحالات إلى ثلاث مجموعات وفقاً لاستخدام مقياس شده التسمم، وكانت غالبية المرضى (٥٥.١٪) من المجموعة الثانية (المجموعة المتوسطة)، بينما (٣١.٤٪) كانوا من المجموعة الأولى و (١٣.٥٪) كانت من المجموعة الثالثة (المجموعة الشديدة). فيما يتعلق ب بيانات الفحص , لوحظ تسارع ضربات القلب في (٥.٨٪) وارتفاع ضغط الدم في (١٣.٥٪) وتسارع في معدل التنفس لدى (١٨٪) و ارتفاع حرارة الجسم في (٣١.٨٪) وكانت نسبه النعاس (٣١.٤٪)، صلابة العضلات (٢١.٥٪)، والتشنجات (٢١.٥٪) ووفقًا لمقياس ريد (REED) لمستوي الوعي، كان (٦٧.٧٪) من المرضي في غيبوبة من الدرجة الأولى، بينما كانت الغيبوبة من الدرجة الثانية في (٠.٩٪) من المرضي, لوحظ ضيق في التنفس لدى (١.٨٪) من المرضى وقد اشتكى ١٧.٩٪ من المرضى من القيء، لوحظ توسع حدقة العين في (١٣٪) من المرضى، بينما لوحظ توسع حدقة العين في (١٨.٨٪)، لوحظ احمرار الجلد في (١٢.١٪) من المرضى, كانت حموضه الدم الناتجه عن اضطرابات الجهاز التنفسي هي الابرزحيث أثرت على ٢٦.٥٪، تم دخول (٦٨.٧٪) من المرضى في وحدة العناية المركزة و تم احتجاز اغلب الاطفال لمده≤٢٤ ساعة في مركز علاج التسمم بجامعة عين شمس وكانت نسبتهم المئويه هي (٦٥.٩ ٪). **الخلاصه:** هناك تزايد في معدل انتشار تسمم القنب الحاد لدى أطفال ما قبل المدرسة بشكل كبير . يمكن تقييم شدة التسمم الحاد بالقنب لدى الأطفال في سن ما قبل المدرسة ببساطة من خلال مقباس شده التسمم. **التوصيات:** يجب التركيز علي التثقيف العام من خلال زيادة الوعي .يمكن أن يساعد كلا من تحليل غازات الدم الشرياني الدقيق وتقييم مستوى الوعي في تحديد المرضى المعرضين للخطر.

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