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Postmortem Toxicology Data of Autopsied Cases in the Northern Border Province, Saudi Arabia: A Six-Year Retrospective Study



بيانات السمية ما بعد الوفاة لحالات تشريح الجثث في مقاطعة الحدود الشمالية في المملكة العربية السعودية: دراسة استرجاعية مدتها ست سنوات.

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Abstract

Autopsy remains the most reliable tool to study mortality causes. This project was conducted to study toxicological findings in relation to gender, age, manners and causes of death among autopsied cases from 2013-2018 in the Northern Border province of Saudi Arabia.

All police, hospitals, toxicology laboratory and autopsy reports related to the autopsied cases within the period of the study were revised.

Among 908 autopsied cases during the study period, 144 autopsies (15.8%) showed positive toxicological findings (136 males; 94.4%) and 8 females (5.4%). Positive toxicological findings were significantly more common in cases aged 20-40 years ($p < 0.0001$) without a significant gender difference ($p = 0.116$). The commonest toxicological finding was alcohol 55 (6.5%) cases followed by cannabis in 27 (2.9%) cases, while 19 (2.1%) cases showed carboxyl-hemoglobin $\geq 10\%$. Most deaths with positive toxicological screens (98 cases; 68.1%) were reported to be accidental. Six cases were recorded as carbon monoxide poisoning (COP), 3 cases were recorded as alcohol toxicity, and 2 cases were registered as hypertensive induced brain haemorrhages. Brain haemorrhages and aspiration pneumonia were reported among deaths related to alcohol, while intraventricular brain haemorrhage was the cause of death in amphetamine deaths. Cherry red hypostasis and pulmonary edema were found among COP deaths.

In conclusion, positive toxicology data were found in a considerable percent of autopsied cases, and they can contribute directly or indirectly to identifying the cause of death. Hence, toxicological screening is mandatory in all suspected deaths and screening should not be neglected in cases with absent suggestive autopsy findings.

Keywords: Forensic science, Alcohol, Amphetamine, Carbon Monoxide Poisoning, Saudi Arabia.



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المستخلص

يبقى تشريح الجثة هو الأداة الأكثر موثوقية لدراسة أسباب الوفيات. وتم إجراء هذا المشروع لدراسة النتائج السمية المتعلقة بالجنس والعمر والأسلوب والأسباب التي حدثت بها الوفاة بين الحالات التي تم تشريحها في الفترة من ٢٠١٣-٢٠١٨ في مقاطعة الحدود الشمالية في المملكة العربية السعودية.

تم تنقيح جميع تقارير الشرطة والمستشفيات ومختبرات السموم وتشريح الجثة المتعلقة بحالات تشريح الجثث خلال فترة الدراسة.

من بين ٩٠٨ حالة تم فيها تشريح الجثث خلال السنوات التي شملتها الدراسة، أظهرت ١٤٤ عملية تشريح (١٥,٨٪) نتائج سمية إيجابية (١٣٦ ذكور (٩٤,٤٪) و٨ إناث (٥,٤٪)). كانت النتائج السمية الإيجابية أكثر شيوعاً بشكل كبير في الحالات التي تتراوح أعمارها بين ٢٠ و٤٠ عاماً (مستوى الدلالة > 0.0001) دون فرق كبير بين الجنسين (مستوى الدلالة = 0.116). وكانت مادة الكحول هي الأكثر شيوعاً بين الحالات المكتشفة (٥٥ حالة (٦,٥٪)) يليها القنب في ٢٧ حالة (٢,٩٪)، في حين أظهرت ١٩ حالة (٢,١٪) تركيز مركب الكربوكسي-هيموغلوبين $\geq 10\%$. معظم الحالات التي تم الإبلاغ عنها وسجلت إيجابية خلال عملية فحص السمية (٩٨ حالة (٦,٨٪)) اكتشفت في قضايا حوادث. وتم تسجيل ست حالات على أنها تسمم بأول أكسيد الكربون (COP)، وسجلت ٣ حالات على أنها سمية كحولية، وسجلت حالتان كنزيف دموي ناجم عن ارتفاع ضغط الدم. الحالات التي تم الإبلاغ فيها عن وجود نزيف في الدماغ والالتهاب الرئوي كانت مرتبطة بالكحول. في حين أن نزيف المخ داخل البطن كان سبب الوفاة فيه في حالات الوفيات المرتبطة بالأمفيتامين. وتم العثور على ترسبات بلون أحمر وردي أو ما يسمى ركود الدوران الأحمر المركزي والوذمة الرئوية بين وفيات حالات تسمم بأول أكسيد الكربون COP.

وفي الختام، تم العثور على بيانات السمية الإيجابية في نسبة كبيرة من حالات تشريح الجثث، ويمكن أن تسهم بشكل مباشر أو غير مباشر في تحديد سبب الوفاة. وبالتالي، يعد الفحص السمي إلزامياً في جميع حالات الوفاة المشتبه فيها ويجب عدم إهمال الفحص في الحالات التي لا توجد فيها نتائج تشريح جثث موحية.

الكلمات المفتاحية: علوم الأدلة الجنائية، الطب الشرعي، الكحول، الأمفيتامين، التسمم بأول أكسيد الكربون.

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1. Introduction

Poisoning is a worldwide leading cause of unnatural deaths. The World Health Organization has reported about 370,000 poisoning-induced deaths annually, among which pesticides, drugs, and alcohol were the main toxic agents [1]. In the United States of America, over 72,000 drug overdose deaths were reported in 2017, including illicit drugs deaths, with more than a threefold increase in comparison to the reported poisoning-related deaths in 2002 [2]. In addition, poisoning deaths were reported to be about 60% of the undetermined unnatural fatalities [3].

Drug overdose deaths are mainly related to their toxic effects on the body organs according to their mechanisms of action. CNS depression, cardiac arrest, hepatic and renal failure are major direct causes in drug related deaths [4,5]. For example, opiates γ -hydroxybutyrate (GHB) or benzodiazepines are represented by coma with central nervous system depression and cardio-respiratory failure. While sympathomimetics such as cocaine and amphetamine (AMP) are manifested as generalized sympathetic manifestations all over the different body systems, and death may occur due to heart failure [6]. Illicit drug overdose is a common accidental cause of death among addicts [7]. Illicit drugs can cause death via CNS depression or cardiac arrest [8]. In addition, they can induce behavioral disorders with depersonalization, increased violence and more susceptibility to attack others. Also, disorientation and lack of attention may occur resulting in a higher incidence of road traffic accidents and deaths [9,10]. Furthermore, decreased inhibition and altered mood may predispose addicts to suicide attempts [11,12].

Toxicities can be caused by suicide attempts, accidental overdose, prescription errors, in compliant patients or accidental ingestions among children. In addition, accidental exposure to toxicants such as occupational exposure to pesticides, carbon monoxide (CO), or poisonous snakes and insects are still important causes of deaths [13,14]. On the other hand, these toxicities may be homicidal, especially among the elderly who are maintained on cardiac or hypoglycemic medications that may be used by some of their relatives to kill them [15]. In addition, exposure to some

drugs and illicit substances may facilitate sexual assault and murder by decreasing their expected vocal and physical resistance [10].

Data regarding poison-related related deaths are deficient in Saudi Arabia with few published data such as data reported from the Eastern Province Toxicology Center [16]. Autopsy remains the most reliable medical tool to study mortality causes, including poisoning-related deaths. This study was conducted to determine the data from toxicological investigations of the autopsied cases in the Northern Border Region in Saudi Arabia from 2013-2018 in relation to gender, age, manners and causes of death with postmortem positive toxicological findings.

2. Materials and Methods

Data collection

According to laws in Saudi Arabia, all suspected unnatural deaths are reported to the police for further investigation into the cause of death for any suspected homicide. In these cases, forensic experts are consulted. Samples for toxicological screening are routinely taken from all autopsied cases. The cause of death is defined by the forensic expert after revising the toxicological report issued by the authorized toxicology laboratory, as these results can change the interpretation of the data in some cases, especially cases with obscure causes of death or road traffic victims and murdered adults who may be under the effect of sedation caused by illicit drugs. In cases of suspected poisoning with clear findings, the toxicological data is mandatory to support the autopsy findings, as chemical analysis is the most confirmatory method for the diagnosis of poisoning.

In this study, all postmortem data at the Forensic Medicine Center in the Northern Border Province were reviewed from the start of January 2013 until the end of December 2018. All postmortem reports with positive toxicological data for illicit drugs, ethanol, CO and other chemicals were identified. Demographic data, autopsy findings, police reports and toxicological findings of the positive cases were recorded.

Analytical methods

Body fluids and tissue samples were sent to Tabouk



Poison Control and Forensic Chemistry Center for analysis. This center is authorized by the Saudi Ministry of Health for forensic toxicology investigations in the region of Tabouk, Northern Border, Al-Jouf and Al-Qurayat. Examination of all samples was done according to the following protocol: Volatiles including ethanol, isopropanol, methanol and acetone were analyzed using headspace-gas chromatography. Ethanol and drugs of abuse (AMP, barbiturates, benzodiazepine, cannabis, cocaine, and opiates) in urine were primarily screened by immunoassay using the ARCHITECT system and in blood, bile and vitreous humor using the RANDOX system. Various tissue samples (ex, liver, kidney, stomach, stomach content, lung, brain bladder, intestine) were digested using the Stomacher 400 circulator and then analyzed using the RANDOX system for primary screening for drugs of abuse. Acidic, neutral and basic drugs were extracted from biological fluids or tissues using solid phase extraction (SPE) followed by instrumental analysis with gas chromatography mass spectrometry (GC-MS). Amphetamine and opiate were extracted by liquid-liquid extraction. The positive controls were prepared in the laboratory. They contained frequently observed drugs at low concentrations to address sensitivity of the assay. In addition, the positive controls contain drugs of various chromatographic retention times (early and late eluting drugs) to ensure the chromatographic conditions are capable of detecting a number of drugs. The screened drugs include narcotics, sedatives pesticides, acetaminophen, non-steroidal anti-inflammatory drugs, antidepressants, stimulants, antihistamines, decongestants, muscle relaxants, anticonvulsants, organic poisons, and antipsychotics. Both amphetamine and methamphetamine were analyzed. Negative Controls were prepared from blood bank samples which were determined not to contain reportable drugs. The procedure may be used to screen for basic, acidic and neutral drugs. Once drugs have been confirmed, the procedure may be used to quantitate drugs, provided at least 3 calibrators are used to generate a response curve. Helium gas was used as a carrier gas. The parameters of GC and mass spectrum assay are shown in table -1.

If carbon monoxide poisoning (COP) was suspected

then carboxyl hemoglobin level (COHb%) was analyzed using an ultraviolet system. Other tests were done upon request. The absorbance of the solution was scanned at a wavelength of 650 nm to 500 nm, using the ultraviolet system. The absorbance ratio at 541nm/A555 nm was calculated and the COHb% was determined for the negative and positive control samples and the case samples from the slope of the known calibration curve. The calibration curve was obtained by saturating negative blood with known concentrations of Hb CO.

Statistical analysis: The data were processed and analyzed by GraphPad Prism V (GraphPad Software Inc., San Diego, CA). Chi square was used for analysis of the categorical data. Data were represented as a percentage of the totals. Significance was considered with p -value <0.05 .

3. Results

Data revealed that a total of 908 cases (84 female; 7.5%) and 824 (92.5%) were males underwent autopsy in the Northern Border Region within the period of the study. Ages ranged from 4 months to 72 years. One hundred and forty-four autopsies (15.8%) showed positive toxicological screens (Table-2). Interestingly, 75% (108/144 cases) of the positive cases were suspected in the police report to have toxicological evidence of illicit drugs. However, 17.3% of the negative cases (132/764) were falsely suspected to have positive toxicological presence of illicit drugs in the police reports.

The distribution of the positive toxicological cases over the years of the study is shown in Table-2. They were significantly ($p=0.0011$) higher among autopsied cases aged from 20-40 years (about 20% of autopsied cases in this age range gave positive toxicological results) with no effect for gender in the distribution of the toxicological positivity among the autopsied cases (136/824 in males and 8/84 in females with $p=0.116$). In addition, there was no significant difference in the type of detected substances in the positive cases in relation to their ages (Table-3). Regarding ages, alcohol was the commonest among the middle-aged and elderly, while AMP was the highest among the autop-



Table 1- Parameters of GC-MS analysis.

1. Parameters for GC	
Linear velocity	Flow control mode
84.1 kPa	Pressure
17.3mL/mint	Total flow
1.30 mL/min	Column flow
41.8 cm/sec	Linear velocity
3 ml/mint	Purge flow
10 °C	Zero Split ratio
70 °C	Column oven temperature
270°C	Injection temperature
Split	Injection mode
70 °C (1) to 280 °C	8(10.9)
(10 °C/ minute then hold (8 minutes)	Oven temperature program
2. Parameters for MS	
240 °C	Ion Source Temp
290 °C	Interface Temp
2.00 min	Start Time
30.00 min	End Time
0.20 sec	Event Time

Table 2- Distribution of cases with positive toxicological findings over the six years of study period.

Year	Number of autopsies	Cases with Toxicological findings	ALC	CAN	AMP	CO	MS
2013	101	19 (18.8%)	7(6.9%)	3(3%)	5 (5%)	2 (2%)	2 (2%)
2014	127	20 (15.7%)	6 (4.7%)	4 (3.1%)	3 (2.4%)	4 (3.1%)	3 (2.4%)
2015	148	28 (18.9%)	13 (8.8%)	4 (2.7%)	4 (2.7%)	4 (2.7%)	3 (2%)
2016	153	25 (16.3%)	8(5.3%)	7(4.6%)	4((2.6%)	3 (2%)	3 (2%)
2017	171	24 (14%)	9 (5.3%)	5(2.9%)	4(2.3%)	2(1.2%)	4(2.3%)
2018	208	28 (5.8%)	12 (5.8%)	4(1.9%)	5 (2.4%)	4(1.9%)	3(1.4%)
Total	908 (100%)	144 (15.9%)	55(6.1%)	27(3%)	25(2.8%)	19(2.1%)	18 (2%)

ALC: alcohol, AMP: amphetamine, CAN: cannabis, CO: carbon monoxide, MS: multiple substances.



Table 3- Documented cases of deaths among the studied cases with positive toxicological findings.

Mode no. (%)	Causes of death	no. (%)	ALC	CAN	AMP	CO	MS
Accidental 98 (68.1)	RTA	56 (38.9)	30(20.8)	11(7.7)	7(4.9)	-	8(5.6)
	Electrocution	5 (3.5)	2(1.4)	-	1(0.7)	-	2(1.4)
	FFH	6 (4.2)	2(1.4)	3(2.1)	1(0.7)	-	-
	Poisoning	11 (7.6)	3(2.1)	-	-	8(5.6)	-
	SND	12 (8.3)	3(2.1)	4(2.8)	1(0.7)	2(1.4)	1(0.7)
	Fire burn	8 (5.6)	-	-	-	8(5.6)	-
Suicidal 24 (16.7)	Hanging	10 (6.9)	4(2.8)	2(1.4)	1(0.7)	-	3(2.1)
	Cut throat/ radial	13 (9)	4(2.8)	2(1.4)	6(4.2)	-	1(0.7)
	Poisoning	1(0.7)	-	-	1(0.7)	-	-
Homicidal 16 (11.1)	Shooting	9 (6.3)	2(1.4)	3(2.1)	4(2.8)	-	2(1.4)
	Stabbing	7 (4.9)	3(2.1)	-	2(1.4)	-	1(0.7)
Undetermined		6 (4.2)	2(1.4)	2(1.4)	1(0.7)	1(0.7)	-
Total		144 (100%)	55(38.2)	27(18.8)	25(17.4)	19(13.2)	18(12.5)

ALC: alcohol, AMP: amphetamine, CAN: cannabis, CO: carbon monoxide, FFH: fall from height, MS: multiple substances, RTA: road traffic accident, SND: sudden natural deaths.

sied cases below 20 years of age. Regarding the source of alcohol detected in the autopsied cases, it was difficult to differentiate between commercially produced alcohol and illegally produced alcohol by the available toxicological screening methods or the data found in the police reports.

Regarding the manner of death, accidental deaths were the commonest (98 cases) among positive cases. Table-4 shows the causes of death in relation to the toxicological laboratory data of the autopsied cases. In parallel, accidental deaths were reported in 71% of the negative cases (542/764), while suicidal and homicidal deaths were reported in 16% (123/764) and 13% (99/764), respectively.

Six cases were recorded as carbon monoxide poisoning (COP) with a COHb range from 56%-65%; 3 cases were recorded as alcohol toxicity, and 2 cases were registered as AMP induced hypertensive brain hemorrhage. Data of the autopsied cases with reported deaths due to poisoning are shown in table (Table-4).

4. Discussion

This study evaluated the toxicological findings in relation to gender, age, manner and cause of deaths among autopsied cases from January 2013-December 2018 in the Northern Border province of Saudi Arabia. Around 16%



Table 4- Autopsy findings in the autopsied cases with documented poisoning or overdose deaths.

Cases with Toxicological findings (no.)	Cause of death	Autopsy Findings
6 Cases	COP	<ul style="list-style-type: none"> - Cherry red hypostasis (5/6 cases) - Pulmonary edema (6/6 cases) - Cerebral edema (5/6 cases) - Cherry red lungs and viscera (5/6 cases) - Cherry red abdominal muscles and intercostal (4/6 cases) - Congested conjunctiva & sub-conjunctival hemorrhage (4/6 cases) - Brain hemorrhages (4/6 cases).
3 Cases	ALC	<ul style="list-style-type: none"> - Pulmonary edema (3/3 cases) - Cerebral, brainstem, and cerebellar hemorrhage. (3/3 cases) - Chronic pancreatitis (2) - Diffuse steatosis (3/3 cases) - Liver fibrosis (partial) (1/3 cases) - Gastritis (3/3 cases) - Aspiration pneumonia (3/3 cases)
2 Cases	AMP	<ul style="list-style-type: none"> - Intraventricular brain hemorrhage (2/2 cases) - Scattered brain petechial hemorrhage (2/2 cases) - Subarachnoid hemorrhage (1/2 cases) - Hypertrophic heart (1/2 cases) - Sub-conjunctival hemorrhages (2/2 cases) - Sub-endocardial and gastric mucosal hemorrhages (2/2 cases) - Teeth grinding and losing (2/2 cases)

ALC: alcohol, AMP: amphetamine, CO: carbon monoxide.

of the autopsied cases showed positive toxicological findings, which were higher among autopsied cases aged 20-40 years. There was no effect for gender in the positive results data with a 17:1 male to female ratio. Regarding age, alcohol was commonest among the middle-aged and elderly, while AMP was highest among the autopsied cases below 20 years old. Accidental deaths were the commonest among positive cases. Six cases were recorded as COP, 3 as alcohol toxicity, and 2 were registered as AMP induced hypertensive brain hemorrhage with characteristic autopsy findings.

Positive toxicological findings were reported among 16% of the autopsied cases, which is slightly lower than reported in the Eastern Province (19.5%) during the years from 2009-2013 [16]. Also, the percentage in this study is double than in Turkey in the period from 1997-2001 [17]. Toxicity was more common among males, especially in the middle-aged group, which is in accordance with previous studies [11,16, 18,19]. This is due to the increased use

of illicit substances among middle-aged males. Also, the higher incidence of positive cases in the middle-aged group can be explained by the higher incidence of autopsy in this age group, which does not actually reflect their presence in the general population. This is understandable, as middle-aged males are more frequently involved in car accidents, crimes, and suspicious deaths which require further medico-legal investigations.

Interestingly, there was no significant difference in the toxicology data of the autopsied cases in relation to their genders (Table-3). However, illicit drugs and substances are expected to be more common in males, as reported previously [16, 18,19]. This difference may be due to the difference of the targeted group in the previous study and the current one, as we were only studying the autopsied cases; whereas, the other studies targeted the pattern of illicit drug use among the general population.

Alcohol and illicit drugs (cannabis and AMP) were reported in 125 cases (86.8%) of the positive toxicologi-



cal results. This is more than twice the percent reported in the Eastern Province study [16]. This may be due to the unavailability in the Northern Borders region, which has no agricultural activities to use pesticides which may be used to commit suicide. In addition, it may be due to other factors. These may include under-reporting of suicidal cases involving drug overdose, accidental overdose of illicit drugs, or accidental household exposure to CO. In Jordan, deaths from illicit drugs are below one quarter of the positive toxicological deaths found in this study. Opioids and benzodiazepines showed significant proportions in the deaths related to illicit drugs. However, cannabis and AMP were not detected in the autopsied cases. This different pattern of illicit substance abuse supports the view that availability of substances plays a major role in their price and controls their rate of abuse [13].

Alcohol was the most common illicit substance found in the studied cases. This is in accordance with the results of the Eastern Province study [16]. The same was reported in studies from Sweden [20] and Jordan [21,22], as alcohol is a widely used illicit substance - even with its religious prohibition and illegal status. Also, local manufacturing and relatively cheap prices have increased its consumption. In addition, its adulteration with methanol was found in ten cases with methanol levels ranging from 67-258 ng/mL. Methanol has a greater depressive effect on the brain center with more incidence of metabolic acidosis [23].

On the other hand, AMP was commonly reported among autopsied cases below 20 years of age, due to the false concepts about its ability to improve their attention and concentration during study. Due to this, students can become abusers of AMP. This trend increase AMP percent among the studied cases. Cannabis was mostly reported among lorry drivers and workers (18 cases) and was common in road traffic accident victims, which is in accordance with other studies such as Carmen del Rio et al. (1999) [24].

Regarding the mode of death, accidental deaths were the commonest among toxicologically positive cases (92

cases (63.8%)). Illicit drugs can play a role in the reported accidental causes of deaths. They may induce impaired consciousness, decrease alertness, and impair motor coordination. They may be used in suicide attempts, which may also involve road traffic accidents, electrocution, or jumping from heights [13-15]. Also, they can predispose users to sudden natural deaths such as sudden cardiac deaths (SCDs) [25-27].

COP was reported in six cases, with reported COH levels over 40% as the cause of death. From these deaths, 3 cases were dead before arrival at the hospital while the other 3 cases were taken to the emergency department with complete loss of consciousness. They were intubated and mechanically ventilated and also treated using the other supportive coma measures. In these cases, clinical parameters gradually deteriorated. One case died within the first 24 hours and the other 2 cases died the second day after admission. Autopsy findings for COP such as cherry red hypostasis and viscera in addition to cerebral hemorrhage and pulmonary edema are in line with the previous published data such as the study by Mehta et al. (2001) [28]. High COHb levels were reported in 13 other cases (COH level 15-30%), from which 9 cases were attributed to dry burns involving more than one third of the body surface area. Burn associated deaths were reported on the first and second day after the burns occurred. Second day cases showed lower levels of COHb, which is expected due to the resuscitation attempts and washing of CO due to the applied treatment protocol. In addition, high COHb levels were reported in 2 cases of cardiac sudden natural deaths with COHb levels of 17% and 22% in which CO may have had a role. This is because CO can contribute to cardiac deaths even with low levels via different mechanisms [29,30].

Autopsy findings for alcohol and AMP were a mix between the pathological effect of the substances on health and the cause of death. In alcohol abusers, liver steatosis, fibrosis, and gastritis were constant findings, which is in line with previous published data about the health effects of alcohol [31] and other published data on autopsy findings.



At the same time in AMP, loss of teeth, hypertensive left ventricular hypertrophy, and cerebral hemorrhage found in the autopsied cases were interesting findings that are in accordance with previously published data [32].

For the other cases where poisoning was not reported as the direct cause of death, autopsy findings were different according to their reported cause of death which is beyond the scope of this study except that these accidental, homicidal or suicidal deaths may be related to the toxicological findings by altered conscious level or depersonalization and suicidal ideation which may be caused by the neuroactive substances.

Limitations

The current study has some limitations such as the under-reporting of toxicity related deaths, especially in cases of accidental deaths due to overdoses of the abused substance and household COP deaths which may be assumed to be natural deaths. Secondly, some autopsied cases were in an advanced stage of putrefaction which may have affected the robustness of their toxicological data. For COHb, levels are affected by resuscitative efforts and the duration between exposure and death and the duration from death to sampling. Despite its shortcomings, the study data is important as it shows the importance of toxicological screening of the autopsied cases, especially with suggestive history. Also the attribution of illicit drugs in accidental, homicidal, and even natural deaths must be considered even in absence of any signs or autopsy finding suggestive of illicit substances. Finally, more legislations and restrictions and religious, health, and moral awareness campaigns are recommended as substances of abuse are the main causes of toxicity induced deaths.

Conflict of Interest

Nil

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