

ORIGINAL ARTICLE

Clinico-epidemiology of Drug Overdose in a Tertiary Care Hospital

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Abstract

Background: Drug overdose is a common health problem and recently, deliberate self-poisoning using medicinal drugs is becoming popular in both urban and rural areas of Sri Lanka. This study aimed to describe the epidemiology and clinical manifestations following drug overdose in adults.

Methods: A prospective clinical study was conducted in Teaching Hospital Ratnapura, Sri Lanka over one year commencing from September 2018 including all adult patients with drug overdose.

Results: There were 202 (21%) adult patients with drug overdose from which deliberate self-poisonings were 200 (99%) and accidental poisonings were 2 (1%). Females were 124 (61%) and the commonly affected age group was 15-30 years (158;78%). The commonest overdosing agent was paracetamol (109;54%). Most patients (96;47.5%) were admitted to the hospital within 1-4 hours of the ingestion (IQR 2-4 hrs). Most of the patients (86;42.5%) were treated at hospital for 2 days (IQR 2-3 days). Decontamination was done for 151 (75%) of patients. Gastrointestinal symptoms including nausea and vomiting occurred prominently and they were 42% (n=89) and 53% (n=113) respectively. Complications were detected in 15 (7.4%) cases from which ECG changes 6 (3%), respiratory failure 5 (2.5%), acute liver failure 4 (2%), acute kidney injury 3 (1.5%) and hypotension 3 (1.5%). Six (3%) were treated at the intensive care unit from which 5 (2.5%) were intubated. There were 2 (1%) deaths and the case fatality rate of drug overdose was 1%.

Conclusions: Drug overdoses are common in intentional type. Young females are mostly affected and the commonest overdosing agent is paracetamol.

Keywords: Drug overdose; Paracetamol; Self-poisoning; Sri Lanka

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INTRODUCTION

Drug overdose is a common health problem in Sri Lanka [1-4] and it may be due to intentional (deliberate self-poisoning or para-suicide) or non-intentional (accidental or homicidal) poisoning. Intentional drug misuse occurs sometimes when people are getting un-prescribed drugs in high doses to produce euphoria for example opiates. Accidental drug overdose is commonly seen in paediatric population [5-7] and it may also be observed in adults as well [8-10]. Particularly, elderly patients may mistakenly ingest the incorrect medication or take the wrong dose of drugs resulting in accidental drug overdose which contributes to significant mortality [8]. Very few drug overdoses are homicidal [11]. It is evidenced that over-the-counter drugs are the most over-dosing agents for example paracetamol in Sri Lanka [12] and barbiturates, benzodiazepines and antiepileptics in India [13,14]. The common drugs used for overdosing are analgesics, antipsychotics, antidepressants, anticonvulsants, antihistamines, anticoagulants, oral hypoglycaemic agents, and benzodiazepines [8,9,15,16]. There are several fatalities

reported in adults and children following pharmaceutical overdoses too [8, 16-19]. The death rate is high in patients on benzodiazepines with the use of opioid analgesics [8,16].

Paracetamol, which is a widely used over-the-counter analgesic and antipyretic is the commonest overdosing agent in the urban and rural areas of Sri Lanka [2,3]. Therefore, the cost of its management has increased more than three-fold over 4 years from 2004 to 2007 [20]. In Ampara-Sri Lanka, the second main cause of acute poisoning is drug overdose (paracetamol) from which the majority are young females [4]. Recently, deliberate self-poisoning using medicinal drugs has become popular in both urban and rural areas of Sri Lanka [2-4]. This trend of increased use of drugs for poisoning accounts for 21% of all poisoning cases, which shows a 1.6-fold rise since 2005 [21]. In Anuradhapura, North Central Province of Sri Lanka, it was shown that 68% of the cases of intentional self-poisoning are due to drug overdose [2]. In another study in Pakistan, 58% of cases of acute poisoning were caused by pharmaceutical agents [9]. It is evidenced that adult drug overdoses are more common in young females in both developed and developing countries [9,22]. In Sri Lanka, medicinal agents are the second

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cause of poisoning in children [5,6] whereas in most other countries, pharmaceuticals are the most common cause of poisoning in children [7]. In Sri Lanka, there are few studies on adult drug overdose, and therefore the understanding of the clinical profile of drug overdose is lacking. This study was designed to fill this knowledge gap, which is essential in managing the poisoning patients. Thus, the objectives of this study were to describe the epidemiology and clinical manifestations following drug overdose in adults.

METHODS

A prospective observational clinical study was carried out for 1 year commencing from September 2018 in Teaching Hospital Ratnapura, Sri Lanka involving all adult patients with a drug overdose. This was a quantitative study and data were collected using an interviewer-administered questionnaire on which epidemiological and clinical information were included. There were no specific exclusion criteria in this study and all adult patients with a history of drug overdose were recruited. Data were analyzed using SPSS version 21. Ethical approval for the study was obtained from the ethics review committee, Postgraduate Institute of

Medicine, University of Colombo (Reference No. ERC/PGIM/2018/120).

RESULTS

There were 964 (0.7%) of all poisoning patients during the study period from which adult drug overdoses were 202 (21%). There were 200 (99%) patients with deliberate self-poisoning and 2 (1%) were accidental poisoning. Demographic and epidemiological features of this cohort are shown in Table 1. Females outnumbered males, which was 124 (61%). The most affected age group was 15-20 years (n=89; 44%). There were elder patients including 13 (6%) with > 50 years of age. Furthermore, there were 2 (1%) pregnant mothers with paracetamol overdose in 6 and 16 weeks of period of amenorrhea. Considering education levels, most people were educated between grades 5-11 (n=91;45%). In this cohort of drug overdose, most people (n=138;68%) were not engaging in any occupation. All patients with drug overdoses were from administrative divisions of Ratnapura district, Sri Lanka. Accordingly, most of the patients were from Ratnapura (62;31%) then from Kuruvita (21;10%) and the next from Gallella (12;6%).

Table 1. Epidemiological features and demographic characteristics of drug overdose

Feature	Number (%)	Demographic feature	Number (%)
Mode of poisoning		Gender	
Intentional	200 (99)	Males	78 (39)
Accidental	2 (1)	Females	124 (61)
Number of drugs		Marital state	
Ingestion of single drug	152 (75)	Married	82 (40.6)
Ingestion of multiple drugs	50 (25)	Unmarried	76 (37.6)
		Schooling	44 (21.8)
Pharmaceutical agents		Occupations	
Paracetamol	109 (54)	No	138 (68)
Unknown	16 (8)	Garment workers	15 (7)
Anti-epileptic drugs	14 (7)	Manual labourers	13 (6)
Psychiatric drugs	12 (6)	Estate workers	13 (6)
Oral hypoglycaemic agents	10 (5)	Three-wheel drivers	7 (3)
Antihistamines	4 (2)	Gem minors	5 (2.4)
Anti-asthmatic drugs	3 (1.5)	Factory workers	3 (1.5)
Anti-hypertensives	2 (1)	Masons	2 (1)
NSAIDs	2 (1)	Businessmen	2 (1)
Benzodiazepines	2 (1)	Others	4 (2)
Others	28 (13.5)		
Time since ingestion to admission		Level of education	
< 1hr	18 (9)	< Grade 5	28 (14)
1-3.59 hr	96 (47.5)	Grade 5-11	91 (45)
4-7.59 hr	30 (15)	Up to Ordinary level examination	66 (33)
8-11.59 hr	24 (12)	Up to Advanced level examination	17 (8)
12-15.59 hr	19 (9)		
16-19.59 hr	6 (3)		
20-23.59 hr	3 (1.5)		
> 24 hrs	6 (3)		
Decontamination		Previous/current medical illnesses	
Done	151 (75)	Psychiatric disorders	12 (6)
Not done	51 (25)	Epilepsy	11 (5)
Psychiatric referral		Asthma	6 (3)
Done	108 (53)	Diabetes	4 (2)
Not done	94 (47)	Others	11 (5)
Transfers from other hospitals			
Yes	58 (29)		
No (direct admissions)	144 (71)		

The commonest overdosing agent was paracetamol (n=109;54%), then anti-epileptic drugs (14;7%) and next psychiatric agents (12;6%) Phenytoin, valproate, carbamazepine, lamotrigine and phenobarbitone were the overdosing anti-epileptics. Main overdosing psychiatric medicines were olanzapine, venlafaxine, amitriptyline, benzhexol, haloperidol and fluoxetine. Commonly used hypoglycaemic agents were metformin, tolbutamide and gliclazide. Losartan, verapamil and enalapril were the anti-hypertensive agents used in this study. Most patients (96;47.5%) were admitted to the hospital within 1-4 hours of the ingestion (median 2 hrs and IQR 2-4 hrs). Early admissions (within 8 hrs of the overdose) were 144 (71%) and late admissions (> 8 hrs of ingestion) were 58 (29%). There were 6 (3%) who sought medical facility after 2 days of overdose. Most of the patients (86;42.5%) were treated at the hospital for 2 days (IQR 2-3 days).

There were 109 (54%) patients with paracetamol overdose of which 77 (71%) were given the antidote [N-Acetyl Cysteine (NAC)]. There were 3 patients (4%) who had allergy to NAC. There were 49 (24%) patients with multiple drugs (two or more drugs) overdose of which 6 patients were found to have self-ingestion of paracetamol with other agents. Therefore, altogether there were 115 patients with paracetamol overdose and the number of ingested tablets ranged from 8 tabs to 96 tabs. There were 4 patients (3.5%) with acute liver failure and one patient (0.9%) with acute kidney injury (AKI) following paracetamol overdose.

Clinical manifestations and complications of drug overdose are shown in Table 2. Gastrointestinal symptoms including nausea and vomiting occurred prominently and they were 42% (n=89) and 53 % (n=113) respectively. In addition, epigastric pain was observed in 40 (20%) patients. Out of central nervous system features, vertigo and confusion were found to have 28 (14%) and 11 (5%) patients, respectively. Cardiovascular features were found less commonly and palpitations occurred in 2% (n=4). Six (3%) were treated at the intensive care unit (ICU).

Complications of drug overdose were detected in 15 (7.4%) cases from which respiratory failure, acute liver failure, AKI, hypotension and ECG changes were more prominent. Respiratory failure was the commonest complication and was observed in 5 (2%) of which 3 (60%) were due to antipsychotics and 2 (40%) were due to carbamazepine overdose. Out of 5 with respiratory failure, 4 (80%) patients were intubated and mechanical ventilation was carried out (Figure 1).

Acute liver failure was observed in 4 (2%) patients of which all were due to paracetamol overdose. Acute kidney injury was detected in 3 (1.5%) patients for which one was due to paracetamol, another was due to antipsychotics and the other was due to multiple unknown drug overdoses. Hypotension occurred in 3 (1.5%) patients, each due to verapamil, losartan and antipsychotic drug overdose. Out of these 3, two were started with 3 inotropes who ultimately died at the ICU. There were 2 (1%) deaths from drug overdoses of which one was due to verapamil and the other was due to antipsychotic drug overdose. The case fatality rate was 1%. A 24-year-old known psychiatric male patient

died following an unknown amount of antipsychotic drug overdose (benzhexol, olanzapine and haloperidol). His postmortem examination revealed loss of corticomedullary demarcation of bilateral kidneys, pulmonary haemorrhage and pulmonary oedema. Histology showed features of acute tubular necrosis in kidneys and pulmonary haemorrhage.

Electrocardiographic Changes

The ECG changes are described in Table 3. There are 6 (3%) patients with ECG changes following drug overdoses. Ischemic changes (T wave inversions) were found in 2 (1%) patients. One was an unknown multiple drug overdose and the other was a previously healthy patient following an overdose of 20 Fe tablets (Figure 2).

Laboratory Findings

Laboratory findings of the study are shown in Table 4 with their mean and SD values. According to statistical analysis, all are in the normal range.

Table 2. Clinical profile and complications of drug overdose

Clinical feature	Number (%)	Complication	Number (%)
Vomiting	113 (53)	ECG changes	6 (3)
Nausea	89 (42)	Respiratory failure	5 (2.5)
Faintness	69 (34)	Acute liver failure	4 (2)
Headache	41 (20)	Acute kidney injury	3 (1.5)
Drowsiness	37 (18)	Hypotension	3 (1.5)
Epigastric pain	40 (20)	Metabolic acidosis	1 (0.5)
Abdominal pain	37 (18)		
Vertigo	28 (14)		
Confusion	11 (5)		
Low GCS	7 (3.5)		
Fever	6 (3)	Outcomes	
Liver tenderness	5 (2.5)	Recovered	186 (92)
Palpitations	4 (2)	Died	2 (0.9)
Hematemesis	2 (1)	Missing from the ward	9 (4.5)
Chest pain	1 (0.5)	Left against medical advice	5 (2.5)
Dizziness	1 (0.5)		
Tremors	1 (0.5)		
Restlessness	1 (0.5)		
Malena	1 (0.5)		



Figure 1. A patient with mechanical ventilation at the intensive care unit due to respiratory failure following an antipsychotic drug overdose

Table 3. Electrocardiographic changes of drug overdose

Serial Number	Gender	Age	Overdosing agents	ECG changes
21	Female	22 yrs	Montelukast 10 mg 10 tabs	Sinus tachycardia
49	Male	40 yrs	Unknown multiple drugs	T wave inversions
60	Male	23 yrs	Unknown multiple drugs	Atrial fibrillation
146	Female	15 yr	Salbutamol 2mg 15 tabs & chlorpheniramine 4mg 5 tabs	Right bundle branch block (RBBB)
188	Female	36 yrs	Fe 200mg 20 tabs	T wave inversions
203	Female	22 yrs	Venlafaxine 37.5mg 2 caps	Sinus tachycardia

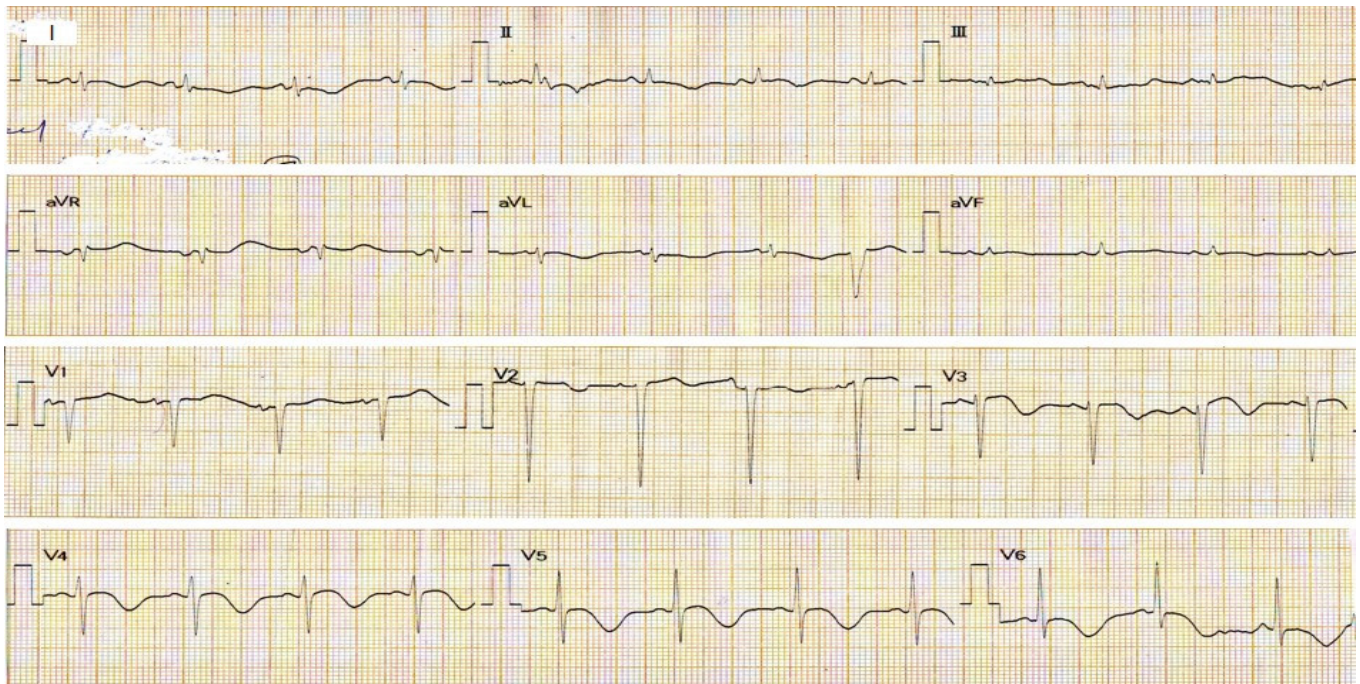


Figure 2. ECG changes (T wave inversions on LI, LII, V₂-V₆) in a 36-year-old female following Fe overdose (200 mg 20 tabs)

DISCUSSION

This study included 202 patients with various drug overdoses. Considering all types of poisonings, drug overdose has become the second cause of poisoning which is compatible with previous studies [3,23]. In Sri Lanka, the commonest poisoning agents were agrochemicals including organophosphate compounds and other pesticides [24,25]. But, since the recent past, this trend has changed to medicinal drugs in both rural and urban areas of Sri Lanka which was seen in our results too. One study in Iran points out that 58% of poisoning cases are due to drug overdose [26]. Drugs are the commonest poisoning agents in the Western part of the world while in Asian and African countries, drugs along with organophosphate compounds are frequently used as self-poisonings.

It was revealed, in our study, that paracetamol is the most common overdosing agent, which was found in more than half of the sample (109;54%). This is compatible with

inferences in other studies in Sri Lanka as well [2,3,12]. According to National Poison Information Centre data, 50% of admissions due to drug overdoses in National Hospital Sri Lanka are due to paracetamol. This is because of the easy availability, accessibility and cheapness as over-the-counter medicine to a normal person without any barriers. This causes an increase in misuse and then intoxication. Next to paracetamol, anti-epileptic and psychiatric drugs cause more overdoses. But, interestingly, even though more patients are treated with anti-diabetic and anti-hypertensive medicines in clinics, those overdoses are few in this study. This may be due to the fact that the overdoses are common in young people and most above clinic attendants are elder people.

It is widely known that drug overdoses are common in females [9,22]. Our study also shows female predominance comprising 61% (n=124). An important finding of our study is that the incidence of overdose is more common in younger population between 15-30 years (n=158 ;78%).

In present study, almost all adults had intentional

Table 4. Haematological and biochemical investigations of drug overdose

Investigation	Reference range	Minimum	Maximum	Mean (SD)
WBC (x10 ³ /μL)	4-11	2	22	9.86 (3.3)
Neutrophils (%)	50 -70	26	96	70.96 (13.4)
Lymphocytes (%)	20 -40	3	72	22.25 (11.6)
Platelets (x10 ³ /μL)	150-450	59	474	276.8 (64)
Hb (g/dL)	11-16	8.1	18.6	12.49 (1.7)
Na ⁺ (mmol/L)	135- 145	121	149	139.6 (3.6)
K ⁺ (mmol/L)	3.5 – 4.5	2.6	6.3	3.868 (0.5)
Creatinine (μmol/L)	60-115	32	301	66.44 (28)
Blood urea (mmol/L)	7.8-20.1	1.2	12.3	3.045 (1.4)
PT (sec.)	10-15	11.0	23.0	14.88 (2.1)
INR	1 - 1.4	.93	1.95	1.256 (0.2)
SGOT(AST) [U/I]	0 - 35	12	309	34.54 (3.6)
SGPT(ALT) [U/I]	0 - 45	6	1922	42.32 (15.6)
RBS (mg/dL)	80-180	76	312	131.6 (42.5)

overdoses except two. It can be assumed that due to acute problems, most people are admitted to the hospital within 4 hours of the ingestion and in the present study, its frequency is 120 (59%). It is evidenced from this study that most of the affected people (68%) are unemployed and they are not engaging in any occupation. In current study, most of the overdosing people are married younger age group and similar results have been obtained in India, too [27]. In contrast, the incidence of poisoning was more commonly observed in unmarried younger people in Pakistan [9]. In Sri Lanka, even though many people are using nonsteroidal anti-inflammatory drugs (NSAIDs) including diclofenac, ibuprofen and celecoxib, we found only 2 (1%) cases of NSAIDs involving ibuprofen and mefenamic acid. This may be, because most of the time these drugs are prescribed only for a few days (short term), not for long-term usage.

This study also revealed that gastrointestinal manifestations such as nausea, vomiting, epigastric and abdominal pain occurred frequently. This is because paracetamol was the most commonly used overdosing agent. Even though the overdoses with psychiatric medicines were few (6%), their complications were severe because they cause depression of the central nervous system (CNS) and those patients need ventilator support at the ICU due to respiratory failure. The second commonly encountered features are related to CNS such as drowsiness, vertigo, confusion and low Glasgow coma scale (GCS) which are mainly due to psychiatric drug overdose.

The complications of drug overdoses were respiratory failure, acute liver failure, AKI, hypotension and ECG changes. Out of these, all cases of acute liver failure were due to paracetamol overdose which is previously well-known [28]. Paracetamol overdose is a leading cause of acute hepatic injury in Western countries [28]. In paracetamol overdose, liver injury occurs due to the production of an

intermediate toxic metabolite, N-acetyl-p-benzoquinonimine (NAPQI) via cytochrome P450 liver enzymes. Normally, NAPQI is detoxified by sulphhydryl groups which are depleted in overdoses. The antidotes are sulphhydryl donors (NAC or methionine) which should be administered within 8 hours of the ingestion to prevent hepatic injury [29]. Acute kidney injury occurs in 1% of overdoses involving paracetamol [30] and this is usually associated with hepatic injury. Interestingly, we observed a patient with AKI without biochemical evidence of hepatotoxicity following self-ingestion of 18 tablets of paracetamol which is an unusual finding. This kind of presentation has previously been reported in Canada too [31]. In this study, cardiotoxicity was seen in overdose with verapamil, losartan, carbamazepine, Fe, venlafaxine, montelukast and antipsychotic drugs. Hypotension and ECG changes were the main features of cardiotoxicity. One patient died due to severe hypotension following a verapamil overdose. Two patients were found to have acute ischemic changes (T wave inversions) on ECG following an overdose of Fe tablets and carbamazepine which are new findings detected in this study.

We found 2 (1%) deaths following drug overdose and in developed countries, there are more deaths related to drug overdoses [16,18,20]. This may be due to, in those countries, opioid analgesics, benzodiazepines and antidepressants are mostly used for overdoses [16,18,20] which have severe effects on the respiratory system and CNS depression. Drug overdoses may cause various derangements of laboratory findings. We found these changes in current study only in a few cases with various complications. However, in the present study, there were no severe changes in laboratory findings and therefore, this should be further evaluated involving more patients. It seems that overdoses with psychiatric medications in Ratnapura region are common in patients, who are regularly taking treatment for psychiatric illnesses and sometimes, these patients may need admission to ICU for ventilator support. These patients might ingest the wrong doses or wrong frequencies and get CNS depression causing aspiration.

LIMITATION

We were not able to measure serum drug levels as those facilities are not available at Government hospitals. Therefore, drug overdose was diagnosed with the patients' history and clinical profile. Patients' history is not always reliable and it would be better if we could have facilities to do plasma drug levels to understand proper clinical profile. But, it is not available even for paracetamol in government hospitals in Sri Lanka.

CONCLUSION

Drug overdoses are common in intentional type. The commonest overdosing agent is paracetamol and young females are mostly affected.

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