ASIA PACIFIC JOURNAL of MEDICAL TOXICOLOGY
APJMT 6;2 http://apjmt.mums.ac.ir June 2017

ORIGINAL ARTICLE

Toxicological Screening of Drug Facilitated Crime among Travelers in Dhaka, Bangladesh

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Abstract

Introduction: Drug-facilitated robberies, primarily of public transport passengers, are a massively increasing public health emergency and law enforcement challenge in Dhaka, the capital city of Bangladesh.
Methods: We conducted a prospective clinical and toxicological study of 38 patients with acute poisoning who had been admitted to Dhaka Medical College Hospital between October 2008 and December 2008 and suspected to be victims of drug-facilitated crimes. Blood samples were obtained on admission and one hour later to identify changing concentrations of the drugs used by the perpetrators. Toxicological screening was performed by LC-TOF/MS and LC-MS/MS analysis of the blood samples of 22 of these patients.
Results: All of the patients in our series were male, 17-60 years of age, and none had any memory of the time between the ingestion of the drug and the onset of unconsciousness. All had lost the valuables they had been carrying at the time of the incident. On admission, 50% of the patients had a Glasgow Coma Score (GCS) of 5-10. Most of them were poisoned while travelling (79%), most frequently by bus (70%). They had been offered tea (21%), other drinks (26%), prickles (18%), herbal medicines (10%) or cigarettes (5%) by the suspected perpetrators. Screening by LC-TOF/MS and LC-MS/MS revealed pharmacologically active concentrations of lorazepam in the blood samples of all 22 cases (191±138 µg/l, mean±SD); midazolam in 12 (149±99 µg/l); diazepam in 3 (217±144 µg/l) and nordiazepam in 6 cases (364±186 µg/l). In five cases the lorazepam concentration of the second blood sample was at least 15% higher than in the sample drawn on admission one hour earlier, indicating continuing absorption. This suggests that only these five patients had been admitted within the 1-2 hour long absorption phase. Almost all of the patients left the hospital unnoticed after clearing up, two likely prematurely within 12 hours of admission, and no mortality was observed.
Conclusions: This study reveals flexibility of the criminals in Dhaka in using different mixtures of benzodiazepines to incapacitate and then rob their victims.The findings of our study have important implications for the clinical management of drug-facilitated crime victims. In particular, they highlight an urgent need to widely deploy rapid diagnostic and analytical forensic and clinical toxicology facilities in Bangladesh, introduce and implement modifications to emergency department protocols, and provide post-recovery psychological support for victims who often suffer existentially threatening economic losses in addition to the poisoning.

Keywords: Benzodiazepine; Commuters; Poisonings

How to cite this article: Basher A, Abul Faiz M, Arif SM, Abul Kashem Khandaker M, Kuch U, Tonnes SW. Toxicological Screening of Drug Facilated Crime among Travelers in Dhaka, Bangladesh. *Asia Pac J Med Toxicol* 2017;6:47-9.

INTRODUCTION

Being poisoned while using public transportation is a common risk in daily life in Bangladesh, where it has become a great social and public health problem especially in urban regions (1). Experience shows that the prevalence of this type of acute poisoning, often called 'commuters' poisoning' is increasing (2). As it involves the intentional application of stupefying agents to unaware victims with the motive of making them helpless and unconscious for a brief period of time, and is invariably associated with a loss (robbery) of the victim's valuable possessions, this worrying phenomenon was identified as a specific type of drug-facilitated crime.

The perpetrators of these crimes in Bangladesh frequently change their modus operandi for the purpose of robbing. In earlier years they were observed to incapacitate their victims with datura and similar compounds of plant origin, but more recently different benzodiazepine drugs are used for this purpose, usually mixed with food items (3-5). To apply these drugs to their prospective victims, the criminals trick them into accepting an invitation to tea, coffee, biscuit, green coconut juice, other cold juices and drinks, fruits, betel nut,

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Received 8 March 2017, Accepted 6 June 2017

popcorn, etc., most frequently during travel in bus, train or launch. Generally, these criminals follow the commuters, chatting friendly with them and lastly offering some food or beverage. Another frequently used method involves advertising and offering at low cost some traditional medicine against skin diseases, asthma, arthritis, etc. Either way, unaware people are easily lured into taking the offering containing the poisoning agent and then become gradually drowsy and finally unconscious. As soon as they think it safe for them, the criminals rob the incapacitated victims of their valuables; in some cases of all possessions they carry with and on themselves, and leave the victim behind in this helpless state. Generally, police or kind people admit the victims of such crimes to the emergency department of public hospitals in Bangladesh (3).

This is not only a potentially serious medical problem for the patients who face various risks, but often also distressing for their families and the medical staff attending such patients. In addition to the acute poisoning suffered by the individual patients, the large numbers of such patients admitted to public hospitals in Bangladesh severely strain limited healthcare resources (3). Additionally, the sometimes existentially threatening economic loss adds to their psychological trauma, disrupting individual domestic and social life. Changing their modus operandi and potentially also the sources and types of incapacitating substances that they use has presumably helped the criminals evade law enforcement. In a previous study, we identified benzodiazepines as the drugs of choice of these criminals in Dhaka (3). Here, we intended to explore the events prior to this type of criminal poisoning, to identify the poisoning agents in urine, and in the case of benzodiazepines, to estimate the applied dose from blood concentrations.

METHODS

Type of study

This prospective study was carried out in the Medicine Department of Dhaka Medical College Hospital in Dhaka, Bangladesh, from October 2008 to December 2008. A total of 38 patients presenting with a history or suspected history of induced poisoning on journey and Glasgow Coma Scores (GCS) of 5 to 14 on admission were evaluated. Patients with a suspicion or diagnosis of deliberate self-harm using substances like pesticides or sedatives, or any organic cause of coma were excluded from the study. Blood and urine samples of 22 patients among these were collected for toxicological analysis.

Data collection

All personal and clinical data were collected on an individual case record form. Blood and urine benzodiazepine levels and other necessary laboratory data were collected and recorded in an attached sheet. Before data collection, written informed consent to participate in the study was taken from the patient himself / herself or his /her attendant.

Blood and urine analysis

For toxicological analysis, blood serum samples and urine samples were collected just after admission. A second serum sample was collected 1 hour after the first. Samples were frozen at -20°C immediately after collection and maintained frozen during air transfer to the forensic toxicology laboratory in Frankfurt am Main, Germany, where they were received within 48 hours of collection and stored at -20°C until analysis. Serum ethanol content was determined using routine headspace-gas chromatography with flame ionization detection. General toxicological screening analyses for unknown substances were performed in 1 ml of sample after enzymatic cleavage of conjugates (pH adjusted to 4.5, β-glucuronidase/arylsulfatase preparation from *Helix pomatia*) and liquid–liquid extraction (pH adjusted to 7.0, 1-chlorobutane/diethylether, 1/1, v/v). Analysis was performed using an Agilent 1100 liquid chromatograph coupled via electrospray interface to an Agilent time-of-flight mass spectrometer (LC–TOF/MS).[3] LC-MS/MS analyses were performed later to determine the concentration of each detected compound.

RESULTS

Patients evaluated for induced poisoning

The average age of the patients was 36 ± 10 years (range 17-60). Most were from Dhaka City (51%) and others traveling from other districts of Bangladesh to Dhaka. The majority of the victims (82%) had a monthly income below 150 US $, and 95% of them lost the equivalent of what they had earned in a month's time due to the drug-facilitated robbery.

The estimated mean time that had elapsed between the incident of poisoning and hospital admission was 4.4 hours (± 3.6 SD; range 1.2-19 hours). The majority of the patients (79%) were poisoned in or on means of transportation and the remaining 21% in various other, usually travel related circumstances like near the car stand or within the market. Ingested items included tea (21%) tea, pickled food (18%), other types of drinks (26%), herbal medicines (10%), cigarettes (5%), betel leaves (5%) and others like biscuits or bananas. Two patients failed to remember what they had ingested. Most of the patients (53%) were found unconscious near or at a bus stand, 11 (29%) were rescued from the street, and 6 (16%) were found in the market. All victims had lost the valuables they had carried, e.g., money, wrist watch, mobile phone, bank or credit card, wedding ring, valuable official documents, etc. We attempted to assess the monetary value of the stolen items and estimated the mean to be 750 US $ per person (range 50 to 8,974 US $).

Clinical features

All patients were admitted within a day of the suspected poisoning incident in drowsy to comatose condition, and none had received treatment prior to admission. During admission 19 patients (50%) had a GCS of 5-10 and the rest had a GCS of 11-14. All patients were assessed for cardiac and respiratory problems, spinal injury or any bruise mark. Bradycardia (<60/min) was present only in 5 patients. Five patients had elevated blood pressure and 3 were hypotensive. Tachypnea (>20/min) was observed in 4 patients.

Twenty-three patients had normal white blood cell counts (4000-11,000/mm^3), 15 had more then 11,000/mm^3 with a maximum of 22,980/mm^3. Blood urea (range 16-37 µg/dl) and serum creatinine values (0.7-1.3 mmol/L) were normal in all patients. One patient had hypokalemia (3.3 mmol/L),

serum chloride was slightly raised among 13 (34%)cases, and one had a very high level (160 mmol/L). Otherwise all assessed laboratory parameters including blood glucose levels were within normal limits in all patients.

Toxicological analysis

Twenty-four hour urine samples were analyzed by toxicological screening using LC-TOF/MS which revealed lorazepam and other benzodiazepines of different concentrations. The corresponding blood samples collected on admission and one hour later contained significant amounts of lorazepam in all cases. The mean (± SD) concentration of lorazepam on admission was 180 ± 145 ng/ml. Midazolam was detected in 12 cases (133 ± 94 ng/ml), nordiazepam in 6 cases (295 ± 133 ng/ml) and diazepam in 3 cases (213 ± 142 ng/ml).

Comparison of the quantitative data obtained for the blood samples on admission and 1 hour later allowed us to assess the pharmacokinetic phase (i.e., absorption or elimination phase). If the values increased in excess of 15% (maximal imprecision of the analytical method) we assumed that the ingestion had occurred less than 2 hours ago because the absorption was still in progress. In 5 of the 22 cases the lorazepam concentration of the second blood sample was at least 15% higher indicating continuing absorption. This suggests that only these 5 patients were admitted within the 1-2 hour-long absorption phase.

For the estimation of ingested doses, the use of the lower boundary of the benzodiazepine volume of distribution and the upper boundary of its bioavailability yields the lowest values in the equation (dose [mg] = concentration [mg/L] × body weight [kg] × volume of distribution [L/kg] / bioavailability [mg]) and is therefore regarded as conservative. From the maximum of the two concentration values (on admission and 1 hour later) the minimum ingested doses can thus be estimated as 0.8 mg for lorazepam, 0.7 mg for diazepam, 0.7 mg for nordiazepam, and 0.8 mg for midazolam), and the upper boundary of their oral bioavailability as 95% for lorazepam, 80% each for diazepam and nordiazepam, and 50% for midazolam. Accordingly, the minimum ingested doses were 10 ± 7 mg (mean ± SD) lorazepam, 13 ± 9 mg diazepam, 20 ± 10 mg nordiazepam and 15 ± 10 mg midazolam (Table 1). The level of GCS varied considerably between individuals. Two patients who were in the absorption phase left the hospital within 12 hours. Two patients with lorazepam levels >250 ng/ml and GCS 5-10 (Table 2) were found to be hypotensive. Almost all of the patients left the hospital unnoticed after clearing up; no mortality was observed.

DISCUSSION

The results of our study indicate that young, economically active persons are the preferred targets of this type of drug-facilitated crime in Dhaka. This is also supported by data collected from the admission records of two big medical college hospitals, two general hospitals and seven primary care hospitals in Dhaka over a period of six months which showed that 87% of the patients admitted with induced poisoning by stupefying agents occurred in the age group of 13-50 years (unpublished data) (6). The sharing of food items during travel is a widely adopted good custom by this age group of people and facilitates their exposure to this type of crime.

The fact that the victims in this series of induced poisoning were all male differs from the proportions observed in other types of poisoning. Possible reasons for this might include more cautious behavior of female travelers in Bangladesh, lower likelihood of women to chat or share food with unknown people during journeys, or an expectation on part of the perpetrators to obtain more money and goods when robbing men.

Table 1. Concentrations and estimated doses of different benzodiazepines detected in 22 cases of travel related poisoning.

	Lorazepam	Diazepam	Nordiazepam	Midazolam
n=(% of all samples)	22 (100 %)	3 (13.6 %)	6 (27.3 %)	12 (54.5 %)
Serum concentration [µg/L]				
Mean±SD	191±138	217±144	364±186	149±99
Median (range)	164 (19–598)	248 (61–343)	394 (151–622)	126 (46–338)
Estimated ingested dose [mg]				
Mean±SD	10.1±7.1	12.8±9.0	19.9±9.6	15.4±10.1
Median (range)	8.9 (1.0–29.2)	14.1 (3.2–21.0)	21.0 (9.0–33.7)	14.5 (4.3–33.5)
Multitude of single therapeutic dose [mg]				
Single therapeutic dose	2.5	10	10	5
Mean±SD	4.0±2.8	1.3±0.9	2.0±1.0	3.1±2.0
Median (range)	3.5 (0.4–11.7)	1.4 (0.3–2.1)	2.1 (0.9–3.4)	2.9 (0.9–6.7)

Table 2. Concentrations of lorazepam and midazolam grouped by Glasgow Coma Score (GCS) and duration of hospital stay (n=22).

GCS	Duration of hospital stay	Lorazepam on admission [µg/L]	Lorazepam 1 hour after admission [µg/L]	Midazolam on admission [µg/L]	Midazolam 1 hour after admission [µg/L]
5–10	0–12 hours	59	102		
		261	237		
		407	375	134	130
		598	328	46	42
	13–24 hours	41	59		
		52	29	55	33
		136	147	272	338
		187	164		
		193	163	54	57
		299	193	270	152
11–14	0–12 hours	10	19	89	98
		49	146	89	147
		60	68		
		64	62	60	117
		94	83	275	163
		142	72	198	165
		146	83		
		149	214		
		180	100		
		189	141		
		239	216	58	44
		405	164		

All patients failed to notice the time when they became unconscious, but the possible times of the incidence and admission times were similar to those observed in other studies (7, 8). Most of the victims remembered that they had been offered various food items which were familiar with this group of victims, popular as fast food, cheap to buy and easily available and thus widely accepted.

All victims had lost their valuables illustrating the purpose of robbery. Criminals engaging in this type of drug-facilitated robbery in Dhaka may be linked with larger organized crime networks, and these need to be identified, neutralized and brought to justice by the law-enforcing agencies of the government to disrupt the criminal chain and to protect the people from being robbed during journeys. Similar trends of drug-facilitated robberies have also been reported from New Delhi and Chittagong where these crimes were especially common on the eve of religious festivals (7, 8).

Regarding their clinical profile, the patients in our series were usually brought by the police in a drowsy or stuporous condition with vitals maintained. Thus, it seems that this type of poisoning is not as serious as that of other poisoned patients treated in this setting.

The massive medico-social emergency of travel-related poisoning in Bangladesh is the result of drug-facilitated organized crime, and the theft of the incapacitated persons' property is not opportunistic but the goal for which they are poisoned. Toxicological screening of the samples obtained in this study revealed different concentrations of lorazepam and other benzodiazepines like midazolam, oxazepam, and diazepam (Table 1). These results are consistent with those of a previous study except for midazolam, which was not found in the earlier study (3). In another earlier study, 26% of the patients were admitted due to datura poisoning (9). This variety of poisoning was also found to be common in the general hospital of Noakhali in 1983 and 1984 (10). However, the present study shows that this has since been replaced by benzodiazepines taken with different food items during travelling.

Drug identification and dose estimation revealed that lorazepam was used in all cases, midazolam in 12 cases and diazepam in 3 cases (Table 1). Nordiazepam was detected in 6 cases and could be interpreted as a metabolite of diazepam. However, we think that the benzodiazepine mixture also contained nordiazepam as such because it was present in considerable concentrations in 3 cases without detection of diazepam, and because even the lowest detected nordiazepam concentration (151 µg/l) cannot be explained by a recent diazepam ingestion (very slow metabolism). For diazepam,

the estimated doses equal a typical therapeutic dose, for nordiazepam and midazolam twice a normal dose. For lorazepam a high dose is only 2.5 mg, therefore the estimates indicate the use of rather high lorazepam dosages. The highest estimate of an ingested lorazepam dose was 29 mg which is about the twelvefold of the recommended maximum dose.

The severity of central nervous system depression as assessed by GCS was less in the victims of travel-related poisoning than in local patients with organophosphate poisoning (Table 2) (11, 12). The patients' normal respiratory rates suggest that the majority of victims of travel-related poisoning were offered hypnotic doses of benzodiazepines that were not sufficient for causing respiratory depression. However, the levels of GCS varied between individuals. The half-life of lorazepam is rather long, therefore the 2 patients who were still in the absorption phase and left the hospital already within 12 hours had a strong chance of experiencing continuing benzodiazepine effects outside of the facility (13). The half-life of different benzodiazepines varies, and a number of drugs have active metabolites. The clinical spectrum of toxicity is almost the same despite their different properties (13). This is due to the distribution of the drug from the brain to peripheral compartments and the development of tolerance to the effects of benzodiazepines that determine the recovery of consciousness rather than the clearance of the drug. They show that a 12-fold overdose of benzodiazepines did not lead to life-threatening symptoms. This result has implications for the clinical management of victims of such drug-facilitated crimes. In the present study the benzodiazepine antagonist flumazenil was not used in any patient. In the absence of adequate clinical toxicology facilities, and due to the much shorter half-life of flumazenil (1–2 h) in comparison to, e.g., lorazepam (10–40 h), a recurrence of symptoms is to be expected (14-19).

Usually, this type of victim does not require specific treatment other than maintenance of clear airways, nutrition, fluid replacement and nursing care. Almost all patients left the hospital unnoticed, probably due to social and medico-legal reasons, which is in marked contrast to other types of poisoning (8, 12). No mortality was observed in the present series. On the contrary, however, there is psychological trauma associated with the criminal poisoning, i.e., the anterograde amnesia, and often substantial loss of property threatening the economic survival of the victim and his family. Therefore, the possible provision of post-recovery psychological support for victims needs to be evaluated. These patients require support from a humanitarian point of view. The syndrome of sudden unconsciousness of travellers and its association with lost property is widely known to the general public in Bangladesh, but it has only recently attracted the interest of the media (20, 21). Steps should be taken by law- enforcing agencies to identify the culprits by better vigilance, and to crush their organized crime networks by bringing them to justice. Social mobilization for safe travel needs to be created. It needs intensive public notification and awareness about the possible health hazards while traveling. If the people, the mass media, the police and justice system, the bus drivers and conductors become more and more alert and active, the incidence of such criminal acts may be reduced.

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