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Poisoning among Commuters in Dhaka, Bangladesh: Prospective Clinical Study and Toxicological Screening

Presented by

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Background

- The poisoning happening during movement using public transport is an social and public health emergency.
- Experience shows, the prevalence of commuters poisoning is increasing.
- Trends of such poisoning using stupefying agents with a motive to make the victim unconscious for a brief period of time with a view to rob his / her valuables.

Background (cont..)

Changing pattern of cheating and robbing by the miscreants help them to carry through their ailing motives and escaping from imprisonment.

Background (cont..)

- Six month base line survey on cases of poisoning conducted in DMCH, CMCH, Jhenaidah General Hospital, Cox's Bazar general Hospital and 7 primary care level health centers on July,2006 revealed total 31,329 cases were admitted in selected health facilities among them **4,553 (14.5%)** were poisoning cases.
- Of them 29.0% poisoning occurs due to pesticide, **37.1% by sedative,** 9.5% by snake bite, 3.0% by kerosine, and rest 22.5% are due to methanol, copper-sulphate, 'potka fish', harpic, drugs except sedative, naphthalene, nail polish, 'dhutura', chlorine gas, depilatory cream, mortein, rat killer, anti-louse, anti-scabies, acid, etc.

Background (cont..)

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Criminal poisoning of commuters in Bangladesh: Prospective and retrospective study

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Objectives

- To know the pattern of event prior to poisoning among the commuters.
- To find out current pattern of offending agent used by the miscreants
- To explore the impact on a family due to loss of valuable.
- To identify the poisoning agents in urine and in case of benzodiazepine substances to estimate the dose from blood concentrations.
- To aware the public and the society for taking adequate measure.

Materials and Methods

- **Type of study:** It was a longitudinal study descriptive in nature.
- **Place of study:** One adult medicine units of Dhaka Medical College Hospital, Dhaka.
- **Period of study:** From February 2008 to January 2009.
- **Selection of subjects:** Patients with / history of induced poisoning on journey or suspected to be such case were evaluated.

Materials and Methods

Inclusion criteria:

- Adult patients admitted in medicine units of Dhaka Medical College Hospital thorough emergency following suspected poisoning during travel.
- Glasgow coma score, 5-14.

Exclusion criteria:

- Diagnosis of any other cause of poisoning by deliberate self harm using substances like pesticide, sedatives etc.
- Presence of any other organic cause of coma.
- Unwilling to give informed consents by patients or patients relatives.

Materials and Methods

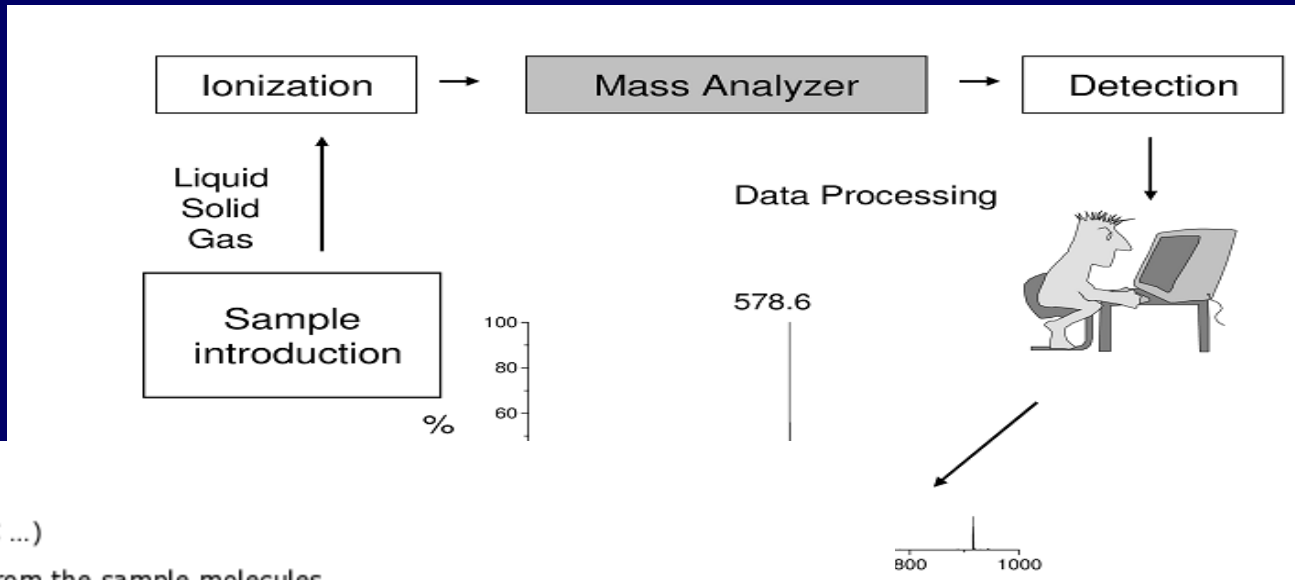
- Benzodiazepine was assayed in home at the Institute of Food Science & Toxicology, BCSIR, Dhaka, Bangladesh and abroad at the Institute of Forensic Toxicology, Centre for Legal Medicine, Johann Wolfgang Goethe University, Frankfurt am Main, Germany for comparison using different methods.

- During the study period additional support was taken through assistance of the Welcome Trust Unit of the Oxford University, UK providing modest patient care and record keeping of all poisoning cases.

- Ethical clearance was obtained from the ethical committee of Bangladesh Medical Research Council

Mass spectrometer

The mass spectrometer is an instrument designed to separate gas phase ions according to their m/z (mass to charge ratio) value. The "heart" of the mass spectrometer is the analyzer. This element separates the gas phase ions. The aim is either to get structure information by fragmenting the ions isolated during the first experiment, and/or to achieve better selectivity and sensitivity for quantitative analysis.



- A vacuum system
- Tools to introduce the sample (LC, GC ...)
- Tools to produce the gas phase ions from the sample molecules
- Tools to fragment the ions, in order to obtain structural information, or to get more selective detection
- A detection system
- Software and computing

Cont…

- **For toxicological analysis,** serum blood samples were collected just after admission, then 1 hour after first sample collection. Another sample was collected at time of discharge or just before the patient left out from Hospital. Urine was also collected after admission.
- Samples were cooled at -20^{0}C immediately after collection and during air transfer to the forensic toxicological laboratory in Frankfurt am Main, Germany, where they were received within 48h of collection and stored at -20^{0}C until analysis.
- For these samples, ethanol content was determined using routine headspace-gas chromatography with flame ionization detection.

Results

- **Total 38 patients** were included who were admitted with unknown poisoning.
- Mean age of total induced poisoning patients was **36SD+10** years. Age varied from 17 to 60 years. No female patients were included or admitted during the study.
- In analysis of present residential addresses, **majority were from Dhaka City (15.8%),** others were traveling from other districts to Dhaka.
  - Bus travel (N=8)
  - Train journeys (N=2)
  - local markets (N=2)
  - The airport area after air travel (N=1),

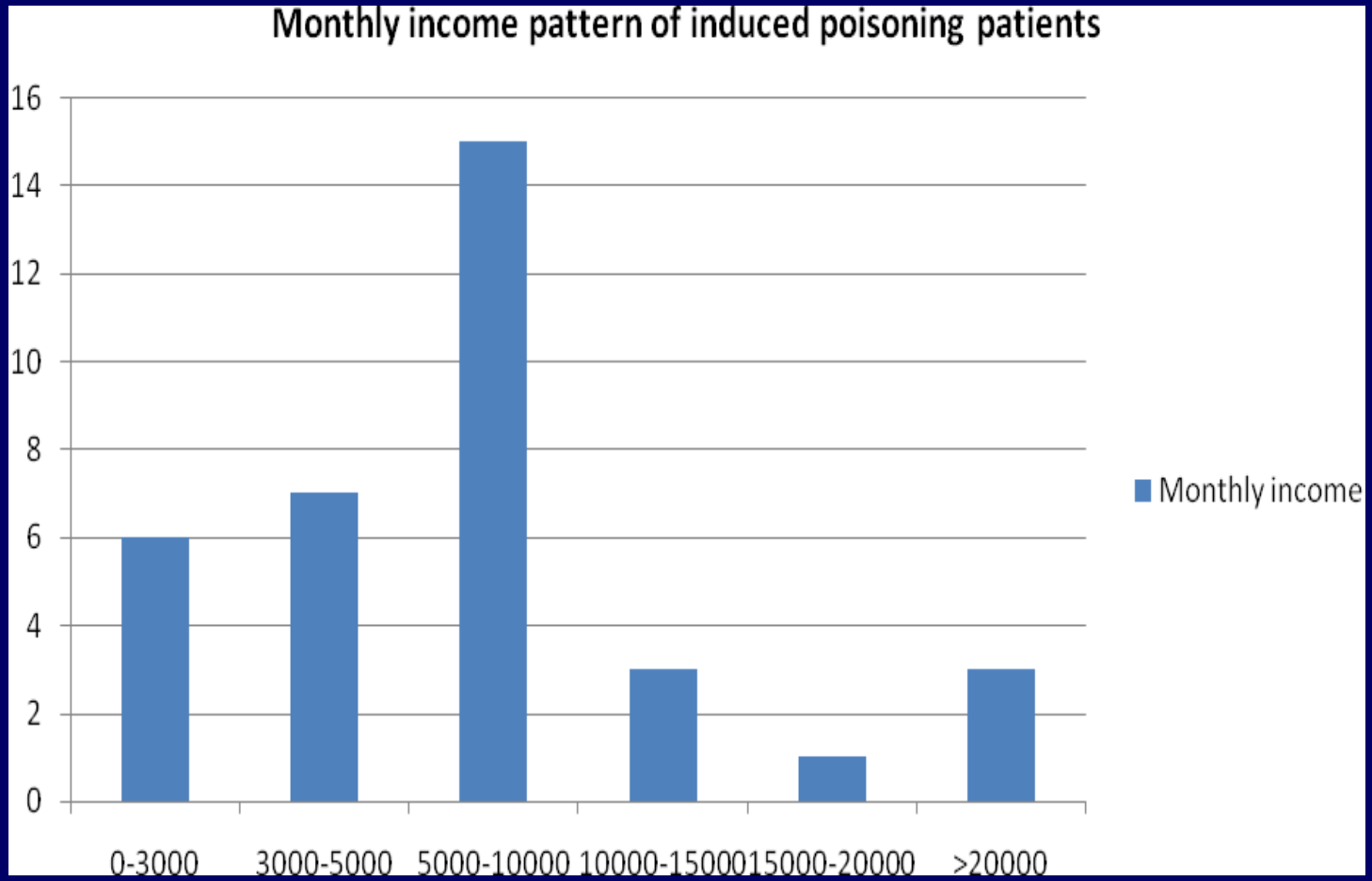
Results (cont....)

Table 1. Other socio-demographic features of the poisoning cases (n = 38)

Other socio demographic features	Number	%
Marital status		
Married	30	78.9
Unmarried	08	21.1
Occupation		
Farmer	3	7.9
Day labour	2	5.3
Govt. employed	7	18.4
Private job	6	15.8
Business	7	18.4
Student	3	7.9
Driver	4	10.5
Others	6	15.7
Education status	14	36.8
Below SSC	10	26.3
SSC- HSC	10	26.3
Graduate and above		

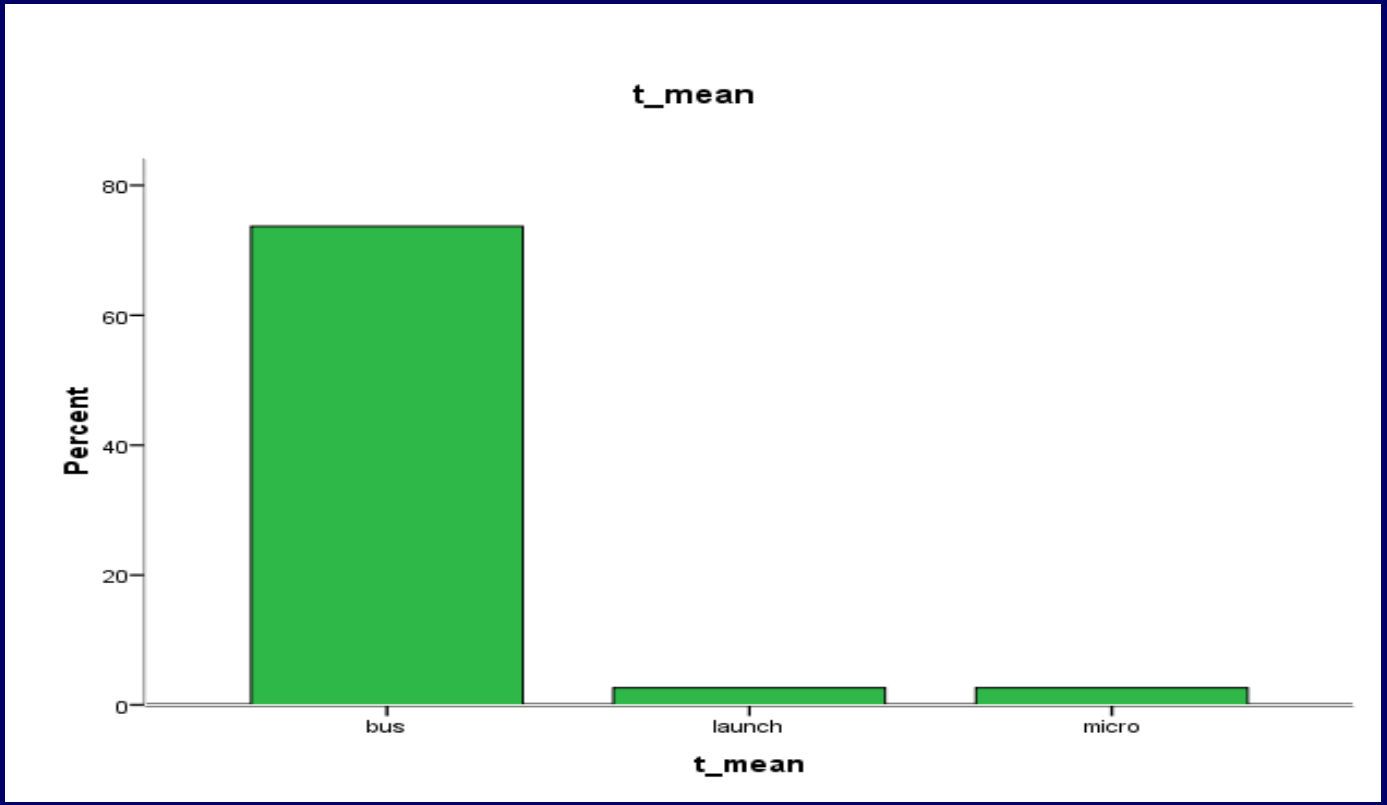
Results (cont....)

Figure – Pattern of monthly income of induced poisoning patients.



Results (cont....)

Figure – Circumstances of induced poisoning patients



Results (cont....)

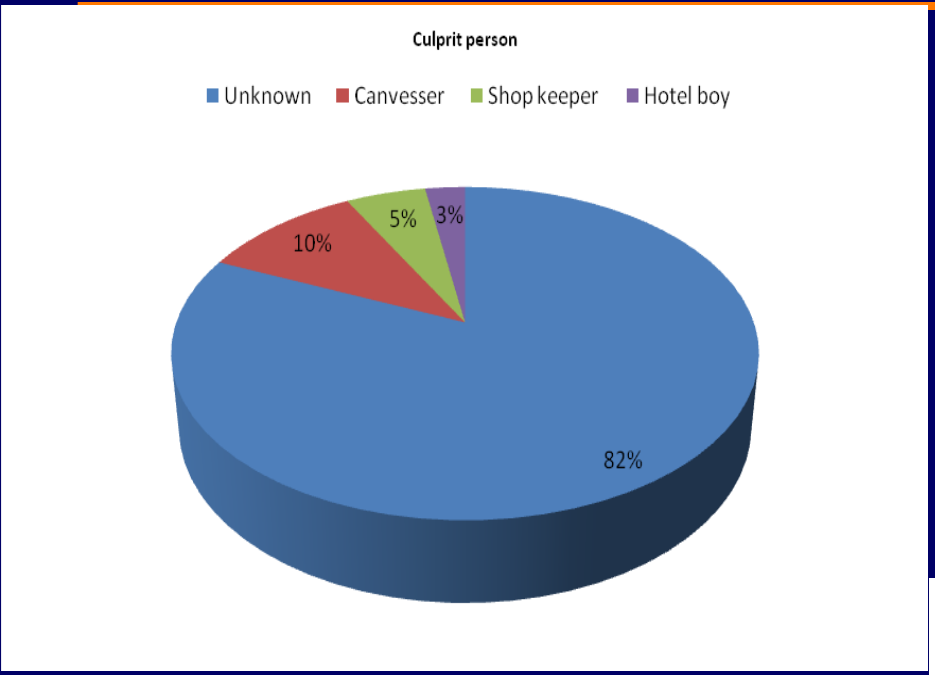
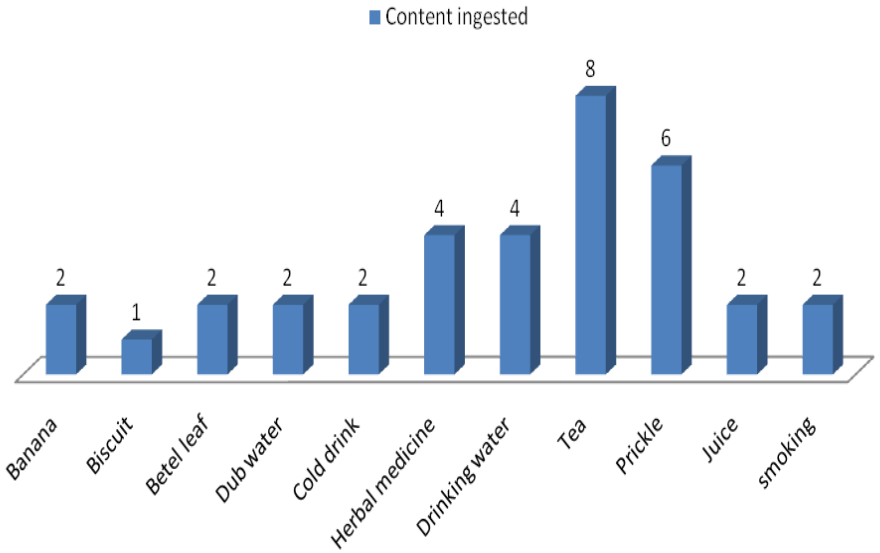


Figure - Culprit people from which patients got the contents.

Figure – Contents ingested by induced poisoning patients.



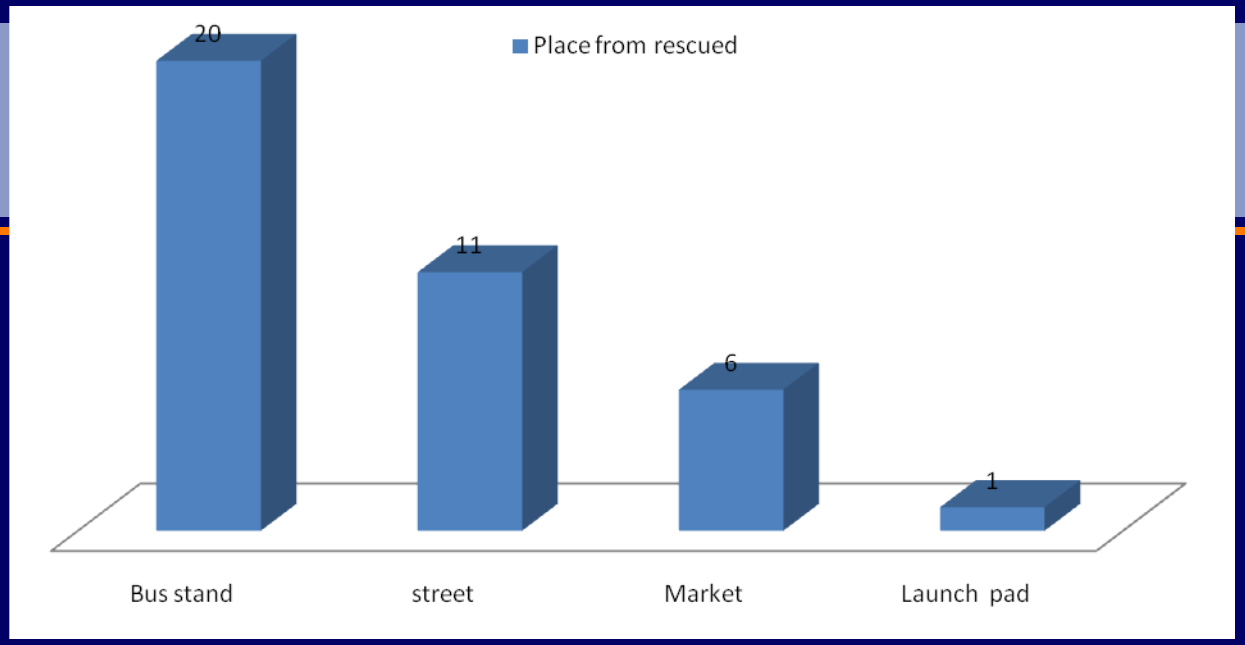


Figure – Pattern of rescuing of induced poisoning patients from different place.

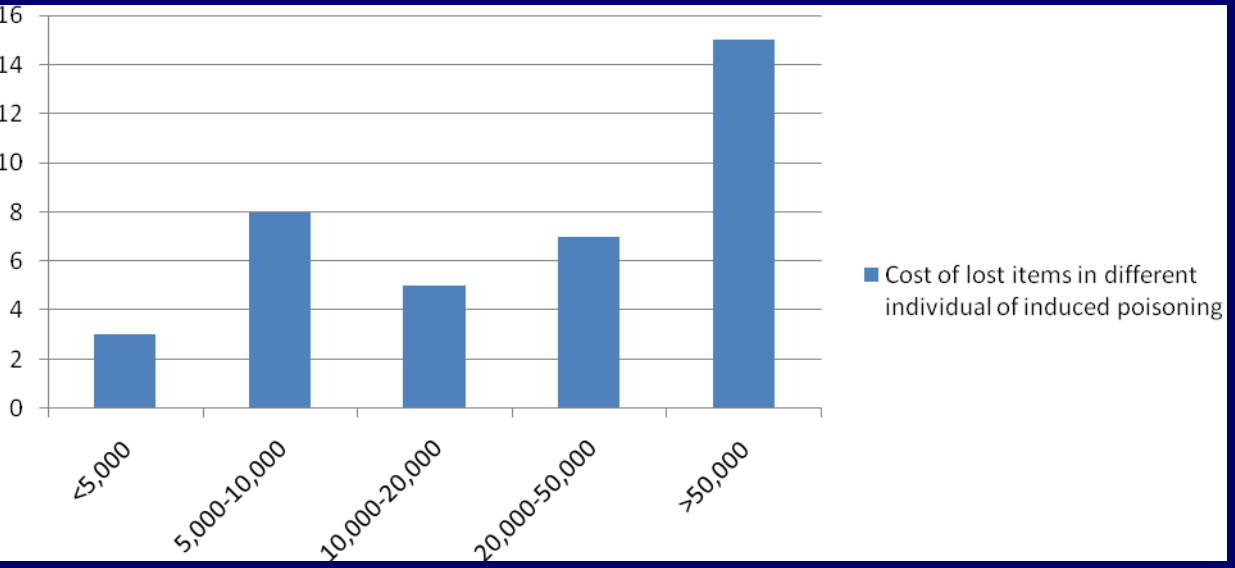
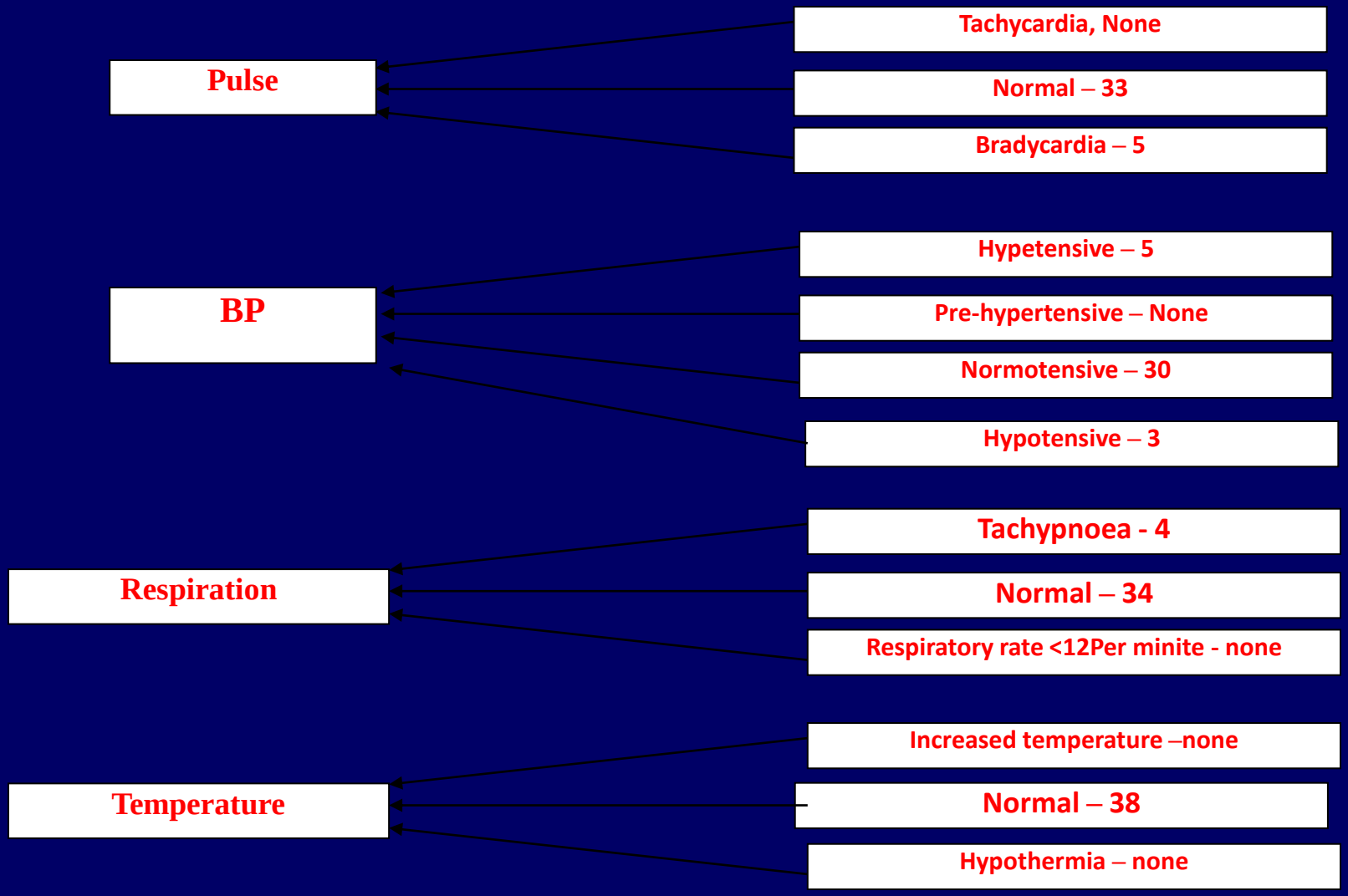
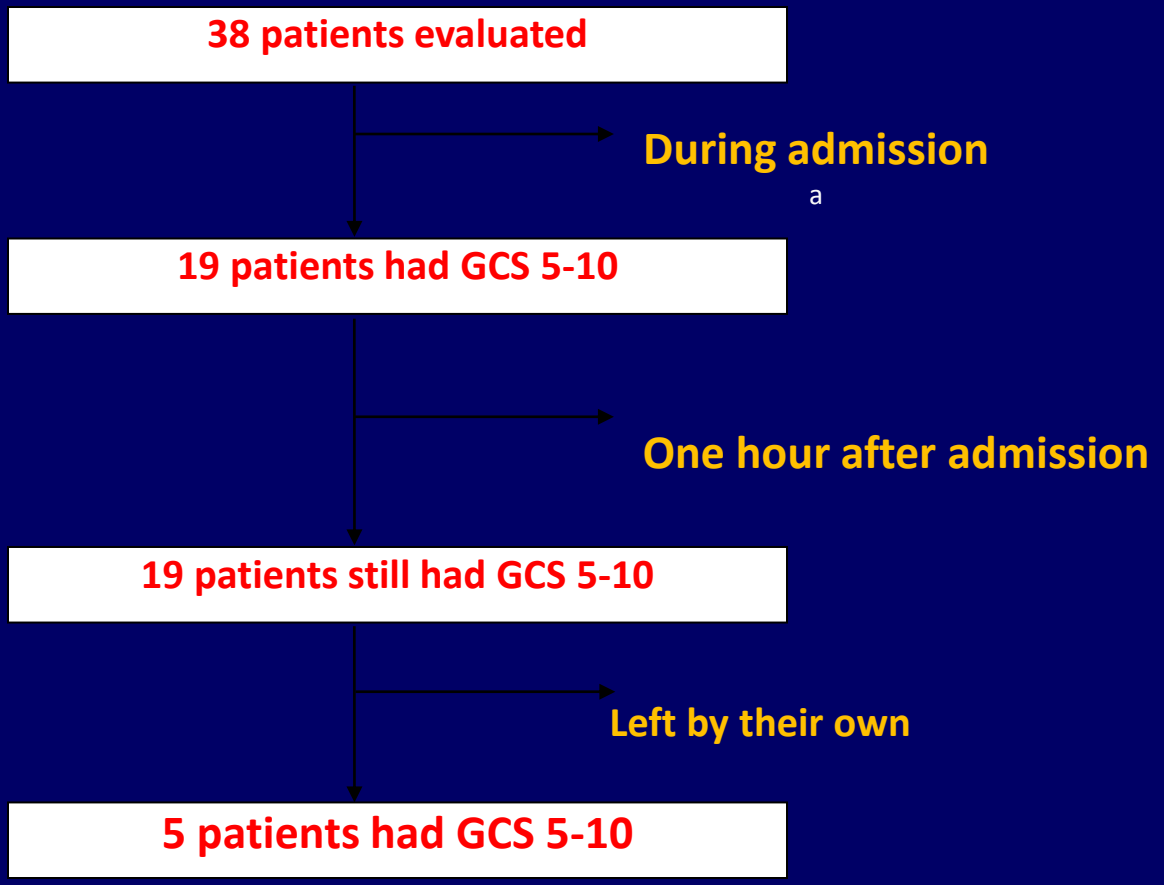


Figure – Lost item evaluation of induced poisoning patients.

Flow Chart : Patients Evaluated for vital parameters.



Flow Chart –: Evaluation of patients for level of consciousness at different time period.



Flow chart: Toxicological screening

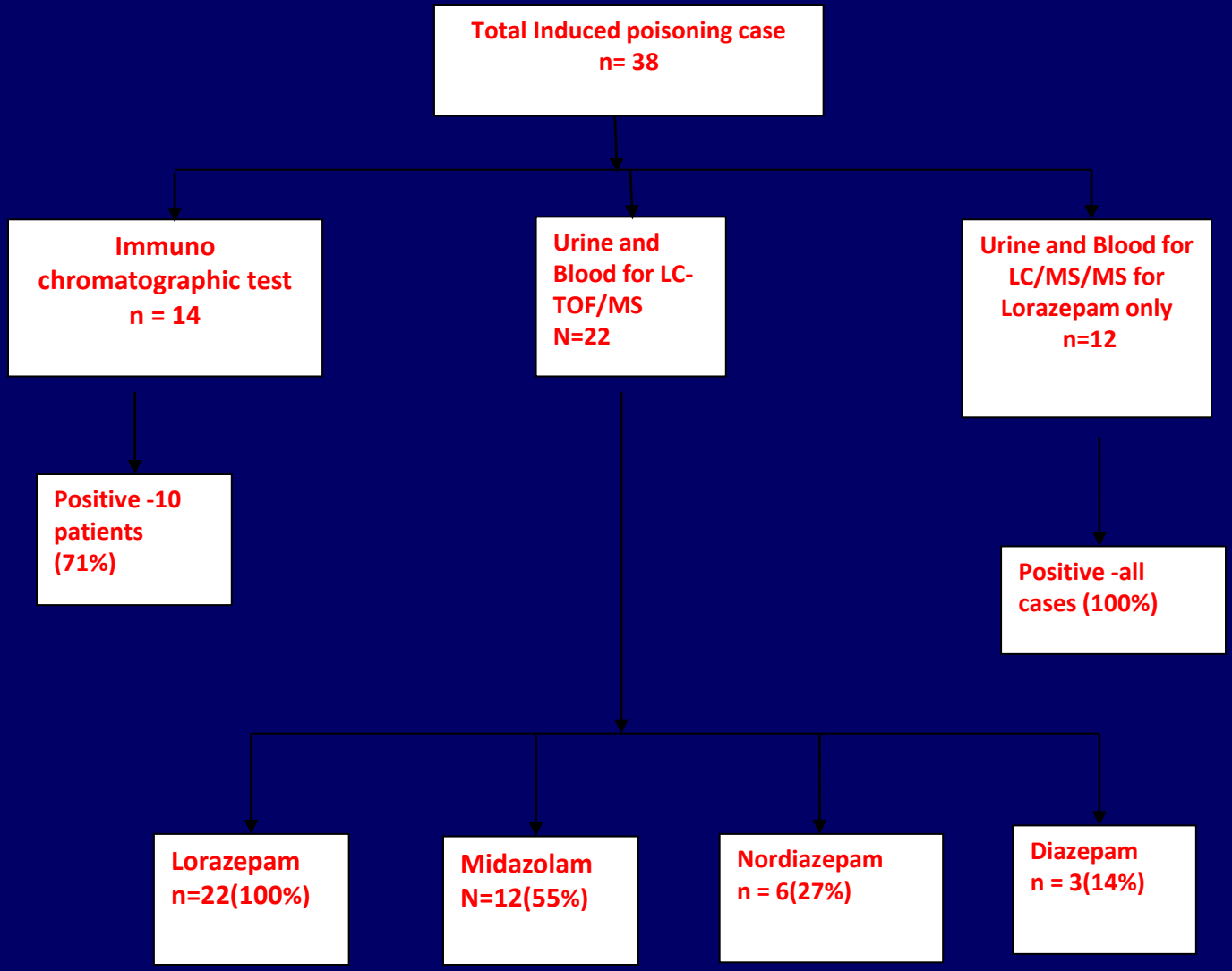


Table - Presence of different groups of Benzodiazepine in urine sample

Urine sample	Lorazepam	Diazepam	Oxazepam	Nordiazepam	Temazepam	Midazolam
13	Present	X	X	X	X	X
14	Present	X	X	X	X	X
15	Present	X	X	Present	X	Present
16	Present	X	X	X	X	Present
17	Present	X	X	X	X	X
18	Present	X	X	Present	X	Present
19	Present	X	X	X	X	Present
20	Present	X	X	Present	X	Present
21	Present	X	X	X	X	Present
22	Present	X	Present	Present	X	Present
23	Present	X	Present	Present	X	Present
24	Present	X	X	X	X	X
25	Present	X	X	X	X	Present
26	Present	X	X	X	X	Present
27	Present	X	X	X	X	X
28	Present	X	X	X	X	Present
29	Present	Present	Present	Present	Present	Present
30	Present	X	X	X	X	Present
31	Present	X	X	X	X	x
32	Present	X	X	X	X	Present
33	Present	X	X	X	X	Present
34	Present	x	X	X	x	Present

Figure – Urine sample showing lorazepam and Midazolam peak in LC MS/MS

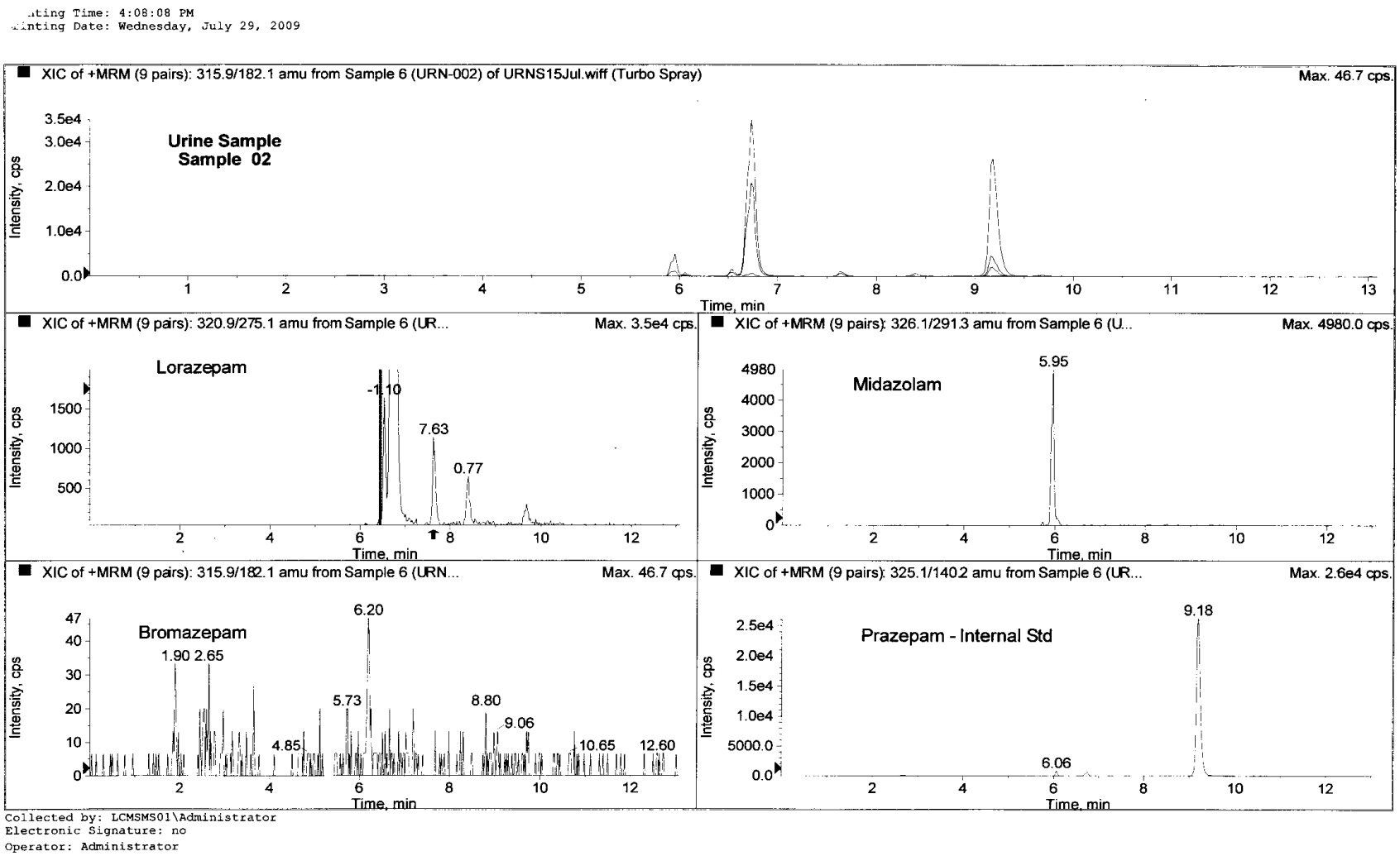


Figure : Blood sample Showing Lorazepam and Midazolam peak at mass no.7.61 and 5.95 ppb in LC MS/MS

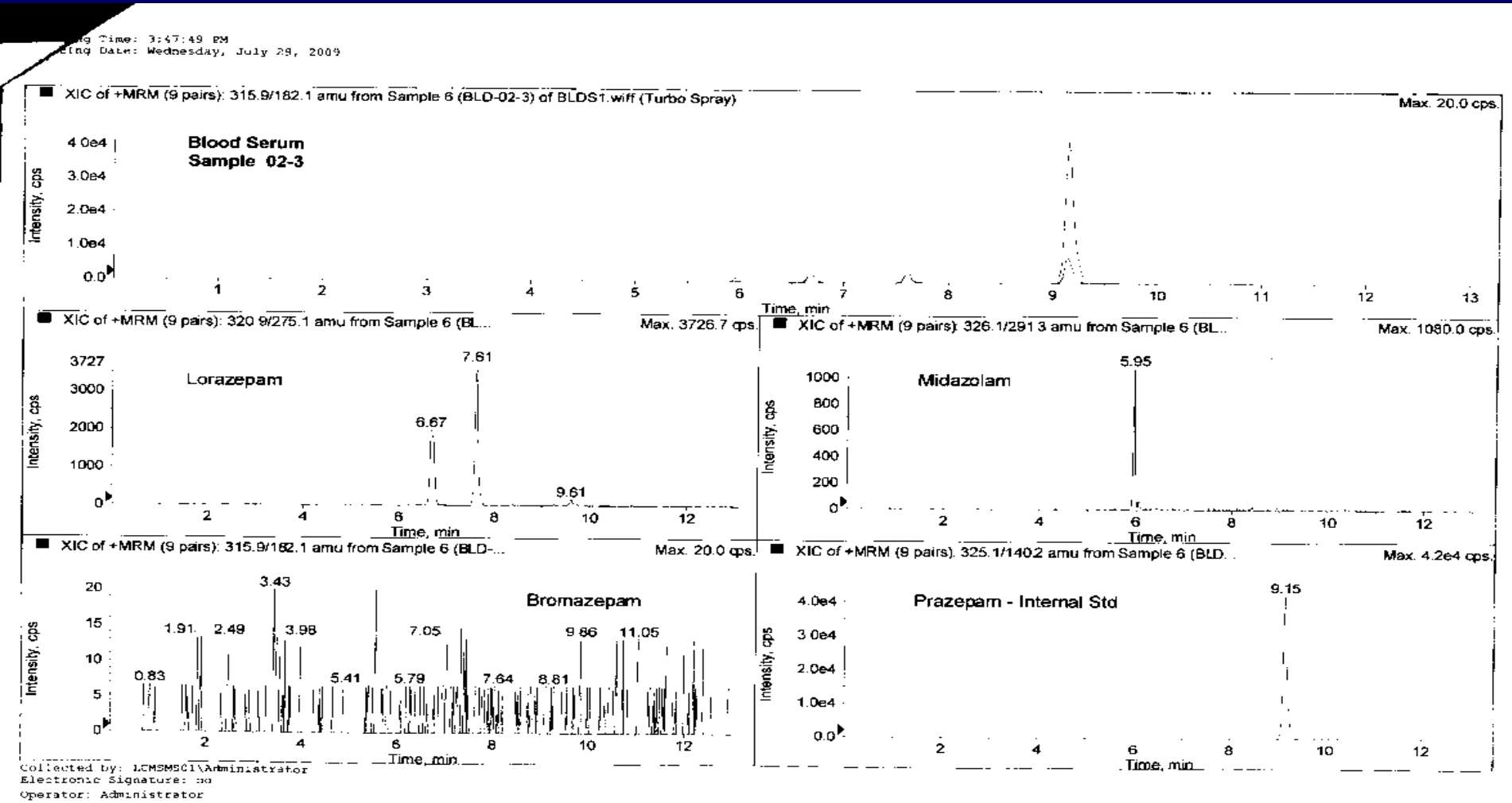


Table: Comparison of different concentration of drugs with GCS and period of hospital stay.

GCS	Duration of Hospital stay		Lorazepam at 0 hour	Lorazepam at 1 hour	Midazolam 0hr	Midazolam 1 hr
GCS 5-10	0-12 hour	1	292	259	.	.
		2	59	102	.	.
		3	407	375	134	130
		4	598	328	46	42
		5	261	237	.	.
	0-12 hour					
GCS 11-14		1	146	83	.	.
		2	94	83	275	163
		3	49	146	89	147
		4	62	62	60	117
		5	10	19	89	98
		6	149	214	.	.
		7	405	164	.	.
		8	189	141	.	.
		9	142	72	198	165
		10	424	24		
		11	180	100	.	.
	13-24 hour				.	.
GCS 5-10		1	153	144	.	.
		2	41	59	.	.
		3	187	164	.	.
		4	193	163	54	57
		5	136	147	272	338
		6	52	29	55	33
		7	299	193	270	152
	13-24 hour					
GCS11-14		1	239	216	58	44
		2	60	68	.	.
		3	279	218	.	.

Table : Estimated doses of different Benzodiazepine were used by miscreants.

	Lorazepam A vs. E	Lorazepam Max [µg/L]	Diazepam Max [µg/L]	Nordiazepam Max [µg/L]	Midazolam Max [µg/L]		Lorazepam Dose [mg]	Diazepam Dose [mg]	Nordiazepam Dose [mg]	Midazolam Dose [mg]
Number of Cases	26					n=	26	3	6	12
Absorption phase	5					Min	1	3	9	4
Elimination phase	21					Median	10	14	21	14
						Max	24	21	34	34
Mean±SD		216,7±131,8	217,3±143,5	363,7±185,6	149,4±99,4	Mean±SD	11,2±6,5	12,8±9,0	19,9±9,6	15,4±10,1
						Single therapeutic Dose ORAL [mg]	2	10	10	5
						Mean multiple of dose	5.6	1.3	2.0	3.1
						Max multiple of dose	11.9	2.1	3.4	6.7

Discussion:

- The observation made from this study included 38 cases of induced poisoning on journey.
- This is the first study using toxicological analysis in a systemic manner in induced criminal poisoning among commuters in Bangladesh.
- On analysis of serum electrolyte 1 patient had found hypokalaemic(3.3mmol/l), serum chloride was found slightly raised among 13(34%) patients, one had very high level 160mmol/L. Otherwise all were within normal limit.

- **Time between poisoning and loss of consciousness were unknown among all patients, The mean time of induced poisoning and hospital admission was 4.42 SD-3.6 hour with minimum 1.2 hour to maximum 19 hour. Similar effect was described by Jain A & Bhatnagar MK.**

- **Time between poisoning and hospital admission was 4 hours for 77% of patients and all were admitted within a day.**

- The analysis also revealed minimum ingested doses, estimated using the lower boundary of the benzodiazepines' volumes of distribution and the upper boundary of the bioavailabilities, was 11±7 mg (mean±SD) lorazepam, 13±9 mg diazepam, 20±10 mg nordiazepam and 15±10 mg midazolam.

- This study reveals flexibility of the criminals in using different mixtures of benzodiazepines (in the earlier study a single drug, lorazepam, was common). This finding also indicates the modifications to emergency department protocols (stomach wash).

- Half life of lorazepam is prolong then other benzodiazepine , so here 2 patients who had in absorptive phase, left the hospital with in 12 hour, had strong chance of again fall outside. Three patients had found hypotensive; 2 were lorazepam level >250ng/ml and GCS-5-10.
- All benzodiazepines are hepatically metabolised with a renal clearance accounting for less than 5%. The half-life of these drugs varies widely and a number of drugs have active metabolites. Drug with a shorter half-life (temazepam, triazolam) and drugs with a longer half-life (diazepam, clonazepam) still have very similar spectrums of clinical toxicity.

- It is actually the development of tolerance to the benzodiazepines that determines the recovery of consciousness rather than the clearance of the drug.

- They show that an up to 12-fold overdose of benzodiazepines did not lead to life-threatening symptoms and have important implications for the clinical management of these drug-facilitated crimes.

- No death was observed in this series during hospital stay. On the contrary, however, the psychological trauma associated with the criminal poisoning, anterograde amnesia, and often substantial loss of property threatening the economic survival of the victim and his family. Therefore, post-recovery psychological supports for victims need to be evaluated.
- In the absence of adequate clinical toxicology facilities, and if it was available at a low price, the administration of a test dose of the antidote flumazenil to patients might instead be considered to diagnose the aetiology of the unconsciousness as benzodiazepine poisoning.

Conclusion

- A team of healthcare professionals including doctors, nurses, paramedics can be build up. A separate day care room close to emergency department can be set up which can be utilized by all admitting adult medicine units in Medical College Hospitals for improved management of such cases.
- These types of patients require support from humanitarian point of view. If the people, the mass media, the police, the bus driver and conductors become alert, the incidence can be reduced.

LIMITATIONS OF THE STUDY

- The higher number of samples could give better information regarding induced poisoning.
- The samples could not be collected from different general hospital of different areas, the data from different hospital could give better information.
- If all the patient sample were analyzed for benzodiazepine, the information could be additional to this above results.

Acknowledgement

- Staff in the Department of Medicine of Dhaka Medical College Hospital
- Institute of Forensic Toxicology of Johann Wolfgang Goethe-University designed
- Institute of Food Science & Toxicology, BCSIR, Dhaka, Bangladesh

N.B..

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