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Prothrombin Time Prolongation in Patients with Acute Intentional Anti-coagulant Rodenticide Intoxication

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Authors' contributions

This work was carried out in collaboration between all authors. Author UZ gave the concept and designed the study. She also did acquisition, analysis and interpretation of data. Author OS drafted the article and did critical revision. Author AF read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Aims: Aim of this study is to determine effects of acute intentional ingestion of superwarfarin compounds for suicidal intentions on homeostatic profile of patients.
Study Design: This is a retrospective observational study.
Place and Duration of Study: This study was conducted at Jinnah Postgraduate medical center in Karachi, Pakistan during the period from 15th October 2015 to 27th December 2015.
Methodology: 74 patients with rodenticide intoxication were included in this study. PT was ordered at the time of presentation. aPTT was done only in few patients because of financial constraints. Symptoms at the time of presentation were recorded. Results were analyzed using SPSS v.20.
Results: 52.7% were males while 47.3% were females. Most common symptom was found to be vomiting which was positive in 38.8% of individuals. No bleeding abnormality was recorded in any

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patient. Mean PT among patients was found to be 10.51 seconds +- 2.38 (control = 11 seconds). PT >14 was found in 5 individuals. Mean INR was found to be 0.94+-0.24. INR greater than 1.5 was found only in 2 individuals.

Conclusion: Majority of studies report no bleeding abnormality in majority of patients associated with rodenticide intoxication while some studies report minor and major symptoms associated with it. However no bleeding abnormality was found in any patient of our study.

Keywords: Prothrombin time; rodenticide intoxication; INR.

1. INTRODUCTION

Rodenticides are compounds which are used to kill rats but are extensively used in Pakistan for suicidal purpose due to easy access and being low priced. Rodenticide intoxication is a rare problem but is very common in east however there is very sparse data available on rodenticide intoxication and its biochemical alterations within human body [1]. Majority of rodenticides have superwarfarin compounds such as brodifacoum and bromadiolone while others have zinc phosphide, bromethalin, cholecalciferol, strychnine, thalium, arsenic, yellow phosphorus, aluminium phosphide [2] Brodifacoum and bromadiolone are known to be superwarfarin compounds. Brodifacoum is present in rodenticides uptil 0.005% [3]. These compounds are very effective as rodenticides because of their high lipid solubility, affinity for hepatic tissue and slow elimination from the body. These compounds have the same mechanism of action as warfarin but are 100 times more potent than warfarin [4]. Clotting factors II, VII, IX and X requires the presence of Vitamin K as activating factor. Superwarfarin compounds thus inhibit formation of active form of vitamin K which results in coagulopathy involving both the intrinsic as well as extrinsic pathway [5]. Other compounds found in rodenticides such as zinc phosphide has the potential of causing cardiovascular and multisystem failure as well as hepatocellular dysfunction [6].

Important factors determining outcome of rodenticide poisoning include type of rodenticide ingested because different rodenticides differ in percentage of superwarfarin compounds present, amount of rodenticide ingested, either it is chronic exposure of acute ingestion, presence of any congenital bleeding disorder, vitamin K deficiency, malnutrition, thrombocytopenias etc [1].

2. METHODS

This retrospective observational study was done in Jinnah Postgraduate Medical Centre, Karachi during the period from 15th October 2015 to 27th December 2015. 77 patients were admitted with rodenticide poisoning during the study duration, 2 of them left hospital against medical advice and were excluded from the study. All patients had intentionally ingested rodenticide for suicidal purpose except one child 5 years old who had unintentionally ingested rodenticide while playing. He was also excluded from the study. The study was approved from ethical review board of Jinnah Postgraduate Medical Center, Karachi.

Majority of rodenticides available in Pakistan contain 0.005% brodifacoum, 0.0375% coumatetralyl, 0.005% bromethalin and 2% zinc phosphide. Diagnosis was based on history from patient as well as patient's attendants, clinical manifestations and laboratory investigations. Patients with unknown poisoning and co-ingestion of rodenticide with other poisons were excluded from the study. Most of the patients were stable at presentation. Signs and symptoms at presentation included vomiting, diarrhea, lacrimation, salivation, fasciculations, sweating, non-reactive pupil, irritability and altered consciousness. No sign or symptom of any bleeding abnormality was found in any patient. Patients were acutely managed with gastric lavage. Gastric lavange was done in all patients. Prophylactic injection of Vitamin K was not given to any patient because of lack of any bleeding abnormality normal PT values. CBC, Serum electrolytes, PT were ordered at the time of presentation. Laboratory value of prothrombin time among normal healthy subjects was 11 seconds. aPTT was done only in few patients because of financial constraints. Results are reported as mean +- S.D. Results were analyzed using SPSS v.20.

3. RESULTS

Among 74 patients admitted, 52.7% (n=39) were males while 47.3% (n=35) were females. 51.4% (n=38) were married while 48.6% (n=36) were unmarried (Table 1). Mean age was found to be

22.98+-8.96. Most cases reported were between ages 17 – 25 years of age (n=35, 21 males and 14 females). Between ages 11-13 were 2 patients (1 male, 1 female), 14 -17 were 18 patients (10 males, 8 females), 25-33 were 10 patients (4 males, 6 females), 33-41 were 6 patients (1 male, 5 females), 41-60 were 2 patients (1 male, 1 female), between 60-80 was only one patient (Fig. 1).

Most common symptom was found to be vomiting which was positive in 38.8% of individuals (n=25, 12 males and 13 females). Other symptoms included: Fasciculations which was positive in 21.6% patients (n=16, 7 males and 9 females), non-reactive pupils in 20.3% (n= 15, 8 males and 7 females), salivation in 12% (n=9, 4 males and 5 females), diarrhea in 10.8% (n=8, 2 males and 6 females), lacrimation in 9.4% (n=7, 3 males and 4 females), urination in 5.4% (n= 4, 1 male and 3 females) (Fig. 2).

Fig. 4 shows occurrence of symptoms in various age groups.

No bleeding abnormality was recorded in any patient. Mean PT among patients was found to be 10.51 seconds +- 2.38 (control = 11 seconds). Fig. 3 shows mean PT, INR and aPTT in different age groups. PT >14 was found in 5 individuals. Mean INR was found to be 0.94+-0.24. INR greater than 1.5 was found only in 2 individuals. Fig. 5 shows mean INR amongst various age groups. aPTT was done only in 19 individuals. Mean aPTT was found in 27.93+-2.93.

No patient died of rodenticide intoxication.

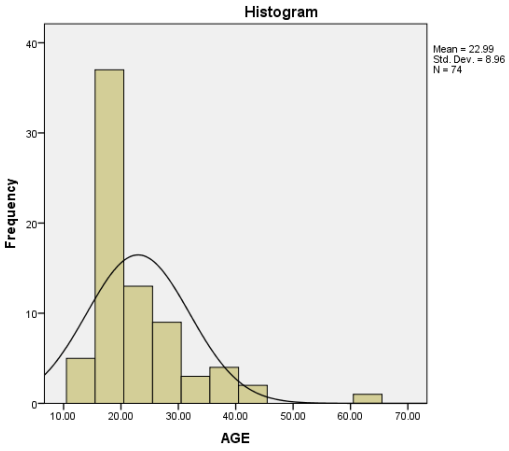

Fig. 1. Ages of individuals

4. DISCUSSION

Rodenticides are a common source of poisoning in Karachi. It has been previously reported that rodenticide poisoning was found in 28% of total poisoning cases being at 2nd place, while the most common source was organo-phosphate ingestion with 33% of total poisoning cases [7]. Our study reports PT and aPTT results with labs collected at the time of admission while literature review shows that PT values increase 48 – 72 hours after ingestion because of longer half life of coagulation factors. Clinical signs can be seen till upto 4 weeks and factors remain decreased till 8 months [8]. But no patient from our study reported with any bleeding abnormality afterwards.

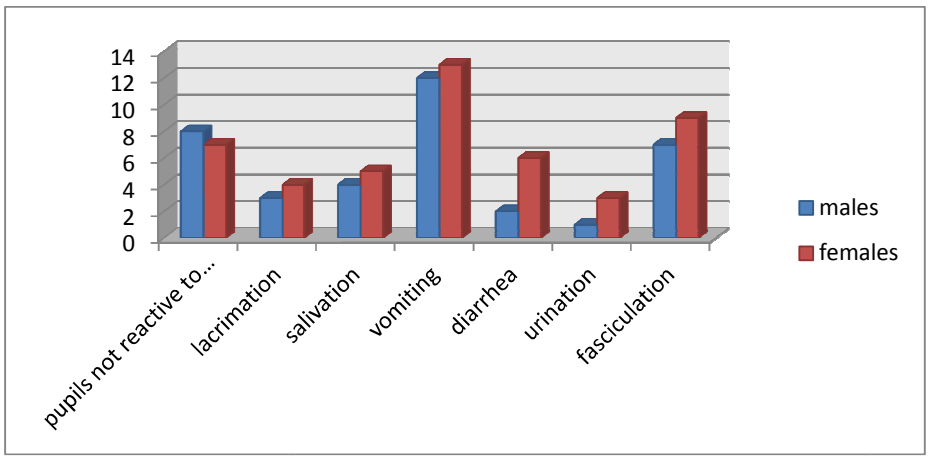

Fig. 2. Association of gender and various symptoms found in patients with rodenticide poisoning

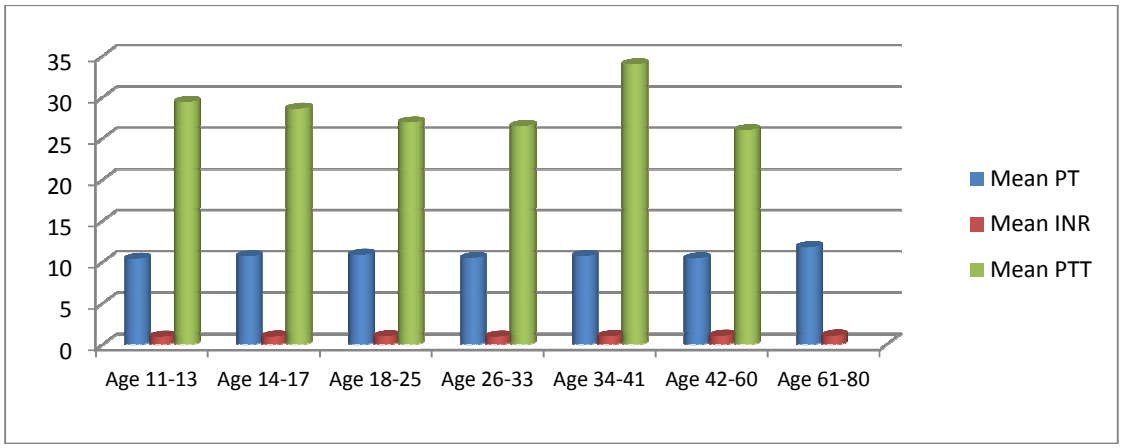

Fig. 1. Mean PT, INR and aPTT in patients of various age groups. (PT control = 11 seconds)

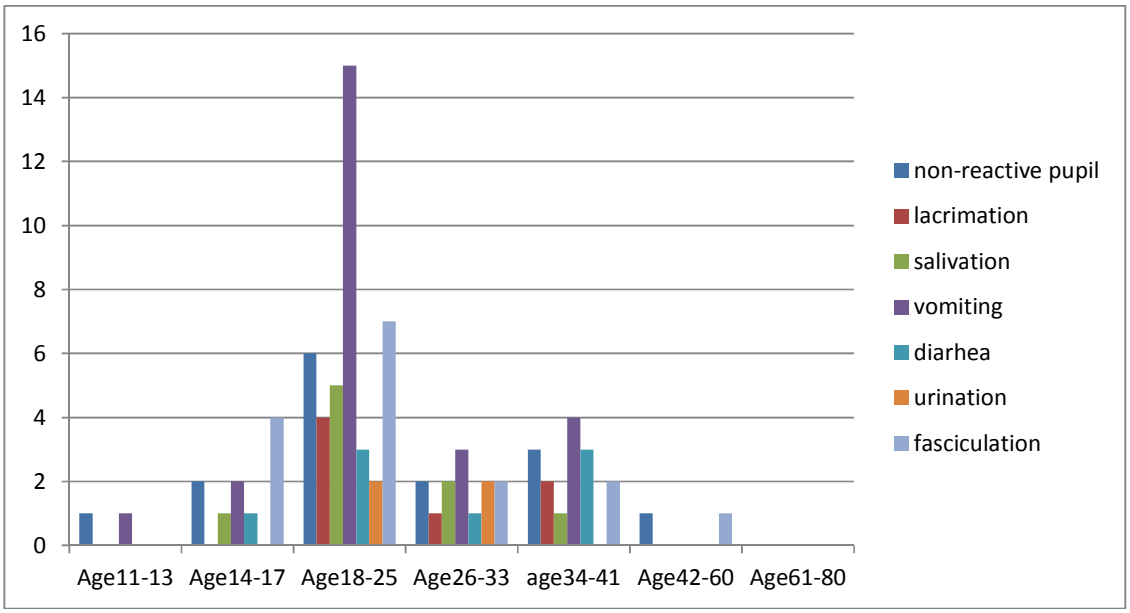

Fig. 2. Distribution of symptoms in amongst various age groups

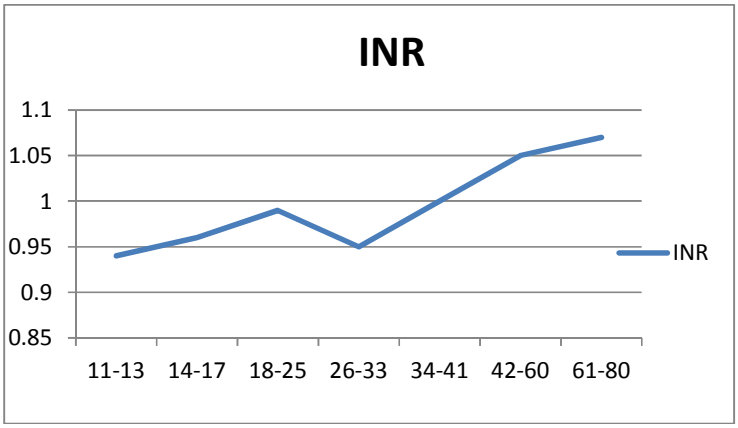

Fig. 3. INR in various age groups

Table 1. Marital status

	Males (n=38)	Females (n=35)
Married	14	24
Unmarried	25	11

Table 2. Demonstration of Fig. 3

	Mean PT (p= <0.001)	Mean INR (p= 0.008)	Mean PTT (p= <0.001)
11-13	10.4	0.94	29.4
14-17	10.71	0.96	28.6
18-25	10.88	0.99	26.94
16-33	10.48	0.95	26.5
34-41	10.75	1.00	34
42-60	10.45	1.05	26
61-80	11.8	1.07	-

Table 3. Demonstration of Fig. 2

	Males	Females
Non-reactive pupil	8	7
Lacrimation	3	4
Salivation	4	5
Vomiting	12	13
Diarrhea	2	6
Urination	1	3
Fasciculation	7	9

It has been shown that majority of bleeding abnormalities with rodenticide intoxication were positive in those with long term chronic exposure as compared to those with acute accidental or suicidal ingestion [9]. Ingels at el reported 595 children younger than 6 years of age with acute unintentional rodenticide ingestion. No bleeding abnormality was found in any of them while only 2 patients had INR greater than 1.5. [10] These results correspond with our study which shows 2 patients with INR greater than 1.5 (age 25 and 30) with no signs and symptoms of bleeding abnormality. On the other hand some studies show hemorrhage and death associated with rodenticide intoxication. Robert et al reported 15 year female child who was found dead in her room. Later investigations revealed rodenticide intoxication 6 months prior [11].

The American association of poison control center (AAPCC) retrospectively examined 10,762 children less than 6 years of age with acute, unintentional rodenticide intoxication. None of the patients died. However, 67 patients developed coagulopathy [12]. Wu, et al. [13] reported hematuria in 8 patients out of 9 with rodenticide intoxication.

5. LIMITATIONS

Limited patient population, lack of diagnostic procedures and poor follow up are some drawbacks of our study which if paid concern can lead to much better conclusion in the fate of rodenticide intoxication. Rodenticide levels have major effect on patient's hemostatic profile. In this study toxin levels cannot be determined and this is one major drawback.

6. CONCLUSION

Mortality rate in our study was found to be zero which is similar to other studies reported earlier in course of rodenticide intoxication. Major factors contributing to this can be gastric decontaimination and urgent referral to hospital. [1].

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this paper and accompanying images.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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