ORIGINAL ARTICLE

INCIDENCE OF PARAPHENYLENE-DIAMINE POISONING IN THREE DISTRICT HEADQUARTER HOSPITALS OF PAKISTAN

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Background: Paraphenylene-diamine (PPD) poisoning is an emerging problem of developing African and South Asian countries. This study was done with the objective to determine the clinical lab diagnostic accuracy of serum creatinine phosphokinase in cases initially reporting facial oedema followed by renal failure and rhabdomyolysis due to paraphenylene-diamine (PPD) poisoning. **Methods**: It was a cross-sectional study in which data was retrospectively collected at District Head Quarter (DHQ) Hospitals. Data was collected over a period of one year from Jan-Dec 2018. Data was collected from the patient file records. Data was analysed on SPSS version 20. **Results:** In the present study, 658 cases of *Kala Pathar* poisoning presented and treated. M: F ratio was 5:20. There were 518 (78.8%) females. Majority of the female patients were married 488 (94%). Most common clinical manifestations included marked facial oedema; dysphagia and stridor. Post complications include rhabdomyolysis and acute renal failure which developed after two to five days. Initial lab investigations within 6–8 hours after ingestion showed marked increase in TLC count, ALT and Na^+ ions. There was marked elevation of serum CPK (1400±200 U/L) levels after 24 hours. **Conclusion:** PPD poisoning is more common in females of younger age group belonging to rural areas. Early diagnosis and prompt supportive treatment within 2–12 hours of ingestion can save many lives. There is no specific antidote available for this poison.

Keywords: Rhabdomyolysis; Para Phenylene Diamine; Acute renal failure; Creatinine Kinese, CK

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INTRODUCTION

Paraphenylene-diamine (PPD) poisoning is an emerging problem of developing African and South Asian countries.[1] PPD is used in industry of making dyes for newspapers and for dyeing leather and fabric. It is also used in small quantity to make tattoos over body by mixing it with *henna.*[2] PPD hair dyes are usually available in the market as paste or powder with a developer. When mixed with a developer (oxidizer) it oxidizes and changes colour from white to black.[3] When the hair dye gives darker colour this mean it has high concentration of PPD. PPD behaves like an allergen and causes mast cell degranulation, capillary leaking, anaphylactic reactions and damage hepatocytes.[4]

Serum creatinine kinase (CK) or creatine phosphokinase (CPK) is an enzyme found in muscle tissue. It catalyzes the conversion of creatine into phosphocreatine and adenosine-triphosphate (ATP) into adenosine diphosphate (ADP). This poison produces highly toxic effect on respiratory, hepatic, renal and cardiac systems by inhibiting cellular oxidation and also have effects on muscles. It also causes rhabdomyolysis, laryngeal oedema, severe metabolic acidosis and acute renal failure.[5] The incidence of suicide poisoning with household items has shown a significant increase in the past five years.[6] Most common incidences of suicide were reported in low socioeconomic status families.[7] The clinical manifestations within 6–8 hours of ingestion include oedema of the face, neck, pharynx, convulsion, muscular cramps and fatigue.[8] Post symptoms include dysphagia, asphyxia, oedema and rhabdomyolysis. It produces very devastating effects on different systems leading to acute renal failure, respiratory acidosis and hepatic failure. Its toxicity depends upon the quantity of dose ingested. When taken orally, death may occur within initial 6–24 hours due to angioneurotic edema.[9] This study was done with the objective to determine the clinical lab diagnostic accuracy of serum creatinine phosphokinase in cases initially reporting facial oedema followed by renal failure and rhabdomyolysis due to paraphenylene-diamine (PPD) poisoning.

MATERIAL AND METHODS

It was a cross-sectional study with data retrospectively collected at District Head Quarter (DHQ) Hospitals of South Punjab (Bakkhar, DG

Khan) and DI Khan of Khyber Pakhtunkhwa (KPK). Data was collected from Jan-Dec 2018. A total of 658 cases of PPD (*kala pathar*) presented to emergency departments over a period of one year. The ratio of male and female cases was 5:20 respectively and age range of both the genders was 15–30 years. Statistical Package for Social Sciences (SPSS) version 20 was used for data entry and analyses. Mean and standard deviation was calculated for age of the patient. Frequency and percentages were calculated for gender, marital status.

RESULTS

In the present study, 503 cases were presented with a history of ingestion of Hair dye (*Kala Pathar*). There were 519 (78.8%) females and 139 (21.2%) males. In adults the age ranged from 12–39 years, average age was 21±11 years for females and 26±13 years for males. Majority of the female patients were married 488 (94%). The socioeconomic status of all the presented cases was below average.

The intention of suicide was determined. Early clinical manifestations included marked oedema of face, dysphagia, and stridor. Rhabdomyolysis, hepatic damage, neuropathy and acute renal failure developed after two to five days. Urine examination showed albinuria and haemoglobinuria. Survival rate was subject to early performance of gastric levage, hemo-perfusion and symptomatic treatment. Out of total 212 (37.5%) of hair dye ingestion arrived within 2 hours of ingestion 291 (57.8%) arrived within 12 hours of ingestion. Table 2 shows data about different presentations.

Initial lab results (2-6 hours of ingestion) showed decrease in Haemoglobin conc. 9.9±2.2 gm/dl in adult females, increase white blood counts of 14000±2000g/dl, platelet counts more than 422,000; serum glutamate-pyruvate transaminase (SGPT) 1365±1186 IU/L, increase Sodium 141 mmol/L, decrease Potassium 3.4 mmol/L, decrease Bicarbonate±24.2 mmol/L. Serum Creatinine phosphokinase (CPK) 1200±200 after 24 hours.

Clinical tests after 12-14 hours showed marked haemolysis [Hb 8.5±1.6 gm/dL (12.1–15.1 gm/dL)], low levels of potassium (K) [2.2±1.1 mEq/L (3.5–5.2 mEq/L)], raised Creatinine (CPK) 1.4±0.2 mg/dl (0.5–1.4 mg/dl), raised WBC that is 15.6±1.7 (4.0-10.0×109/L) (Table-3). Diagnostic accuracy of serum creatinine phosphokinase (CPK) showed that its sensitivity was 92.38% for the detection of PPD poisoning, specificity was 88.89%, positive predictive value was 99.37%, negative predictive value was 38.10% and overall diagnostic accuracy was 92.20%.

The mortality rate was quite high. On average survival rate was less than 20% (n=119). The median for duration of stay in the hospital was 7±2 days (inter-quartile range=6.45). Out of 518 female patients 26 (5.0%) had pregnancy and 44 (8.6%) had left the hospital against medical advice.

Table-1: Demographic characteristics of the patients (n=658)

Gender	Poisoning due to Para Phenylene Damine	
	Children (5 >12 years)	Adults
Male	22 (68.7%)	118 (18.7%)
Female	11 (33.3%)	507 (81.1%)

Table-2: Clinical Features and outcome of *Kala Pathar* poisoning

Clinical Features	n=658 (%)
Pain in Throat	416 (63.2)
Oral Erythema	376 (57.1)
Cervicofacial Oedema	658 (100)
Dysphagia	317 (48.1)
Dysphonia	416 (63.2)
Difficulty in Opening of Mouth	311(47.6)
Muscle Aches/Rigidity	100 (15.1)
Dark urine	134 (20.3)
Rhabdomyolysis	309 (46.9)
Oliguria/Anuria	405 (61.5)
Acute Renal Failure	406 (61.5)
Hyperkelemia	303 (47.8)
Hepatitis	314 (48.1)
Hemodynamic shock	203 (30.8)
Sinus bradycardia	103 15.6)
Sinus tachycardia	213 (32.3)
Outcome	n (%)
Tracheotomy	324 (49.2)
Ventilator	212 (32.2)
ICU stay (days)	6.43±3.61
Mortality	06 (37.5)

Table-3: Laboratory parameters

Laboratory parameters	Mean±SD	Normal Range
TLC (4.0–10.0 X 109/L)	15.6±1.7	(4.0–10.0×109/L)
CPK (U/L)	1200±200	22–198
AST (U/L)	1365.18±1186.28	10–40
ALT (U/L)	851.19±1604	7–56
Serum Creatinine (mg/dL)	1.98±1.6	0.50–1.2

DISCUSSION

During the last decade, the tendency of suicide has been increased specially in youngsters.[10] PPD is cheap and salty in taste in contrast to most of the poisons with bitter taste that is why it has become popular choice among household suicidal poisons.[11] Most of the cases reported from low socioeconomic rural areas located in southern districts of Punjab and KPK. In Arabian Peninsula and Gulf countries most of the victims were young females who use it with suicidal intention.[12,13] In current study 518 victims were females and most of them were married (n = 488).

The chemical composition of *kala pathar* compounds are harmful for kidneys and liver.[14] The metabolites cause renal tubular necrosis leading to

hyperkalaemia and raised SGPT.[15] Raised SGPT is not a reliable indicator as it has very high levels in other metabolic disorders. The toxicity of Para-phenylene-diamine is dose dependent with estimated lethal dose of oral 0.5–0.8 mg/kg or 7–10 grams orally.[16]

In about one third cases PPD causes unconsciousness leading to coma. In other studies, done in 2011 and 2014 percentage was 20 and 26.3%.[17,18] Haemolysis, acute septicaemia and myocarditis might be the underlying cause. Hyperkalaemia was observed in 12.5% cases. Hyperkalaemia was noted to be 20% and 26.3% in patients in other studies conducted in Mirpur khas (Sindh) and in Southern Punjab.[19-20] Rhabdomyolysis and ARF may be the cause of hyperkalaemia.[21] Skeletal muscle fatigue was evident in 62.4% patients in our study due to rhabdomyolysis. ARF occurred in 37.5% of patients whereas in other studies it was 47.4% and 40%.[22-23] We also found that the SGPT a marker of hepatitis was significantly higher in our patients but also higher in other non-poisoned patients. Acute renal failure (ARF) developed as a consequence of tubular necrosis[23]. ARF developed only in patients who ingested more than 100 ml of *kala-pathar.* Cervicofacial oedema was not dose dependent it was present in all victims. In 324 patient's tracheotomy was performed to clear airway obstruction, rests of the patients were given 100% Oxygen. Angioedema, Dysphagia, Rhabdomyolysis were observed in more than 60% of the patients. Opinion of the scientific committee on cosmetic products and non-food products (SCCNFP) intended for consumers concerning p-phenylenediamine was that this compound is not safe for human ingestion in any form, it is highly toxic and 1% PPD if remained in contact with skin for 15 mins can cause severe hypersensitivity reaction.[24] Further studies at different places and with different designs are required

CONCLUSION

PPD poisoning is more common in females of younger age group belonging to rural areas. Early diagnosis and prompt supportive treatment within 2-12 hours of ingestion can save many lives. There is no specific antidote available for this poison. Laboratory tests such as RFTs, LFTs, CPK levels may be the indicators of prognosis. There is a need to specify criteria for the diagnoses of PPD. It is also suggested that sale of *Kala Pathar* should be legally restricted by government.

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AUTHORS' CONTRIBUTION

RZA: Conception, study designing, planning, experimentation, study conduction, analysis, interpretation, discussion, manuscript writing. AHK, SY: Experimentation, study conduction, analysis, interpretation, discussion. AUH, ZUK: Manuscript writing, critical review.

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