



Paraphenylenediamine poisoning: clinical features, complications and outcome in a tertiary care institute

Muhammad Saleh Khaskheli¹, Shamsuddin Shaikh², Munazzah Meraj³, Hamid Raza⁴, Iqra Aslam⁵

ABSTRACT

¹Department of Anesthesiology, Peoples University of Medical & Health Sciences for Women (PUMHSW), Nawabshah (Pakistan)

²Department of Medicine, PUMHSW, Nawabshah (Pakistan)

³Department of Biochemistry, PUMHSW, Nawabshah (Pakistan)

⁴Department of Anesthesiology, Liaquat University of Medical & Health Sciences, Jamshoro (Pakistan)

⁵Department of Biochemistry, Government College University, Faisalabad, (Pakistan)

Correspondence:

Prof Muhammad Saleh Khaskheli, Department of Anesthesiology, Peoples University of Medical & Health Sciences, Nawabshah, (Pakistan); Phone: 03360868593; E-mail: beesaleh@hotmail.com

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Background: Paraphenylenediamine (PPD) is a substance present in hair dyes which is metabolized in the body cytochrome P450 system, and is further oxidized to a toxic product that can lead to multi organ failure

Objective: To determine the frequency of clinical features, complications and outcome in PPD intoxicated patients admitted to the ICU of Peoples Medical College Hospital Nawabshah S.B.A, Sindh, Pakistan.

Methodology: This retrospective study was conducted at the Intensive Care Unit of Peoples Medical College Hospital, Nawabshah between January 2011 and December 2016. A detailed clinical history was recorded including demographic profile, symptoms signs and outcome. Diagnosis of PPD poisoning was based on history of ingestion and clinical manifestations

Results: There were 1032 patients of hair dye (PPD) poisoning. There were 350 (33.91%) males and 682 (66.09%) females (mean age 22.08 ± 8.42 years). Dysphagia was observed in 1032 (100%), cervicofacial swelling in 939 (90.99%), dyspnea in 927 (89.82%), generalized body ache with muscle weakness in 712 (68.99%), decreased urine output in 185 (17.93%) and chocolate brown color urine in 776 (75.19%) cases. Regarding the reason of ingestion of poison, suicidal intention was observed in 1021 (98.94%), accidental ingestion in 8 (0.77%), homicidal in 1 (0.097%) and in 2 (0.193%) patient's intention could not be determined. All patients consumed local stone (black stone) based hair dye by oral route. Thirty nine patients were lost to follow up. Mortality rate in rest 993 patients was 14.5% (n=139) in male and 17.52% (n=172) in females.

Conclusion: PPD poisoning was more common in females (66%) for suicidal purpose due to easy availability, and is associated with an overall mortality rate of 31.6%.

Key word: Paraphenylenediamin; Mortality; Morbidity; Poisoning

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INTRODUCTION

Paraphenylenediamine (PPD) is an aromatic amine, alanine derivative locally known as 'kala pathar' (black stone). It is solid and white in physical appearance but on oxidation quickly changes to a black color. PPD has been used in industry and cosmetics, however, its main use is in hair dyes and

in combination with henna.^{1,2}

A number of reports of fatal ingestion of hair dye containing PPD have been published. It can cause rhabdomyolysis and acute kidney injury, flaccid paralysis, severe gastrointestinal manifestations, cardio toxicity and arrhythmias.³⁻⁵ There is no definite diagnostic criteria, and the diagnosis requires a high

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degree of suspicion based on comprehensive history, clinical examination and laboratory investigation.⁶

In Pakistan, females buy it commonly in raw form to dye hair and literature published in Pakistan has shown that it is a suspected cause in several cases of poisoning either due to accidental ingestion, or attempted suicide.^{7,8} The aim of the current study was to assess the cause, presentation and outcome of this condition in a large cohort of such patients

Table 1: Demographic variables, duration, route, intention, outcome, renal recovery and mortality in patients presenting with PPD poisoning

Variables	No. of patients	%
Gender		
Male	350	33.91
Female	682	66.09
Duration of poisoning		
Within 2±0.45 hrs.	53	5.14
Within 2-4±1.39 hrs.	256	24.81
More than 4±2.76 hrs.	723	70.05
Route of poisoning		
Oral	1032	100
Inhalation	00	00
Percutaneous	00	00
Intent of poisoning		
Suicidal	1021	98.94
Accidental	08	0.77
Homicidal	01	0.097
Undetermined intention	02	0.193
Outcome		
Prolong hospitalization > 7 days	206	19.96
Renal recovery		
Complete	886	94.96
Partial	52	5.04
Left against medical advice during acute phase	01	0.097
Patients recovered	682	66.08
Referred to Karachi	39	3.78
Mortality (excluding patients referred to Karachi)		
Total	311	31.67
Male	139	14.15
Female	172	17.52
Mortality due to cardio toxicity	67	21.54
Mortality due to renal failure	61	19.61

who presented to our ICU. Our objective was to determine and document the frequency of different clinical features, complications and outcome in PPD intoxicated patients at Peoples Medical College Hospital, Nawabshah.

METHODOLOGY

This retrospective, observational study was conducted on 1032 patients of PPD (hair dye) poisoning, hospitalized in our Intensive Care Unit and were referred from the medical units of Peoples Medical College Hospital Nawabshah over a period of 6 years from January 2011 to December 2016. Formal approval was obtained from the Ethical Review Committee of the university. Data were collected from the patients' hospital record files. Diagnosis of PPD poisoning was based on history of ingestion and clinical manifestations, intention of poisoning, time interval between consumption of poison and first medical attention, nature of symptoms and physical examination and complications

Following parameters were noted from the records; demographic details, clinical presentation, management, reason for ingestion, laboratory results, and outcome.

Management was supportive as no specific antidote was available. Gastric lavage was done with activated charcoal. Oxygen was administered if SpO₂ was < 90%, proven hypoxia on arterial blood gas analysis or presence of severe angioedema. Chlorpheniramine maleate was also used for 3-5 days. Intravenous corticosteroid (hydrocortisone / methylprednisolone) for angioneurotic edema was the main stay of treatment. Vasopressors (dopamine / noradrenaline) were used if hypotension persisted even after adequate fluid therapy. Forced alkaline diuresis (sodium bicarbonate along with loop diuretics) was used to prevent myoglobin mediated renal tubular injury.

Hemodialysis was done in selected cases of renal failure, metabolic acidosis and hyperkalemia.

Laboratory investigations recorded were serum creatinine, leucocyte count, SGPT, SGOT, serum bilirubin, serum alkaline phosphatase, serum, potassium, & calcium, serum CPK and evidence of myoglobinuria

RESULTS

Record files of one thousand thirty two (1032) cases with PPD poisoning were reviewed, out of which 350 (33.91%) were males and 682 (66.09%) were females with age range of 12 to 40 years (mean 22.08 ± 8.42 years) (Table.1).

Regarding reasons of ingestion, suicidal intention

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was observed in 1021 (98.94%), in 8 (0.77%) patients it was accidental, in one (0.097%) homicidal and in 2 (0.193%) patients intention could not be determined. All 1032 patients ingested local made, black stone-based hair dye via oral route. The time interval to reach hospital ranged from 1 to 24 h with a mean duration of 5.36 ± 4.67 h. Seventy percent of the patients (n=723) were brought to hospital emergency after 4 ± 2.76 h, 24.81% within $2-4 \pm 1.39$ h and only 53 patients (5.14%) were brought within 2 ± 0.45 h of ingestion (Table 1). Patients who reached the hospital emergency (first medical attention) early had less morbidity and mortality.

Clinical symptoms noted are given in Table 2. The clinical presentation of patients was proportionately associated with the amount and the type of dye consumed. Most common presentation was dysphagia which was present in all patients. The cervico-facial swelling was also a common symptom present in 939 (90.99%) patients. Swelling involved tongue, floor of mouth, eyelids and conjunctiva and was observed in late comers possibly due to prolonged time of contact with oropharyngeal mucosa. The next common presentation was dyspnea, tachypnea, generalized body ache and muscle weakness, tachycardia, cyanosis, hypotension and bilateral basal crepitation's (Table 2). These patients had history of immediate swallowing of large amount of hair dye and developed features suggestive of myocarditis immediately and or later. Chocolate brown / cola colored urine was present in 75.19% cases, especially in those who had pronounced muscle pain, tenderness and cervico-facial swelling.

Serum bilirubin, SGPT, SGOT, and serum alkaline phosphatase were raised in variable number of cases suggestive of cholestasis and hepatic injury. 17.93% had had decreased urine output (Table 3).

Serum creatinine and CPK were raised (Table 3). Maximum elevation of CPK was up to 90,000 and serum creatinine up to 12 mg/dl. These patients needed multiple sessions of dialysis, leading to increased hospital stay, morbidity and mortality.

Electrolyte abnormalities were reported in 4.52% cases (Table 3). Hyperkalemia was associated with increased mortality despite appropriate medical management and dialysis.

As regards outcome, 682 patients (52.6%) recovered, and 311 died. Thirty nine patients were referred to Karachi and were lost to follow-up. Mortality rate in 993 patients who were followed up was 31.67% with 139 males (14.15%) and 172 females (17.52%) (Table 2).

Table 2: Clinical symptoms and physical signs observed in PPD poisoning

Clinical signs / symptoms	No. of patients	%
Cervicofacial swelling	939	90.99
Dysphagia	1032	100
Dyspnea	927	89.82
Generalized body ache with muscle weakness	712	68.99
Chocolate brown color urine	776	75.19
Decreased urine output	185	17.93
Tachypnea (RR>18/min)	958	92.83
Tachycardia (heart rate>100/min)	989	95.83
Decreased air entry due to laryngeal edema	825	79.94
Cyanosis	206	19.96
Hypotension	196	18.99
Bilateral basal crepitation	103	9.98

Table 3: Investigations at the time of admission in PPD poisoning.

Investigations	Normal values	Increased N (%)
Leucocyte count	4000-11000	30 (2.91)
Liver profile		
SGPT	< 40 IU	815 (78.97)
SGOT	< 40 IU	812 (78.68)
S. Bilirubin	< 1mg/dl	381 (36.91)
S. Alkaline phosphatase	> 120 IU	319 (30.91)
Renal profile		
S creatinine	< 1.4mg/dl	938 (90.89)
S. Na+	135-145 meq/L	30 (2.91)
S. K+	3.5-5 meq/L	16 (1.55)
S. Ca++	9-10.5meq/L	08 (0.78)
Urine		
Routine/microscopic for myoglobin	Myoglobin +	92 (8.91)
Serum		
CPK level	≥ 190	959 (92.93)

Prolonged hospitalization was required in 73.84% cases. Cardiotoxicity and renal failure accounted for mortality in 21.54 % cases.

DISCUSSION

PPD (C6H8N2) is the commonest and cheapest form

paraphenylenediamine poisoning

of dye available in North Africa and the Middle East, known as stone dye, and contains the highest concentration of PPD (from 70 to 90%).^{9,10} Other branded hair dyes contain lesser concentrations of PPD, typically from 2 to 10%.¹¹ The formation of oxide derivatives of PPD such as benzoquinone diimide is responsible for destruction of muscle cells by a mechanism of membrane lipid peroxidation which leads to muscle necrosis and also produces fatal effects on various organ by causing angio-neurotic edema, myocarditis and rhabdomyolysis.^{4,5,12,13} Due to its improper handling, easy availability and low cost, it becomes a common mode of self-poisoning in rural areas of Pakistan and India. Moreover, absence of specific antidote is also a matter of concern regarding its fatal outcomes.^{14,15}

Females have been found to be more affected by hair dye ingestion intoxication.^{7,9,18} This is because females are exposed to PPD more than men as henna is used to enhance the color of hair and also as a skin cosmetic for making tattoos. These findings are similar to the studies conducted by other researchers.^{2,16,17,18}

The intent of poisoning was suicidal in 98.94% of our cases; however psychological evaluation was found to be normal in all these patients. This indicated that most of suicidal attempts were impulsive precipitated by either scolding from parents, family quarrels or socioeconomic reasons.^{14,15} In our study, all patients were exposed to hair dye (black stone) through oral route probably due to ease of administration. This was similar to what was observed by Perumal et al.¹⁵ and by Khan et al.⁹ who found suicidal intent in 94.74% of their cases. Shafiq et al.¹⁹ also found it in 90% of cases. These findings are in line with other studies; Akbar et al from Pakistan reported suicidal intention in 60%, Amira et al. from Tunisia 84% and Shankar et al. from India as 90%.^{20,21} These findings show its high use for suicide and there must be some steps taken regarding its availability. The accidental exposure of PPD is not very common in the developed countries, neither is its exposure through the skin. The mean time to arrive in hospital was recorded 5.36 ± 4.67 h. This value is similar to that of Shankar et al. who report it as 4.63 ± 1.73 h.¹²

The main physical signs in our study were tachycardia, tachypnea, decreased air entry, cyanosis and hypotension. These findings were due to very high toxicity of PPD secondary to development of laryngeal edema, leading to decreased air entry, development of cyanosis, tachycardia and hypotension

due to myocardial damage. The myocarditis due to hair dye poisoning has also been reported in various studies.^{4,13,16}

Various biochemical investigations have found PPD to be hepatotoxic. Tiwari et al. also reported high levels of SGPT/SGOT in their study of hair dye poisoning. In our study, the overall incidence of renal failure was 58.46% while other investigators showed renal failure of more than 70%.^{12,22}

The mortality rate in our study was 31.67% which is comparable to that reported by other researchers.^{5,8,17,21-23}

PPD poisoning is more pronounced among youngsters, illiterate and poor people of the developing countries especially in rural areas. The high rate of morbidity and mortality has raised health concerns associated with PPD poisoning. Intensive supportive care, appropriate interventions including tracheostomy is the mainstay of management. PPD containing hair dyes are a great hazard and have been banned in countries like Germany, France and Sweden. However, in Pakistan it is still commonly used due to easy availability and access in many parts and needs to be banned. Public education and awareness of PPD related health hazards is urgently required so that PPD should be used for 'dyeing only and not for dying'. Moreover, the need of quality research should be emphasized in order to find out effective antidote for PPD to reduce morbidity and mortality.

CONCLUSION

PPD poisoning in patients admitted to our ICU was seen more commonly in female patients (66%). Commonest presenting symptoms were dysphagia, cervicofacial swelling & dyspnea, and overall mortality was 31.6% in 993 patients who were followed. Majority of patients had taken it for suicide.

Conflict of interest: None declared by the authors

Authors' contribution:

MSK: Concept, conduction of study work, design the study, final manuscript approval

SS: Edited final manuscript

MM: Wrote the protocol and first draft of the manuscript

HR: Statistical analysis

IA: Analysis of the study

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