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

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ABSTRACT

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

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. 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. 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

<table>
<thead>
<tr>
<th>Variables</th>
<th>No. of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>350</td>
<td>33.91</td>
</tr>
<tr>
<td>Female</td>
<td>682</td>
<td>66.09</td>
</tr>
<tr>
<td>Duration of poisoning</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Within 2±0.45 hrs.</td>
<td>53</td>
<td>5.14</td>
</tr>
<tr>
<td>Within 2-4±1.39 hrs.</td>
<td>256</td>
<td>24.81</td>
</tr>
<tr>
<td>More than 4±2.76 hrs.</td>
<td>723</td>
<td>70.05</td>
</tr>
<tr>
<td>Route of poisoning</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral</td>
<td>1032</td>
<td>100</td>
</tr>
<tr>
<td>Inhalation</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Percutaneous</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Intent of poisoning</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suicidal</td>
<td>1021</td>
<td>98.94</td>
</tr>
<tr>
<td>Accidental</td>
<td>08</td>
<td>0.77</td>
</tr>
<tr>
<td>Homicidal</td>
<td>01</td>
<td>0.097</td>
</tr>
<tr>
<td>Undetermined intention</td>
<td>02</td>
<td>0.193</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prolong hospitalization &gt; 7 days</td>
<td>206</td>
<td>19.96</td>
</tr>
<tr>
<td>Renal recovery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete</td>
<td>886</td>
<td>94.96</td>
</tr>
<tr>
<td>Partial</td>
<td>52</td>
<td>5.04</td>
</tr>
<tr>
<td>Left against medical advice</td>
<td>01</td>
<td>0.097</td>
</tr>
<tr>
<td>Patients recovered</td>
<td>682</td>
<td>66.08</td>
</tr>
<tr>
<td>Referred to Karachi</td>
<td>39</td>
<td>3.78</td>
</tr>
<tr>
<td>Mortality (excluding patients referred to Karachi)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>311</td>
<td>31.67</td>
</tr>
<tr>
<td>Male</td>
<td>139</td>
<td>14.15</td>
</tr>
<tr>
<td>Female</td>
<td>172</td>
<td>17.52</td>
</tr>
<tr>
<td>Mortality due to cardio toxicity</td>
<td>67</td>
<td>21.54</td>
</tr>
<tr>
<td>Mortality due to renal failure</td>
<td>61</td>
<td>19.61</td>
</tr>
</tbody>
</table>

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 ± 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).

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%). Other branded hair dyes contain lesser concentrations of PPD, typically from 2 to 10%. 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. 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.

Females have been found to be more affected by hair dye ingestion intoxication. 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.

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. 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. and by Khan et al. who found suicidal intent in 94.74% of their cases. Shafiq et al. 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%. These findings show its high use for suicide and there must be some steps taken regarding its availability.

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.

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%.

The mortality rate in our study was 31.67% which is comparable to that reported by other researchers.

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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