

Paraphenylenediamine Containing Hair Dye

An Emerging Household Poisoning

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Abstract: Paraphenylenediamine poisoning is among one of the emerging causes of poisoning in Asian countries, because it is a constituent of hair dye formulations and is easily available in market at low cost. Hair dyes are rampantly used in Asian households compared with the western world. Locally, hair dye constituents may have allergic adverse effects, and acute systemic poisoning presents with characteristic angioedema, upper airway obstruction, rhabdomyolysis, methemoglobinemia, myoglobinuria, and acute renal failure. This study reports about the death of a 24-year-old Indian housewife who committed suicide by taking hair dye emulsion. She had an argument with her husband, and because of fit of rage, took a bowlful (80 mL) of hair dye emulsion kept prepared for the use by husband. She developed angioedema, cervical swelling, and rhabdomyolysis and died of acute renal failure within 24 hours. Toxicological analysis of viscera and blood revealed varying levels of paraphenylenediamine. Histopathological samples of kidney showed features of acute tubular necrosis and myoglobin casts in renal tubules. The aim of the study is to create awareness about the adverse effects of the hair dye, its poisoning outcome, and possible preventive measures.

Key Words: hair, dye, myoglobin, paraphenylenediamine, angioedema, renal, tubular, cast

(*Am J Forensic Med Pathol* 2015;00: 00–00)

LEARNING OBJECTIVES

After completing this activity, the learner will be better able to do the following:

1. Assess the global burden of hair dye poisoning and its varying clinical presentation.
2. Evaluate the clinical findings, prognosis, and medicolegal management of hair dye poisoning cases.
3. Interpret the medical and medicolegal findings of hair dye poisoning cases.

In developing countries, suicidal poisoning has increased by 60% for the last 50 years, resulting in 1 million fatalities every year. It is a preventable public health problem.^{1,2} Poisoning is a preferred method of suicide and is one of the major problems encountered in the emergency department (ED) of hospitals.³ Poisoning with paraphenylenediamine (PPD) is a newer trend of intentional self-harm, especially in some parts of Asia and Africa.⁴ Paraphenylenediamine is a synthetic aromatic amine

(C₆H₄[NH₂]₂) derived from paranitroaniline (a coal-tar derivative) and is widely used as a constituent of hair dye. The major oxidation product of PPD is Bondrowski's base, an allergenic, mutagenic, and highly toxic. It is an oxidant and, hence, widely used as hair dye.⁵ It is also used as dye in textile, fur industries, dark cosmetics, temporary tattoos, photographic development, gasoline, etc.⁵ Most PPD poisoning cases are associated with high mortality rate due to unavailability of any specific antidote.⁶ In Africa, Middle East, and Indian subcontinent, PPD is commonly mixed with henna (leaves of *Lawsonia alba*) and traditionally applied to color palms, soles, and feet and to give hair a dark red shade.^{7–11} The reported mortality rates from PPD poisoning is between 12% to 42%.² The first case of PPD poisoning was reported in a hairdresser, in 1924 due to exposure to PPD-containing hair dyes.¹² Ingestion of PPD leads to angioedema, asphyxia, dysphagia, oliguria/anuria, acute renal failure, rhabdomyolysis, intravascular hemolysis, coagulation derangements, and toxic myocarditis. Fatality is related to acute renal failure or myocardial damage.^{11,13,14} Acute poisoning presents with the characteristic triad of angioneurotic edema leading to swollen, dry, protruding tongue, chocolate brown urine due to myoglobinuria, and acute renal failure.^{15,16} Other less common clinical presentations include flaccid paralysis, gastrointestinal manifestations, and arrhythmias.^{17,18} The ingredients of the commonly marketed hair dye are PPD, resorcinol, propylene glycol, sodium EDTA, preservatives, and perfumes, and the major contributor of toxicity is PPD. The combined effects of the individual toxicants result in significant morbidity and mortality.^{10,11,19} This case report provides autopsy and toxicological findings in a case of suicidal ingestion of a paraphenylenediamine containing hair dye preparation (SuperVasmol 33, Hygienic Research Institute Pvt Ltd, India). A 24-year-old housewife, who had died within 24 hours of the ingestion. SuperVasmol 33 is an emulsion-based hair dye commonly available in the markets of India at a very cheap price.

CASE REPORT

The body of a 24-year-old married woman was brought by the police for autopsy. The case was registered by the police under the section of 174 criminal procedure codes, which deals with the investigation of unnatural death cases by police. The history from police records and from the accompanying relatives of the deceased revealed that she had ingested a bowlful (approximately 80 mL) of hair dye solution (SuperVasomol 33), which was prepared by her husband for his own use and kept near the kitchen wash basin. There was a quarrel between the couple on some issues, which also had happened many times before. Hence, because of fury and frustration, she had ingested the entire bowl of hair dye solution present nearby when the husband was out to garden for a while, and the husband came to know about it after 30 to 45 minutes of her ingestion. She was shifted to a nearby primary health center, where she was given supportive treatment, and due to lack of adequate poisoning management facilities, she was referred to a tertiary care center. After 6 to 8 hours of

Manuscript received July 5, 2013; accepted February 14, 2014.

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The authors report no conflict of interest.

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ISSN: 0195-7910/15/0000-0000

DOI: 10.1097/PAF.0000000000000165

ingestion of hair dye solution, she had reached to the ED of our hospital. At admission, she had complaints of breathing difficulty, stridor, and hoarseness of voice. Swelling of lips, tongue, neck, and eyelids were the prominent physical findings. Blood biochemistry revealed severe metabolic acidosis (pH, 6.9; bicarbonate, 6.7 meq/L; pCO₂, 14.8 mm Hg; pO₂, 140.5 mm Hg), uremia (creatinine, 4.3 mg/dL; urea, 120 mg/dL) with hypokalemia (serum potassium, 2.9 meq/L), and muscle enzymes (creatinine phosphokinase, 1278 U/L; creatine kinase-MB, 671 U/L). Urine was dark brown, and volume decreased to 20 mL per 12 hour and showed positive for myoglobin. Urine ketones were negative. Treatment was ensued in the line of acute PPD poisoning with angioedema, rhabdomyolysis, metabolic acidosis, and acute renal failure. The patient required ventilator support and tracheostomy for obstructing edema of the upper respiratory tract. To start with, she was conscious, was oriented to time, place, and person, but gradually became delirious with deranged coma score and loss of consciousness after 6 hours of admission. She had developed convulsion and succumbed to the complications after 24 hours of ingestion of hair dye. Clinically, the cause of death was thought to be due to acute renal failure and complications thereof.

On postmortem examination, we found swollen protruding tongue, swelling of lips, neck, and face, and a tracheostomy wound in situ (Fig. 1). No other injury was found. First, the skull was opened to have a blood less field during examination of neck structures. The brain was edematous and congested to a variable degree. Multiple subcortical petechial hemorrhages were found scattered at multiple places of both cerebral hemispheres. On neck dissection, cervical soft tissues were found to be congested and edematous. There were features of angioedema of larynx and fauces obliterating the upper airway (Fig. 2). The lungs showed features of pulmonary edema. The heart was congested and had multiple, confluent areas of petechial hemorrhages over the

surface. On cut section, all chambers contained dark-red fluid blood. Multiple, confluent patches of subendocardial hemorrhage were found on the papillary musculature. The kidneys were congested and edematous and were found to be hemorrhagic on cut sections with cloudy degeneration of cortex. Stomach contained approximately 130 mL of mucoid fluid without any specific odor. Multiple confluent patches of corrosions and submucosal hemorrhages were found over the mucosa of pylorus and greater curvature including first part of duodenum. Pancreas was edematous and hemorrhagic. Chemical analysis of postmortem samples using thin layer chromatography and other quantitative tests revealed varying quantities of PPD. In the stomach and intestine, PPD content was 1.3 mg% whereas in the liver, spleen, and kidneys, it was 0.79 mg%. Blood showed positive results for methemoglobin (8 mg%). The liver was congested, enlarged (weight, 720 gm), and hemorrhagic on cut section. The rest of all abdomino-pelvic organs were congested to a variable degree. Light microscopy features of kidney were a characteristic of myoglobin-induced acute tubular injury (Fig. 3). Granular reddish-brown, globular deposits of myoglobin casts were found within the lumen of the renal tubules and collecting ducts, which was confirmed by the immunoperoxidase staining with specific antibodies against myoglobin. Viral cytopathic changes and acute cellular or vascular rejection was excluded. The opinion as to the cause of death is acute renal failure due to myoglobinuria as a complication of PPD-induced rhabdomyolysis.

DISCUSSION

Review of literatures revealed that PPD is emerging as a suicidal poison in Indian households. Similarly, findings were also recorded by authors from other Asian and African countries. Paraphenylenediamine is used as a suicidal agent because of its easy availability in households, low cost, and tolerable taste (salty taste), which fulfills the requirements for an ideal suicidal poison.^{14,20,21} An 11-year (1992–2002) retrospective study of PPD poisoning taking 374 cases revealed female predominance (77%) and that approximately 21.1% of poisoning cases were fatal.²² The deceased in our study is a female in her third decade of life. Some authors observed that consumption of 100 to 300 mL of hair dye suspension is usually found to be fatal and in our case, the deceased had consumed approximately 80 mL of hair dye emulsion and died after 24 hours of consuming the emulsion.^{11,13}

The hair dye SuperVasomol 33 is an emulsion of 4% PPD, liquid paraffin, cetostearyl alcohol, sodium lauryl sulfate, disodium EDTA, resorcinol, and propylene glycol often mixed with henna.²³ The postmortem chemical analysis report of the stomach and intestine showed a PPD level of 1.3 mg%, whereas in the liver, spleen, and kidneys, the level was 0.79 mg%. This much PPD concentration is usually associated with fatal outcome. On oxidation of PPD, several intermediates byproducts are produced in vivo and the major product formed is Bondrowski's base, which is an allergen and mutagen and is responsible for the clinical features.^{24,25} According to some authors, the toxicity of hair dyes is also due to disodium EDTA in addition to PPD. Another component of hair dyes "resorcinol" is a corrosive agent and causes methemoglobinemia.^{11,13} In the present case, the deceased had methemoglobinemia too. The PPD itself has a direct toxic effect on the kidney due to its aromatic structure, which is easily reabsorbed and concentrated in distal tubules leading to renal epithelial cell necrosis and acute tubular necrosis.²⁶ The major challenge in the late presentation is renal failure and toxic myocarditis because the rate of morbidity and mortality are increased once the renal failure develops.^{27–29} It can cause rhabdomyolysis with the deposition of myoglobin casts within the distal tubules,



FIGURE 1. Swollen, protruding tongue and swollen lips, face, and neck (triangle). In situ tracheostomy wound (arrow).



FIGURE 2. Epiglottises, laryngeal inlet, fauces, base of tongue, and lumen of trachea show disproportionate swelling and congestion of mucosa obliterating the upper airway.

collecting ducts and hemolysis with resultant hemoglobinuria causing acute tubular necrosis.³⁰ In our case, histopathology of kidneys showed intra-tubular proteinaceous deposits in renal tubules and collecting ducts suggestive of myoglobin casts, and diffuse tubular epithelial necrosis. These findings occurred due to rhabdomyolysis as a complication of PPD.

Early manifestations, that is, cases presenting within 4 to 6 hours of ingestion, include numbness, burning of mouth and throat, and vomiting along with characteristic angioedema of the face and neck and subsequent development of stridor, respiratory distress, and dysphagia.²⁴ Conversely, cases present after 12 hours of ingestion show rhabdomyolysis, which may manifest as muscle aches, tenderness, muscle edema, cola-colored urine, raised creatine phosphokinase, intravascular hemolysis, myoglobinuria, oliguria, acute renal failure, and often toxic myocarditis.^{7,17} The present case was hospitalized after 8 hours of ingestion of hair dye, and the predominant clinical manifestations were cervical and upper respiratory tract edema, rhabdomyolysis, and acute renal failure. In a study by Kallel et al,¹⁵ the frequency of cervical or upper respiratory tract edema and acute renal failure is 68.4% and 47.4%, respectively. In that study, orotracheal intubation was performed in 68.4% of patients and emergency tracheostomy in 15.8% of patients.¹⁵ Yagi et al⁹ recommended early tracheostomy at presentation with intensive medical management thereof. In the present case, although emergency tracheostomy was performed at admission, she had died, maybe due to delayed hospitalization, that is, after 8 hours. The characteristic angioedema of the face and neck, on initial presentation with difficulty in breathing, secondary to upper respiratory tract edema and cola-colored urine, may be considered as pathognomonic of PPD poisoning in absence of laboratory facilities and/or if proper history is lacking.^{27,31} Early airway intervention, forced alkaline diuresis, and hemodialysis are the 3 strategies in the management of PPD poisoning, which may be helpful in reducing the mortality.³¹

Hair dye is not a regular suicidal poison; rather, it is an “at the reach household agent,” which is readily available at any moment of time and is the reason of rampancy of its use as a suicidal agent. Accidental ingestion of hair dye solution or powder by the children is more common occurrence followed by suicidal attempts. Often, family conflicts are the reason of poisoning and it is usually used to threaten the other members of family if the demands are not met.¹⁰ In our case, the deceased had committed suicide due to fit of rage, because she was upset with her husband. In view

of raising incidence of hair dye poisoning, it is time to control its rampant use. In some countries such as Germany, Japan, and United Kingdom where PPD is produced, it is considered an occupational health hazard. Germany banned the use of PPD in early 1990s, subsequently France and Sweden in 1964. Since 2008 in Sudan, legislations are made to prevent PPD trade and use in the local market. The health authorities there have developed a standard level of contamination of 0.1-mg/m³ PPD in air, to control pollution of working atmosphere. However, in Japan and India, it is still a common component in hair dyes and rampantly sold in open market.³² We hardly find any literatures on “PPD-containing hair dye poisoning” with affiliations from United States or other western countries, suggestive of relative paucity of such cases in the West. Nevertheless in the East, people have black hair and habituated to dye the grayed hair at home. Very few numbers of people do visit salons or parlors for hair dying.

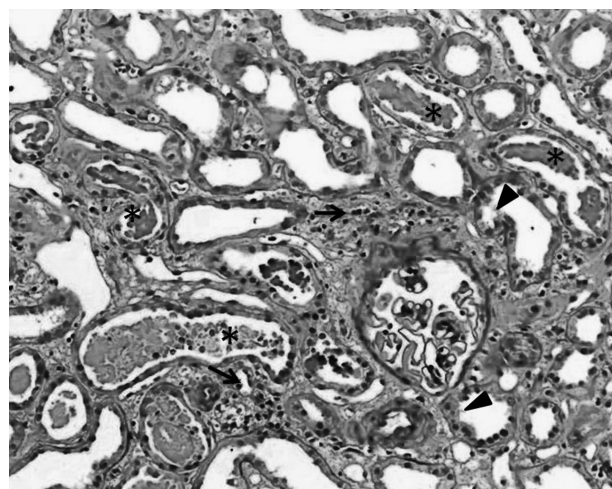


FIGURE 3. Low power periodic-acid-Schiff stain shows widespread tubular epithelial cell necrosis with thinning of cytoplasm and loss of brush borders (spearhead). Multiple reddish-brown granular periodic-acid-Schiff positive proteinaceous (myoglobin) casts are present within the tubules (asterisk). The interstitium shows variable degree of edema and mononuclear infiltrate (arrow). A small artery and glomerulus are unremarkable.

This may be the reason of more number of PPD poisoning cases in Asia compared with the United States and Europe.

CONCLUSIONS

The poisoning from PPD-containing hair dyes seems more commonly in Asian countries compared with the western world. It is alarmingly emerging as a suicidal agent next to organophosphates. Many countries in Asia including India have banned the rampant use of pesticides to curtail number of poisoning cases, and similar steps may be helpful in the use of containing hair dyes too. Unlike pesticides, the potential ominous effects of PPD-containing hair dyes are still not so commonly known among the general public. Hence, we recommend creating public awareness regarding the potential dangerous effects of careless use of hair dyes and that statutory policy should be devised to restrict its rampant sale by the stakeholders. The volume of the currently available 50- and 100-mL sachets of hair dyes should be reduced to 25 mL, thereby decreasing the toxin burden in accidental or suicidal exposures. Early diagnosis of rhabdomyolysis, acute renal failure, and institution of emergency tracheostomy in severe upper airway obstruction may have a better outcome in such poisoning cases.

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Questions

1. Paraphenylenediamine is used as a constituent more commonly in ____.
A. Sunscreen lotions
B. Ayurvedic medicine
C. Tanning leather
D. Hair dyes
2. Hair dye poisoning is more commonly seen in ____.
A. Asia
B. America
C. Europe
D. Australia

3. The most common complication of PPD-containing hair dye poisoning is ____.
 - A. Optic atrophy
 - B. Hepato-cellular carcinoma
 - C. Anaphylactic shock
 - D. Myoglobin-induced acute tubular injury
4. The most common clinical presentation of PPD-containing hair dye poisoning is ____.
 - A. Tachyarrhythmia, stridor, and vomiting
 - B. Hematemesis, pain abdomen, and polyuria
 - C. Shrunken visual field with central scotoma
 - D. Stridor, hoarseness of voice, as well as swelling of lips, tongue, and neck
5. The most common mode of PPD-containing hair dye poisoning is ____.
 - A. Homicidal
 - B. Suicidal
 - C. Accidental
 - D. Iatrogenic
6. Paraphenylenediamine is metabolized in body to form Bondrowski's base, which is a ____.
 - A. Reductant
 - B. Oxidant
 - C. Free radical
 - D. Alkaline byproduct
7. Specific antidote of choice in acute poisoning by PPD-containing hair dye is ____.
 - A. Atropine sulfate
 - B. Penicillamine
 - C. Obidoxime
 - D. None of the above
8. The renal complications due to hair dye poisoning are commonly due to ____.
 - A. Hemolytic uremic syndrome
 - B. Focal segmental glomerulosclerosis
 - C. Myoglobin-induced acute tubular necrosis
 - D. Formation of PPD casts in distal tubules
9. The urine microscopy in the cases of hair dye poisoning can show all of the following, EXCEPT ____.
 - A. Hemoglobinuria
 - B. Myoglobinuria
 - C. Methemoglobinuria
 - D. Albuminuria
10. The treatment of choice for acute poisoning by PPD-containing hair dye is ____.
 - A. Emergency tracheostomy, forced alkaline diuresis, and hemodialysis
 - B. Gastric lavage, catharsis, and elective tracheostomy
 - C. Forced acidic diuresis and selective beta-blockers
 - D. Cardiac defibrillation and Digoxin infusion

Answers

1. D
2. A
3. D
4. D
5. C
6. B
7. D
8. C
9. A
10. A