Super Vasmol Poisoning: Dangers of Darker Shade

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Introduction
The ancient science of cosmetology is assumed to have originated in India and Egypt. Available evidences indicate that highly advanced ideas of hair care and hair dressing among men and women were practiced in ancient India. The earliest records of art of dyeing hair with henna, indigo, and vegetable dyes date back to circa 2500 and 1550 B.C., to the Indus valley civilization, and their preferred colors were black or orange-red.

The secrets of art and nature as well as the various methods of hair coloring like black, gold, green, red, yellow, and white were described as early as 1661. The development of synthetic dyes for hair in the laboratory is traced back to 1856, and permanent hair dyes have been in commercial use more than 10 decades ago. The systemic toxicity of paraphenylenediamine (PPD) was first documented in a hairdresser handling dye in 1924 due to occupational exposure. Super Vasmol is an emulsion-based popular hair dye used in India, and the poisoning due to it is emerging as a major cause of suicide in the developing world since it is cheap and freely available over-the-counter.

Toxic Cocktail
The active ingredients of Super Vasmol include PPD, propylene glycol, liquid paraffin, resorcinol, cetostearyl alcohol, sodium lauryl sulfate, sodium ethylenediaminetetraacetic acid, preservatives, and perfumes. The main compound responsible for the toxicity is paraphenyl-diamine [C₆H₄(NH₂)₂], which is a key ingredient for most of the hair dyes, and it is used for color enhancement. It is an aromatic amine derived from coal tar and is used for commercial purposes.

PPD is available in the form of white crystals when it is pure and rapidly turns to brown when exposed to air. It has a molecular weight of 108 Dalton with a boiling point of 267°C and melting point of 140°C. It is easily soluble in ethanol, ether, benzene, chloroform, and acetone and partially soluble with agitation in water. The concentration of PPD in hair dye formulation varies from 70% to 90% in stone hair dye and 2 to 10% in branded dyes.

A 100-mL Super Vasmol contains 12 g of PPD, and the minimal dose required to produce systemic features of poisoning is approximately 3 g. The fatal dose after oral ingestion is 7 g or more.

Exact concentrations of PPD in different formulations are not known as these formulations are patented. Paraphenylenediamine is quickly absorbed into systemic circulation through mucous membranes of the digestive tract after oral intake. It is acetylated into N-acetyl-PPD and N,N-diacetyl-PPD as major metabolites for detoxification and excreted in the urine. Bandrowski’s base is formed by the oxidation reaction of PPD with base in an alkaline medium, which is allergenic, mutagenic, and highly toxic.

Resorcinol found in hair dyes is a phenol derivative, which is chemically designated as 1,3-dihydroxybenzene or 3-hydroxyphenol. It is highly corrosive in nature. Propylene glycol is used as a solvent in the hair dyes. Among all the active ingredients of Super Vasmol PPD, resorcinol and propylene glycol are found to have systemic toxicity and has the most life-threatening effects.

Toxic Effects
A three-stage progression has been witnessed in PPD poisoning with inflammatory stress characterized by a relative immunodepression in the first 3 days, proinflammatory state (due to rhabdomyolysis) from third to sixth day, and immunomodulatory action (due to oxidative metabolism) from the sixth day.

It causes systemic inflammatory reaction specific to a cytotoxic cell effects. The pathophysiologic mechanisms could be due to increased free radical formation, skeletal and cardiac muscle necrosis (scattered coagulation necrosis), formation of highly nephrotoxic quinine diamine (an oxidation product of PPD metabolites), renal tubular occlusion due to myoglobin casts, and acute tubular necrosis. Hoarseness of voice, pneumothorax, hepatitis, convulsions, coma, cardiac toxicity, hypotension, and sudden cardiac death are on the toxic end of the spectrum.

Clinical Features
The characteristic triad of Super Vasmol poisoning is early angioneurotic edema of face and neck with hoarseness of voice and stridor, rhabdomyolysis with dark brown colored urine and acute kidney injury (AKI) even in the absence of laboratory facilities or in the absence of proper history. These patients have obvious orofacial swelling with swollen hard protruding tongue and...
edematous bull neck, which are the earliest manifestation following ingestion of the dye. The most bulbous edema is provoked by PPD, and it appears to be exceptionally specific and selectively limited in the head and neck. It was suggested that the toxic effect of the PPD is due to its oxidation product quinone diamine, which is responsible for severe local irritation. Some authors thought that PPD toxicity is due to the consequence either on the blood colloids or on vascular permeability. Moreover, it was understood that the PPD toxicity is due to altered vascular permeability and involvement of the parasympathetic nervous system. Deamination and formation of aniline from PPD are also claimed to be accountable in part for the toxic symptoms. The differences in opinion as to the reason of PPD edema appear due to the fact that the exact number and nature of the oxidation products are not known. These results are dependable based on the view that oxidative stress may be an essential part of the preimmunological phase in the induction of the allergic contact dermatitis by PPD.

Super Vasmol is a potent nephrotoxic cocktail; the extent of renal involvement in hair dye poisoning varies between transient proteinuria and oliguric AKI. Acute kidney injury is a late manifestation of PPD poisoning, which usually develops few days after PPD exposure. The development of AKI in PPD intoxication does not occur in all patients, and it differs from 47.3% to 100%. Naqvi et al. had reported a cohort of hundred patients presented to his institution with AKI following PPD poisoning.

The mechanisms of AKI following hair dye poisoning are several. Paraphenylenediamine itself has a direct toxic effect on kidney due to its aromatic structure, making its reabsorption and concentration in tubule easy, and it can also cause acute tubular necrosis. Rhabdomyolysis is the main cause of renal failure and is a recognized complication of hair dye poisoning. Paraphenylenediamine causes rhabdomyolysis by promoting calcium release and leakage of calcium ions from the smooth endoplasmic reticulum, followed by continuous contraction and irreversible change in the muscle’s structure, which results in deposition of myoglobin cast within the renal tubules, and hemolysis leading to acute tubular necrosis and AKI. Hypovolemia and toxic metabolites of PPD also contribute to AKI. Propylene glycol is associated with hyperosmolality, raised serum creatinine, hyperphosphatemia; and mortality rates varied between 0.03% and 60%.

Interestingly PPD is banned in certain countries like Germany, France, Sweden, Sudan, etc. Free availability contributes to Super Vasmol poisoning, but restricted use or introduction of alternatives may likely bring down the incidence of Super Vasmol poisoning. In addition, community awareness and health education help towards early diagnosis and prevention to some extent.

The management of Super Vasmol poisoning is mainly dependent on maintaining airway patency and preventing acute renal failure. Currently, no specific antidote is available to neutralize the toxic effects of PPD. Hence, the treatment is mainly supportive and depends on the clinical situation. It is preferable to consider tracheostomy over cricothyroidotomy as an emergency surgical airway in the presence of extensive neck swelling and difficulties encountered in identifying landmarks. However, endotracheal intubation done in early stages of edema or prophylactic intubation before development of edema can avoid tracheostomy. Antihistamines and steroids are commonly used in the management of airway edema possibly due to hypersensitivity reaction to PPD even though there is no therapeutic trial to substantiate their benefits.

Timely institution of alkaline diuresis using isotonic saline, sodium bicarbonate, and osmotic diuretics and maintenance of a high urine output can prevent acute renal failure due to rhabdomyolysis. Paraphenylenediamine is non-dialyzable compound and dialysis is only part of the supportive therapy. However, trials of PPD removal were attempted using hemoperfusion and hemodialysis, with variable results. The most consistent predictors of mortality are the amount of hair dye ingested, the time interval between consumption and intervention, hyperkalemia, hypocalcemia, and hyperphosphatemia; and mortality rates varied between 0.03% and 60%.

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**Learning Points**

- A diagnosis of Super Vasmol poisoning is made invariably on the basis of characteristic clinical trial.
- Early endotracheal intubation can preclude tracheostomy.
- Possibility of pneumothorax has to be considered if hypoxia persists or worsens or in case of cardiorespiratory arrest.
- Serum creatinine kinase level is not a reliable indicator of myocardial injury.
- Urine may not contain myoglobin if the patient presents late.

**References**