Journal of Forensic Chemistry and Toxicology
Volume 2 Number 1, January - June 2016
DOI: http://dx.doi.org/10.21088/jfct.2454.9363.2116.5

Review Article

Phenol Poisoning with Analytical Aspects and Its Management

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Abstract

Phenol or carbolic acid has been used in households since time immemorial. It has also been used extensively for medicinal purposes since Lister first published his paper titled 'On the Antiseptic Principle in the Practice of Surgery'. With time, the side effects of using phenol have also been noticed, resulting in decreased medicinal use of phenol. However, continued household use of phenol and its derivatives makes it one of the most common cause of medico-legal presentation in casualty.

This paper has been written with the aim of highlighting the presentation and management with focus on analytical aspects of phenol poisoning.

Keywords: Phenol; Poisoning; Analysis; Management.

Introduction

Phenol or carbolic acid [Hydroxybenzene, Phenylic acid, Phenylic alcohol, C_6H_5OH] [1-3] was first extracted from coal tar in 1834 [4]. The use of phenol in surgery by Sir Joseph Lister resulted in drastic fall in fatalities [5]. In 1867 Lister published his landmark paper 'On the Antiseptic Principle in the Practice of Surgery' [6] and it proved to be a turning point in health care [7]. Subsequently the use of carbolic acid was done in treating conditions like typhoid fever, mucous tubercles, primary syphilitic sores, psoriasis, pityriasis, prurigo and chronic bronchitis [8,9]. However, there were numerous instances, when the use of carbolic acid during treatment resulted in toxicity, leading to a limited use of phenol. Phenol is one of the most common household poisons. In one study done by Patil A et al it was concluded that Phenol poisoning was the most common cause of medico-legal presentation in casualty of Navi Mumbai hospital, India [10].

Sources of Carbolic Acid

1. Antiseptic and disinfectant especially for sterilising floors, walls, furnishing, glassware and instruments [3].
2. Phenol is used in the production of resins, which are used in the plywood, construction, automotive, and appliance industries [11].
3. It is used for manufacture of plastics [11].
4. It is also used in preservatives.
5. Medical Sources [3] are
   a. Face peel in plastic surgery.
   b. Neurolysis for spasticity.
   c. Treatment of localised skin disorders (Castellani's paint) and as a local anaesthetic.
   d. Ear and nose drops, throat lozenges, and mouthwashes.
6. Cresol which is derivatives of phenol is used as

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disinfectant and antiseptic [12,13].

7. Creosote – is a mixture of phenols and consists mainly of cresol and guiacol. It is used as household remedy for coughs and is found in many proprietary preparations [12,13].
8. Resorcinol which is a derivative of phenol is a colourless crystalline substance and is used for the treatment of various skin diseases including ringworm, psoriasis, eczema etc [12,13].
9. Dettol is chlorinated phenol; parachlorometaxylenol. Although it is said to be practically nontoxic in adults, deaths have still been reported [13-15].
10. Thymol is an alkyl derivative of phenol obtained from volatile oils of thymus vulgaris, Monarda punctata or Trachyspermum ammi. It occurs in colourless crystals with characteristic pungent odour and taste. It was used earlier as an antihelminthic, antifungal and antiseptic [13,14].

Exposure of Phenol

Phenol is a pure acid which consists of short, colourless, prismatic, needle like crystals [4,13]. These crystals turn pink on exposure to air [2,4]. Phenol has a characteristic phenolic or carbolic odour or hospital odour [3,13]. It is sparingly soluble in water, but freely soluble in alcohol, benzene, ether, glycerine and fat and hence can attack the nervous system [13]. It is not a true acid as it does not turn litmus paper red [13]. Common routes of exposure are usually inhalational, oral and dermal. Few Points about Exposure of Phenol are

1. Breathing air contaminated with phenol.
2. Drinking water contaminated with phenol. Phenol in soil usually drains into groundwater.
3. Overdose of phenol and its derivatives during treatment.
4. Accidental ingestion of phenol instead of another liquid like cough remedy/ medicine.
5. Breathing air at work sites like petroleum industry, manufacture of nylon, epoxy resins and polycarbonates, herbicides, wood preservatives, hydraulic fluids, heavy-duty surfactants, lube-oil additives, tank linings and coatings, and intermediates for plasticizers and other specialty chemicals [11].
6. Breathing fumes while treating a patient.
7. Dermal contact by products containing phenol.
8. Eating food materials like smoked summer sausage, smoked pork belly, mountain cheese, fried bacon, fried chicken, and black fermented tea, where a low level of phenol is found [11].

Pharmacokinetics

Mechanism of Action

Phenol is a protoplasmic poison. Because it is an irritant, tissue damage, inflammation, or other irritation effects may occur at the sites of absorption. Phenol impairs the stratum corneum and produces coagulation necrosis by denaturing and precipitating proteins. It causes widespread capillary damage and clotting in superficial blood vessels. It also causes central nervous system depression, metabolic acidosis and renal damage. The toxicity is due to phenol and the metabolites formed during the metabolism of phenol i.e. hydroquinone, catechol, and benzoquinone. These three metabolites exhibit potency similar to phenol [2-4,11,13,16].

Metabolism

Phenol is readily absorbed from all routes i.e. rectum, gastrointestinal tract, respiratory tract, serous cavities, skin, vagina and wounds [1,2,12-14,16]. Conjugation with glucuronic acid and conjugation with sulfate are the main routes of detoxification of phenol. Phenol is excreted in the urine as phenyl glucuronide and phenyl sulfate metabolites [2]. Phenol is metabolised to pyrocatechol and hydroquinone in the liver. These metabolites are also excreted in the urine. These get oxidized in air and because of this, initially colourless urine turns to greenish or blackish on standing (Carboluria). Phenol is also excreted by lungs, salivary glands, stomach and skin. There is no information on levels of phenol in human breast milk [11]. The time required for complete excretion is 36 hours.

Phenol in Environment

Phenol enters the air, water, and soil as a result of its manufacture and use. Phenol has a short half-life in air, less than 1 day. In air, it reacts with photochemically produced hydroxyl radicals. Phenol generally remains in soil only about 2–5 days. In soil, phenol biodegrades under both aerobic and anaerobic conditions. Phenol is rapidly degraded in water, but it can remain in water for upto 9 days. Phenol does not accumulate in fish, other animals, or in plants [17,18].

Exposure Limit for Phenol

NIOSH REL - TWA 5ppm (19mg/m3) C 15.6 ppm

(60 mg/m3), OSHA PEL - TWA 5ppm (19mg/m3). The biological exposure index (BEI) for occupational exposure to 5 ppm phenol is 250 mg total phenol in urine/g creatinine. Environment Protection Agency has determined that exposure to phenol in drinking water at a concentration of 6 milligrams per liter (mg/L) for up to 10 days is not expected to cause any adverse effects in a child. EPA has determined that lifetime exposure to 2 mg/L phenol in drinking water is not expected to cause any adverse effects. The FDA has determined that the phenol concentration in bottled drinking water should not exceed 0.001 mg/L. [1, 11, 17, 18]

Fatal Dose and Fatal Period

***Fatal Dose*:** Literature report of human LD_{LO} by the oral route range from 0.14 to 14 g/Kg. [1,18]. U.S. Department of health and human services records that the minimal lethal oral dose of phenol is approximately 70 mg/kg in adults. Other estimates indicate that an oral dose as low as 1,000 mg could be fatal in humans, but patients occasionally survived doses as high as 65,000 mg [11].

***Fatal Period*:** Fatal period of phenol is 3-4 hours. [4, 12-14, 16]

Normal / Reference Values

Phenol is a normal constituent of urine. The total phenol concentration in the urine of unexposed individuals does not exceed 20 mg/L and the mean is usually <10 mg/L.[11, 17]

Signs and Symptoms of Phenol Poisoning (Carbolism) [2-4, 12-14, 16, 19-24]

Signs and symptoms of phenol poisoning are detailed in Table 1.

Table 1: Signs and symptoms of phenol poisoning

		Features
Acute poisoning	Local effects	• Skin: Numbness, burns (heal leaving a brown stain) • GI tract: nausea, vomiting, pain, lips & mouth & tongue are corroded, deglutition and speech becomes difficult.
	Systemic effects	• General – Odour in breadth *(phenolic)*, pupils - miotic, breathing - stertorous, pulse -feeble, irregular and rapid, face covered with cold sweat, dusky cyanosis. • CNS - Initial stimulation followed by depression especially of respiratory centres. • CVS - Hypotension, tachycardia, arrhythmias, infrequent gasps, laryngeal and pulmonary edema, bronchitis, bronchopneumonia. • Hepatorenal – oliguria, carboluria, renal and hepatic failure • Blood- hemolysis, methemoglobinemia • Metabolic acidosis and respiratory alkalosis • **Rabbit syndrome**- fine rapid rhythmic contractions of the perioral musculature resembling the chewing movement of rabbit. • Lock jaw
Chronic poisoning (Phenol Marasmus)		• General – anorexia, headache, vertigo, weight loss • Urine – dark • Pigmentation – yellowish (ocher like) discoloration of cartilages, sclera (oochronosis)

Biomarkers for Phenol Poisoning

Biomarkers are broadly defined as indicators signalling events in biologic systems or samples. They have been classified as markers of exposure, markers of effect, and markers of susceptibility. Measurement of total phenol in the urine is the most useful biomarker following inhalation exposure to phenol (ACGIH 2001). The test is nonspecific and should not be used when workers are exposed to benzene, to household products, or to medications containing phenol. Dermal exposure may also result in overestimation of inhalation exposure. Dark urine occurs in individuals exposed to phenol. Phenol can also be measured in the urine after oral exposure, although a dose-response relationship between oral exposure to phenol and phenol in the urine has not been established. Specific biomarkers used to characterize effects caused by phenol have not been identified. The biological monitoring for exposure to phenol is possible by measuring blood or urine levels of the parent compound whose toxicity is suspected. The sample of urine to be tested can be stored in the refrigerator for 4 days or frozen for at least 3 months before analysis [11].

Diagnosis of Phenol Poisoning

Diagnosis of phenol poisoning can be made by

1. Typical odour.
2. Initial colourless urine that changes in colour to green or black.
3. To 10 ml urine add 1 ml of 10% ferric chloride. A purple or blue colour appears that persists even on heating.

Analytical Tests & Diagnosis (Phenols) [25, 26]

Qualitative Tests

- ***Iron (III) Chloride Test***

1. Iron (III) chloride test is used for water soluble phenols
2. 1 ml of distillate is taken in a clean and dry test tube.
3. 0.5 ml of water or water- alcohol mixture is added to it.
4. 1 to 2 drops of 1% aqueous iron (III) chloride solution is added to it.
5. A red, blue, green, or purple color formation indicates the presence of phenol.
6. The iron (III) chloride test for phenols is not completely reliable for acidic phenols.

- ***Iron (III) Chloride – Pyridine Test***

1. Iron (III)Chloride – Pyridine Test is used for water insoluble phenols.
2. 1 ml of distillate is taken in a clean and dry test tube.
3. 0.5ml of methylene chloride is added to it.
4. 3-5 drops of a 1% solution ferric chloride in methylene chloride is added to it
5. A drop of pyridine is added to it and stirred.
6. Addition of pyridine and stirring will produce a color if phenols or enols are present
7. This is more sensitive test for phenols.

- ***Quinonechloroimides Test***

Quinonechloroimides are slightly soluble in water. Quinonechloroimides decomposes slowly in alkaline buffers so the solutions to be tested should be very dilute, not stronger than 1 or 2 parts of phenol in 1000 parts of solution, should be brought to an alkalinity ranging between pH 8 to 10, preferable 9.4.2 or 3 drops of the test solution, carrying some of the quinonechloroimide in suspension, are added to 10 to 50 cc. portions of the solution to be tested. In the presence of reacting phenols the blue color of the indophenol develops, in the more concentrated solutions intense blue appears.

- ***Bromine water Test***

An unknown sample is treated with a small amount of elemental bromine in an organic solvent, such as dichloromethane or carbon tetrachloride. Presence of unsaturation and/or phenol in the sample is shown by disappearance of the deep brown coloration of bromine when it has reacted with the unknown sample. The formation of a brominated phenol in form of a white precipitate indicates that the presence of phenol. The more unsaturated an unknown is, the more bromine it reacts with, and the less colored the solution will appear.

Quantitative Test

The quantitative determination of phenol is done by UV-Visible spectrophotometer by making colour complex with suitable reagents and absorbance is measured at 610 nm. The color formation observed at a time intervals measured in minutes until the maximum of absorption is shown which requires from 10 to 20 minutes.

Management

Pre-Hospital Management [27]

Secondary contamination by victims exposed to phenol vapour is not a threat. However, victims whose skin or clothing are contaminated with liquid phenol can secondarily contaminate response personnel by direct contact or through off-gassing vapour from heavily soaked clothing or from vomitus. Hence, it is important that the clothes of the victim are removed as soon as possible. If inhalation exposure is there then the person should be removed from the site of exposure.

Hospital Management [4, 11-14, 16, 28]

- *Contact:* Remove clothes immediately. Clean skin with polyethyl glycol (PEG 400), isopropranol (70%), ethyl alcohol (10%), methylated spirit and olive oil. The use of water is dubious as in different studies varying results have been found. It is preferable not to use water for decontamination.
- *Ingestion:* Gastric lavage with water mixed with castor oil or olive oil or glycerine (10%), magnesium or sodium sulphate or saccharated lime or soap solution. When lavage is complete, 30 mg of magnesium sulphate or medicinal liquid

paraffin should be left in the stomach. Gastric lavage should not be done if esophageal injury is suspected.

- Demulcents, Egg white, Normal saline with sodium bi carbonate can be given.
- Increase hydration (glucose saline) to induce diuresis.
- Hemodialysis is not effective.
- On Inhalation - Patient should be removed from the contaminated area and given 100% humidified oxygen and ventilatory support.
- Cardiovascular support includes the use of intravenous saline and vasopressors to support the blood pressure. Lidocaine can be used to treat ventricular dysrhythmias and bretilium for lidocaine-refractory arrhythmias.
- Administration of sodium bicarbonate intravenously for central nervous system depression in the presence of metabolic acidosis.
- If methemoglobinemia > 30%, then administer methylene blue.
- Other supportive measure - artificial respiration, tracheal aspiration of froth/secretions

Post Mortem Appearance

Asphyxia (due to failure of respiration and edema of glottis and complications) and syncope[4]. Viscera should be preserved in saturated solution of sodium chloride and never in alcohol or rectified spirits. For histology, viscera should be preserved in formal saline solution [27].

Table 2: Post mortem appearance [4, 12-14, 16]

Post-mortem examination	Findings
External	• Smell – of phenol • Corrosion of skin • Tongue is white, swollen or hardened • Lips mouth throat – mucus membrane is coagulated, corrugated, detached, opaque, sdden and swollen, • Colour – whitened, brown or gray • Numerous small submucous haemorrhages are present.
Internal	• Esophagus- same as mouth • Stomach – contents – reddish fluid mixed with mucus and shreds of epithelium, smell of phenol. Thick and leathery mucosa. • Furrows are more damaged • Respiratory tract (inhalational phenol poisoning) - Coagulation necrosis of mucosa, sever congestion of submucous layers, laryngeal and pulmonary edema. • Liver, spleen – white hardened patch where stomach is in contact with them • Kidney – hemorrhagic nephritis • Brain – congested and edematous • Blood – dark, semifluid, partially coagulated.

Conclusion

Phenol is used in manufacture of many chemicals and substances. It is important to control the emission and release of phenol in surroundings to prevent air, water and soil pollution as it has been classified as an environmental pollutant and human health hazard. Though no record of carcinogenicity and bioaccumulation has been noted with phenol, it is still considered as extremely hazardous substance with reportable quantity (RQ) limit of 1000 pounds.[11] Periodical monitoring and adequate protective measure are required for prevention and early diagnosis of phenol poisoning. Medically, Phenol is often used as a disinfectant and preservative for vaccines and sera. Suicidal and Homicidal poisoning is rare because of taste and color of phenol, but accidental poisoning is due to carelessness in storage or misguided medical treatment like application to raw wounds or accidental overdose of phenol during treatment as analgesic [19] etc has often been reported.

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