POISONING OF PARAPHENYLENE DIAMINE "KALA PATHAR": BLACK STONE, A LETHAL SUICIDAL AGENT: MINI REVIEW

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ABSTRACT

OBJECTIVES

To objective of review was to gather the knowledge about the clinical aspects of PPD poisoning as suicidal agent and its treatment and outcomes.

METHODOLOGY

The data regarding the poisoning cases was collected from online databases, the toxicological effects of paraphenylene diamine Kala Pathar poisoning (Scopus, Dimensions, Google Scholar, Science Direct, and Web of Science using these keywords Kala Pathar poisoning, Paraphenylene Diamine). The duration of the study was July - December 2023. This review shows that PPD poisoning is very lethal, quick treatment can save the mortality and morbidity, poor countries have little sources of research to do over it, so wealthier countries should come forward to invest in creation of antidote and improve the treatment options.

KEYWORDS: *Toxicological Effects, Kala Pathar, Paraphenylene Diamine*

INTRODUCTION

The World Health Organization (WHO) reports that suicide is becoming more common each year, raising public health concerns.[1] Intentional suicide with poisoning is the most common method. A study observes, every 20 seconds a suicide death occurs, and every 1-2 seconds, a suicide attempt occurs this number will rise to almost 1.53 million deaths.[2] Additionally, there will be 10-20 times more suicide attempts worldwide. High rate of suicide is primarily due to such reasons like, socio-economic, psychiatric diseases and psychological disturbances. In addition, there are a number of medical conditions that are linked to suicidal behavior, including chronic illnesses, malignancies, AIDS, liver, and renal failure.[3] Due to a variety of factors, the suicide trend has transferred from Western Europe to Eastern Europe and is currently in Asia.[4] Suicide and homicide poisoning frequently include the use of substances or agents that are simple to obtain, inexpensive, and easy to administer. Suicide is seen as a legal concern in many Asian countries, where it accounts for around 1 million mortalities annually.[5] In the past ten years, suicide rates have surged 60% worldwide, in both developed and developing countries. One of the most popular and preferred methods of suicide is poisoning, which is a major source of suicide. Both men and women kill themselves. Males typically finish suicide successfully compared to females with fewer attempts due to their aggressive and violent tactics.[6] However, the method of poisoning differs quite a little between countries. The most common drugs that cause poisoning in affluent countries include opiates, analgesics like Paracetamol, anxiolytics, and antidepressants. However, one of the most common causes of suicide poisoning in developing countries is exposure to organophosphorus chemicals, which are used in pesticides. Additionally, many visits to emergency rooms are related to failed suicide attempts.[7] Pesticide poisoning continues to be the biggest cause of sickness and mortality in Pakistan.[8] Pakistan lacks accurate data on suicide deaths and has no vital records. The estimated age-standardized suicide rate in Pakistan is 4.4 per 100,000 persons, which is lower than the global suicide death rate for both genders in 2017 of 9.98 per 1 million, India, Bangladesh, and Sri Lanka, which are neighbors, had suicide death rates of 13.33, 5.73, and 7.55 per 100,000 inhabitants, respectively.[9] Socioeconomic factors, masculine gender dominance, low levels of literacy, lax government employment rules, and restrictions on the use of illegal drugs or chemicals are the causes of these incidents. Paraphenylene Diamine (PPD), also known as Kala Pathar (Black Stone) in Urdu, has recently become widely used as a method of suicide poisoning in many underdeveloped countries of the world. Due of its high fatality rate, it is one of the suicide methods that the majority of individuals favor. Due to its inexpensive cost and cosmetic application, it is also readily available in the market. In Pakistan, Kala Pathar (PPD) poisoning is a new kind of deliberate suicide with a significant death rate. This hair colour is often chosen for suicide due of its simple availability, low cost, and swiftly detrimental effects. It can be mistakenly consumed or used as a suicide tool.[11] Paraphenylenediamine (PPD) is an organic compound

with chemical formula C6H4 (NH2). It is an aromatic amine, solid and white in color, which turns black on oxidation. If ingested it is metabolized in the body cytochrome P450 system, and is further oxidized to a toxic product that can lead to multi organ failure.[12] And is a main ingredient of many locally produced hair dyes. It is produced in Germany, Japan, and the United Kingdom.[13]

Uses of Paraphenylenediamine (PPD) as a Chemical: PPD is a derivative of coal tar that, when combined with ammonia and hydrogen peroxide, produces an aromatic amine derivative of aniline and a par nitro aniline derivative that is used as a hair dye. Because of darker effect it produces when combined with henna, it is also used for tattooing.[14] Many industrial operations routinely use PPD in hair dyes, the photochemical process, hair dye oxidation, dyeing furs, vulcanizing tyres, and the rubber business are all examples of hair dyes.[15] Since PPD has a significant tendency to speed up the dying and dyeing processes, many women have used it since 1863 for cosmetic purposes. It is frequently utilized in industrial products like dyes for textiles or fur, dark cosmetics, temporary tattoos, photographic development and lithography plates, photocopying and printing inks, black rubber, oils, greases, gasoline and more.[15]

Route of Administration of Paraphenylenediamine (PPD) for Poisoning Purposes.

The most common route of administration of PPD, found in various articles is Oral ingestion. The majority of the time, this substance is used for self-suicidal purposes, however it can also be accidentally consumed and utilized with homicidal intent.[16] PPD consumption is commonplace, which makes it a popular choice for suicide. Adult population PPD consumption was primarily for intentional suicide/suicide.[17] On the other hand, unintentional ingestion was the main reason for consumption in children. Toxicity might also result from local absorption. There have been cases of transdermal absorption, but the main worries are related to its suicidal consumption; it is extremely poisonous when taken by mouth, and the outcome is mostly dose dependent.[18] When consumed, PPD is a dangerous and deadly drug that can be accidently consumed, taken orally for suicidal purposes, or even given to a person to try murder.[19] Humans are most commonly exposed to PPD through their skin and through inhalation during the dyeing process.[20] PPD can result in severe edema, rhabdomyolysis, renal impairment, skin irritation, contact dermatitis, and rhabdomyolysis. These issues show that this substance is extremely hazardous.[21]

Mode of action of Paraphenylenediamine:

Clinical Features and Complication Reported by Various Research Studies: Depending on the method of intoxication, the amount consumed, and the length of time before presenting to the hospital, patients may exhibit a variety of symptoms and indicators. Documents reveal that aromatic amines like PPD have highly common toxicological characteristics. The triggering of apoptosis through an increase in reactive oxygen species (ROS) is one of these crucial characteristics. This poison is very irritant to local organs like mouth, tongue, lips and pharynx and causes' rapid damage of the tissues and ultimately causing angioedema leading to dysphasia and respiratory distress, rhabdomyolysis, intravascular hemolysis, abrupt renal failure, and liver necrosis.[22] Angioedema and chocolate-brown urine are two signs of PPD poisoning that may be present. PPD produces edema of the face, neck, tongue, throat, and larynx after consumption. Rhabdomyolysis, angioneurotic edema, and renal failure are some effects of its poisoning.[23] The malfunctioning of numerous organs is a documented effect of PPD. The malfunctioning of numerous organs is a documented effect of PPD. Due to severe cardiac toxicity or angioneurotic edema, death might occur within 6–24 hours.[24] For the first time, Chugh reported on two patients who had PPD intoxication-related oligo urea and acute renal failure (ARF). In Sudan, 31 patients with PPD poisoning were recorded, all of them had severe angioneurotic edema; 15 of these patients required an immediate tracheostomy; there were five ARF patients; and 13 of these patients passed away in the hospital within 12 hours.[25] Oral ingestion of PPD for suicide purposes quickly develops edema on the face, throat, neck, larynx, and tongue at first, and later results in rhabdomyolysis. In addition, it causes oliguria/anuria, dysphagia, acute renal failure, asphyxia, IV hemolysis, toxic myocarditis, and rhabdomyolysis. Death is caused by myocardial injury and acute renal failure ARF, brown urine, urine retention, and a projecting tongue are among symptoms of acute PPD poisoning. Finally, ARF supervenes as renal tubular necrosis develops as a result of the buildup of toxic PPD metabolites, ultimately leading to death if immediate treatment is not instituted.[26] PPD can cause angioneurotic edema or cardio toxicity, which can cause lethal arrhythmias and mortality during the first six to 24 hours of intake.[27] Within the first week, moderate doses can result in acute renal failure. PPD can also lead to allergies and skin rashes that could intensify many reactions, including anaphylaxis. Anaphylaxis reaction with facial and oral cavity edema, dysphagia, as well as damage to the throat, tongue, and upper gastrointestinal system, are among the signs and symptoms (GIT).[28] Additionally, it can result in severe hepatitis, renal failure, various arrhythmias, and electrolyte imbalance, tissue damage and the development of hypersensitive allergic responses.[29] Due to myoglobin casts, it causes renal tubular obstruction

and necrosis of the skeletal and cardiac muscles. Renal tubules are extremely prone to be damaged by this poison.[30] There are both early and late clinical consequences of PPD toxicity. Laryngospasm, cardio toxicity, acute pulmonary edema, and angioneurotic edema made up the majority of the early clinical presentation.[31] On the other hand, late symptoms of PPD poisoning include renal failure and liver damage. Acute and late clinical manifestations, however, depend on a number of variables, including the quantity of PPD consumed, the timing of the consumption, the amount of time it took to get to the hospital emergency room, and other timely interventions like gastric lavage, endotracheal intubation, and tracheostomy.[32] PPD poisoning is distinguished by symptoms including rhabdomyolysis, cervicofacial angioedema, and swelling of the tongue and lips. Major clinical problems of the black stone include angioedema, rhabdomyolysis, and renal failure.[33] See Table No: 01

Table 1: Most Common Complications of Paraphenylenediamine (PPD) Toxicity

Complications	Frequency in Published Articles
Skin Rash	80-90 %
Respiratory Distress	70-60%
Anaphylactic Reaction	60-50%
Swelling of Face/Neck	60-50%
Rhabdomyolysis	50%
Cardiovascular Effects	35%
Gastrointestinal Issues	55%
Neurological Symptoms	35%
Renal Dysfunction	50%
Hepatic Dysfunction	30%
Hematological Effects	30%

Paraphenylenediamine (PPD) Poisoning Diagnosis: The diagnosis of PPD intoxication is largely dependent on history, clinical manifestations and some laboratory findings. The clinical features are rather unique and in the absence of laboratory facilities in many developing countries the angio-edema of the face and neck together with the hard protruding tongue and the chocolate-brown color of the urine are used for clinical diagnosis.[34] urine can be tested for PPD using thin layer chromatography which is essential for medico-legal purposes. However, this test is not routinely available and there is a need for a rapid test to demonstrate PPD in blood or urine. Various other tests are also performed for diagnosis like Blood complete test, serum creatinine, leucocyte count, SGPT, SGOT, serum bilirubin, serum alkaline phosphatase, serum potassium & calcium, serum CPK, and evidence of myoglobinuria by thorough urine report are all shown in studies.[35]

Treatment for Paraphenylenediamine (PPD) Poisoning: Since there is no cure for this illness, all efforts are focused on symptomatic management in an effort to lower mortality and morbidity.[36]All researchers in papers address this issue and place emphasis on the need for scientific research in institutions to develop a remedy for this extremely lethal and toxic poison. Treatment is based on the route of administration, the time, the quantity, and the concentration of the poison consumed. Anti-inflammatory medications, such as steroids, are given along with anti-allergic medications to reduce the edema of the face, oropharynx, tongue, and esophagus. The possible therapy is the immediate administration of steroids and water. The tracheotomy is additionally regarded as effective emergency management.[37] Early diagnosis and therapy are essential for management. With a focus on airway control and the prevention and treatment of renal failure, since there was no specific antidote available, management offered support. Activated charcoal can be used to lavage the stomach. If the arterial blood gas study reveals hypoxia or if there is severe angioedema, oxygen should be provided along with Chlorpheniramine maleate and injection of corticosteroids for 3-5 days. For angioneurotic edema, intravenous corticosteroids (hydrocortisone/methylprednisolone) is the mainstay of therapy. If hypotension persists despite receiving adequate fluid therapy, vasopressors (dopamine/norepinephrine) should be administered. To stop myoglobin-mediated renal tubular damage, sodium bicarbonate and loop diuretics were utilized to force an alkaline diuresis. Mechanical air conditioning.[38] An investigation in Multan, Bahawalpur, (100%), Nawabshah, (87.5%), and South India found that 60% of tracheostomies were inserted. Patients in this study who had upper airway tract obstruction required an emergency life-saving tracheostomy in 68.5% cases.[39] Depending on the clinical symptoms upon presentation, the primary form of treatment is supportive. Some patients may require endotracheal intubation, and a tracheostomy is a life-saving procedure for an obstruction of the airway. Due to the potential for a hypersensitive reaction to PPD, antihistamines and steroids are frequently employed, however there is no evidence to support this course of treatment. Myoglobinuria is managed with alkaline diuresis, with mixed success, employing sodium bicarbonate, isotonic saline, and diuretics.[40] According to a study the effectiveness of tests to remove PPD using hem perfusion and hemodialysis was inconsistent, and there is no specific antidote available. However, in cases of oliguria or anuria AKI, dialysis is a useful supportive therapy.[30] See Table No: 02.

Table 2: Common Signs, Symptoms, and Treatment Options of Paraphenylenediamine (PPD) Toxicity

Signs and Symptoms	Treatment Options
Skin irritation and rash	Supportive care
Swelling of the face or neck	Intravenous fluids
Itching and burning sensation	Oxygen therapy
Redness and blistering	Topical corticosteroids for rash
Difficulty breathing	Antihistamines
Rapid heart rate	Pain relievers
Dizziness and fainting	Monitoring and observation
Nausea and vomiting	Treatment of complications
Abdominal pain	Antispasmodics
Dark urine	I/v fluids
Yellowing of the skin	fluids
Confusion or agitation	Anxiolytics

According to the study by Muhammad Ahmed Khan et al, 98% of patients had tracheostomies. In the study by Akbar et al.6 60% of cases had a tracheostomy, and in the study by Khuhro et al.[13] 87.5% of cases had one. There is no known antidote for PPD poisoning, thus treatment focuses mostly on supportive care. Patients who experience acute renal failure need dialysis, but none of patients of that study did. The biggest danger to life is respiratory failure. Therefore, tracheostomy, assisted ventilation, and endotracheal intubation were essential and life-saving procedures.[42] A study at Multan shows 60% of patients at Nishtar Hospital in Multan had tracheostomies, an other study by Shivani Nautiya et al shows 108 of patients went under tracheostomies.[43,44] the management of PPD poisoning requires several specializations assistance for the best management. Interdisciplinary coordination between the fields of otolaryngology, anesthesia, nephrology, medicine, and laboratory medicine is necessary for effective care. Muhammad Ahmed Khan and colleagues' investigation reveals As a result of the gross enlargement of the neck, tongue, and intraoral tissue brought on by this poison, which also causes dyspnea and stridor, tracheostomies were performed in these cases to ease breathing difficulties and imminent suffocation. Nearly 1173 (98.01%) of the cases received tracheostomy surgery.[42]

CONCLUSIONS

Paraphenylenediamine ―Kala Pathar‖ is a very deadly chemical, its use in suicide and homicidal cases are increasing day by day in Pakistan and other developing countries so governments should impose ban on this compound and its easy availability should be restricted because no any antidote is available to rescue the patients from mortality. The proper awareness campaign regarding availability and dangerous aspects of black stone (kala Pathar) also is warranted for future.

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AUTHORS CONTRIBUTION

Masood Ahmed Unar - *Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Critical Revision; Supervision; Final Approval*

The authors accept responsibility for all aspects of the work and will ensure that any concerns regarding the accuracy or integrity of any part are properly investigated and resolved.