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Research Article

Role of Methylprednisolone and Cyclophosphamide in Paraquat Poisoning Treatment

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ABSTRACT
Background: Paraquat is a herbicide with a chemical composition of 1,1′-dimethyl-4,4′-bipyridinium dichloride. The primary use of paraquat is for weed control. Accidental or deliberate self-harm can lead to inhalation and ingestion of the compound. It is hydrophilic and does not penetrate intact skin. However, there is mention about dermal exposure. Paraquat is rapidly inactivated in soil. The clinical signs and symptoms can range from the development of oral ulceration, abdominal pain, reduced urine output, renal failure, jaundice, and hypoxemic respiratory failure leading to acute respiratory distress syndrome (ARDS).
Objectives: 1. Role of methylprednisolone and cyclophosphamide in paraquat poisoning treatment.2.Study the Role of methylprednisolone and cyclophosphamide in paraquat poisoning treatment.3.Study the clinical profile of paraquat poisoning cases in a tertiary care center.4.Study the outcome among paraquat poisoning cases in a tertiary care center.
Methods: Study Design: A prospective observational study. Study Setting: Medicine Department of Government medical college Jalgaon, Maharashtra. Study population: All cases with paraquat poisoning admitted in medicine department of Government medical college Jalgaon, Maharashtra. Study Duration: 1 January 2024 to 31 December 2025.Sample size: 16
Results: Majority cases found in 17-25 years age group 8 (50%) cases followed by 5 cases (31.25%) found in 26-35 years age group and 3 (18.75%) cases observed in 36 and above years age group. Most of cases were males 14 (87%) and 02 females (12.5%). Majority of cases from rural area 14 (87.5%) and 2 cases from urban area (12.5%). Most of the cases were farmers 9 (56.255) followed by 2 cases were housewife and 1 student. majority of cases presented with vomiting 13 (81.25%) followed by Increased serum creatinine 11 (68.75%), lethargy 10 (62.5%), leukocytosis 7 (43.75%), respiratory failure 7 (43.75%), acute hepatitis 7 cases (43.75%) and shock 7 cases (43.75%). mortality was 43.75%, 7 cases death during treatment and 7 cases survive (43.75%) and 2 cases DAMA
Conclusions: Majority cases found in 17-25 years age group, Most of cases were males, Majority of cases from rural area, Most of the cases were farmers, majority of cases presented with vomiting and mortality was 43.75%.

Keywords: Paraquat Poisoning, Methylprednisolone, Cyclophosphamide, Mortality Rate, Outcome.

Introduction

Paraquat is a herbicide with a chemical composition of 1,1′-dimethyl-4,4′-bipyridinium dichloride [1, 2]. The primary use of paraquat is for weed control. Accidental or deliberate self-harm can lead to inhalation and ingestion of the compound. It is hydrophilic and does not penetrate intact skin. However, there is mention about dermal exposure [3]. Paraquat is rapidly inactivated in soil [4] The clinical signs and symptoms can range from the development of oral ulceration, abdominal pain, reduced urine output, renal failure, jaundice, and hypoxemic respiratory failure leading to acute respiratory distress syndrome (ARDS) [5, 6]. The mortality remains high, ranging between 50 and 90% [1, 2].

The intensivist should have a high index of suspicion as the timely initiation of treatment can significantly improve patient outcomes. The mechanism of toxicity is due to the generation of reactive oxygen species (ROS) and free radicals. Para quat is reduced by nicotinamide adenine dinucleotide phosphate (NADPH). Paraquat stimulates the formation of ROS and acts on NADPH oxidase and nuclear factor kappa B (NFkB). [4]. It causes extensive inflammation, triggering a cytokine response.
The respiratory system is predominantly involved. Paraquat is absorbed in the lungs through an energy-dependent process, resulting in a higher concentration in the lungs than plasma. Progressive lung damage is seen similar to ARDS [4, 7]. The ROS causes

damage to proximal tubules, resulting in acute kidney injury [8]. Painful oral ulcers are a characteristic feature of paraquat poisoning [9]. A urine or plasma dithionate test helps to determine the paraquat level quantitatively [10]. The initial management of any poisoning includes reducing further absorption, using renal replacement therapy (RRT) for rapid excretion, treating with the antidote, and supportive therapy. For paraquat, initial treatment involves gastric lavage. Early use of charcoal and hemoperfusion helps to decrease plasma levels of paraquat rapidly [11, 12]. As paraquat causes severe inflammation, immunomodulators, such as cyclophosphamide and steroids, either methylprednisolone or dexamethasone, have been used and showed mixed results.

Mechanism of Toxicity of Paraquat Self-Poisoning: [13-16]

Generation of free radicals and oxidative stress Paraquat-induced toxicity is a manifestation of its ability to undergo redox-cycling and subsequent generation of reactive oxygen species (ROS) [13]. Paraquat is metabolized by several enzyme systems (NADPH-cytochrome P450 reductase, xanthine oxidase, NADH-ubiquinone oxidoreductase and nitric oxide synthase)[14].

Its metabolism through these systems generates a paraquat mono-cation radical (PQ.+). Inside the cell, PQ.+ rapidly gets Pq2+ O2 Gut Activated charcoal Blood 1 2 HD HF NADP+ NADPH 7 NADP+ Pq2+ O2− SOD re-oxidized to PQ2+ and in the process it generates super oxide (O2.-).O2 acts as an electron acceptor and NADP as an electron donor in this reaction. This further gives rise to formation of the hydroxyl free radical (HO.) in the presence of iron via the Fenton reaction. NO. combines with O2.- to generate peroxinitrite (ONOO-) which is a very strong oxidant and a nitrating intermediate.

NO. is enzymatically produced from L-arginine by NO synthase, and PQ also directly or indirectly induces NO synthase mediated nitric oxide production [15]. Generation of highly reactive oxygen and nitrite species results intoxicity in most organs but the toxicity is particularly severe in the lungs as paraquat is taken up against a concentration gradient in to the lung.[16]

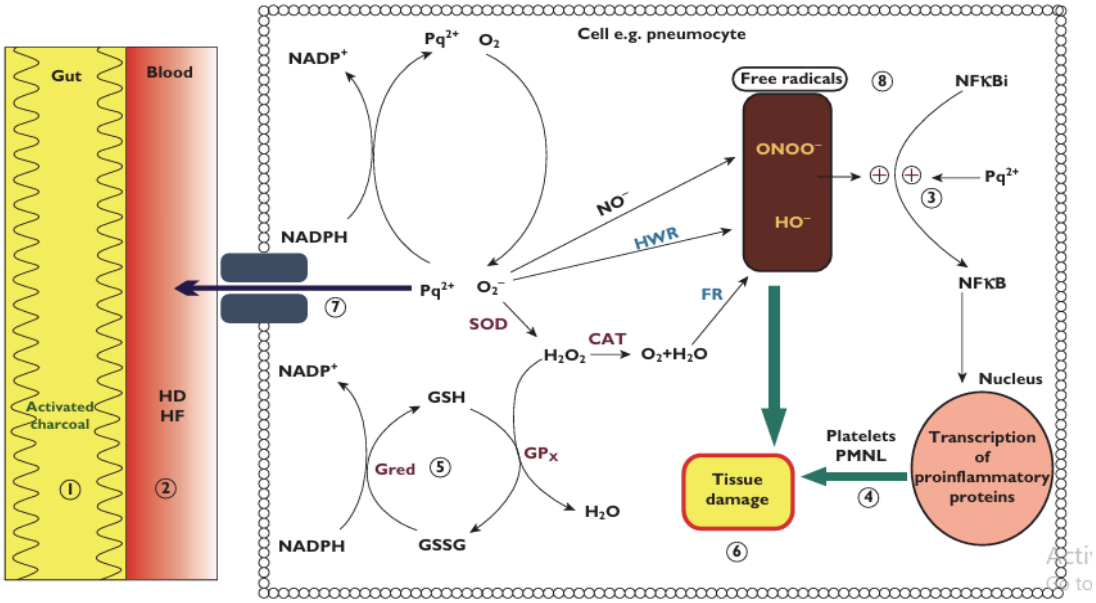

Figure 1 – Graphical Representation of Paraquat Toxicity Inside A Pneumocyte and Potential Sites of Antidotal Therapy

SOD, superoxide dismutase; CAT, catalase; Gred, glutathione reductase; Gpx, glutathione peroxidase; FR, Fenton reaction; HWR, Haber-Weiss reaction. 1–8: potential sites of action by available treatment options. 1: activated charcoal and Fuller's earth; 2:dialysis; 3, 4, 6 and 8:salicylates; 5 and 8:N-acetylcysteine; 7 (P-glycoprotein induction):dexamethasone; 4: immunosuppression

Aim and Objectives

Aim: Role of methylprednisolone and cyclophosphamide in paraquat poisoning treatment

Objectives

1. Study the Role of methylprednisolone and cyclophosphamide in paraquat poisoning treatment
2. Study the clinical profile of paraquat poisoning cases in a tertiary care center
3. Study the outcome among paraquat poisoning cases in a tertiary care center.

MATERIAL AND METHODS

Study Design: A prospective observational study. **Study Setting:** Medicine Department of Government medical college Jalgaon, Maharashtra. **Study Population:** All cases with paraquat poisoning admitted in medicine department of Government medical college Jalgaon, Maharashtra. **Study Duration:** 1 January 2024 to 31 December 2025**. Sample Size:** 16

Inclusion Criteria

1. All cases with paraquat poisoning admitted in medicine department of Government medical college Jalgaon, Maharashtra.

Exclusion Criteria

1. Not willing to participate in the study
2. In complete information
3. Cases with Unknown poisoning

Approval for the study

Written approval from Institutional Ethics committee was obtained beforehand. Written approval of Medicine and another related department was obtained. After obtaining informed verbal consent from all patients with paraquat poisoning admitted to Medicine ward of Government medical collage Jalgaon, Maharashtra such cases were included in the study.

Methods of Data Collection and Questionnaire

Predesigned and pretested questionnaire was used to record the necessary information. Questionnaires included general information, such as age, sex, religion, occupation, residential address, and date of admission.

Medical history- chief complain, past history, general examination, systemic examination. Data on demographic profile of paraquat poisoning, investigation, personal history, medical past history, treatment modalities, and clinical outcome data collected from patients admitted in medicine ward. Relevant investigations like complete blood count, random blood sugar, renal function test, liver function test, serum albumin and protein, serum electrolytes, lipid profile, ECG and urine routine examination was done.

Data Entry and Analysis

The data were entered in Microsoft Excel and data analysis was done by using SPSS demo version no 21 for windows. The analysis was performed by using percentages in frequency tables and correlation of stroke. $p<0.05$ was considered as level of significance using the Chi-square test.

RESULT AND OBSERVATIONS

This present prospective study conducted on all paraquat poisoning cases admitted in medicine department of government medical college, Jalgaon, Maharashtra during study period such 16 cases were included in the study.

Table No.1: Distribution of Cases as Per Age (N=16)

Age (in Years)	Frequency	Percentage
17-25	08	50%
26 -35	05	31.25%
36 and above	03	18.75%
Total	16	16 (100%)

The above table shows that majority cases found in 17-25 years age group 8 (50%) cases followed by 5 cases (31.25%) found in 26-35 years age group and 3 (18.75%) cases observed in 36 and above years age group.

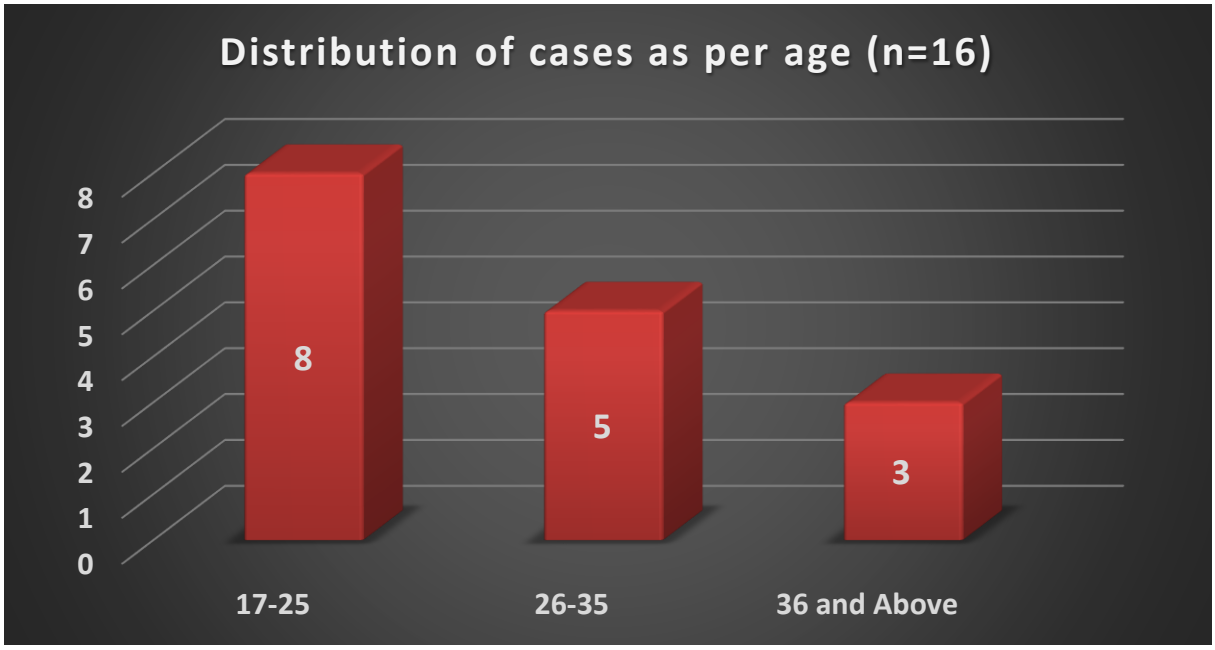

Table No.2: Distribution of Cases as Per Gender (N=16)

Gender	Frequency	Percentage
Male	**14**	**87.5%**
Female	**02**	**12.5%**
Total	**16**	**16 (100%)**

The above table shows majority of cases were males 14 (87%) and 02 females (12.5%).

Table No.3: Demographic Profile (n=16)

Place of residence	Frequency	Percentage
Urban	02	12.5%
Rural	14	87.5%
Occupation		
Farmer	09	56.25
Labourer	04	25
Student	01	6.25
Housewife	02	12.5

Majority of cases from rural area 14 (87.5%) and 2 cases from urban area (12.5%). Most of the cases were farmers 9 (56.255) followed by 2 cases were housewife and 1 student.

Table No.4: Distribution of Cases as Per Clinical Features (N=16)

Clinical features	Frequency	Percentage
Vomiting	13	81.25
Loss of consciousness	07	12.5
Lethargy	10	62.5
Shock	07	43.75
Leukocytosis	07	43.75
Increased serum creatinine	11	68.75
Respiratory Failure	07	43.75
Acute hepatitis	07	12.5

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The above table shows majority of cases presented with vomiting 13 (81.25%) followed by Increased serum creatinine 11 (68.75%), lethargy 10 (62.5%), leukocytosis 7 (43.75%), respiratory failure 7 (43.75%), acute hepatitis 7 cases (43.75%) and shock 7 cases (43.75%).

Table No.5: Treatment Given (N=16)

Treatment Given	Frequency	Percentage
Methylprednisolone	15	93.75%
Cyclophosphamide	16	100%
Dialysis	10	62.5%

The above table shows all cases given Cyclophosphamide and Methylprednisolone given in 15 cases and dialysis 10 cases

Table No.6: Distribution of Cases as Per Outcome (N=16)

Outcome	Frequency	Percentage
Survival	07	43.75%
DAMA	02	12.5%
Death	07	43.75%
Total	16	16 (100%)

The above table shows mortality was 43.75%, 7 cases death during treatment and 7 cases survive (43.75%) and 2 cases DAMA.

DISCUSSION

Paraquat is rapidly but incompletely absorbed and then largely eliminated unchanged in urine within 12-24 h. Clinical features are mainly due to generation of intracellular reactive oxygen species which cause cellular damage via lipid peroxidation, activation of nuclear factor kappa B, mitochondrial damage and apoptosis in many organs. Paraquat is actively taken up against a concentration gradient into lung tissue leading to pneumonitis and lung fibrosis.

Paraquat also damages the heart, kidneys, liver, adrenal glands, central nervous system, muscles and spleen causing multiple organ failure. Clinical reports associated paraquat poisoning with acute lung injury, pulmonary hypertension, leukocytosis, metabolic acidosis, enlarged heart, acute kidney injury, generalized edema and increased level of amylase, glucose and creatinine. Until now, there has been no effective antidote.

In current study shows Majority cases found in 17-25 years age group 8 (50%) cases followed by 5 cases (31.25%) found in 26-35 years age group and 3 (18.75%) cases observed in 36 and above years age group. Similar finding observed in the study conducted by Delirrad M et al [17] he reported that the most of the cases found in 21-30 years age group 19 (46.3%) followed by 14-20 years 10 (24.4%), 31-40 age group 3 (7.3%), 41-50 age group 1 (2.4%),51-60 years 4 (9.8%) and above 60 years 4 (9.8%).Another study by Soloukides A et al [18] found that the majority of cases 21-30 years age group 52% followed by 31-45 years age group 32% and above 50 years age group 16%.

In current study shows Most of cases were males 14 (87%) and 02 females (12.5%). Similar finding observed in the study conducted by Delirrad M et al [17] he reported that the most of the cases were males 23 (56.1%) and females 18 (43.9%). Another study by Soloukides A et al [18] found that the majority of were males 64% and 36% were females. Tan JT et al [19] Reported that the 78% cases were males and 28% were females.

Majority of cases from rural area 14 (87.5%) and 2 cases from urban area (12.5%). Similar finding observed in the study conducted by Delirrad M et al [17] he reported that the most of the cases from rural area 23 (56.1%) and 18(43.9%) cases from urban area. Soloukides A et al [18] found that the majority of cases from rural area 62% and 38% from urban area.

Most of the cases were farmers 9 (56.255) followed by 2 cases were housewife and 1 student. Similar finding observed in the study conducted by Delirrad M et al [17] he reported that the majority of cases were farmers 63% and 24% students 13% labourer.

In current study shows majority of cases presented with vomiting 13 (81.25%) followed by Increased serum creatinine 11 (68.75%), lethargy 10 (62.5%), leukocytosis 7 (43.75%),

respiratory failure 7 (43.75%), acute hepatitis 7 cases (43.75%) and shock 7 cases (43.75%). Similar finding observed in the study conducted by Delirrad M et al [17] he reported that the main symptoms and signs of studied patients include nausea (53.7%); vomiting (43.9%); epigastric pain (36.6%); mucosal lesions of oral cavity and pharynx (85.4%); loss of consciousness as mild to moderate lethargy (9.8%); and fever (9.8%).Leukocytosis was seen in 41.7% of patients (n=17). Acute hepatitis was seen in 31.7% (n=13) of patients. Significant increases in serum creatinine (Cr) were seen in 61% of patients (n=25).

In current study shows mortality was 43.75%, 7 cases death during treatment and 7 cases survive (43.75%) and 2 cases DAMA. Similar finding observed in the study conducted by Delirrad M et al [17] he reported that the mortality was 23.40% and survival rate was 76.6%. Soloukides A et al [18] found that the mortality rate was 32% and survival rate was 68%. Tan JT et al [19] Reported that the mortality rate was 19%.

CONCLUSION

Majority cases found in 17-25 years age group, Most of cases were males, Majority of cases from rural area, Most of the cases were farmers, majority of cases presented with vomiting and mortality was 43.75%.

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