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# MIXED POISONING OF PARAQUAT AND ORGANOPHOSPHORUS POISONINGS ASSOCIATED WITH ACCELERATED RENAL DAMAGE

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## ABSTRACT

Organophosphosphates (OP) and paraquat poisoning is the major cause of death in developing countries. Very few cases reported in the literature regarding the mixed OP and paraquat poisoning and its management. In the present study we reporting a case admitted with consumption of Monocrotophos (OP compound) and Gramoxane (paraquat). Patient managed symptomatically, even though there was consistent increase in urea and creatinine levels indicating renal failure. This deterioration probably due to the effects of both compounds due to oxidative stress. Due to constant renal failure patient underwent hemodialysis along with atropine, glycopyrrolate, pralidoxime, midazolam, furosemide, immunosuppresants, antioxidants and antibiotics. There was no improvement was observed in the patient and he discharged against the medical advice.

**Key Words:** paraquat, op, mixed poisonings, renal failure, oxidative stress.

## INTRODUCTION

Acute pesticide poisoning is the major clinical problem throughout the world and accounts about 3,00,000 deaths annually.[1] Among these pesticides a majority of the deaths are due to organophosphorous and paraquat compounds. [1] Poisoning due to these chemicals is commonly observed due to the easy availability as over counter medicine, improper storage methods and lack of awareness of the potential harm.[1-2]

OP compounds contribute to a major part of suicidal poisoning in India[1]. Acute toxicity of these compounds results from its inhibition of acetyl cholinesterase which is mainly responsible for the initial cholinergic crisis.[1] The standard treatment mainly includes gastric decontamination, supportive care, and use of specific antidote like atropine and oximes.[1] Paraquat is non-selective bipyridyl herbicides which is an important cause of acute poisoning. High case fatality is seen in the cases which are mainly due to its inherent toxicity and the lack of effective treatment. To prevent systemic toxicity due to intoxication of these chemicals immediate medical care is needed. In case of paraquat ingestion, gastric lavage or whole-gut irrigation using adsorbents such as Fuller's earth, bentonite or activated charcoal is recommended. Immunosuppressive therapy with cyclophosphamide, along with antioxidant therapy with N-acetylcysteine, vitamin E & vitamin C can also be considered as alternative treatment for paraquat poisoning. In some cases hemodialysis or hemoperfusion is recommended as alternative therapy. [3] However information regarding OP and Paraquat mixed poisoning is not available in the literature. Here we are reporting a case on OP and Paraquat mixed poisoning admitted to the tertiary care hospital.

## CASE HISTORY

A 21-year-old-man was admitted to emergency centre with a history of alleged consumption of about 30-40 ml of mixture of Monocrotophos (OP compound) and Gramoxane (paraquat) in a tertiary care hospital, south India. The complaints on admission were burning sensation in the upper throat and upper abdomen region. At the time of admission he was conscious and oriented to time, place and person. During the admission his pulse rate was 86 beats per minute and blood pressure (BP) was 130/80 mm Hg. Systemic examination was normal except for tenderness in abdomen epigastric region.

**Table:I Arterial blood gas analysis**

| Parameters | D4 | D5 | D6 |
|---|---|---|---|
| PH | 7.02 | 7.07 | 7.07 |
| P02 | 60.8mm Hg | 60.6mm Hg | 51mm Hg |
| PCO2 | 62.4mm Hg | 66.0mm Hg | 83mm Hg |
| HCO3 | 12.1meq/l | 13.9meq/l | 22.9meq/l |

**Table:II Renal Function Tests(RFT) and Liver Function Tests(LFT)**

| Parameters | D1 | D2 | D3 | D4 | D5 | D6 |
|---|---|---|---|---|---|---|
| Urea | 12mg/dl | 37mg/dl | 93mg/dl | 148mg/dl | 209mg/dl | 170mg/dl |
| Creatinine | 1.2mg/dl | 2.8mg/dl | 3.9mg/dl | 5.3mg/dl | 9.1mg/dl | 6.0mg/dl |
| Sodium | 135meq/l | 136meq/l | 138meq/l | 142meq/l | 140meq/l | 137meq/l |
| Potassium | 3.4meq/l | 3.0meq/l | 3.5meq/l | 5.6meq/l | 5.4meq/l | 4.9meq/l |
| Total bilirubin | 0.8mg/dl | - | - | 1.3mg/dl | - | - |
| Direct bilirubin | 0.2mg/dl | - | - | 0.7mg/dl | - | - |
| AST | 35 IU/L | - | - | 58 IU/L | - | - |
| ALT | 22 IU/L | - | - | 48 IU/L | - | - |
| ALP | 79 IU/L | - | - | 56 IU/L | - | - |
| cholinesterase level | 262 IU/L | - | - | - | - | - |

Initially he was admitted to primary care hospital, where stomach wash was done and ryles tube was inserted. On the day of admission his biochemical investigations were normal except cholinesterase level which was found to be very low (Table 2). Hematologic investigation showed that his WBC count (24900cells/$mm^3$) was elevated. Urinary analysis shows that presence of protein, sugar, RBC and WBC.

On the second day onwards there was progressive worsening of biochemical parameters from day 4 and patient developed acidosis on the $7^{th}$ day of admission. Parameters as shown in the table 2. There was a consistent increase in the urea and creatinine level indicating the acute renal failure probably contributed by the acute poisoning. On the day $4^{th}$ patient was ventilated and his arterial blood gas reports were progressively worsening (Table1).

Here on the day of admission he was started with atropine 5amp stat dose and followed by 2ml/hr infusion along with glycopyrrolate infusion at the rate of 2ml/hr, Inj. pralidoxime 1gstat was started and continued as 1g iv q8hrly along with iv methylprednisolone (1g/24hourly) and cyclophosphamide (750mg in 500 ml DNS at the rate of 150ml/hour). The antibiotics like piperacillin and tazobactum, azithromycin was also added on the day of admission. All the other medication given during the course of treatment except for cyclophosphamide, pralidoxime azithromycin which were are discontinued on $2^{nd}$,$3^{rd}$,$4^{th}$ day respectively.

Inj.pantoprazole, intravenous fluids were co-administered as a supportive therapy On second day from admission urea and creatinine levels were increased and T.N-acetycysteine 600mg BD, Inj.midazolam 3mg, Inj.mesna added to therapeutic regimen. T.N-acetycysteine was

continued during his hospital stay while Inj.mesna, Inj.midazolam were discontinued on 3rd and 4th day respectively. On 3rd day from admission Inj.Lasix (furosemide) was added to the treatment as patient had a decreased urine output. Due to continuous increase in urea and creatinine level, patient was recommended to undergo hemodialysis on the 3rd, 5th, and 6th days. On the 6th day from admission, patient was continued on ventilator support and even though there was improvement in the urea and creatinine levels (Table2), but his arterial blood gas progressively worsened (table1). This was explained to relatives, but they were willing to discharge him against medical advice due to financial constraints.

## DISCUSSION

Patient was admitted in the hospital with a history of consumption of monocrotophos and paraquat. Monocrotophos on ingestion is absorbed rapidly and accumulates in the liver and kidney.[8] Paraquat also undergoes rapid absorption by gastrointestinal mucosa, reaches peak plasma concentration within 0.5 to 2 hours after ingestion and thereafter a rapid decline in concentration is seen over the next 12 to 24 hours. This is probably due to deposition of the paraquat in organs like lungs, heart, kidney and liver.[3-4] It follows the two compartment model probably due to its deposition in the organs like lung, liver and kidney in the initial stages followed by redistributions.[3] About 90% of the parent molecule is excreted through kidney and clinical studies showed that majority of patients admitted with acute toxicity of paraquat associated severe lung injury along with hepatic and renal failure which results probably due to tubular necrosis.[3] The probable mechanism of renal and damage may be associated with redox cycling and oxygen toxicity.[3] This is probably due to generation of free radicals due to oxidative stress.[3] The OP compounds also contributed for the renal damage by the same mechanism and there is no literature available regarding the effect of the mixture of these compounds on the renal system.[5-6] The combination of these compounds may probably result in the accelerated renal damage due to additive effect. Moreover no standard guidelines for treatment of mixed poisoning exist. The treatment in the hospital mainly focuses on improving the kidney and liver function. In this case patient underwent hemodialysis for 3 days and even though his renal functions were improved, he was discharged against medical advice due to financial constraints.

## CONCLUSION

We are reporting a mixed OP and paraquat poisoning associated with acute renal failure probably due to additive effective of both the compounds. Dialysis is the main course of

treatment along with antioxidants, cyclophosphamide, atropine and pralidoxime. Both the compounds contributed renal damage probably due to oxidative stress and there is no clear picture of the effect of two compounds when consumed together.

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**ABBREVATIONS**

OP- organophosphorus

AST- Aspartate transaminase

ALT- Alanine transaminase

ALP- Alkaline phosphatase

RBC- Red blood cells

WBC-White blood cells