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ORIGINAL ARTICLE

Outcome of Paraquat Poisoned Patients Treated with a Commonly Used Therapeutic Flowchart: A Case Series

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Abstract

Background: Paraquat poisoning is a medical emergency challenge due to its inherent severe toxicity and unavailability of specific antidote for it. In this paper, a series of patients who were treated according to a commonly used treatment flowchart are presented.
Methods: This prospective observational study was carried out on paraquat poisoned patients admitted to District Hospital, Chamarajanagar and Shimoga institute of Medical Sciences, Shimoga, Karnataka, India, during January 2013 to December 2014.
Results: Six patients (4 women and 2 men) with median age of 23 [min-max: 18-42] years were studied. The majority of patients had respiratory distress (with an average SpO_2 of 60%), i.e. 4 out of 6 cases manifested with respiratory distress associated with dryness and burning sensation in mouth, throat and chest. Oxygen therapy with mask in one case and by ventilator in rest of cases was required. Except one patient who died on the first day and no further measurement of serum creatinine could be taken from her, all other patients developed increased creatinine. Five out of 6 patients died mainly due to pulmonary sequels. In the only survived patient, gastrointestinal symptoms were predominant followed by acute renal failure and pulmonary congestion which were reverted with medical care indicated in the therapeutic flowchart. In post-mortem investigations, inflammatory infiltration in lungs was noted in all cases and acute tubular necrosis was seen in 3 cases.
Conclusion: Renal insufficiency and pulmonary damage following severe paraquat poisoning are indicators of poor prognosis and may not be reversible with commonly used treatment approaches.

Keywords: Clinical Protocols; Paraquat; Poisoning; Renal Insufficiency; Respiratory Insufficiency

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INTRODUCTION

Paraquat poisoning is a medical emergency challenge due to its inherent severe toxicity and unavailability of specific antidote for it (1). Even though paraquat toxicity can be managed partially with decontamination methods, increased renal excretion (rigorous fluid therapy), administration of anti-inflammatory and immunosuppressive drugs (2,3); no standardized treatment approach has been established, to date. Paraquat toxicity predominantly affects the pulmonary system as it can be accumulated in lungs reaching up to 6 to 10 times higher than plasma levels. Moreover, paraquat remains retained in lungs even when blood levels start to decrease (Figure 1) (2,4). The fatal pathophysiology in paraquat poisoning has been explained by pulmonary failure following alveolar epithelial cells (type I and II pneumocytes) and bronchiolar Clara cells disruption, hemorrhage, edema, hypoxemia, infiltration of inflammatory cells into the interstitial and alveolar spaces, proliferation of fibroblasts and excessive collagen deposition and sometimes by disseminated intravascular coagulation (3,5).

Easy accessibility of paraquat in some countries including India has resulted in many human exposures, by both unintentional and deliberate self-poisonings (6-10). The majority of paraquat poisoning cases requires immediate treatment and close monitoring in a hospital setting. The management is primarily supportive and directed toward poison removal from gastrointestinal (GI) tract, increased excretion of the poison from blood circulation, as well as therapeutic measures to control pulmonary damages (2,3). In 2008, Dinis-Oliveira et al introduced a treatment flowchart to manage paraquat poisoned patients (3). This flowchart provides a step by step treatment based on the underlying mechanisms of paraquat toxicity. In the present paper, we presented a series of patients who were treated according to this flowchart at a tertiary care hospital in India.

METHODS

This prospective observational study was carried out on paraquat poisoned patients admitted to District Hospital, Chamarajanagar and Shimoga institute of Medical Sciences, Shimoga, Karnataka, India, during January 2013 to December 2014. Patients with concomitant poisoning with other poisons were excluded. paraquat poisoning was confirmed by taking

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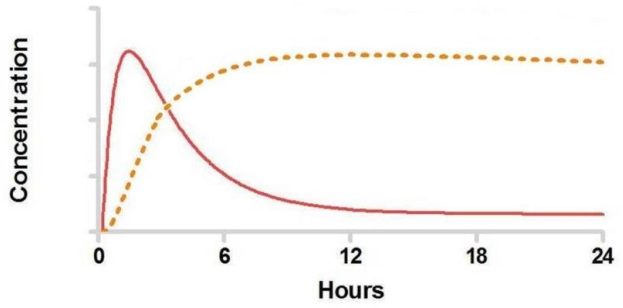

Figure 1. Paraquat concentration in blood and lung after hemodialysis (red line indicates plasma and dotted orange line indicates lung concentration) [Adopted from Gawarammana et al and Pond et al. (2,4)]

history from the patients, as well as clinical and laboratory investigations.

After admission, a urine spot test using alkali and sodium dithionite reagent was performed for all patients. Moreover, 5 mL of venous blood was analyzed for blood urea nitrogen and serum creatinine on patient's admission and subsequently on days 2, 4 and 6 (Totally 4 visits/ measurements). The arterial oxygen saturation level was recorded by using pulse oximeter.

RESULTS

Clinical findings

In this study, 6 patients (4 women and 2 men) with median age of 23 [min-max: 18-42] years were included. The majority of patients had respiratory distress (with an average SpO_2 of 60%), i.e. 4 out of 6 cases manifested with respiratory distress associated with dryness and burning sensation in mouth, throat and chest. Oxygen therapy with mask in one case and by ventilator in rest of cases was required. All cases had fever, nausea, vomiting and dry cough. Except one patient who died on the first day and no further measurement of serum creatinine could be taken from her (case 4), all other patients developed increased creatinine (Table 1). Figure 2 shows the trend of mean serum creatinine of the patients during the 4 visits. Five out of 6 patients died mainly due to pulmonary sequels. In the only survived patient (case 2), gastrointestinal symptoms were predominant followed by acute renal failure and pulmonary congestion which were reverted with medical care indicated in the therapeutic flowchart. His oxygen saturation was at an average of 88%. In cases 4, 5 and 6, severe respiratory distress was predominant rather than renal impairment. The survival period of the deceased cases varied between 8 hours and 6 days.

Post-mortem findings

Five patients who died were referred for post mortem examinations. All of them had mucosal erosion of the upper gastro-intestinal tract. The stomach mucosa was hemorrhagic in all cases. Lungs were congested and edematous which yields foamy exudation on cut section. All organs were congested. Based on histopathological investigations, inflammatory infiltration in lungs was noted in all cases and acute tubular necrosis was seen in 3 cases.

DISCUSSION

Paraquat poisoning predominantly affects the respiratory and renal systems apart from the common gastro-intestinal irritations (3,5). This type of poisoning is associated with high mortality rate despite current treatment approaches (7-10). In the present study, the majority of cases died as a result of uremia due to acute renal failure and hypoxemia due to severe pulmonary damage. Post-mortem findings well correlated with the features of ante-mortem manifestations. The triad of congestion, edema and petechial hemorrhage were visible on the organs in post-mortem investigations. Dinis-Oliveira et al similarly showed presence of alveolar collapse, vascular congestion, enlargement of alveolar walls with leukocyte infiltration, alveolar hemorrhage and fibrin-like deposits within alveolar space in post-mortem lung specimens (11). In addition, they found renal tubular necrosis, interstitial edema, thickening

Table 1. Serial reports of renal function biomarkers, average oxygen saturation and outcomes of patients

Case n.	Age (year)	Gender	BUN ((mg/dL)				SCr (mg/dL)				Average SpO_2 during admission	Circumstances / outcome
			Day 1	Day 2	Day 4	Day 6	Day 1	Day 2	Day 4	Day 6		
1	21	Female	15	80	158	169	1.26	6.3	8.2	9.97	70%	Death on 6th day
2	25	Male	19	48	40	38	0.85	1.33	1.33	1.33	88%	Discharged in good condition
3	24	Female	70	77	80	-	9.13	9.73	9.9	-	57%	Case referred two days post-exposure/ Death on 6th day
4	18	Female	27	-	-	-	0.73	-	-	-	40%	Severe respiratory distress / death on 1st day
5	22	Female	63	-	-	-	1.9	-	-	-	45%	Severe respiratory distress / Death on 1st day
6	42	Male	33	44	-	-	1.1	1.93	-	-	60%	Severe respiratory distress/ Death on 4th day

BUN: Blood Urea Nitrogen, SCr: Serum creatinine, SpO_2: Blood oxygen saturation level

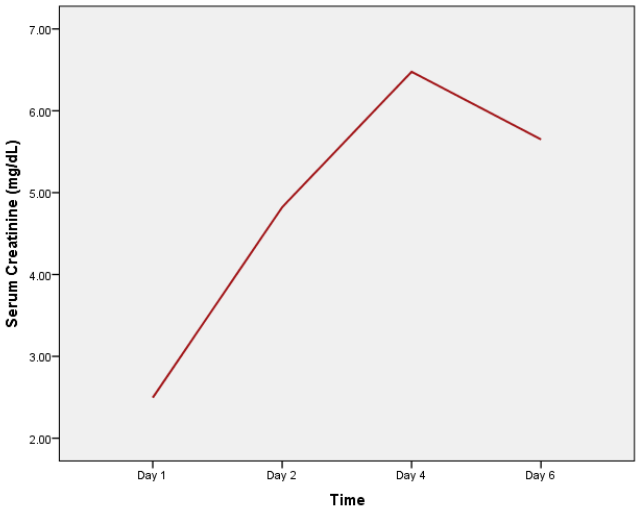

Figure 2. Trend of mean serum creatinine of the patients during the 4 visits

of vascular endothelium and parietal layer of Bowman's capsules, global necrosis of glomeruli and substitution by fibrinoid-like deposits (11).

It has been shown that the concentration of paraquat in lungs is inversely proportional to the concentration in blood after 2-3 hours (2,4). Thus, systemic toxicity demands immediate therapeutic measures to modify the toxokinetics of the poison, to suppress inflammation and to prevent reactive oxygen species generation (2,3,11). In this context, Dinis-Oliveira et al proposed a step by step treatment flowchart. Hemoperfusion, in this flowchart, is to facilitate rapid elimination of poison from blood and prevent subsequent effects. Hong et al ascertained adequate hemoperfusion as an indispensable treatment for patients with acute paraquat poisoning (12). However, we could not perform hemoperfusion for our patients due to limitation in hospital facilities. In addition, anti-inflammatory drugs, which are recommended in Dinis-Oliveira et al's flowchart, may help suppress overt inflammation and prevent consequent tissue damages following paraquat poisoning (3,13). Nonetheless, this may not be the case for patients advanced tissue damages following severe poisonings (13). It seems that once the parenchymal damage of kidney and lung following paraquat toxicity establishes, use of immunosuppressive and anti-inflammatory agents does not yield good results. In our study, 5 out of 6 patients died although they received the recommended medical care (except hemoperfusion) in the flowchart. However, this may not undermine the efficacy of the flowchart as we only studied a limited number of patients whom the majority of them had very severe systemic poisoning and presented late to the hospital. In this study, only one patient who had near to normal arterial oxygen saturation and mild increase in creatinine could survive. The other patients with marked decrease in oxygen saturation and highly increased creatinine died. This is in agreement with many studies which showed poorest prognosis in paraquat poisoned patients with respiratory distress and renal dysfunction (7,9,14).

LIMITATIONS

The small number of patients presented in this article is one of the major limitations of this article. Hemoperfusion was not performed for our patients, although it is indicated in the Dinis-Oliveira et al's treatment flowchart (3).

CONCLUSION

Renal insufficiency and pulmonary damage following severe paraquat poisoning are indicators of poor prognosis and may not be reversible with commonly used treatment approaches.

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