CLINICAL FEATURES AND PROGNOSIS OF PARAQUAT POISONING: A REVIEW OF 27 CASES

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SYNOPSIS

27 patients were admitted into Toa Payoh Hospital after having ingested paraquat. 21 patients died, giving an overall mortality rate of 77%. Of the fatal cases 10 (47%) died within 24 hours from cardio-respiratory collapse. This preceded any other clinical signs of tissue toxicity such as the development of mouth ulcers, liver or renal damage. Survivors of paraquat poisoning showed a decrease in the diffusing capacity and a restrictive pattern on lung function tests. Urine paraquat concentration determination is a simple and reproducible test. When performed within 8 hours of paraquat ingestion ($n = 12$), no one with a urine concentration of 10 mg/100 ml survived ($n = 7$). Conversely, 3 out of 5 patients with a urine concentration $\leq$ 10 mg/100 ml survived ($P < 0.05$, X^2 test with Yates correction). Paraquat ingestion is a serious and lethal form of poisoning. Determination of urinary paraquat concentration early in the course of paraquat poisoning may be helpful in predicting prognosis.

INTRODUCTION

Paraquat is a bis-quarternary compound that was made commercially available in 1962 as a domestic and commercial herbicide. Since the first report of death from paraquat poisoning in 1966 (1) numerous reports in the medical literature have attested to the deadlines of paraquat as a human poison. Paraquat poisoning was seen in Singapore as early as 1969 (2). An earlier paper (3) described three survivors of paraquat poisoning. This paper is a review of the clinical data of 27 patients who had ingested paraquat and examines urine paraquat determination as a prognostication tool.

MATERIALS AND METHODS

Twenty-seven patients admitted to the Toa Payoh Hospital over a nine year period (1976—1984) were included in the study. All the patients had ingested 'gramoxone' a liquid formulation containing 20% paraquet. Twenty-four patients were seen within 34 hours of ingestion. The remaining three were seen after 48 hours, 72 hours and 16 days after ingestion. The age, and sex distribution of the patients are shown in Table 1. Paraquat poisoning was suspected on clinical grounds in all the patients and confirmed by presence of paraquat in body fluids (blood, stomach contents, urine or bile). Serial haemotological and biochemical tests were available as were the X'rays and blood gas analyses.

Urine paraquat concentrations determined by thin layer chromatography were available in 14 patients. All the patients except one who was admitted 16 days after ingestion, were treated with gastric lavage, oral bentonite and magnesium sulphate mixture and forced diuresis. Steroids were administered. Only 2 patients received hypoxic therapy through a respirator delivering 15—19% oxygen.

TABLE 1
PARAQUAT POISONING: AGE, SEX

Age	Male	Female
10—20	3	4
21—30	5	3
31—40	3	2
41—50	3	1
51—60	1	0
Above 61	1	1
Total	16	11

TABLE 2
TIME OF DEATH AFTER INGESTION

Time	No.	Percentage
Less than 24 hours	10	47.6
1 — 7 days	7	33.3
More than 1 week	4	19.0
Total	21	100%

RESULTS

Fatal Cases

Of the 27 patients, 21 died giving a mortality rate of 77%. Slightly less than 50% died within 24 hours; a third died within the first week while one fifth survived beyond one week. The 10 patients that died within 24 hours of ingestion took a mean ingested dose of 17.2 gms. A characteristic clinical picture was noted. The patients appeared well initially, were anicteric with no oral ulcers seen but rapid deterioration with oliguria and cardic-respiratory collapse occurred. Chest X'rays were normal. At post-mortem, pulmonary haemorrhage and oedema was found.

Those that perished within the first seven days of ingestion developed mouth ulcers after 48 hours. None developed jaundice (Table 3) but all had impaired renal function. Chest X-rays showed acute pulmonary oedema. All died from acute respiratory failure. The mean ingested dose was 5 gms.

Those who perished after the first week had mouth ulcers, clinical jaundice and impaired renal junction and progressive respiratory failure (Table 4). The mean ingested dose was 5 gms.

TABLE 3
CLINICAL FEATURES OF FATAL PARAQUAT POISONING (1—7 DAYS)

Patient	Mouth Ulcers	Serum Bilirubin (Normal 0.2—1.4 mg%)	Blood Urea (Normal up 40 mg%)
1	+	1.4	88
2	+	1.4	58
3	+	0.9	58
4	+	0.9	73
5	+	0.1	156
6	+	0.6	86

TABLE 4
CLINICAL FEATURES OF FATAL PARAQUAT POISONING (>1 WEEK)

Patient	Mouth Ulcers	Serum Bilirubin (Normal 0.2—1.4 mg%)	Blood Urea (Normal up 40 mg%)
1	+	3.0	91
2	+	5.2	268
3	+	7.7	452
4	+	3.7	73

Survivors

The clinical data of the six survivors are summarised in Tables 5 and 6. All the patients had mouth ulcers and impaired renal function. Only 1 was jaundiced. Except for 1 patient, all had lung function tests that showed a restrictive ventilatory pattern with a decrease in the diffusing capacity. In one patient, the decrease in diffusing capacity improved over a 48 month period from 30% of the predicted value of 62%. Chest X-rays in 3 patients showed fibrosis. The mean ingested done was 4 gms.

Urine Paraquat Concentration

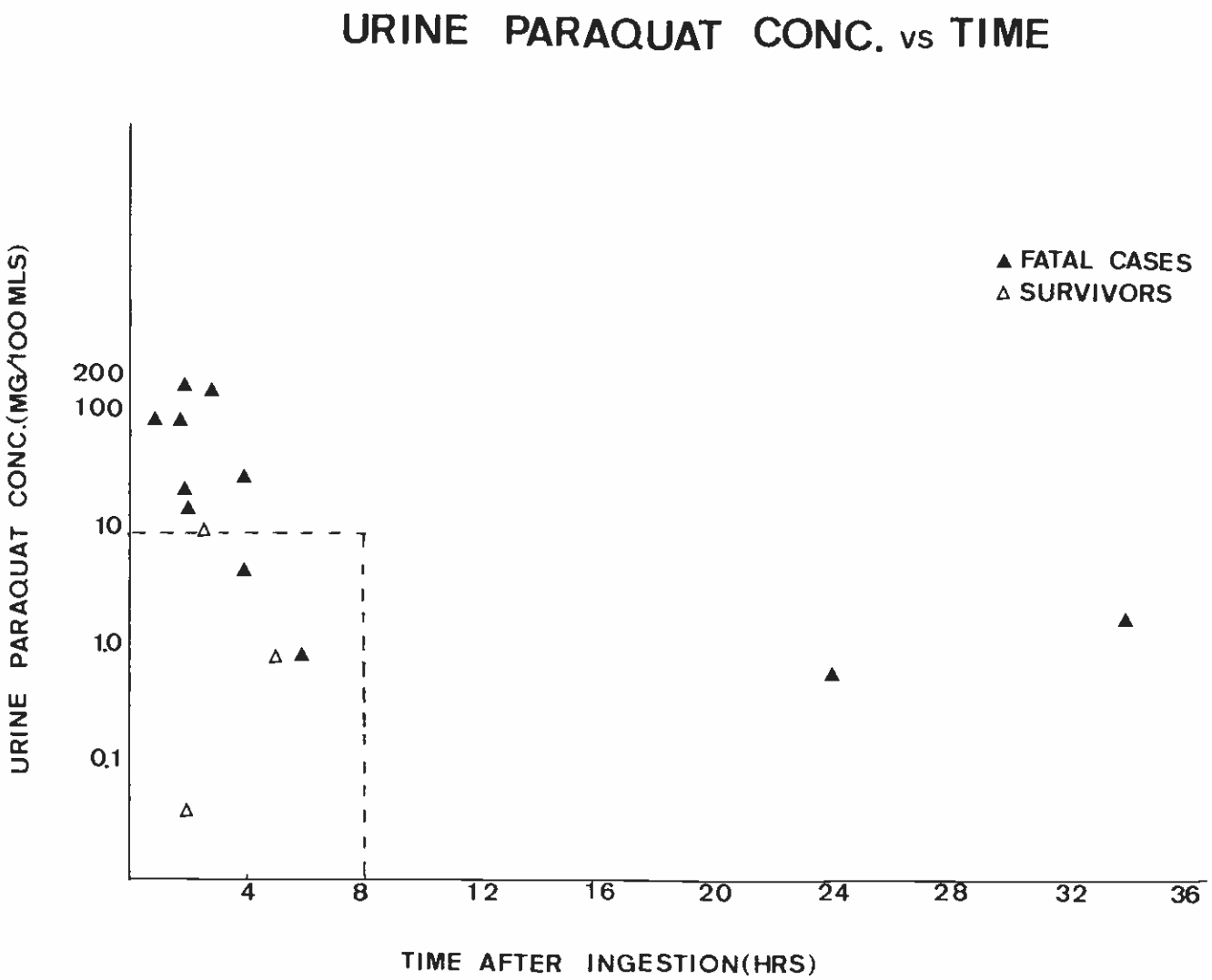
The urine paraquat concentrations were available in 14 patients. This was related to the time after ingestion and outcome and is shown in Figure 1. None of the patients with a urine paraquat concentration of 10 mg/100 ml within 8 hours of ingestion survived (n = 12). Conversely, 3 out of 5 patients with a urine concentration < 10mg/100 ml survived (p 0.005).

TABLE 5
CLINICAL FEATURES OF NON-FATAL PARAQUAT POISONING

Patient	Mouth Ulcers	Serum Bilirubin (Normal 0.2—1.4 mg%)	Blood Urea (Normal up 40 mg%)
1	+	0.5	56
2	+	0.3	72
3	+	5	220
4	+	0.1	30
5	+	1.4	51
6	+	1.8	150

TABLE 6
LUNG FUNCTION TESTS OF NON-FATAL PARAQUAT POISONING

Patient	Vital Capacity (Litres)	FEV_1 (Litres)	Total Lung Capacity (Litres)	Transfer Factor mls/min/mm Hg
1	0.85 (1.95)	2.61 (2.79)	1.17 (2.55)	5.2 (17)
2	2.33 (3.74)	2.7 (3.25)	4.87 (5.29)	15.0 (20.8)
3	2.33 (2.44)	2.04 (2.12)	3.15 (3.67)	6.6 (13.3)
4	2.53 (2.59)	2.46 (2.35)	3.78 (3.67)	13.3 (18.0)
5	1.44 (3.36)	1.48 (2.76)	2.85 (5.29)	7.03 (14.3)



DISCUSSION

Paraquat, used extensively as a herbicide, is an extremely lethal human poison with no known antidote. There is a high mortality rate of 60—70 percent (4,5) associated with paraquat poisoning. The mortality is related to the ingested dose and the formulation ingested. The minimal lethal dose with the liquid formulation containing 20% paraquat (gramoxone) is as little as 10 mls while that of the granular preparation 'Weedol' containing only 2.5% paraquat and 2.5% diquat is 1 sachet or roughly 1.5 gms. Enthusiastic treatment with forced diarrhoea, forced diuresis, haemodialysis, haemoperfusion, hypoxic therapy have not significantly altered the outcome (6,7).

The mortality rate of 77 per cent in this series is somewhat higher than the reported mortality although it must be pointed out that the patients included in the study have taken larger amounts of paraquat. Paraquat commonly affects four major organ systems of the body: lung (8,9) liver, (10) kidney (11) and the upper gastrointestinal tract. Less frequently affected are the myocardium, adrenal (12) and the brain (13). The clinical presentation is determined by the amount ingestted as shown in the present study and three groups could be recognised. Those that died within 24 hours have taken a mean ingested dose of 17.2 gms. Cardio-respiratory failure occurred before ulceration of the upper gastric-intestinal tract, liver and renal damage developed. Those that took 5 gms of paraquat developed mouth ulcers after 24-hours and evidence of hepatic and renal damage were present. Death from acute respiratory failure occurred within the first week. A sub-group of 4 patients died after the first week. Amongst the patients, the survivors ingested the smallest amount of paraquat. They went through an acute phase not unlike that seen in the fatal cases with mouth ulceration, liver and kidney damage, and in three cases, a period of respiratory failure before recovery. On lung function tests, a restrictive ventilatory pattern was found, whilst chest X'ray suggested pulmonary fibrosis. Serial lung function tests showed that there was significant improvement in the diffusing capacity over a 48 month period in one patient. This observation supports an earlier report (14) and seems to suggest that paraquat lung injury may be partially reversible.

It is important to assess the severity of paraquat poisoning for two reasons. Firstly, to allow objective evaluation of new modalities of treatment, such as radiotherapy (15) and lung transplantation (16). Secondly, to avoid unnecessary treatment in minimally poisoned patients. Several ways of assessment have been reported. Fitzgerald et al (5) found that the estimated oral dose could be one way of assessment. Urinary excretion rate of 1 mg/hr or more 8 hours after ingestion has been found to correlate with mortality (17). Proudfoot et al (18) demonstrated that patients with plasma paraquat concentrations less than 2.0, 0.6, 0.3, 0.16 and 0.1 mg/L at 4, 6, 10, 16 and 24 hours respectively are likely to survive. Nevertheless, there have been reports of survival with plasma concentration in excess of these levels (15,19). Using a statistical approach, probability of survival curves relating to plasma paraquat concentration have been compiled (20). The present study has shown that urine paraquat concentration prior to treatment and within 8 hours of ingestion of more than 10 mg/100 mls is not compatible with survival employing the treatment outlined. Survival below this level is not always assured as only 3 out of 5 patients survived. More studies will be required to determine the upper limits of urine paraquat concentration that is compatible with survival.

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