IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 4 Ver. 15 (April. 2018), PP 39-45
www.iosrjournals.org

A Study on the Clinical Outcome of Paraquat Poisoning Cases

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Abstract
Background :
Agricultural poisoning is one of the leading causes of poisoning related Morbidity and Mortality worldwide Paraquet[2]though of the lesser incidence is very important because of its very high mortality. It mainly affects the Kidneys , liver and lung and causes multiorgan failure[3]. Although Kidneys are the most affected the primary cause of death is pulmonary Fibrosis affecting the Lungs.
Aims and Objectives :
To study the clinical outcome of paraquet poisoning in Coimbatore medical college hospital.
Material and methods :
Prospective study
Results and Conclusion: Lack of specific antidote is a significant cause of mortality and morbidity associated with Paraquet poisoning.
Keywords*; Paraquet, poisoning, Acte Kidney Injury, pulmonary Fibrosis.*

Date of Submission: 12-04-2018 Date of acceptance: 30-04-2018

I. Introduction

Poisoning by agricultural chemicals[1] and pesticides is a major public health issue worldwide. It imposes health problem mainly in developing world. There are about 20,000 mortalities & hospitalizations exceeding 2 million due to poisoning by agricultural chemicals and pesticides every year world wide. There were around 3.4lakh number of poisoning cases from agriculture , found in the US during 1985 to 1990.There were nintyseven deaths among those cases. Eventhough grammaxane[1] poisoning resulted only 0.34% of the above cases, it accounted for the higher death rate, causing about 13% of all expired patients.Grammaxane contains 24% paraquat dichloride[1], 1% cocoamineethoxycar, 0.1% silicone defoamer, 0.05% acid blue dye, pyrimidine .Severe grammaxane poisoning leads to multiple-organ failure, kidneys, liver and lungs are commonly involved. Eventhough kidney is the main organ affected in grammaxane poisoning, pulmonary fibrosis associated lung damage is the important factor leading to mortality . Therefore it is an essentiality to have a prompt diagnosis and early initiation of treatment .

II. Methodology

The study is will be undertaken on paraquat poisoning patients in the Coimbatore Medical College and Hospital, Coimbatore during the study period (July 2015 to June 2016). A total of 50 newly detected patients of paraquat poisoning will be included in the study.

The study excludes minors, those with chronic illnesses like renal failure, heart disease, chronic liver disease, chronic pulmonary or airway disease.

Study begins with detailed history taking and clinical examination of paraquat poisoning patients to assess the quantum of poison ingested and system of involvement. All patients were asked about amount of paraquat consumed, time of consumption, time of presentation and intention behind consumption.Their complaints following consumption of poison such as vomiting, abdominal pain, difficulty in swallowing, breathing difficulty, reduced urine output ,yellowish urine etc.All baseline laboratory tests to detect the severity of systemic involvement are to be done. The patients' response to treatment and the outcome with regard to morbidity and mortality is assessed. Cyclophosphamide or steroids will be given to randomly selected patients and their role in preventing pulmonary fibrosis is statiscallyanalysed.

III. Observation And Results

Among the study population most of them were males (male:female – 1.94:1), with the mean age of the patients were 43-34years. The amount of poison ingested were divided into <25mml, 26-50ml, 51-75ml,>75ml. twenty four patient took around 26-50ml of paraquat. Most of the patient admitted in the hospital with in 6 hours of consumption of poison. Out of 50 patients 49 had blood urea above 30mg/dl, 43 had acute kidney injury. Among the study population 86% were developed acute kindey injury. All the patient with acute kidney injury underwent haemodialysis. Out of 43 patients who had undergone hemodialysis 8 needed more than 10 times. Among the study population 22% had respiratory failure and Serum bilirubin was found to be raised in 32% , 66% had elevated SGOT, 16 had raised SGPT level. 18% patients were presented with circulatory failure and shock. Gastro intestinal manifestations were presented as dysphagia, oral ulcer, loose stools, mucositis. Of these oral ulcers accounting for 42%.Multiorgan dysfunction syndrome was seen among 36% of patients.

BASELINE CHARECTERISTICS	
NUMBER OF PATIENTS	50
MALE:FEMALE RATIO	1.94:1
MEAN AGE	43.34 YRS
AMOUNT OF PARAQUAT INGESTED	
<25 ML	7
26-50 ML	24
51-75 ML	14
>75 ML	5
DURATION OF INGESTION TO ADMISSION	
<6 HRS	33
6-12 HRS	14
> 12 HRS	3
RENAL PARAMETER	
MEAN BLOOD UREA	101.62
MEAN SERUM CREATININE	3.06
AVERAGE DIALYSIS REQUIRED	6.78 TIMES
HEPATIC INVOLVEMENT	17
DIGESTIVE TRACT INVOLVEMENT	12
RESPIRATORY FAILURE-FIBROSIS	11
CIRCULATORY FAILURE	9
MULTI ORGAN DYSFUNCTION	18

Table 1 showing basic characteristic among the study population

Among study population 28 patients were randomly selected and administered both steroids and cyclophosphamide.

PROGNOSIS	
RECOVERED	19
DEATH	31
< 5 DAYS	6
5-10 DAYS	15
>10 DAYS	10
AVERAGE TIME OF DEATH AFTER INGESTION	9.06 DAYS
CAUSE OF DEATH	
RESPIRATORY FAILURE	5
ACUTE RENAL FAILURE	9
SHOCK	2
MULTIORGAN DYSFUNCTION	15

Table 2 showing the outcome of the patients.

Out of 50 patients 31 died and the mortality rate is 62%, among those who died out of poisoning 48.4% had acute renal failure . most of the deaths were happened in the second week of ingestion (48.4%).
Among the study population who treated with cyclophosphamide 28 patients only 3 patients developed pulmonary fibrosis, Out of 28 patients who received steroids only 3 developed respiratory failure

FIBROSIS	CYCLOPHOSPHAMIDE	
	GIVEN	NOT GIVEN
ABSENT	25	14
PRESENT	3	8
P VALUE	0.03	
SIGNIFICANT	SIGNIFICANT	

Table 3 showing correlation of absence of fibrosis on treatment with cyclophosphamide.

FIBROSIS	STEROIDS	
	GIVEN	NOT GIVEN
ABSENT	25	14
PRESENT	3	8
P VALUE	0.03	
SIGNIFICANT	SIGNIFICANT	

Table 4 showing correlation of absence of fibrosis on treatment with steroids.

Correlation of all parameters between alive and dead using chi square method, mannwhitney u test.

	MEAN AGE(IN YRS)
ALIVE	39.95
DEAD	45.52
P VALUE	0.143
SIGNIFICANCE	NOT SIGNIFICANT

Table 5 showing Correlation between age of patients and mortality.

The amount of paraquat ingested is found to be more in patients who died than those survived

	MEAN AMOUNT OF PARAQUAT(IN ML)
ALIVE	32.37
DEAD	61.94
P VALUE	0.001
SIGNIFICANCE	SIGNIFICANT

Table 6 showing Correlation between mortality and amount of paraquat ingestion.

It is found that patients who died had undergone more number of dialysis

	MEAN NO OF TIME OF DIALYSIS
ALIVE	4.75
DEAD	7.84
P VALUE	0.003
SIGNIFICANCE	SIGNIFICANT

Table 6 showing correlation between mean time of dialysis and mortality.

The mean creatinine level in patients who died is found to be higher than those who survived

	MEAN CREATININE
ALIVE	2.421
DEAD	3.465
P VALUE	0.003
SIGNIFICANCE	SIGNIFICANT

Table 7 showing correlation between serum creatinine and mortality

Among the study population mean SGPT level is found to be higher in those who died than survived.

	MEAN SGPT
ALIVE	36.74
DEAD	73.97
P VALUE	0.002
SIGNIFICANCE	SIGNIFICANT

Table 8 showing correlation between mean SGPT and mortality

There is no correlation found between time lag for admission and mortality in the study

PROGNOSIS	TIME INTERVAL-INGESTION TO ADMISSION		
	< 6 HRS	6-12 HRS	> 12 HRS
DEAD	20	8	3
ALIVE	13	6	0
P VALUE	0.367		
SIGNIFICANCE	NON SIGNIFICANT		

Table 9 showing Correlation between time lag for admission and mortality is insignificant

Among those who died all patients had acute kidney injury

PROGNOSIS	ARF	
	PRESENT	ABSENT
DEAD	31	0
ALIVE	12	7
P VALUE	0.001	
SIGNIFICANCE	SIGNIFICANT	

Table 10 showing Correlation between acute kidney injury and mortality

Out of 31 patients who died 17 had hepatic involvement .

PROGNOSIS	HEPATIC INVOLVEMENT	
	PRESENT	ABSENT
DEAD	17	14
ALIVE	0	19
P VALUE	0.001	
SIGNIFICANCE	SIGNIFICANT	

Table 11 showing correlation between hepatic involvement and mortality is found to be significant.

Among those who died 18 had multi organ failure and there is significant correlation between MODS and mortality.

PROGNOSIS	MODS	
	PRESENT	ABSENT
DEAD	18	13
ALIVE	0	19
P VALUE	0.001	
SIGNIFICANCE	SIGNIFICANT	

Table 12 showing correlation between multi organ failure and mortality is significant.

IV. Discussion

Paraquat (1,1'-dimethyl 4,4'-bipyridylium dichloride) is a widely available herbicide used in agriculture . Around 40 to 50 cases of poisoning are reported every year in Coimbatore medical college. There is no adequate data or study report on paraquat poisoning in south India. Paraquat poisoning is associated with severe multi organ dysfunction[9] and high mortality. The aim of the study was to analyse the clinical symptoms, signs and outcome of paraquat poisoning cases admitted in Coimbatore medical college.

This is a prospective study including 50 cases of paraquat poisoning hospitalized during the period of July 2015 to June 2016.all the patients admitted to emergency department is given stomach wash followed by activated charcoal. the amount of poison consumed was assessed by taking one mouthful as 30ml. The time of consumption and delay in admission to hospital was also noted.

Most of the patients were above 50 years of age. There was significant correlation between age of patient and outcome ie. mortality rate is more in older age group than others. Out of total study population 66% were males and 34% were females. But there was no significant correlation between sex category and outcome in the study. About 48% of the patients had consumed 26-50ml of paraquat. Most of the victims had presented within 6hours of consumption and there is no direct relation between delay in hospitalization and mortality. That may be because those who had consumed large amount of poison is more likely to get admitted early.

Among the study population 86% had acute kidney injury which is diagnosed as those with serum creatinine above 2mg% and all of them had undergone hemodialysis[16]. Out of which 18.6% had hemodialysis more than ten times. Out of the 43 patients who developed acute kidney injury 12 survived with hemodialysis and supportive measures.

The whole study population was presented with intentional ingestion of paraquat and there was no dermal exposure. The overall mortality was 62% and multiorgan failure was the most important cause for mortality in the study. The other significant predictor of mortality was the development of respiratory failure. Patients who had low arterial oxygen saturation and those who required ventillatory support were included in this category. Oxygen supplementation[5] was restricted to patients with FiO2 less than 50 as there are previous studies showing controversy in the use of oxygen to paraquat intoxicated patients. It is to prevent free radical injury oxygenation is restricted to a certain level. Though respiratory failure is anticipated in late stages of intoxication as per other studies 22% of our study population developed features of respiratory distress during hospital stay. It is associated with 100% mortality.

Among the study population only 18% had circulatory failure ie. systolic blood pressure less than 100mmHg .Those patients were managed with intravenous fluids and ionotropes, but was found to cause 100% mortality in this study. Gastrointestinal manifestations[15] were also a feature of paraquat poisoning found in 24% of the study population. This may present as painful swallowing, vomiting, oral ulcers or burning erythematous oral mucosa. In this study 42% of the patients had oral ulcers. Such cases were treated symptomatically. It has less association with mortality following paraquat intoxication. Toxin induced hepatitis[12] was found in 34% of the study population. The total bilirubin and transaminases were elevated. Other causes of hepatitis like viral infections and alcoholism were ruled out in such cases. They were treated symptomatically with hepato protective medications. Compared to other system involvement hepatic involvement poses less risk for significant morbidity or mortality.

Among the study population 36% had multiorgan failure which was an important predictor of mortality .There was 100% mortality in those patients and in most cases respiratory or circulatory failure associated with acute kidney injury predicted the outcome.

The use of steroids and cyclophosphamide[6] in paraquat poisoning to prevent pulmonary fibrosis is still controversial .In this study we have randomly selected paraquat intoxicated patients and were given dexamethasone(5 mg every 6hourly) and cyclophosphamide(2 mg/kg per day) for 14 days. it was found that the pulse therapy with steroid and cyclophosphamide[13] has significant role in preventing respiratory failure[11]

with a p value of 0.03.The antiflammatory[3] action of those two drugs could prevent the retard the development of pulmonary fibrosis. The statistical methods used in the study were chi square test mannwhitney u test , unpaired t test and anova.

We noticed some limitations in our study .we could not measure the serum level of paraquat. since this is a prospective study confined to hospitalized patients the future of patients who get discharged could not be assessed. several studies have already been proven the possibility of delayed onset pulmonary fibrosis[8] leading to mortality which may happen a few months after intoxication .The main issue is that there is no specific antidote for this dangerous toxin. More effective scientific research is needed in this regard. Many countries like Canada have banned paraquat due to its potential to cause mortality even at low doses. Even then it is widely available in our country as herbicide .It would have been a worth decision if government could restrict the use of paraquat. Educating the public and health care professionals regarding the toxic effects of paraquat helps to prevent many cases of accidental exposure and further complications.

V. Summary

The study population was 50 with male sex predeliction. all patients were given first aid immediately after admission with stomach wash adsorbant and supportive measures. Those with comorbidities especially hepatic, cardiac and pulmonary disease were excluded from the study. The morbidity and mortality is determined mainly by the quantum of poison ingested, age of the person and comorbidities .the mortality rate was 62%.the most important cause being multisystem failure closely followed by acute kidney injury, respiratory and circulatory failure. Among the total cases 86% developed renal failure and underwent hemodialysis. Hemodialysis could revive 12 patients. Circulatory failure was the complication in 18% cases and respiratory failure in 22% cases. Both were managed symptomatically and with supportive measures including mechanical ventilation .there was 100% mortality in both the scenario. The case fatality is found to be very high despite the availability of newer modalities of inpatient treatment.

Dexamethasone and cyclophosphamide pulse therapy was given to randomly selected patients and their role in preventing respiratory distress is assessed. There is significant correlation found between the treatment and prevention of respiratory failure.

The gastrointestinal and hepatic involvement were seen in 24% and 34% of the study population respectively. This was not complicating the clinical picture to the extent of mortality unlike other system failure. There is no antidote for paraquat and symptomatic treatment is the only possible mode of therapy. Early admission ,immediate treatment and careful monitoring of all patients anticipating all the complications so as to provide necessary interventions is that could do as health care professionals. Furthur studies are needed to find out specific antidote for paraquat.

VI. Conclusion

Paraquat is a double edged weapon which is being used as a weedicide and misused as most potent poison. The lack of specific medicine for detoxification of paraquat is the main issue behind managing the intoxication. There are not much studies in this regard. Since the basic pathology causing tissue injury is freeradical production, anti-inflammatory drugs play a significant role in limiting the progression of tissue damage. Still, the case fatality rate is very high in patients with both accidental orintensional exposure to paraquat.

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Maniappan "A Study on the Clinical Outcome of Paraquat Poisoning Cases."IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 4, 2018, pp 39-45.