Research Paper

Volume : 4 | Issue : 7 | July 2015 • ISSN No 2277 - 8179

A Study on the Effectiveness of Therapy with Different Doses of Pralidoxime in Acute Organophosphorus Poisoning

Medical Science

KEYWORDS : OP, AChE, PAM, WHO, MG, GM, KG,ICU, EEG, ACTH, ECG, ATP, ARDS,RCT, IV, No., CNS, RS, CVS,PA

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ABSTRACT

Background: *Organophosphorous (OP) compound poisoning is a major health problem not only in the developing countries but also in western countries. OP compounds are easily available as insecticides in shops and have resulted in a gradual increase in suicidal & accidental poisoning.*

The diagnosis is based on the history of exposure and features of cholinergic overactivity. Standard treatment includes attempts to reduce OP absorption with gastric lavage and/ or activated charcoal, plus administration of atropine and oximes to counter the cholinergic effects of the pesticide. Although the use of high doses of atropine is well established, the use of oximes is more controversial. Pralidoxime is the oxime most often used worldwide.

Objective: *In this study we aim to evaluate the efficacy and outcome with different dosages of pralidoxime.*

Study design: *Fifty (50) patients presenting to the emergency department of BGS Apollo hospital, Mysore, between April 2008 to March 2009 with acute organophosphorus compound poisoning were included in the study. All the patients received a bolus dose of 2gm pralidoxime in the emergency room after emergency treatment using a standard protocol, following which patients were randomized into 3 categories depending on the dose of pralidoxime they received, into 250mg, 500mg and 1000mg(1gm) categories.*

The three groups were evaluated for the parameters and appropriate analysis was done.

Various kinds of poisons were encountered in current study, of which Roger was the most common.

Results: *This study concluded that Dosage of Pralidoxime does not have any significance in patients with organophosphorous compound poisoning with respect to the outcome parameters like Need for Intubation, Duration of Ventillation and Mortality. Also development of Intermediary syndrome is more common with higher dosage of Pralidoxime. Patients receiving high dosage of pralidoxime require longer intensive care management as compared to those receiving low dose of pralidoxime. Development of Respiratory distress does not have any direct correlation with dosage of pralidoxime.*

INTRODUCTION

Organophosphorous (OP)compound poisoning is a major health problem not only in developing countries but also in western countries.[1] Hospital based statistics suggest that nearly half of the admissions to emergency with acute poisoning are due to Organophosphorous compound poisoning.[2] OP compound poisonings are found to be a leading cause of death in agricultural countries globally.[3,4]

These were first discovered more than 100 years ago are at present the predominant group of insecticides employed globally for pest control.[5]

OP compounds poisoning affects globally approximately 3 million population and causes 2,00,000 deaths annually, most of these occur in developing countries.[6]

OP compounds are easily available as insecticides in shops and have resulted in a gradual increase in suicidal & accidental poisoning. Nearly 90% of the poisoning are suicidal with a fatality rate of >10%. 8-10% accidental and <1% homicidal. Occupational exposure accounts for 1/5th of accidental poisoning with fatalities of <1%.[7]

OP compounds are the organic derivatives of phosphorous containing acids. The phosphonate, which are organic derivatives of phosphoric acid are not used as insecticides but are used as chemical warfare agents.

OP compounds combine with esteratic sites of acetyl cholinesterase, that is phosphorylated & phosphorylated esteratic sites undergo hydrolysis. The phosphorylated enzyme is inactive and thus unable to hydrolyze acetylcholine. The biological effects of organophosphorous compound are as a result of accumulation of endogenous acetylcholine at sites of cholinergic transmission. This causes disruption of transmission of nerve impulses in both peripheral & central nervous system.

Most organophosphorous compounds are readily absorbed through respiratory, oral mucous membrane, GIT mucous and through intact skin, as they are lipid soluble. This binding is irreversible, except with early pharmacological intervention.[8]

The diagnosis is based on the history of exposure and features of cholinergic overactivity.[9] Standard treatment includes attempts to reduce OP absorption with gastric lavage and/ or activated charcoal, plus administration of atropine and oximes ot counter the cholinergic effects of the pesticide.[11,12,13] Although the use of high doses of atropine is well established, the use of oximes is more controversial.

Oximes reactivate AChE by removing the phosphoryl group. Pralidoxime is the oxime most often used worldwide and occurs in two common forms: the chloride (2-PAM; molecular weight 173; used worldwide) and the mesylate.[14] The great majority of its effects are on the peripheral nervous system, since its lipid solubility is low and its entry into the CNS limited. The main therapeutic effect of pralidoxime is predicted to be the recovery of neuromuscular transmission at nicotinic synapses. Although oximes should be given as soon as possible before ageing occurs, a beneficial response as long as 24 hours after exposure has been reported.[15] Oximes are believed to be effective and to be especially useful in treating moderate or severe OP poisoning. Oximes may also reverse the CNS effects of OP.[16]

Current WHO guidelines recommend giving a 30mg/kg loading dose of pralidoxime over 10-20 minutes followed by a continuous infusion of 8-10/kg/h until clinical recovery or seven days have elapsed, whichever is later.[10,12]

In this study we aim to evaluate the efficacy and outcome with different dosages of pralidoxime.

MATERIALS AND METHODS

Fifty (50) patients presenting to the emergency department of

BGS Apollo hospitalMysore between April 2008 to March 2009 with acute organophosphorus compound poisoning were included in the study. The patients having concomitant chronic lung disease were excluded from the study. A consent was obtained from all the patients or the nearest relative for participating in the study and hospital ethical committee clearance was obtained. Emergency treatment was done according to the standard protocol, which included decontamination, gastric lavage and atropine administration. All the patients received a bolus dose of 2gm pralidoxime in the emergency room, following which patients were randomized into 3 categories of pralidoxime dose they received 250mg, 500mg and 1000mg(1gm) categories.

Daily monitoring was done for development of atropinisation (increase in heart rate,pupil dilatation,decrease bronchorrhoea, increase in temperature ,psychosis etc)

The outcome was evaluated using the following parameter: Need for the ventilation Duration of ventilation Duration of ICU stay Development of intermediary syndrome Any other complications Mortality The three groups were evaluated for the parameters and appropriate analysis was done.

OBSERVATIONS AND RESULT

The study involved 50 patients with organophosphorus poisoning admitted to Apollo BSG Hospital from April 2008-March 2009.

Age distribution:

There were 50 patients included in the study.Age of the patients included in this study varied from 11-50 yrs.The mean age was 35yrs.The lowest incidence was noted in the age group of 11-20yrs,highest incidence was noted in the age group of 31-40 yrs.(TABLE NO 1)(FIGURE 1)Majority of the patients in this study were young adults in the age group of 21-30 years (22), and 31-40 years (23).

2.Gender Distribution:

Of the total 50 patients, majority were male (40), as compared to Female (10) (TABLE NO 2)(FIGURE NO 2)

3.Number of Patients in each category of pralidoxime test group:

There were 19 patients in 250mg of pralidoxime category, 25 in 500mg of pralidoxime and 06 patients in 1000mg category of pralidoxime.(TABLE NO 3)(FIGURE NO 3)

4.Nature of poison:

Various kinds of poisons were encountered in current study, of which Roger was the most common poison with 28 cases. In 15 cases poison was unknown. There were 3 cases of Metacid poisoning, and 1 each of chlorpyriphos, super killer, shikari and Hamla.(table no 4)(figure no 4)

5.Presenting Symptom

The patients presented to the emergency department with one of the three symptoms which included vomiting, unconsciousness and drowsiness.(table no 5)(figure no 5)

Vomiting was the most common presenting symptom which was 78.9%, followed by unconsciousness which was 5.3% and drowsiness which was 15.8%,and unconsciousness 5.3%.

6.Need for Intubation:

Total of 12 patients out of 50 patients (24%) required intubation. 3 (15.79%) patients in 250mg and 3 (50%) in 1gm category were intubated, and 6 (24%) were intubated in 500mg category.(table no 6)(figure no 6)

7.Duration of Ventillation:

Average number of days on ventilation in each category was evaluated.Mean, Std deviation, Std error, F and P values were calculated, Duration of ventilation of patients who required intubation and ventilation .N represents total patients in each group. (table no 7)(figure no 7)

Result: The F value for duration of ventilation was 0.761, and P value was 0.495, which is not significant , using Oneway Anova.

8.Duration of ICU stay:

Duration of ICU stay was analysed using oneway Anova test.N indicates the number of patients.The mean value for the number patients with 250mg of PAM was 2.7368 -/+ 1.9 days , 500mg of PAM was 3+/-2.0 days and 1gm of PAM was 5.8333 +/- 3.98 days. (table no 8)(figure no 8) Anova was applied to ICU days, and f value and p value were calculated.F value was 4.516 and p value was 0.016, this was found to be significant.

9.Intermediary syndrome:

3(6%) patients in total developed intermediary syndrome. This included 1(4%) patient in 500mg category and 2(33.3%) in 1gm category. No patient in 250 mg category developed intermediary syndrome.(table no 9)(figure no9)

Result:The significance was calculated using Contingency coefficient, which was 0.009 which is found to be significant.

10.Respiratory distress:

Total 15 patients developed respiratory distress, out of which 3(15.8%) were in 250mg category, 8(32%) in 500mg and 4(66.7%) in 1gm category respectively.(table no 10)(table no 10)

The Contingency coefficient was 0.320 and p value 0.057 which was not statistically significant.

11.Mortality:

There were 5(10%) deaths in total. 1(5.3%) patient died in 250mg category, and 2 each in 500mg and 1gm category(8% and 33.3% respectively). 5 patients went against medical advised and hence the outcome of these patients could not be traced.(table no 11) (figure no 11)

Contingency coefficient for mortality was 0.273 and p value is .164 which was not statistically significant

12.Other Complications:

Other complications which were noticed in this study were Renal failure and cardiac arrest.(table no 12)(figure no 12)

Results: one patient developed renal failure who was in 500mg category. 3 patients in total developed cardiac arrest, out of which 2 were in 500mg category and 1 in 1gm category.

DISCUSSION

Acute organophosphorous poisoning is one of the most frequent poisonings encountered in our institute.

Among the 50 cases studied, majority of the patients were in the age group of 21-30 and 31-40 years (44% and 46% respectively), which correlate with the study done by Sungur M and Guven M[16]. In the current study, 80% of the patients were male. This correlates with the findings of previous studies. However in the series of Sungur M and Guven M[16] majority of the patients were female (53%).

Vomiting was the most common presenting symptom in our series (80%). This correlates with the study of Goel et al[17], in which vomiting was the presenting symptom in 97.08% of the patients. Vomiting was probably due to chemical gastritis.

In this study, total of 12 patients required intubation. 3 patients in 250mg and 1gm category were intubated, and 6 were intu-

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bated in 500mg category. The p value for this was 0.232, which is not significant. This differs with the studies published. In the series of Johnson S et al[18], higher requirment of intubation was observed in high dose group (p=0.09). In contrast, Pawar KS et al[19] found a less need for intubation in high-dose pralidoxime regimen (P=0.0001).

But study of Peter J V et al[73] found no statistically significant association of oxime therapy with ventilatory requirements (risk difference 0.16, 95% confidence interval -0.07 to 0.38). This correlates with our findings.

For the duration of ventilation, no statistical significance was found in current study (F =0.761, P =0.495). This result is similar to that obtained by Peter JV et al[20]. In contrast, Pawar KS et al[19] found that patients receiving low dose pralidoxime required ventilatory support for longer.

Regarding Intermediary syndrome in this study, patients in 250mg category fared better with no case developing intermediary syndrome. 3(6%) patients in total developed intermediary syndrome. This included 1(4%) patient in 500mg category and 2(33.3%) in 1gm category. .Contingency coefficient, was 0.009 which is found to be significant. Similar results were obtained by Johnson S et al[18] who observed higher prevalence of intermediate syndrome (p=0.08) in high dose group. Whereas Peter JV et al[20] found no statistically significant association for the incidence of intermediate syndrome (risk difference 0.16, 95% confidence interval -0.12 to 0.45).

The duration of stay in ICU varied between the three groups, with patients in 1gm category requiring longer stay in ICU(Mean: 5.8333), as compared to those in 250mg category(Mean:2.7368) and 500mg category(Mean:3). The F value was 4.516 and p value was 0.016, this was found to be significant. This correlates with the literature[20,21].

In the current study, there were 5(10%) deaths in total. 1(5.3%) patient died in 250mg category, and 2 each in 500mg and 1gm category (8% and 33.3% respectively).Contingency coefficient for mortality was 0.273 and p value is .164 which was not statistically significant. Most of the studies in the literature support this finding[23,22,20]. But the study of Peter JV, Cherian AM[1] found higher mortality rate with high dose pralidoxime. In contrast, Pawar KS et al[19] found that high-dose regimen of pralidoxime reduces mortality.

One major limitation of our study was that, the sample size in patients receiving 1gm pralidoxime was small (n=06), and hence the statistical comparison with the two groups was inadequate.

Secondly, 5 patients went against medical advised, out of which 4 were in 500mg category and 1 patient from 250mg category, and hence the outcome of these patients could not be traced.

TABLES AND FIGURES

Table no 1 : Age distribution of the patients admitted with OP poisoning

Age group(in years)	Number
11-20	02
21-30	22
31-40	23
41-50	03

Figure 1 –Graph showing the age distribution of the patients

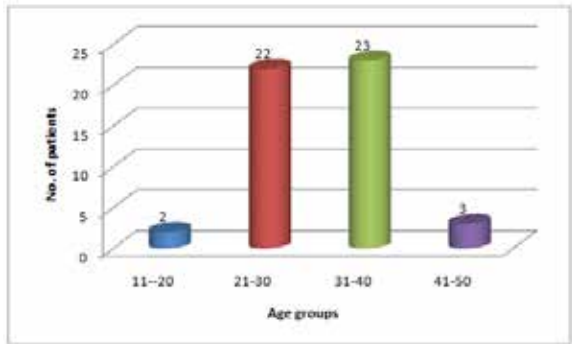

Table -2 : Gender distribution of the patients admitted with OP poisoning

Gender	Number
Male	40
Female	10

Figure 2-Graph showing the gender distribution of the patients

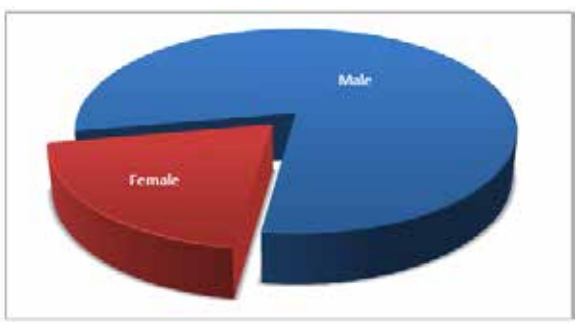

Table – 3: Showing total no of patients in each category

Dose of P2AM	Number of Patients
250mg	19
500mg	25
1000mg	06

Figure 3-Graph showing the number of patients in each category

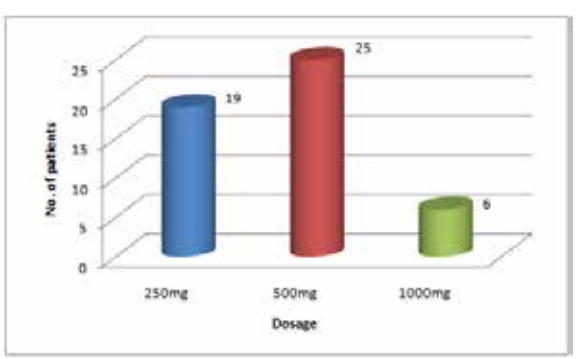

Table-4 : Showing nature of poison in each category

Poison	250mg	500mg	1Gm
Chlorpyriphos	1	0	0
Cypermethrin	1	0	0
Unknown	6	8	1
Dimethoate	11	14	3
Methl Parathion	0	1	2
Delta Methlyn+Trizophos	0	1	0
Chlorpyriphos+Cypermethrin	0	1	0

Figure 4-Graph showing the nature of poison in patients in each category

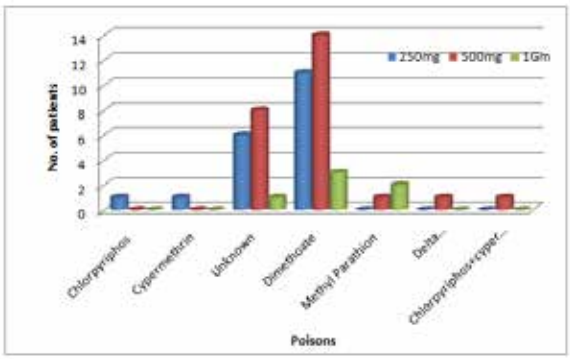

Table-5 : showing symptom wise distribution in each category

	250mg	500mg	1gm	Percentage
Vomiting	15	23	02	78.9%
Unconsciousness	1	1	1	5.3%
Drowsiness	3	1	3	15.8%

Figure 5-graph showing the symptoms wise distribution in each category of pralidoxime.

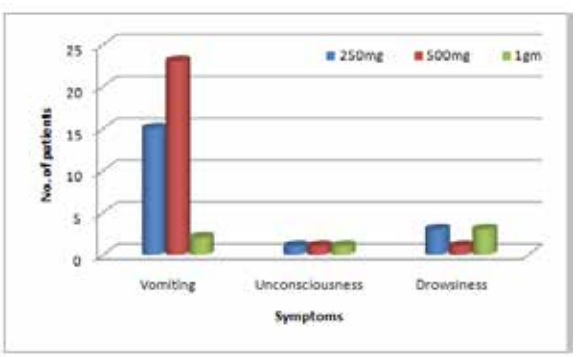

Table – 6: showing no of patients requiring intubation in each category

	Total number of Patients	Total no of patients intubated	Total no of patients not intubated	P value	cc
250mg	19	03 (15.19)	16	.232(ns)	.235
500mg	25	06 (24%0	19		
1gm	06	03 (50%)	03		
Total	50	12 (24%)	38		

Figure - 6 : showing distribution of patients requiring intubation

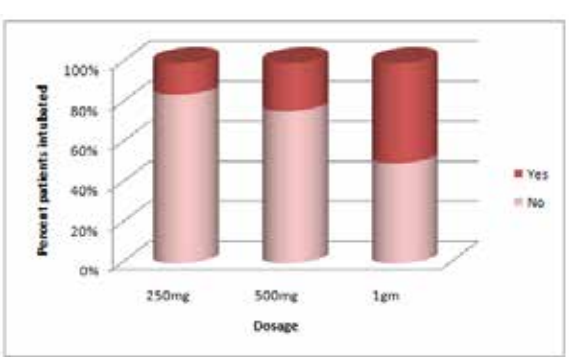

Table – 7 : Analysis of no of patients for Duration of Ventilation among the intubated patients

	N	Mean	Std Deviation	Std error	F	P
250mg	3	4.3333	1.52753	.88192	.761	.492(ns)
500mg	6	3.3333	2.33809	.95452		
1Gm	3	5.1538	2.98608	1.49304		
TOTAL	12	4.1538	2.37508	.65873		

Figure– 7 : Graph showing Duration of Ventillation in each category in days Figure– 7 : Graph showing Duration of Ventillation in each category in days

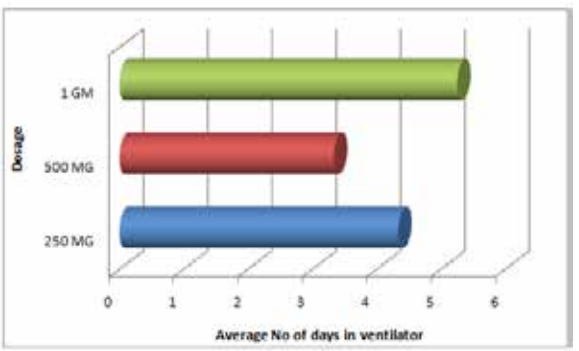

Table – 8 : Showing duration of ICU stay:

Dose	Mean days	Std deviation	F	Sig.
250mg	2.7368	1.91027	4.516	.016
500mg	3	2.02073		
1Gm	5.8333	3.97073		

Figure– 8 : Graph showing Duration of ICU stay in each category

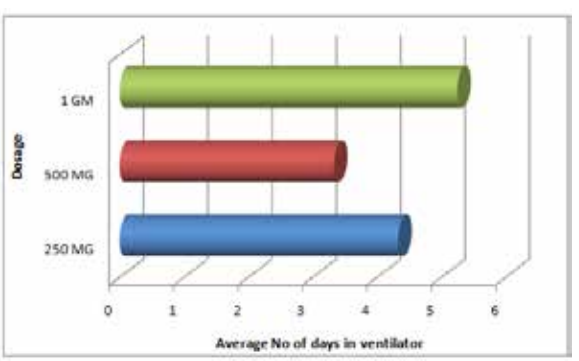

Table – 9 : Showing distribution of patients with intermediary syndrome

	250mg	500mg	1gm	Contingency coefficient	Pvalue
No	19	24	04	0.397	.009
Yes	00	01	02		

Figure – 9 : Graph showing ddistribution of patients with intermediary syndrome

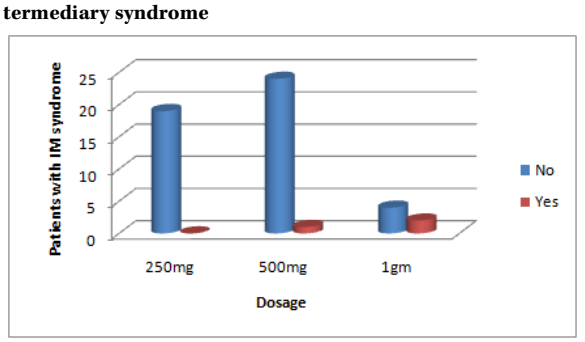

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Table – 10 : Showing distribution of patients with Respiratory distress

	250mg	500mg	1gm	Contingency coefficient	P value
No	16	17	02	0.320	.057
Yes	03	08	04		

Figure - 10 : Graph showing distribution patients with Respiratory distress

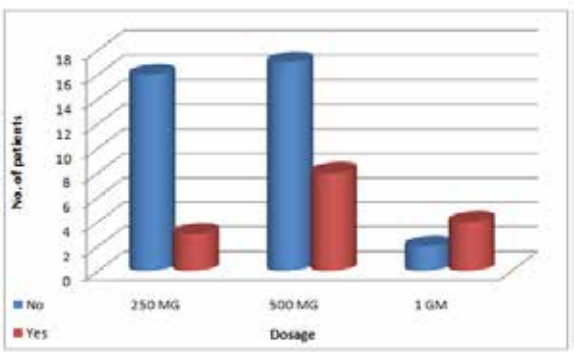


Table – 11 : Showing distribution of Mortality

	250mg	500mg	1gm	Contingency coefficient	P value
No	17	19	04	0.273	.164
Yes	01	02	02		

Figure- 11 : Graph showing mortality distribution

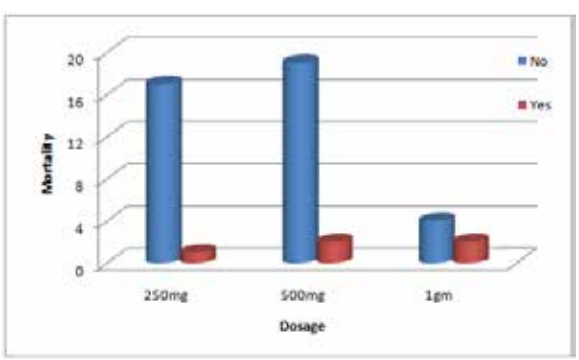
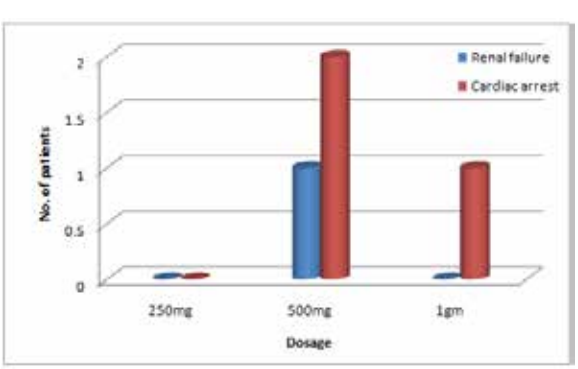
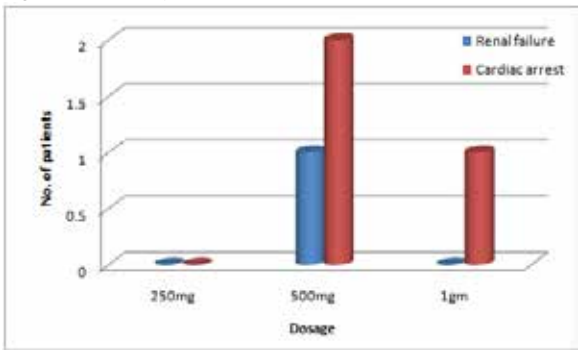


Table – 12 : Analysis of Compilcation



Dosage of P2AM	Renal failure	Cardiac arrest
250mg	0	0
500mg	1	2
1gm	0	1

Figure -12 : Analysis of Complication



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