

Effects of Early N-Acetyl Cysteine in the Management of Rodenticide Consumption: A Prospective Study**Namburu Sindhura¹, Koniki Priyanka², P Tabitha R J Chandrika³, Siva Sankar Annangi^{4*}, Srinivasula Sri Ranga Pravallika⁵**^{1,2}Assistant Professor, Department of General Medicine, Guntur Medical College, Guntur³Associate Professor, Department of General Medicine, Guntur Medical College, Guntur⁴Assistant Professor, Department of Cardiology, Guntur Medical College, Guntur⁵Senior Resident, Department of General Medicine, Guntur Medical College, Guntur

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Abstract:**Background:** A poison is a substance that is capable of causing illness or harm to a living organism on contact or upon introduction to the body. Rat poisons (Ratol) paste contains yellow phosphorus also called as Rodenticides. There is no antidote for rodenticide poison, and consumption is often fatal. The Role of N acetyl cysteine (NAC) in acetaminophen induced ALF is well established.**Aim and Objectives:** To find out the outcome of patients treated with NAC in rodenticide poisoning admitted in rural tertiary care hospital.**Material and Method:** This was the Hospital based prospective observational study, conducted on patients with consumption of Rodenticide poisoning, during period from May 2021 to December 2022 (18 months), at one of Tertiary care hospital - Guntur Medical College, Guntur. In the study we have included 100 patients, selected by using simple random sampling method admitted for rodenticide poisoning in the hospital after following inclusion and exclusion criteria.**Results:** Mean age of the study population was found to be 37.6 ± 12.45 years and maximum patients were lying in the age group of 31-40 years. 83% of cases were found to be Suicidal followed by accidental. mean duration of Hospitalization was found to be 6.42 ± 4.12 days. There was statistical significant difference between proportion of survival and non-survival due to treatment of NAC (P-value=0.0007).**Conclusion:** Early use of NAC which is inexpensive and relatively safe among rodenticide poisoning, patients shows significant impact on the recovery of the patients. Mortality rate was found low among the patients treated before 12 hours with NAC.**Keywords:** N acetylcysteine, Rat poisons, Rodenticides, Yellow phosphorus etc.

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Introduction

A poison is a substance that is capable of causing illness or harm to a living organism on contact or upon introduction to the body. Poisoning is a significant global public health problem. Rat poisons (Ratol) paste contains yellow phosphorus (White phosphorus with its impurities is called yellow phosphorus), also called as Rodenticides, and also rat poisons are heterogeneous cluster of compounds, that are used for agricultural and domiciliary purposes, account for one amongst the frequent varieties of poisoning in India.

India being a primarily rural country, rodenticides are widely used. They're offered in varied forms like powders, pastes, baits, or blocks. A perfect rodenticide is one that's extremely toxicant to rodents in little quantities, nontoxic to nontarget species. In South India, Rodenticides commonly

available as rat killer paste (3%). Yellow phosphorus causes hepatotoxicity by the production of phosphoric acid, which causes free radical damage. [1]

In 2016, deaths due to suicide were around 800 000 worldwide, implying an annual world suicide rate of 10.5 per 100 000 population. However, in India the suicide rate is almost double (18.5 suicide deaths for 100 000 population). Majority (79%) of suicides occur in low-income and middle-income countries. Ingestion of poison is one of the most common modes of suicide in low-income and middle-income countries such as India. [2] Among poisons, pesticides contribute to majority of cases of poisoning in India. [3] Pesticide poisoning in India is highly prevalent due to the widespread use

of pesticides for agricultural and household activities.

N-acetylcysteine (NAC) is a well-tolerated mucolytic drug that moderates clinging mucous secretions and enhances glutathione S-transferase activity. During oral administration, deacetylation reaction of NAC happens while passing along the small intestine as well as liver, thus its bioavailability is decreased to 4-10%. NAC stimulates glutathione biosynthesis, promotes detoxification, and acts directly as a scavenger of free radicals. It is a powerful antioxidant. The critical antioxidant power of NAC is due to its role as a precursor of glutathione, which is one of the most important naturally occurring antioxidants.

There is considerable clinical evidence to support the fact that oral and intravenous NAC are equally effective in the prevention of hepatotoxicity.[4] There is no antidote for rodenticide poison, and consumption is often fatal. The Role of N acetyl cysteine (NAC) in acetaminophen induced ALF is well established. Additionally, some studies have shown that it may be useful in non-acetaminophen induced ALF also. Cases with ALF secondary to suicidal rodenticide consumption have been reported, and some reports show that NAC is beneficial in these cases.

There is considerable clinical evidence to support the fact that oral and intravenous NAC are equally effective in the prevention of hepatotoxicity.[5] Hence this study is conducted to find out the outcome of patients treated with NAC in rodenticide poisoning admitted in rural tertiary care hospital.

Materials and Method

This was the Hospital based prospective observational study, conducted on patients with consumption of Rodenticide poisoning, during period from May 2021 to December 2022 (18 months), at one of Tertiary care hospital - Guntur Medical College, Guntur. In the study we have included 100 patients, selected by using simple random sampling method admitted for rodenticide poisoning in the hospital after following inclusion and exclusion criteria bellow and after approval of institutional ethical committee.

Inclusion Criteria:

- Patients admitted with alleged history of rodenticide poisoning.

Exclusion Criteria:

- Patients who do not give consent
- Patients with history of liver disease
- Patients with history of jaundice in the recent past
- Patients with history of chronic alcoholism
- Patients consuming the poison along with alcohol or other compounds

Method: During the admission of patients details of the patients were entered in the case report form. Demographical details such as age, medical history were recorded. The type and quantity of the Rodenticide consumed, duration of hospitalization, time-lag between poison consumption and initiating NAC treatment, symptoms and complications of the patients during admission, laboratory parameters and if any pre-hospitalization treatment given to the patients were recorded. General treatment approaches and the route, dose, and duration of treatment provided with NAC, adverse effects of the treatment, any extracorporeal methods used, ventilation and survival outcomes in terms of the clinical status at the time of discharge were evaluated.

Statistical Analysis : Collected data were entered in the Microsoft excel 2016, for further analysis, qualitative data were presented with proportion and percentages while quantitative data were presented by mean and standard deviation. Qualitative analysis (association or proportion difference) were assessed by using chi-square test. P-value less than 0.05 was considered as statistically significant. For statistical Analysis SPSS software version 25 was used.

Observation and Results

Demographic profile of the rodenticide poisoning cases among study population showed mean age of the study population was found to be 37.6 ± 12.45 years and maximum patients were lying in the age group of 31-40 years followed by 41 – 50 years. We have observed male dominance in our study. We have found 23% of the patients were consuming alcohol, while 12 patients were chewing tobacco. Hypertension and diabetes mellitus were dominant comorbid condition among study population.

Table 1: Demographic distribution of study population

Parameters	Frequency	Percentage
Gender		
Male	51	51
Female	49	49
Age (Years)		
< 20	3	3
21-30	48	48

31-40	18	18
41-50	24	24
51-60	6	6
> 60	1	1
Comorbid Conditions		
Diabetes	18	18
Hypertension	32	32
Tuberculosis	3	3
Hypothyroid	6	6
Any other Habits		
Alcohol Consumption	21	21
Tobacco Chewing	18	18

We have observed male dominance in our study. 83% of cases were found to be Suicidal followed by accidental. Among rodenticide distribution majority of rodenticide was Yellow Phosphorous followed by Zinc Phosphide and Super warfarin and treatment for rodenticide, it was observed that almost 93 of the patients were treated with N-acetylcysteine, followed by gastric lavage, vitamin K1, activated charcoal and 7 patients were by using ventilation, shown in bellow table.

Table 2: Distribution of type of poisoning, rodenticides and treatment given among population.

Parameters	Frequency	Percentage
Type of Poisoning		
Suicidal	83	83
Accidental	13	13
Homicidal	0	0
Rodenticide		
Unknown	16	16
Yellow Phosphorous	71	71
Superwarfarin	4	4
Zinc Phosphide	9	9
Treatment		
N-acetylcysteine	93	93
Vitamin K1	57	57
Gastric Lavage	71	71
Activated Charcoal	12	12
Ventilation	7	7

Table no.3 showed that the mean duration of Hospitalization was found to be 6.42 ± 4.12 days and maximum patients were stayed for 3 to years of hospital stay. Majority of the patients were came in the hospital with symptoms of vomiting, followed by abdominal pain, nausea.

Table 3: Distribution of Clinical symptoms and duration of Hospital among population

Parameters	Frequency	Percentage
Clinical Symptoms		
Nausea	26	26
Abdominal Pain	36	36
Jaundice	9	9
Hepatitis	23	23
Vomiting	57	57
Duration of Hospital		
0 - 2 Days	19	19
3 -5 Days	64	64
> 5 Days	17	17

Table 4: Association of NAC treatment and final outcome among study population

NAC Treatment	Outcome		Total	Chi-square	P-value
	Survived	Non-Survived			
Yes	81(87.1%)	12(12.9%)	93(100%)	15.8**	0.0007
No	2(28.6%)	5(71.4%)	7(100%)		
Total	83(83%)	17(17%)	100(100%)		

**P-value<0.05, statistically highly significant at 5% level of significance. Among all study population 17% of the patients were expired and 83% were survived. Those who have not treated with NAC among them 71.4% of

the patients non-survived and among treated patients with NAC only 12.9% of the patients were non-survived and this difference in the proportion between survived and non-survived between treated and not treated patients was statistically highly significant.

Table 5: Association of NAC treatment and final outcome among study population

Time of initiation of NAC	Frequency	Percentage	Died after Complication
0 - 2 Hours	4	4.3	0(0%)
2- 4 Hours	9	9.7	0(0%)
4 - 6 Hours	9	9.7	0(0%)
6 - 8 Hours	19	20.4	0(0%)
8 - 10 Hours	13	14	1(7.7%)
10 - 12 Hours	11	11.8	0(0%)
12 - 14 Hours	11	11.8	4(36.4%)
14 - 16 Hours	7	7.5	3(42.9%)
16 - 18 Hours	4	4.3	1(25%)
18-20 Hours	4	4.3	2(50%)
> 20 Hours	2	2.2	1(50%)
Total	93	100	12(12.90%)

In the above table it was showed that maximum patients were treated with NAC before 12 hours only and those treated after 12 hours mortality was observed maximum among the patients treated with NAC after 12 hours

Discussion

Poisoning is a major health problem worldwide. It is deliberate self-poisoning that causes the great majority of deaths and the immense strain that pesticides put on hospital services, particularly in developing countries like India. Pesticides like rodenticide are a heterogeneous group of compounds usually intended for killing rats and mice. These compounds, however, show sharply distinctive toxicities among humans and rodents.[6] The number of cases of pesticide poisoning is on the increase globally, with around 300,000 cases being reported every year [7]. Rodenticides are composed of superwarfarins, thallium, barium carbonate, aluminium phosphide (AIP) and zinc phosphide. They are inexpensive and highly toxic pesticides [8]. They are easily available in the Indian subcontinent and are common agents in deliberate self-harm, especially among the agricultural community. The high fatality due to ALF induced by rodenticides makes the need for an antidote urgent and imperative.

In the present study of 100 patients, included in the study irrespective of age and gender. It was observed that there was predominance of male was observed in the study compared to the female and ratio of male is to female was 1.04 : 1, we have also observed that majority of the patients were from the age group of 31 -50 years, means more than 50% of the population and mean age of our study population was be 37.6 ± 12.45 years. Nearly among all 83% of the cases were suicidal followed by accidental and homicidal, 21 patients were consuming alcohol while 12 patients were chewing

tobacco. Various studies on poisoning did in India Banerjee *et al.* in West Bengal also noticed most commonly affected age group was 20–40 years.[9] according to the study by Chandravanshi J. et al. [10] out of all patients, females 27 (54%) were higher than males 23 (46%) and it was supported to our study as well as similar to study conducted by Seetha 33 (58.92%). Another study by Acharya R et al incidence of rodenticide poisoning was slightly more in Males than females [11]. Our study observed that maximum patients admitted by common symptoms of vomiting, followed by abdominal pain followed by nausea. Zinc phosphide poisoning, and Aluminium phosphide showed these kind of clinical features but initiation of these symptoms are late in aluminium phosphide[12, 13].

Present study found that majority of the patients were observed with hypertension and diabetes, it was observed that it quite common comorbidities among the old age people. Study by Saravanan and Karthik et al [14] observed of the 30 patients studied, 13 patients (43.34%) developed complication and in that 5 patients (16.67%) died. One more study conducted by Mohideen S, Kumar K et al[15] found that, onset of these complication was not there initially but sudden patients shows the complications like pancreatitis, Cardiac Arrhythmia, Encephalopathy, Fulminant Hepatic failure which will be the risk factors for death.

Our study found that majority of the rodenticide were unknown but that rodenticide were observed among that Yellow phosphorous was more common followed by surperwarfarin, and Zinc phosphate. Among the all rodenticide, yellow phosphorous is more commonly observed rodenticide, rat killer contains yellow phosphorous and at every home it is available, Yellow phosphorus is a protoplasmic poison and is both hepatotoxic and cardiotoxic. The first phase

consists of nausea, vomiting, abdominal pain, and smoking stools. Then, in the second phase, the patient may feel symptomatically better and the third stage consists of systemic organ damage due to absorbed phosphorous. Study conducted by Chandravanshi J et al observed that based on the type of rodenticide poison ingestion, intake of rodenticide paste poison constitutes 25 (50%) also supported to our study, study by Saravanan et al observed rat killer paste poisoning was most common and their sample size was 30 patients. one more another study by Acharya R et al supported our study, they also observed yellow phosphorous was most common rodenticide in their study.

In our study among all the patients most of the patients, around 93% of the patients were treated by using N-acetylcysteine, followed by Vitamin K1, gastric Lavage, and activated charcoal, also we have observed we had 12 patients were treated with ventilation. Study by Chandravanshi et al treated there all patients with NAC, one more another study by Saravanan found that with the early use of N-acetylcysteine therapy in rat killer paste poisoning. In present study we have observed mortality rate was 17% among all the patients. Study conducted by Acharya et al showed that there was mortality observed among 35.7% of the patients which was more than our study, another study Saravanan and Karthik observed mortality rate equal to our study, A recent study conducted in South India showed that yellow phosphorus was the most common rodenticide used in suicide attempts in the region and carried a 30% mortality despite maximal supportive therapy.

Also in our study those who have treated with NAC, among those 81.7% of the patients were treated less than 12 hours found good recovery of the patients, but remaining 19.3% of the patients treated after 12 hours among them recovery rate was less and maximum mortality was observed among that group only. Study by Saravanan and Karthik et al observed that among 30 patients studied, five patients died, seven patients developed hepatitis, one patient developed acute kidney injury with hepatitis, and one patient developed hyponatremia. During the treatment with NAC we have encountered with some adverse effect of NAC in that most common adverse effect was vomiting, diarrhoea and sever cough. Supported with our study by Mumtaz K et al[16] observed adverse effects of treating with NAC.

Conclusion

Early use of NAC which is inexpensive and relatively safe among rodenticide poisoning, patients shows significant impact on the recovery of the patients. Mortality rate was found low among the patients treated before 12 hours with NAC. Also we have observed that males and

female were equally encountered with rodenticide poisoning and most of the patients were of young age

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