ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 11, Issue, 01, pp.672-675, January, 2019

DOI: https://doi.org/10.24941/ijcr.33948.01.2019

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

A STUDY ON THE ROLE OF N-ACETYL CYSTEINE IN YELLOW PHOSPHOROUS POISONING (RATOL) AND POSTMORTEM TOXICOLOGICAL FINDINGS

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ARTICLE INFO

Article History:
Received 15th October, 2018
Received in revised form
14th November, 2018
Accepted 20th December, 2018
Published online 31st January, 2019

Key Words:
Yellow phosphorous (ratol),
Liver failure, NAC.

ABSTRACT

Context: Ratol is a rodenticide (rat killer paste) ,it contains yellow phosphorus, a severe local and systemic toxin causing damage to gastrointestinal, hepatic, cardiovascular, and renal systems. Among these liver is the most commonly affected organ and acute liver failure with coagulopathy is the most dreaded complication. These toxins damages the liver by depleting glutathione stores. NAC acts by stimulating the glutathione synthesis and enhances glutathione transferase activity.Therefore, treatment with NAC, which is inexpensive and relatively safe, would be a viable treatment option for patients admitted with yellow phosphorous consumption with ALF but those who are not eligible for liver transplant. **Aim of The Study:** 1. To study the prevalence of yellow phosphorus poisoning in our hospital 2. To evaluate the usefulness of N-Acetyl cysteine in yellow phosphorous poisoning 3. Postmortem findings in liver and kidney. **Settings and Design:** Prospective cross sectional observational study. **Materials and Methods:** The study was conducted on 25 patients with history of yellow phosphorous poison (ratol) consumption who fulfill the inclusion and exclusion criteria getting admitted at Government Rajaji Hospital & Madurai Medical College during the period of June to September 2017. • The control group patients are taken from retrospective data obtained in year 2016 at GRH, who had similar management protocol except for NAC. **Results:** Morbidity and Mortality was reduced to 50% in the study group who was admitted early and treated with NAC, even though they consumed lethal dose of Ratol. **Conclusions:** Most patients admitted with history of suicidal consumption of ratol (yellow phosphorous) were young and belonged to poorer socio-economic sections. Therefore treatment with NAC, which is inexpensive and relatively safe, would be a viable treatment option for patients admitted with ratol consumption.

Citation: Dr. Alaga Venkatesan, V.N., Anandhi, P.G., Shridharan, P. and Manikandan, **2019.** "A study on the role of n-acetyl cysteine in yellow phosphorous poisoning (ratol) and postmortem toxicological findings", *International Journal of Current Research*, 11, (01), 672-675.

INTRODUCTION

Poisoning is a major problem globally and its incidence is rising due to rapid industrialization and urbanization. The exact incidence of acute poisoning is not known in India because of lack of any central poison registry. The toxins involved in acute poisoning cases vary from place to place. In western countries, the commonest toxins are medicinal agents. In contrast, in India, insecticide, pesticides and rodenticide are the most commonly consumed agents in adults. Ratol is a rodenticide (rat killer paste), it contains yellow phosphorus, a severe local and systemic toxin causing damage to gastrointestinal, hepatic, cardiovascular, and renal systems. Among these liver is the most commonly affected organ and acute liver failure with coagulopathy is the most dreaded complication. Other fatal complications are acute tubular necrosis, hepatorenal syndrome, hypotension and arrhythmias. Clinical manifestations of yellow phosphorous poisoning has three stages. First stage has gastrointestinal symptoms like nausea and vomiting in the absence of any laboratory abnormalities. Second stage occurs after 24– 48 hours characterised by rising rising transaminases, although the patient may be asymptomatic. In some cases, this progresses to the third stage characterised by acute liver failure with coagulopathy and encephalopathy, which can be fatal. The Role of N acetyl cysteine (NAC) in acetaminophen induced Acute fulminant hepatic failure (ALF) was well established. Additionally some studies have shown that NAC may be useful in non-acetaminophen induced ALF like yellow phosphorous poisoning also.

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These toxins damages the liver by depleting glutathione stores. NAC acts by stimulating the glutathione synthesis and enhances glutathione transferase activity. Other beneficial effects of NAC are anti-inflammatory, inotropic and vasodilatory effects .Therefore, treatment with NAC, which is inexpensive and relatively safe, would be a viable treatment option for patients admitted with yellow phosphorous consumption with ALF but those who are not eligible for liver transplant. A post-mortem liver biopsy shows hydropic or fatty infiltration of hepatocytes, collapsed reticulin framework with fibrosis between the hepatocytes and periportal necrosis suggestive of an acute fulminant hepatitis

MATERIALS AND METHODS

The study was conducted on 25 patients with history of yellow phosphorous poison (ratol) consumption who fulfill the inclusion and exclusion criteria getting admitted at Government Rajaji Hospital & Madurai Medical College during the period of june to september 2017. The control group patients are taken from retrospective data obtained in year 2016 at GRH, who had similar management protocol except for NAC.

Inclusion criteria: All patients admitted with history of yellow phosphorous poison (ratol) consumption at Government Rajaji Hospital & Madurai Medical College during the period of june to september 2017.

Exclusion criteria

- Patient who have ingested other substance in addition to yellow phosphorous will be excluded
- Patients who are known to have preexisting liver disease
- Patients with chronic kidney disease
- Patients with heart disease
- Absconded within 24hrs of admission.

Study protocol

Informed consent obtained from all patients to be enrolled for the study. In all, the patients relevant details will be collected in a predesigned proforma. The patients are selected based on history of yellow phosphorous poisoning, clinical examinations, biochemical tests and ultrasound abdomen, toxicological autopsy findings of expired patients.

Design of study: Prospective cross sectional hospital based observational study PERIOD OF STUDY: 4 MONTHS (June 2017 to september 2017) METHODOLOGY: History was taken from patients who consumed yellow phosphorous poisoning, about time of consumption, amount of consumption, any prior hospital admission and treatment before arriving to our hospital. History regarding details and duration of alcohol intake was taken, and history of vomiting, abdominal pain, loose stools, altered sensorium also noted. Clinical examination about presence of icterus, anemia, edema legs, features of encephalopathy, abdominal tenderness was noted during admission. After stomach wash and initial resuscitation, oral Loading dose of 140 mg/kg of N Acetyl cysteine was started and then followed by 17 doses, each at 70 mg/kg, given 4th hourly. The total duration of the treatment course is 72 hours.

Time of stomach wash and intiation of N Acetyl cysteine was noted. serial monitoring of vitals and complete blood count, blood sugar, urea, creatinine, serum bilirubin, AST, ALT, prothrombin time, INR ,urine analysis, ECG, USG abdomen was estimated. Post-mortem toxicological findings of liver and kidney was noted in all expired patients.

Statistical analysis

All data were entered in Excel 2007 and statistical analysis was "performed using the statistical software SPSS 16.0.Data were expressed as mean values with standard, deviation". For continuous variables "Mann Whitney U-test was performed to find the differences between two groups and for categorical variables Pearson's chisquare test was performed". Results were defined as statistically significant when the P value was less than 0.05.

RESULTS

1. Age Distribution

Age in years	Study	control
15-25	14	15
26-35	7	7
36-45	4	2
46-55	0	1
Total	25	25
Mean	26.52	25.72

2. Gender Distribution

Sex	study	Control
Male	10	8
Female	15	17
Total	25	25

3. Relation to alcohol consumption

Alcoholic	study	Control
Yes	3	3
No	22	22
Total	25	25

4. Amount of poison consumption

Amount of poison consumed	study	Control
<1 gm	5	6
>1 gm	20	19
Total	25	25
Mean	3.74	2.56

5. Comparison of presence of icterus

Presence of icterus	study	control
yes	18	18
no	7	7
total	25	25

6. Comparison of presence of hepatic encephalopathy

Encephalopathy	study	control
yes	5	13
No	20	12
Total	25	25
P value	0.039 significant	

7. Comparison of Hypotension

Hypotension	Study	control
Yes	6	14
No	19	11
Total	25	25
P value	0.043 significant	

8. Comparison of oliguria

Oliguria	Study	control
Yes	5	13
No	20	12
Total	25	25
P value	0.039 significant	

9. Comparison of leucopenia

Leucopenia	study	control
Yes	3	9
No	22	16
Total	25	25
P value	0.098 not significant	

10A. Liver function test

LFT	Study	control
Elevated	19	18
Normal	6	7
Total	25	25

10B. Time to NAC initiation

Time to NAC initiation	study
< 1 day	14
> 1 day	11
Total	25

10C. Response to NAC (recovery)

Response to NAC	Study	control
Yes	17	0
No	8	25
Total	25	25
P value	<0.001 significant	

10D. Serum bilirubin response to NAC

CASE NO.	1ST DAY	3RD DAY	6TH DAY
C1	1.1	1.5	0.9
C2	0.9	2.9	1.3
3	1.2	7.9	1.9
4	1.1	2.5	1.3
5	1	2.7	1.2
6	2.1	5.6	3.1
C7	5.4	23.9	8.1
C8	0.8	4.1	1.4

10E. Liver enzyme (ALT) response to NAC

CASE NO.	1ST DAY	3RD DAY	6TH DAY
C1	40	39	31
2	21	118	53
3	51	213	70
4	39	139	56
5	29	105	41
6	33	71	34
7	198	720	232
C8	21	255	63

11. Comparison of renal function test

RFT	study	control
Elevated	7	12
Normal	18	13
Total	25	25
P value	0.244 not significant	

12. Outcome of the study

Outcome	study	Control
DEATH	8	17
DISCHARGE	17	8
TOTAL	25	25
P value	0.024 significant	

DISCUSSION

Our study was done to identify the prevalence of yellow phosphorus poisoning in our hospital and to evaluate the usefulness of N-Acetyl cysteine in yellow phosphorous poisoning and also study the postmortem findings in liver and kidney. Out of 50 patients 25 were study group those who were treated with N Acetyl cysteine (NAC) and another 25 patients were taken from retrospective data collected from those who not treated with NAC. Our study showed that most vulnerable age group of yellow phosphorous (ratol) poisoning was 15 to 25 years. More than 60% of the victims were females. So influence of alcohol is not much significant. Calculated Lethal dose of YP in previous study was >1mg/kg. This study also told that, 80% of the admitted patients consumed more than 1gm of poison and has more mortality. Most of the patients were admitted with vomiting, abdominal pain. On 3rd day pt developed icterus, feature of hepatic encephalopathy, bleeding manifestation, hypotension, tachycardia and oliguria , some patients had respiratory failure also. In our study approximately 20% of the patients in the study group and 50% in the control group had features of hepatic encephalopathy, hypotension and oliguria.

These data pointed that earlier admission and treatment with NAC prevents from occurrence of above said complications. Both group have leucopenia, but control group (36%) is affected more than study group (12%). 3/4 of patients in the both group had elevated LFT value, remaining 1/4 of patients had near normal LFT, probably they did not consumed poison or had very minimal consumption. Among 25 patients, 14 reaches our hospital within 24hrs of poison consumption, so NAC initiated early. Remaining patients were admitted in peripheral hospital and referred later after pt had features of toxic hepatitis. In the study group 17 patients have good response to NAC, among them 8patiens had elevation of LFT (bilirubin, AST, ALT, prothrombin time) mostly in the 3rd and 4th day of admission. That LFT values become near normal on 6th or 7th day due to timely treatment with NAC. It is statistically more significant (p value is 0.001). In the study group among 25 yellow phosphorous consumed patients, 8patients (32%) died inspite of NAC treatment mostly due to delayed admission with features of acute liver failure. In the control group 17 patients (68%) died. So treatment with NAC REDUCES 50% OF MORTALITY. It is statistically more significant (p value is 0.024).

Conclusion

Most patients admitted with history of suicidal consumption of ratol (yellow phosphorous) were young and belonged to poorer socio-economic sections. Mortality was reduced to 50% in the study group who was admitted early and treated with NAC, even though they consumed lethal dose of ratol. Therefore treatment with NAC, which is inexpensive and relatively safe, would be a viable treatment option for patients admitted with ratol consumption.

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