N Acetylcystine: Role in non-acetoaminophen acute liver failure

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Abstract

Background: Acute liver failure (ALF) is not an uncommon entity now a days.

Objective: To determine the efficacy of N-acetyl cysteine for management of non acetaminophen Acute Liver Failure.

Methodology: Setting; Shaikh Zayed Hospital, Rahim Yar Khan Study design: Comparative study Duration: 1st June to 31st December 2015. In the present study, the cases in the age range of 15 to 70 years, irrespective of their gender, suffering from non acetaminophen acute liver failure were enrolled. The diagnosis of ALF was made on history and laboratory data like INR> 1.5 and encephalopathy of any grade with no history of previous cirrhosis and total duration of symptoms less than 26 weeks. The subjects were subdivided into two groups. Group A was given placebo and group B was administered N-acetyl cysteine. The subjects were assessed for their final outcome in terms of survival and discharge (to label length of hospital stay).

Results: In this study, out of 68, 34 were in each group. The mean age was 31.13 $\pm$ 10.81 vs 32.71$\pm$9.57 years in group A and B. There were 24 (70.59%) males in group A and 26 (76.48%) in group B. Mean hospital stay in group A and B was 11.37 $\pm$ 3.32 vs 8.53 $\pm$ 1.89 days with p= 0.27. Survival was seen in 24 (70.59%) cases in group A vs 31 (91.17%) in group B with p= 0.02.

Conclusion: N-acetyl cysteine is significantly better than placebo in terms of survival rate, in non acetaminophen acute liver failure.

Key words: N-acetyl cysteine, Survival, INR, Acute liver failure.

Introduction

Acute liver failure (ALF) is not an uncommon entity but has a high degree of fatality. It's an acute insult to the liver with high degree of inflammation and necrosis which results in architectural distortion and wide array of physiological and structural changes in liver. It markedly reduces its metabolic and synthetic functions which add to its eventual failure and a high degree of symptomatology. Its exact burden is not known; but it has a high degree of morbidity and mortality. In developed countries, its prevalence is around 2 thousand cases annually.[1] It can be denoted on the basis of acute liver failure in cases with no prior history of hepatitis and lead to severe coagulopathy in terms of INR more than 1.5, varying degree of hepatic encephalopathy; all occurring in a duration of less than 26 weeks.[2-3]

The other clinical features to add on are jaundice and severe hemodynamic dysfunctions that might be due to an ongoing internal bleeding. The mainstay of the treatment is supportive therapy with definitive can be achieved liver transplant; though uncommon.[4-5]

The basis underlying pathophysiology included release of highly obnoxious free radical that cause intense tissue injury and keeping in view, few of the agents have been formed that can act upon this and help reducing the injury by scavenging these cells. N-acetylcysteine (NAC) which have a ring, which contains a thiol group where these free radicals are attached.[6-7] The data is variable and has shown promising results in cases with ALF especially in cases with acetaminophen poisoning.[5,8] It has the tendency to vasodilate the microvasculature and increased the perfusion to the hypoxic end organs.[9] As NAC can work in a variety of ways, that's why its postulated to have a role in other ALF as well other than acetaminophen only for which this study was planned.[10-12] The objective of the study was to determine the efficacy of N- acetyl cysteine for management of non acetaminophen acute liver failure.

Methodology

This comparative study, was carried out at Sheikh Zayed Hospital, Rahim Yar Khan during 1st June to 31st December 2015, in which the cases of non

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acetaminophen associated ALF were selected via non-probability consecutive sampling technique. The cases were selected in the age range of 15 to 70 years irrespective of their gender. The diagnosis of ALF was made on history and laboratory data like INR> 1.5 and encephalopathy of any grade with no history of previous cirrhosis and total duration of symptoms less than 26 weeks. The subjects were subdivided into two groups. Encephalopathy was assessed on the basis of West Haven Criteria. The cases were subdivided into two subgroups via random number allocation method. The cases in Group A were offered placebo and the ones in B group were offered N-Acetyl cysteine. The subjects were assessed on daily basis to look for final outcome in terms of survival/ death and discharge (to label length of hospital stay). SPSS version 20 was used for data analysis. The data was stratified and both independent sample t test and chi square tests were applied for numerical and categorical data respectively and post stratification p value < 0.05 was taken as significant. Ethical approval was taken from institutional review board.

Results

In the present study, 68 cases were enrolled with 34 in each group. The mean age was 31.13 + 10.81 vs 32.71+9.57 years in group A and B. There were 24 (70.9%) males in group A and 26 (76.48%) in group B. There were 12 (35.3%) cases in group A and 16 (47.1%) in group B with grade I encephalopathy as in table I.

Table II describes the laboratory data of both groups. Mean hospital stay in group A and B was 11.37 + 3.32 vs 8.53 + 1.89 days with p= 0.27. Survival was seen in 24 (70.59%) cases in group A vs 31 (91.17%) in group B with p= 0.02 as displayed in table III.

Table I: Encephalopathy in study subjects (n= 34 in each group)

Encephalopathy Grade	Group A	Group B
	No (%)	No (%)
I	12 (35.3)	16 (47.1)
II	12 (35.3)	9 (26.4)
III	7 (20.6)	7 (20.6)
IV	3 (8.8)	2 (5.9)

Table II: Laboratory investigations of study subjects (n= 34 in each group)

Laboratory data	Group A	Group B	P value
	Mean ±SD	Mean ± SD	
PT (mg/dL)	10.47 ± 4.13	9.89 ± 2.79	0.7 6
Bilirubin (mg/dL)	9.37 ± 3.27	8.31 ± 1.83	0. 41
Albumin (mg/dL)	3.71 ± 0. 35	3.95 ± 0. 53	0. 63
Creatinine (mg/dL)	1.23 ± 0.1 7	1.41 ± 0. 23	0.57
ALT (mg)	165 ± 31.23	267 ± 37 .89	0.003

Table III: Comparison of Survival (n= 34 in each group)

Survival outcome	Group		P Value
	A (Placebo)	B (NAC)	
Yes	24 (70.59 %)	31 (91.17 %)	0.02
No	10 (29.41 %)	3 (8.83 %)	
Total	34	34	

Discussion

Acute liver failure (ALF) is an acute liver injury to noxious agents and can be fatal despite aggressive treatment. Liver transplantation is considered as the mainstay of the treatment, but its not widely available and has a great cost.[13-15] NAC has been tested for acetaminophen association ALF and work being done for its utility in other causes of liver failures.[10]

In this study, the age of the subjects was 31.13 ± 10.81 and 32.71±9.57 years in group A and B respectively these results were according to the findings of the previous studies. According to one study conducted by Alvi H, et al [13] found that mean age of their participants was 31.4±15.1 years. Moreover, in the present study there was male dominance where these were seen to suffer from ALF as 70.9% and 76.48% of the cases. which was also similar to their study as well where there was also male dominance and they were seen in more than 60% of their cases. Mumtaz A, et al also had the almost similar mean age and was noted as 27.7 ± 11.8 years.[1]

In the present study, the survival was seen in 24 (70.59%) of the subject in group A and 31 (91.17%) subjects in B (p=0.02) with a statistically significant

difference. The data regarding NAC is scarce especially in non acetaminophen ALF but studies have shown the favourable outcomes with this. Kortsalioudaki et al[8] also carried out a similar study where NAC was administered in 111 cases with non acetaminophen associated ALF and it was observed that favourable outcome in terms of efficacy was seen in 75% of their intervention with NAC in contrast to 50% with conventional supportive treatment with p= 0.009.[12] Lee et al,[14] also found better results with NAC but this was a non significant difference with p value of 0.28. Furthermore, they found that change in the grade of hepatic encephalopathy was significantly better with NAC ac compared to placebo (p= 0.01).

Khuroo et al[15] found the survival benefit in their 72.8% of subjects managed by NAC and also decreased in length of hospital stay which was also supported by the findings of Kortsalioudaki et al where this stay was seen in 1-264 days with placebo as compared to 19 1-201 days in cases managed with NAC.[8] Similarly no significant difference was seen in the present study in terms of hospital stay; though the stay was far low as compared to their data. The reason can be due to low health care facilities in the developing countries as compared to developed ones

Conclusion

N-acetylecystine is significantly better than placebo in terms of survival rate in non-acetaminophen acute liver failure patients.

Authors Contribution: JM: Design of work, Interpretation of Data, revising and final approval. **MAM:** Conception of work, Drafting and final approval. **AH:** Design of work, revising and final approval. **GF:** Design of work, revising and final approval. **HR:** Acquisition and analysis of data, drafting and final approval. **SA:** Analysis of data, drafting and final approval.

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