Use of N-acetylcysteine in non-acetaminophen induced acute liver failure and its effect on total bilirubin, ALT, and INR

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BACKGROUND

- Acute liver failure (ALF) is an uncommon medical emergency that has significant mortality and need for transplantation associated with it.
- Acetaminophen toxicity is the most common cause of ALF and patients respond well to treatment with N-acetylcysteine (NAC)
- Non-acetaminophen induced acute liver failure (NAI-ALF) however, has a high mortality rate.
- A growing amount of evidence has demonstrated NAC to improve systemic hemodynamics, tissue oxygen delivery, hepatic blood flow, or through other mechanisms to potentially benefit NAI-ALF, particularly in early coma grades.
- A decrease in alanine aminotransferase (ALT), total bilirubin, and international normalized ratio (INR) have shown to reduce the rate of transplantation or death in this population.
- The purpose of this study is to examine the use of NAC in patients with NAI-ALF and its effect on total bilirubin, ALT, and INR.

METHODS

- Retrospective chart review of patients admitted between December 5, 2012 and September 26, 2015
- Single academic medical center
- Inclusion criteria: adults, treated with acetylcysteine (oral or intravenous), meet the American Association for the Study of Liver Diseases' (AASLD) classification of ALF (INR ≥ 1.5 and any degree of encephalopathy).
- Additionally, patients with liver cirrhosis were included because a high percent of our population has cirrhosis, patients with ALF are regularly transferred for higher level of care, and may receive a transplant
- Exclusion criteria: acute liver failure due to acetaminophen toxicity or shock/ischemic liver.

ENDPOINTS

Primary endpoint:

- Effect of NAC on total bilirubin, ALT, and INR in patients with NAI-ALF

Secondary endpoints:

- Survival at end of hospital stay and at 3 weeks

BASELINE CHARACTERISTICS

	Control (N=17)	Study (N=19)	P-value
Male	6	13	0.093
Age (years)	52.4 +/- 17.2	56.2 +/- 17.5	0.522
Weight (kg)	95.6 +/- 26.4	107.1 +/- 34.7	0.271
Total Bilirubin (mg/dL)	14.5 +/- 12.8	12.5 +/- 10.3	0.608
AST (U/L)	235.5 +/- 235.1	1035.8 +/- 1500.6	0.033*
ALT (U/L)	139.2 +/- 164.7	676.0 +/- 891.0	0.018*
INR	2.0 +/- 1.1	3.1 +/- 3.0	0.123
PT (seconds)	21.7 +/- 12.8	31.4 +/- 26.8	0.171
Scr (mg/dL)	2.1 +/- 1.5	2.3 +/- 1.5	0.686
Jaundice	13 (76.5)	9 (47.4)	0.097
Cirrhosis	13 (76.5)	12 (63.2)	0.481
ICU	12 (70.6)	16 (84.2)	0.281
MELD	28.3 +/- 9.4	30.5 +/- 10.3	0.511

*statistical significance

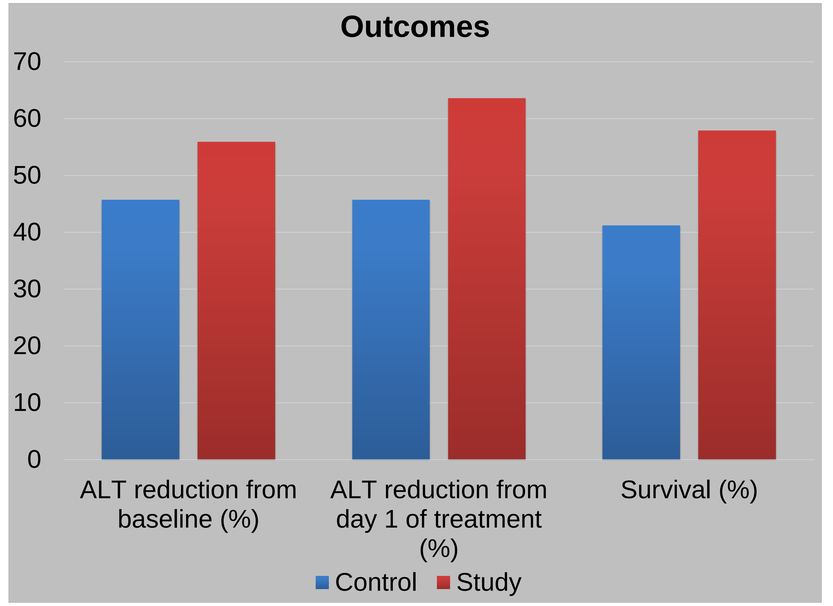
Two differences in baseline characteristics were observed, the study group had higher baseline AST and ALT. Despite this, the groups liver functions were similar as demonstrated by the calculated MELD scores, rates of jaundice, and cirrhosis.

RESULTS

	Baseline	Day 1 of Treatment	7 days post treatment	P-value
Total Bilirubin, Control	14.5 +/- 12.8	-	15.1 +/- 12.8	0.759
Total Bilirubin, Study	12.5 +/- 10.3	-	16.4 +/- 13.5	0.037*
Total Bilirubin, Study	-	12.8 +/- 11.3	16.4 +/- 13.6	0.079
ALT, Control	235.5 +/- 235.1	-	128.2 +/- 206.6	0.861
ALT, Study	676.0 +/- 890.9	-	271.7 +/- 391.8	0.051
ALT, Study	-	734.2 +/- 875.5	271.7 +/- 391.9	0.017*
INR baseline, Control	2.0 +/- 1.1	-	3.0 +/- 2.9	0.216
INR baseline, Study	3.1 +/- 3.0	-	3.0 +/- 3.1	0.971
INR, Study	-	2.5 +/- 1.4	3.0 +/- 3.2	0.524

*statistical significance

RESULTS



The results showed a significant increase in total bilirubin from baseline and a decrease in ALT from day 1 of treatment in the study group; otherwise there was no difference in outcomes. Additionally, the survival at the end of hospital stay was the same as at 3 weeks.

CONCLUSIONS

The results showed show a portion of the data to be skewed. After using the log function to transform these variables, the only difference was the addition of a significant reduction in the study group's baseline ALT to 7 days post treatment. While the ALT percent reduction and survival were not significant, there was approximately a 15% higher reduction in ALT and 17% higher survival rate in the NAC group. As of now, it is difficult to support the use of NAC in this population based on these results as there was an increase in bilirubin, decrease in ALT, and similar survival rates. With the addition of more patients in the future, this study will provide greater insight.