NAC ATTACK: An Emerging Therapy for Ischemic Hepatopathy

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AIM

The aim of this study is to evaluate and compare the trend of hepatic function tests, use of vasopressor requirements, and length of intensive care stay for patients admitted with ischemic hepatopathy who received the 72-hour-NAC protocol compared to those who did not.

BACKGROUND

Acute ischemic hepatopathy, or shock liver, is diffuse hepatic injury due to hypoperfusion and accounts from 1 to 2.5 percent of patients admitted to an intensive care unit. This phenomenon leads to a profound elevation in aminotransferases. Recent studies have shown that N-Acetylcysteine (NAC) provides mortality benefit and improves transplant-free survival in patients that have non-acetaminophen induced acute liver injury, however there have been no studies that show the effects on ischemic hepatopathy from cardiogenic, septic, or hypovolemic shock. In studies utilizing murine models, NAC has been shown to be beneficial in ischemic injury by eliminating reactive oxygen species and attenuating hepatic apoptosis.

MATERIALS & METHODS

In this retrospective single-center study, we identified adult patients with cardiogenic, septic, or hypovolemic shock from 2016 to 2019 with ischemic hepatopathy defined by an acute increase in aspartate aminotransferase (AST) and alanine aminotransferase (ALT) to 20-times the upper limit of normal without other identifiable causes (drug-induced, acute viral hepatitis, autoimmune). Chart review was performed and data trends in transaminases, bilirubin, coagulation tests, creatinine, volume status, vasopressor requirements, and the number of ICU days were collected. Univariate analysis was performed.

Clinical Characteristics and Trends Between Patients With and Without 72-hour NAC Protocol

Clinical Characteristics and Trends Between Patients With and Without 72-hour NAC Protocol

	No NAC (n=18)	NAC (n=20)	p-value
Age	67.5 (21,89)	67.5 (21,82)	0.6821
Gender			
Male	12 (67%)	15 (75%)	0.5717
Female	6 (33%)	5 (25%)	
Length of Stay *(in days)*			
Hospital Admission	13.0 (4,36)	16.0 (3,100)	0.4842
Intensive Care Admission	6.5 (3,31)	10.0 (2,100)	0.7146
Intensive Care Unit Location			
Adult Surgical Heart Unit	5 (28%)	10 (50%)	0.2590
Cardiothoracic Vascular Transplant Unit	1 (6%)	2 (10%)	
Medical Intensive Care Unit	12 (67%)	8 (40%)	
Shock Etiology			
Cardiogenic	10 (56%)	17 (85%)	0.1054
Hypovolemic	1 (6%)	1(5%)	
Septic	7 (39%)	2 (10%)	
Apache II Score At Time of ICU Admission	25.1 ± 7.3	21.5 ± 8.7	0.1731
Vasopressor Days	7.0 (3,32)	2.5 (0,120)	**0.0322**
Fluid Volume Over 72-Hour Period *(in liters)*			
Total Volume of Fluids	6.0 (0.5, 13)	10.0 (2, 25)	**0.0015**
Total Volume of Fluids without NAC	6.0 (0.5, 13)	8.9 (1, 24)	**0.0340**
Net Balance	-1.1 (-10, 10)	-0.3 (-12.0, 19)	0.5587
Net Balance without NAC	-1.1 (-10, 10)	-2.1 (-13, 17)	0.5786
Laboratory Trends (% Change)*			
Albumin	-13.6 (-43, 29)	-8.1 (-33, 55)	0.2139
Aspartate Aminotransferase (AST)	-72.0 (-97,2)	-93.5 (-99,-33)	**0.0001**
Alanine Aminotransferase (ALT)	-52.6 (-85,41)	-61.3 (-92,-15)	0.0845
International Normalized Ratio (INR)[1]	-15.9 (-50,136)	-24.0 (-74,156)	0.5488
Prothrombin Time (PT)	-21.8 (-48,129)	-25.4 (-70,113)	0.4281
Creatinine (Cr)[2]	20.6 (-77,121)	-46.3 (-75,2)	**0.0003**
Total Bilirubin	31.3 (-47,595)	-12.9 (-63,229)	0.1178
Platelet Count	-51.5 (-90,126)	-30.1 (-71,230)	0.0537
Mortality	9 (50%)	5 (25%)	0.1107

*Values are presented as median % change (range). Change is calculated as (initial value – value at 72 hours) / initial value x 100.
[1]In NAC group, 2 patients were excluded as they were on coumadin and had higher goal INR.
[2]In NAC group, 1 patient was excluded and in non-NAC group, 4 patients were excluded due to continuous renal replacement therapy requirement.

RESULTS

A total of 38 patients with ischemic hepatopathy were included; 20 patients received the 72-hour NAC protocol and 18 patients did not. There were no differences found in age, gender, and APACHE II score among both groups (p=0.6821; p=0.5717; p=0.1731). The shock etiology among both groups was predominantly cardiogenic (85% in NAC group, 56% in non-NAC group). Patients in the NAC group received more volume over the 72-hour period compared to the non-NAC group (10.0L vs 6.0L, p=0.0015), even when NAC was controlled for (8.9L vs 6.0L, p=0.0340). However, there was no difference in the net fluid balance over the 72-hour period between the two groups (-0.3L vs -1.1L, p=0.5587). A statistical improvement in AST (-93.5% vs -72.0%, p=0.0001) and creatinine (-46.3% vs 20.6%, p=0.0003) was observed in the NAC group compared to the non-NAC group. Median vasopressor days was significantly less in the NAC group (2.5 vs 7.0, p=0.0322). There was no significant difference among length of stay and mortality between the two groups.

CONCLUSION

NAC is associated with improved renal function at 72 hours. The NAC group showed a more rapid improvement of AST, ALT, and bilirubin compared to the control group, however only AST reached significance, likely due to the small sample size. In addition, the NAC group received more volume over the 72-hour period, even when the NAC volume was controlled. The NAC group required fewer vasopressor days compared to the non-NAC group. This pilot study shows clinical benefit of NAC as a treatment modality for ischemic hepatopathy. Double blind, randomized controlled trials are needed to further validate this observation.