

ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH: A CASE REPORT ON ROLE OF N-ACETYLCYSTEINE IN NON-ACETAMINOPHEN-RELATED ACUTE LIVER INJURY

ANOOJA THAMPI^{1*}, JINU JOY¹, GIREESH KUMAR², SREEKRISHNAN TP², AJITH V²

¹Department of Pharmacy Practice, Amrita Vishwa Vidyapeetham, AIMS Campus, Kochi, Kerala, India. ²Department of Emergency Medicine, Amrita Vishwa Vidyapeetham, AIMS Campus, Kochi, Kerala, India. Email: anoojathampi@yahoo.com

Received: 08 July 2016, Revised and Accepted: 13 August 2016

ABSTRACT

Acute liver failure (ALF) is a clinical entity associated with a high mortality rate, and the majority of these patients may require liver transplantation. N-Acetylcysteine (NAC), an antioxidant agent that replenishes mitochondrial and cytosolic glutathione stores, is an antidote for acetaminophen poisoning. However, their role in non-acetaminophen-related ALF is still not proven. Here, we discuss a 67-year-old male patient diagnosed with hepatitis with an acute liver injury who was admitted to Emergency Medicine. He was treated with NAC infusion for an average of 48 hrs, and later, it was found that his liver function tests improved. In this study, we could find that NAC plays a major role in improving the liver function test of patients with non-acetaminophen-related ALF.

Keywords: Acute liver injury, N-acetylcysteine, Emergency medicine.

© 2016 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) DOI: <http://dx.doi.org/10.22159/ajpcr.2016.v9i6.13978>

INTRODUCTION

Acute liver failure (ALF) is defined as the development of impaired hepatic synthetic function with coagulopathy and the development of hepatic encephalopathy in the absence of underlying liver disease in <2-3 months time [1]. The specific pathogenesis of the liver injury is dependent to a large degree on the etiology. These injuries to hepatocytes cause cell damage or cell death by necrosis or apoptosis and these processes may coexist [1]. Triggering of the mitochondrial permeability transition by injury is mainly associated with apoptosis (if adenosine triphosphate (ATP) stores are preserved) and necrosis if there is ATP depletion [1]. ALF has many potential causes. A few of the more common causes include: Acetaminophen-an overdose of this drug is the most common cause. Viruses-hepatitis A, B, and E, as well as Epstein-Barr virus, cytomegalovirus, and herpes simplex virus, are all known to cause ALF. Autoimmune hepatitis, a disease in which the immune system attacks liver cells, can also cause ALF. A number of risk factors are thought to be associated with the development of drug-induced liver injury (DILI) [2]. In general, older age is a risk factor for DILI occurring more commonly in adults compared with children. While there seems to be a biological basis for age as a risk factor, it may also reflect that adults are more frequently exposed to potential hepatotoxins compared with children [2].

N-Acetylcysteine (NAC) is a thiol-containing agent that scavenges free oxygen radical and replenished cellular mitochondrial and cytosolic glutathione stores [3] and was first used as a treatment for paracetamol overdose which has been firmly established as an effective and safe treatment for this condition [4]. NAC has also shown to be safe and effective outside of paracetamol overdose. It has been evaluated as a treatment option for non-paracetamol ALF in adults and pediatric patients [2]. Treatment with NAC for these patients is beneficial either by improving systemic hemodynamics, tissue oxygen delivery, or via other favorable effects on the acutely injured liver [5,6].

CASE REPORT

A 65-year-old male patient, with history of chronic obstructive pulmonary disease (COPD), came with complaints of pedal edema and

breathlessness since 2 weeks. On evaluation, he was found to have coronary artery disease-non-ST elevation myocardial infarction. His lower respiratory tract infection worsened and was intubated; later, he developed multiorgan dysfunction syndrome (MODS). Computer tomography of the chest was done to rule out any features for tuberculosis, and it showed features of interstitial lung disease. On the basis of blood culture report, he was started treatment with intravenous antibiotics (injection meropenem 600 mg). Subsequently, his condition

Days	SGOT (IU/L)	SGPT (IU/L)
day 1	610	627
Treated with injection NAC 300 mg/hrs intravenous		
day 2	304	396
day 3	190	187.2
day 4	57.2	104.7

SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamate pyruvate transaminase, N-Acetylcysteine: NAC

improved and was extubated. Since there was saturation drop, he was on BIPAP for 1 day and later shifted to ward on nasal prongs. Injection meropenem was then changed to injection levofloxacin 500 mg once daily and fluconazole 200 mg once daily.

During his course at the hospital, his lab investigations showed elevated liver function test which was diagnosed as acute liver injury.

This was treated with injection NAC 300 mg/hrs intravenous infusion for 2 days, and his liver function test showed steady improvement within 2 days.

DISCUSSION

Although liver failure usually develops slowly over the course of many years, ALF due to acetaminophen or non-acetaminophen develops in a matter of days. Earlier, there was no established treatment for non-acetaminophen-induced ALF other than liver transplantation. Later, studies suggest that transplant-free survival was improved by NAC if this is diagnosed early [5]. NAC, which has been used in conventional

medicine for many years, primarily as a mucolytic agent was found to be safe with minor side effects that can be self-limited or resolved. These do not require treatment in intensive care and can also be given in community hospitals. Here, in this case, initially patient was admitted with acute infective exacerbation of COPD, and further, his condition worsened due to bilateral pneumonia with sepsis, coronary artery disease, and MODS. Later, it was found that his liver enzymes were elevated which on treatment with NAC was improved significantly. This highlights the importance of NAC in non-acetaminophen-related liver injury and improving the transplant-free survival rate.

CONCLUSION

ALF is the end stage of many acute viral and drug-induced hepatic diseases [7]. Survival of patients who have ALF depends on the etiology, with spontaneous or non-transplant recovery being the best option in patients with acetaminophen or non-acetaminophen-induced injury who receive timely treatment with NAC [1]. Through this study, we found that NAC for non-acetaminophen-induced ALF appeared to be safe with less duration of hospital stay and a higher incidence of native liver recovery.

REFERENCES

1. Schilsky ML, Honiden S, Arnott L, Emre S. ICU management of acute liver failure. *Clin Chest Med* 2009;30(1):71-87, viii.
2. Chughlay MF, Kramer N, Werfalli M, Spearman W, Engel ME, Cohen K. N-acetylcysteine for non-paracetamol drug-induced liver injury: A systematic review protocol. *Syst Rev* 2015;4:84.
3. Squires RH, Dhawan A, Alonso E, Narkewicz MR, Shneider BL, Rodriguez-Baez N, *et al.* Intravenous N-acetylcysteine in pediatric patients with nonacetaminophen acute liver failure: A placebo-controlled clinical trial. *Hepatology* 2013;57(4):1542-9.
4. Kortsalioudaki C, Taylor RM, Cheeseman P, Bansal S, Mieli-Vergani G, Dhawan A. Safety and efficacy of N-acetylcysteine in children with non-acetaminophen-induced acute liver failure. *Liver Transpl* 2008;14(1):25-30.
5. Lee WM, Hynan LS, Rossaro L, Fontana RJ, Stravitz RT, Larson AM, *et al.* Intravenous N-acetylcysteine improves transplant-free survival in early stage non-acetaminophen acute liver failure. *Gastroenterology* 2009;137(3):856-64, 864.e1.
6. Bass S, Zook N. Intravenous acetylcysteine for indications other than acetaminophen overdose. *Am J Health Syst Pharm* 2013;70(17):1496-501.
7. Holt AW. Acute liver failure. *Crit Care Resusc* 1999;1(1):25-38.