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Efficacy of L-Ornithine L-Aspartate in Recovery of Patients Suffering from Acute Viral Hepatitis

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ABSTRACT

Objective: To assess the efficacy of L-Ornithine L-Aspartate (LOLA) compared with non-LOLA Group in the recovery of patients with acute viral hepatitis.

Study Design: Quasi-experimental study.

Place and Duration of Study: Department of General Medicine, Railway Hospital, Rawalpindi Pakistan, from Aug 2020 to Jan 2021.

Methodology: All patients of either gender, aged >18 years with acute viral hepatitis were included. All patients were divided into two groups. LOLA-Group (Group-A) was given as an infusion over 24 hours at a dosage of 300 grams for three consecutive days. Whereas Group-B had patients to whom L-Ornithine L-Aspartate (LOLA) was not administered. The efficacy was defined as no signs and symptoms in comparison to baseline (clinical improvement), LFTs improved to more than half compared to baseline, and INR was <1.2 at seven days' follow-up.

Results: Of 128 patients, the median age was 28 years (20-32). A significant median difference in total bilirubin on the seventh day (*p*-value 0.044) was observed for the L-Ornithine L-Aspartate (LOLA)-Group. In addition, the efficacy was found to be significantly higher among patients in the Control Group as compared to the patients in the Treatment Group, i.e., 54(84.4%) and 40(62.5%), respectively (*p*-value 0.005).

Conclusion: This study showed that the outcome of L-Ornithine L-Aspartate (LOLA) is not very effective in managing patients with acute viral hepatitis.

Keywords: Acute viral hepatitis, Efficacy, L-ornithine L-aspartate.

How to Cite This Article: *Bilal E, Burney S, Sajid MU, Zulfiqar A, Farooq M, Shaukat N. Efficacy of L-Ornithine L-Aspartate in Recovery of Patients Suffering from Acute Viral Hepatitis. Pak Armed Forces Med J 2023; 73(3): 642-645. DOI: https://doi.org/10.51253/pafmj.v73i3.6473*

INTRODUCTION

Acute hepatitis is a common diagnosis of several acute inflammatory or hepatocytic disorders. It is an increasing health concern and could lead to severe complications.[1] Hepatitis is classed as acute if it improves in less than six months, and it is categorized as chronic hepatitis if irregular results last longer than six months.[2,3]

It is reported in various published studies that acute viral hepatitis could occur due to various reasons, including drug relation, causes, alcoholism, autoimmune disorder, and other associated disease like cholestatic, pregnancy-associated hepatic abnormalities, and shock.[4,5]

However, many efforts have been made to manage viral hepatitis effectively. However, still, a breakthrough is required to combat the disease prevalence and its related complications.[6,7] In Pakistan, the burden of viral hepatitis is continuously on the rise.[8] It is reported in various studies that increased ammonia levels negatively affect liver function & can exacerbate liver dysfunction.[9,10]

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Received:18 Mar 2021; revision received: 15 May 2021; accepted: 18 May 2021

In our practice, LOLA is also used to manage patients with acute viral hepatitis. However, this efficacy has yet to be reported by our population and from international studies. Therefore, we planned this research to determine the outcome of LOLA in treating patients with acute viral hepatitis.

METHODOLOGY

The quasi-experimental study was conducted at the Department of General Medicine Railway Hospital, Rawalpindi Pakistan, from August 2020 to January 2021. Institutional approval was obtained prior to conducting the study (ERC#Riphah/IRC/20/211). Non-probability consecutive sampling technique was applied. OpenEpi sample size calculator was used to estimate sample size, taking efficacy in Treatment Group as 63%, efficacy in Non-Treatment Group as 86%.[11]

Inclusion Criteria: All patients of either gender, aged >18 years with acute viral hepatitis were included in the study.

Exclusion Criteria: Patients having sepsis, chronic liver disease, acute on chronic liver failure, acute liver failure, obstructive jaundice, and choledocholithiasis were excluded.

Acute hepatitis has been described as a patient with at least two of the following signs and symptoms: fever, jaundice, upper abdominal pain, nausea or vomiting along with Alanine aminotransferase (ALT) level of more than 500, and positive any of the acute hepatitis viral serology like anti-hepatitis A virus immunoglobulin M (HAV-IgM), Anti-hepatitis E (HEV)-IgM, hepatitis B core-IgM, anti-hepatitis D virus (HDV).[12]

In Group-A, LOLA was administered at a dose of 300 gram daily per infusion over 24 hours for three days, while in Group-B were patients in whom LOLA was not administered. Demographic characteristics were noted along with clinical characteristics like fever, jaundice, upper abdominal pain, and nausea/ vomiting at baseline and seven days follow-up. The efficacy was defined as no signs and symptoms in comparison to baseline (clinical improvement), LFTs improved to more than half compared to baseline, and INR is <1.2 at seven days follow-up.[13]

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. Median and interquartile range was computed for quantitative variables. Frequency and percentages were calculated for quantitative variables. Inferential statistics were explored using the chi-square, Mann-Whitney U, and Wilcoxon sign rank tests. The *p*-value of ≤0.05 was considered significant.

RESULTS

Of 128 patients, the median age was 28(20-32) years. Most patients, 112(87.5%), were presented with hepatitis A, while 16(12.5%) were presented with hepatitis B. (Table-I) Fever at baseline was observed in 34 (26.6%) while on the seventh day in none 0(0%) of the patients. Jaundice at baseline was observed in 111(86.7%) while on the seventh day in 59(46.1%) patients. Upper abdominal pain at baseline was observed in 68(53.1%) while on the seventh day in 9(7%) patients (Table-II). A significantly higher proportion of jaundice was observed in patients presented in the Treatment Group as compared to the patients in the Control Group, i.e., 40(67.8%) and 19(32.2%), respectively (*p*-value <0.001). Similarly, a significantly higher proportion of nausea and vomiting were observed in the Treatment Group as compared to the patients in the Control Group, i.e., 24(72.7%) and 9(27.3%), respectively (*p*-value 0.002) (Table-II). A significant median difference in total bilirubin on the seventh day (*p*-value 0.044) was observed for the Group. (Table-III) Stratification based on the Treatment Group showed a significant median difference of INR, total bilirubin, and ALT at baseline and on the seventh-day follow-up in both groups (*p*-value <0.05) (Table-IV). The efficacy was found to be significantly higher among patients in the Treatment Group as compared to the patients in the Control Group, i.e., 54(84.4%) and 40(62.5%), respectively (*p*-value: 0.005).

Table-I: Comparison of Baseline Characteristics (n=128)

	L-Ornithine-L-Aspartate (n=64)	Non-L-Ornithine-L-Aspartate (n=64)	*p*-value
	Median (IQR)	Median(IQR)	
Age, years	29(21-31)	20(18-36)	0.027
Height, m	1.7(1.6-1.7)	1.7(1.6-1.7)	0.558
Weight, kg	62(56-67)	60(58-72)	0.954
BMI, kg/m2	23(19-23)	21(20-23)	0.567
	n(%)	n(%)	*p*-valueß
Age, years			
≤28	32(50.0)	36(56.3)	0.479
>28	32(50.0)	28(43.8)	
Gender			
Male	48(75.0)	37(57.8)	0.040
Female	16(25.0)	27(42.2)	
BMI, kg/m2			
<22.5	24(37.5)	45(70.3)	<0.001
22.5-25	32(50.0)	10(15.6)	
>25	8(12.5)	9(14.1)	
Etiology			
Hepatitis A	59(92.2)	53(82.8)	0.109
Hepatitis B	5(7.8)	11(17.2)	

¥Mann-Whitney U test, ßChi-square test applied

DISCUSSION

Viral hepatitis remains one of the world's main causes of acute liver failure. Its effective and prompt treatment could prevent various health issues.[14,15] The current study was conducted to assess the efficacy of the LOLA Group versus non-LOLA Group in the recovery of patients with acute viral hepatitis. L-Ornithine-L-aspartate, a mixture of two endogenous amino acids, is one such agent.[16]

The findings of the study have reported that a significantly higher proportion of jaundice was observed in patients presenting in the LOLA Group as compared to the patients in the non-LOLA Group, i.e., 67.8% and 32.2%, respectively.

Table -II: Comparison of Treatment Outcome (n=128)

	L-Ornithine-L-Aspartate (n=64)	Non-L-Ornithine-L-Aspartate (n=64)	*p*-value
	n (%)	n (%)	
Fever at Baseline			
Yes	16(47.1)	18(52.9)	0.689
No	48(51.1)	46(48.9)	
Fever on 7th day			
Yes	0(0)	0(0)	-
No	64(50)	64(50)	
Jaundice at baseline			
Yes	56(50.5)	55(49.5)	0.795
No	8(47.1)	9(52.9)	
Jaundice on 7th day			
Yes	40(67.8)	19(32.2)	<0.001
No	24(34.8)	45(65.2)	
Upper Abdominal Pain at baseline			
Yes	32 (47.1)	36(52.9)	0.479
No	32(53.3)	28(46.7)	
Upper Abdominal Pain on 7th day			
Yes	0(0)	9(100)	0.003
No	64(53.8)	55(46.2)	
Nausea/Vomiting at baseline			
Yes	0(0)	0(0)	-
No	64(50)	64(50)	
Nausea/Vomiting on 7th day			
Yes	24(72.7)	9(27.3)	0.002
No	40(42.1)	55(57.9)	

Table-III: Median difference of Clinical Characteristics (n=128)

Variables	Group		*p*-value
	L-Ornithine-L-Aspartate (n=64)	Non-L-Ornithine-L-Aspartate (n=64)	
	(n (%)	(n (%)	
INR at baseline	1.4(1.2-1.9)	1.3(1.2-1.6)	0.426
INR on 7th day	1.2(1.1-1.3)	1.2(1.1-1.2)	0.583
Total Bilirubin at baseline,mg/dl	10(8-11)	8(6-10)	<0.001
Total Bilirubin on 7th day, mg/dl	3(3-4)	3(2-4)	0.044
ALT at baseline, U/L	2190(1862-2807)	1893(1603-2260)	0.001
ALT on 7th day, U/L	425(334-866)	425(375-903)	0.848

Mann-Whitney U test applied

Similarly, a significantly higher proportion of nausea and vomiting were observed in the Treatment Group compared to the patients in the Control Group, i.e., 72.7% and 27.3%, respectively. However, a significantly higher proportion of upper abdominal pain on the seventh day was observed in the Control group compared to the patients in the Treatment Group, i.e., 27.3% and 0%, respectively. According to the current study fin-dings, a significant median difference in total bilirubin on the seventh day was observed for the group. However, a non-significant median difference of INR on the seventh day and ALT on the seventh day was observed between groups. Furthermore, the efficacy was significantly higher among patients in the Control Group than in the Treatment Group, i.e., 84.4% and 62.5%, respectively.

Table-IV: Median Difference of Clinical Characteristics at Baseline and at the Time of Follow-Up (n=128)

	Baseline	7th Day Follow-up	
	Median (IQR)	Median (IQR)	*p*-value
L-Ornithine-L-Aspartate (n=64)			
INR	1.4(1.2-1.9)	1.2(1.1-1.3)	<0.001
Total Bilirubin, mg/dl	10(8-11)	3(3-4)	<0.001
ALT, U/L	2190(1862-2807)	425(334-866)	<0.001
Non-L-Ornithine-L-Aspartate (n=64)			
INR	1.3(1.2-1.6)	1.2(1.1-1.2)	<0.001
Total Bilirubin, mg/dl	8(6-10)	3(2-4)	<0.001
ALT, U/L	1893(1603-2260)	425(375-903)	<0.001

Wilcoxon Sign Rank test applied

Though studies on the efficacy of LOLA in managing acute viral hepatitis are scarce.[17] However, Acharya et al.reported the efficacy of LOLA in patients with acute liver failure and also reported the same finding. Acharya *et al*. reported that LOLA did not improve the ammonia level or survival of the patient.[18] Butterworth *et al*. [14] and Varakanahalli *et al*.[19] in their published trials, reported effectiveness in lowering systemic ammonia levels and improving psychometric performance in patients with cirrhosis using both oral and intravenous L-ornithine l-aspartate.

The current study findings are also supported by the findings of a recent Cochrane meta-analysis conducted in patients with hepatic encephalopathy that also indicated the evidence of the effective outcome of LOLA is not strong. However, the outcome of LOLA needed to be better. Still, acute viral hepatitis and related hepatic diseases are major concerns. A large number of the population in Pakistan belong to rural areas and have poor socio-economic status. Therefore, most patients reported very late due to a lack of medical facilities and financial constraints compared to other developed countries. Therefore, it is important to investigate the current status of it in our country so that treatment of such patients should be anticipated in appropriate clinical lines, which will be helpful in quick recovery.

CONCLUSION

This study showed that the outcome of LOLA is not very effective in managing patients with acute viral hepatitis. Patients who did not receive LOLA also showed better efficacy regarding signs and symptoms and other clinical characteristics.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

EB & SB: Conception, study design, drafting the manuscript, approval of the final version to be published.

MUS & AZ: Data acquisition, data analysis, critical review, approval of the final version to be published.

MF & NS: Data interpretation, critical review, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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