L-ornithine L-aspartate lowers ammonia and improves cognitive function but not mortality in hepatic encephalopathy from acute on chronic liver failure

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Introduction

While hyperammonia is the primary cause of hepatic encephalopathy (HE) in acute liver failure (ALF), in acute-on-chronic liver failure (ACLF) its importance is reduced as many other factors may also impair cerebral function. The evidence for improving ammonia and HE using L-ornithine L-aspartate (LOLA) is debated and patients with ACLF underrepresented in randomised trials of LOLA.

Objective:
The aim of this project is to explore the efficacy of LOLA in patients with ACLF in a Liver intensive therapy unit (LITU) and report the clinical outcome.

Methods and Materials

A retrospective case-control study was performed of patients admitted to LITU in King's College Hospital between October 2017 and May 2020.

In all patients HE (grade >2 with associated hyper-ammonaemia) was a major and persistent component of the ACLF presentation.

LOLA was given in the treatment arm as either an IV infusion, (20g loading dose over 4hours followed by 20g over 24hours) or oral sachets (3-6g BD-TDS), for an average of 5 days.

The non-LOLA treated control group was matched by age, sex, aetiology of liver disease and mortality scores (acute physiology and chronic health evaluation (APACHE) and simplified acute physiology score (SAPS), chronic-liver-failure acute-on-chronic liver failure score (CLIF-C ACLF). The initial raised ammonia is termed early ammonia and after 5 days is termed late ammonia.

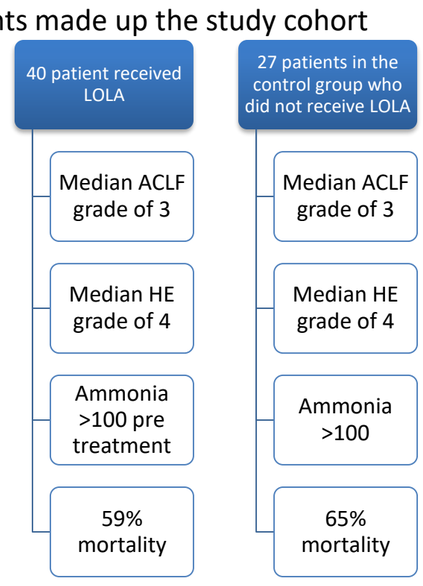
Table 1. Baseline Characteristics of the study participants by treatment group

Characteristic	LOLA	Control	P Value
Demographics			
M:F	25:15	19:09	0.157
Age (mean)	50	50	0.87
Aetiology [n; (%)]			
ALD	18 (45)	16 (59)	0.18
NAFLD	9 (23)	5 (19)	0.7
Autoimmune	4 (10)	1 (0.4)	0.34
Other	12 (30)	8 (30)	0.97
Mortality Scores on admission [mean (SD)]			
APACHE II	24.7 (6)	25.4 (7)	0.77
CLIF-C-ACLF	14.1 (2.3)	14.4 (2.3)	0.7
Ventilated [n; (%)]	27 (68)	13 (65)	0.7
CVVHDF [n; (%)]	14 (35)	12 (60)	0.05
Medication [n; (%)]			
Laxatives	4 (10)	6 (30)	0.08
Rifaximin	1 (2.5)	2 (7.4)	0.157

CLIF-C-ACLF European Foundation for the study of chronic liver failure acute consortium acute on chronic liver failure score

Results

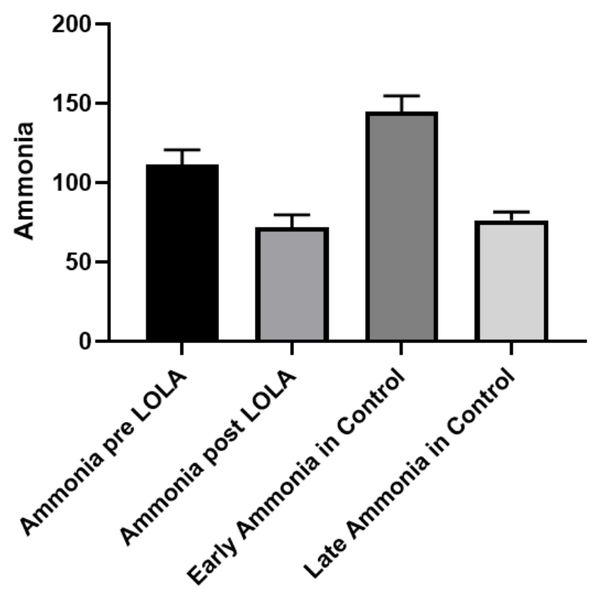
Sixty-seven patients made up the study cohort



•A significant reduction in ammonia (p=0.008) with a mean ammonia of 115.63 (61) pre LOLA and a mean ammonia of 78.7(52) post LOLA.

•The control group also had a significant reduction in the ammonia (p=0.01) with a mean early ammonia at 144.9 (52) and a late mean ammonia of 76 (27).

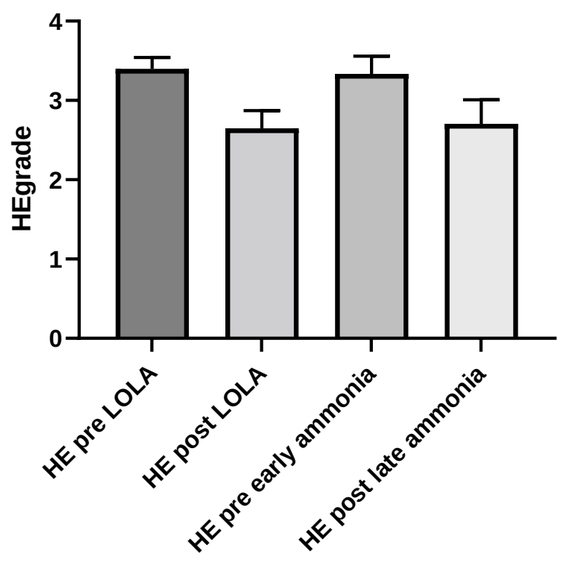
Graph 1



•A significant reduction in the HE grade (p=0.03) was seen in the group that received LOLA.

•However no significant reduction in the HE grade (p=0.08) was seen in the control group.

Graph 2



•Both the control and LOLA group saw a significant reduction in SAPS II score however only the control group had a significant reduction in APACHE II score.

Conclusions

In an intensive care setting, LOLA significantly reduces HE grade and plasma ammonia in patients with ACLF and HE.

In our retrospective case control study, LOLA did not appear to improve mortality or non-HE related organ failure severity.

Further investigation is required to assess its efficacy in early administration in ACLF driven by HE is required, ideally in a randomised controlled trial.

References

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