



PROGNOSTIC RELEVANCE OF ARTERIAL AMMONIA LEVELS IN HEPATIC ENCEPHALOPATHY

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ABSTRACT

Objectives of the study is to establish a correlation between arterial ammonia levels and the grade of hepatic encephalopathy and also to determine if the levels of arterial ammonia can be used as a prognostic marker of hepatic encephalopathy. This will result in better management of the patients and also improve the quality of life and reduce the cost burden on our health care system.

Methodology : This prospective study was carried out on 100 patients of medicine and gastroenterology department in a tertiary care hospital over a period of 3 months after taking written informed consent Mental status was assessed and graded on admission using THE WEST HAVEN CRITERIA for grading of mental status. Also the APRAXIA CHART method was used for the same for patients in hepatic encephalopathy grade 1. The diagnosis of hepatic encephalopathy was made when mental status was altered and appropriate laboratory and diagnostic tests excluded other causes.

Results : In this study we found a strong correlation of arterial ammonia with grade of hepatic encephalopathy. The highest level of arterial ammonia was seen with grade 3 or 4 of hepatic encephalopathy. Patients with grade 1 or 2 had arterial ammonia < 150 $\mu\text{mol/l}$ mostly. Out of 100 patients :- 0 patients – grade 0 - with no signs and symptoms, 24 patients – grade 1 (24%), 30 patients – grade 2 (30%), 26 patients – grade 3 (26%), 20 patients – grade 4 (20%) On follow up of 60 patients, 80% (24 out of 30) patients in grade 3 and 4 taken together, improved, that is, their ammonia levels decreased with fall in grade of hepatic encephalopathy. Similarly, 90.9% patients in grade 2 improved (20 out of 22) and 50% patients in grade 1 (4 out of 8) showed improvement.

Conclusion: This correlation between arterial ammonia levels and hepatic encephalopathy and use of this as a prognostic marker will result in better management of the patients and also improve the quality of life and reduce the cost burden on our health care system

KEYWORDS : Arterial Ammonia, Hepatic Encephalopathy, Grade, Mental Status

INTRODUCTION

Hepatic encephalopathy is defined as a chronic neuropsychiatric syndrome characterised by disturbances in consciousness and behaviour, personality changes, fluctuating neurological signs, asterix or flaps and distinctive EEG changes.

The pathogenesis of hepatic encephalopathy in chronic liver dysfunction is widely accepted to be due to failure of hepatic clearance of toxic products from the gut(1). The exact toxins involved remain controversial, but ammonia is thought to be an important factor(2).

This debilitating condition can negatively impact quality of life for patients and their families(3).

Furthermore, admissions for hepatic encephalopathy commonly result in prolonged hospital stays and a costly burden on our health care system.(4)

The determination of arterial ammonia (NH_4) levels is often performed in the clinical setting to support the diagnosis of hepatic encephalopathy. However, this practice has been scrutinized over the past decade with poor correlation between NH_4 levels and hepatic encephalopathy.(5)

Poor sampling technique can artificially elevate NH_4 measurements.(6) However, the correlation between arterial ammonia levels and severity of hepatic encephalopathy is not consistent (8-9). Perhaps because the previous researchers have used suboptimal blood sampling sites (Eg: venous instead of arterial) and older and less reliable ammonia assays.

This study is of significant concern because :

(1) It will help obtaining a good correlation between degree of

hyperammonemia and grade of hepatic encephalopathy.

(2) Also in establishing if ammonia reproducibly precipitates episodes of coma along with compounds that form ammonia in GIT such as blood from haemorrhage or protein meals.

The purpose of this study is to examine the correlation between arterial ammonia levels and grade of hepatic encephalopathy and also to establish if arterial ammonia levels can/cannot be used as a prognostic marker of hepatic encephalopathy or if it can form a basis of follow up of such patients.

This will result in better management of the patients and also improve the quality of life and reduce the cost burden on our health care system.

MATERIALS AND METHODS

This prospective study was carried out on 100 patients of medicine and gastroenterology department in a tertiary care hospital over a period of 3 months after taking written informed consent and obtaining Institutional Ethics Committee approval.

Inclusion Criteria

Patients of ALD, CLD, Cirrhosis

Exclusion Criteria

1. Patients with altered sensorium due to primary CNS diseases or any other organic diseases.
2. Patients on hemodialysis.

Collection Of Data.

Details of the patients admitted in Medicine units and GE units were noted. Clinical and Laboratory information was collected at the time of admission only after the informed consent was obtained from the patient.

Laboratory Data Included:

- (1) Complete blood count
- (2) Arterial ammonia levels-by newer and more reliable enzymatic method.
- (3) Biochemical Examination:
 - (i) Renal function tests
 - (ii) Liver function tests
 - (iii) Urine routine examination
- (4) Microbiological Tests (wherever indicated)
- (5) Radiological investigations (wherever indicated)
- (6) Mental status was assessed and graded on admission using THE WEST HAVEN CRITERIA for grading of hepatic encephalopathy.

Also the APRAXIA CHART method was used for the same for patients in hepatic encephalopathy grade 1 .

OBSERVATIONS AND RESULTS

Out of 108 patients whom we approached for the study, eight patients did not meet the exclusion and inclusion criteria (2 did not have cirrhosis, 3 were on hemodialysis , 3 died within hours of admission).

The remaining 100 patients were included in the final analysis. The mean age selected was patients between 25 to 65 years of age.

Out of 100 patients :- (Table 1)

- 0 patient - grade 0 (0%)
- 24 patients – grade 1 (24%)
- 30 patients – grade 2 (30%)
- 26 patients – grade 3 (26%)
- 20 patients – grade 4 (20%)

Table 1 : Percentages Of Patients In Each HE Grade

Grade Of Hepatic Encephalopathy	Percentage Of Patients
Grade 0	0%
Grade 1	24%
Grade 2	30%
Grade 3	26%
Grade 4	20%

The highest level of arterial ammonia was seen with grade 3 or 4 of hepatic encephalopathy, mostly > 150umol/l. Patients with grade 1 or 2 had arterial ammonia < 150 umol/l mostly.

Therefore higher the grade higher was the ammonia levels showing a positive correlation between the arterial ammonia levels and hepatic encephalopathy grading.

To find the association between arterial ammonia levels we used Chi square test method for statistical Analysis (Table 2)

Table 2 : Arterial Ammonia Levels And HE Grade

GRADE	ARTERIAL AMMONIA LEVELS < 60 umol/L (NORMAL)	ARTERIAL AMMONIA LEVELS > 60 umol/L (DERANGED)	Chi Square value 5.27 (p > 0.05)
1.	12	12	
2.	14	16	
3.	8	18	
4.	0	20	

Calculated chi square value = 5.27

Since the calculated chi square value is less than table value, that is 5.99 at (2df), so the result is not significant. Although the values showed a positive association but the results are statistically insignificant. This could be due to small pool of patients taken under study. Therefore to correlate the levels of

arterial ammonia with grade of hepatic encephalopathy we need a large pool of patients and a large study to make the results statistically significant.

Therefore we were able to fulfill our first objective of our study, that is, a positive correlation was established between levels of arterial ammonia and grade of hepatic encephalopathy (though the results were statistically insignificant).

Now to fulfill our 2nd objective, that is, to see if arterial ammonia can be used as a prognostic marker of hepatic encephalopathy, we had to follow up the patients taken under study. Around 60 patients were taken for follow up (since the rest 40 were already discharged). These 60 patients were being given ammonia lowering therapy for their treatment.

The follow up study showed that 80% (24 out of 30) patients in grade 3 and 4 taken together , improved on follow up, that is, their ammonia levels decreased with fall in grade of hepatic encephalopathy.

Similarly, 90.9% patients in grade 2 improved (20 out of 22) and 50 % patients in grade 1 (4 out of 8) showed improvement.

Paired t test was performed to correlate our findings statistically.

Paired t test = 8.59
df = 30
p = 0.00

Since p < 0.05, the test is significant and correlated statistically.

Therefore, the improvement in patients on ammonia lowering therapy shows that ammonia is an important indicator to assess the severity of hepatic encephalopathy and can also be used as a prognostic marker.

DISCUSSION

We found a strong correlation between ammonia levels and the severity of hepatic encephalopathy. To overcome some of the limitations of previous studies, we optimized the conditions under which the relation between hepatic encephalopathy and ammonia levels was examined.

Ammonia measurement was performed using a newer and more reliable enzymatic method, and grading of encephalopathy was blinded to the ammonia measurements. Under these conditions, ammonia levels correlated strongly with the severity of hepatic encephalopathy.

In the study by Ong and colleagues (2003) – the conclusion was that “because of the substantial overlap in total ammonia levels and partial pressures between cirrhotic patients with and without hepatic encephalopathy, a single level has little clinical utility in the diagnosis of hepatic encephalopathy”.

In our study too the arterial levels showed a strong correlation with grade of hepatic encephalopathy , however the presence of substantial overlap of arterial ammonia could not be denied. To rule this out, a follow up of 60 patients was done which showed that the level arterial ammonia falls with the fall in grade of Hepatic encephalopathy , thus , supporting our study of correlation between the arterial ammonia levels and grade of hepatic encephalopathy.

In another study by Nicolao and co-workers (2003) (5), the authors came to conclusion that “ammonia levels are limited both for diagnosis of hepatic encephalopathy and for clinical management.” However, in our study we found that ammonia

levels acted as a good diagnostic indicator as well as a useful tool on which clinical management was based. Patients on ammonia lowering therapy (non absorbable disaccharides and oral antibiotic) improved rapidly with decline in arterial ammonia levels as well as grade of hepatic encephalopathy. This indicates that ammonia does have a significant role to play in hepatic encephalopathy.

CONCLUSIONS

Our study showed that 80% (24 out of 30) patients in grade 3 and 4 taken together, improved on follow up, that is, their ammonia levels decreased with fall in grade of hepatic encephalopathy. Similarly, 90.9% patients in grade 2 improved (20 out of 22) and 50% patients in grade 1 (4 out of 8) showed improvement.

Thus our study concludes that ammonia levels show a positive correlation with grade of hepatic encephalopathy.

This study can help in establishing a correlation between arterial ammonia levels and the grade of hepatic encephalopathy and also helps in determining the prognostic significance of arterial ammonia levels with hepatic encephalopathy grading. This will further result in appropriate management of the patients with hepatic encephalopathy based on ammonia lowering therapy and thus rapid recovery of patients. Hence, reducing the burden of mortality as well as cost in our country.

Conflicts Of Interest - None

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