Indian Journal of Clinical Biochemistry, 2007 / 22 (2) 136-139

ROLE OF HELICOBACTER PYLORI AND HYPERAMMONEMIA IN SUBCLINICAL HEPATIC ENCEPHALOPATHY IN CIRRHOSIS OF LIVER

C. Rekha, M. Srinivasa Phanidhar*, A. Vidya Sagar*, A. Revathi and W. A. Asra

*Deaprtments of Biochemistry and *Medicine, Gandhi Medical College & Hospital, Secunderabad, Andhra Pradesh.*

ABSTRACT

In a prospective study of 47 patients of subclinical hepatic encephalopathy in cirrhosis of liver, aged between 23 and 60 years, 49% showed Helicobacter pylori positivity by rapid urease test. The baseline characters of patients (mean age, serum creatinine, sereum albumin, serum bilirubin, prothrombin time) were similar among patients with and without Helicobacter infection in all the patients. There was no statistically significant difference in blood ammonia levels in either group of patients. Blood ammonia values showed good correlation with the functional state of liver function but they did not show statistically significant difference between two groups of patients in any of Child Pugh classes. It is concluded that Helicobacter pylori does not contribute significantly to blood ammonia levels and the severity of hepatic encephalopathy.

KEY WORDS

Helicobacter pylori, Hyperammonemia, Cirrhosis of liver, Hepatic encephalopathy.

INTRODUCTION

Hepatic encephalopathy (HE) is defined as an alteration of mental state in the absence of other causes of encephalopathy, due to impaired liver function and/or abnormal shunting of blood from the portal to systemic circulation. This is often accompanied by abnormal E.E.G.,elevated blood ammonia, and absence of other causes of encephalo-pathy (1). The exact pathogenesis of this remains unknown (1,2). Pathogenesity of Helicobacter pylori is related to its ability to produce large amounts of enzyme urease many times greater than that of urease positive bacteria (3). This ability to hydrolyse urea to produce ammonia has been the rationale for proposing the involvement of H.pylori infection (4-7). The importance of H.pylori as an independent risk factor for the development of HE is not yet clear,but it may play a contributory role in at least a subset of patients with cirrhosis and HE. Therefore, this prospective study was conducted, between July 2001 and January 2003, to determine the contribution of H.pylori to blood ammonia levels in patients of hepatic encephalopathy and to correlate various indicators of portal systemic encephalopathy with blood levels of ammonia and H. pylori status.

Address for Correspondence :

Dr. C. Rekha
Assoc. Prof. of Biochemistry
Gandhi Medical College & Hospital,
Secunderabad, Andhra Pradesh.
E-mail : drcrekha@yahoo.co.in

MATERIALS AND METHODS

Patients of chronic liver failure presenting to the out patient department and acute medical care unit of department of medicine and gastroeneterology, Gandhi Hospital (a tertiary level teaching hospital), Secunderabad were included in this study. However, patients with acute precipitating events for HE like spontaneous bacterial peritonitis, gastrointestinal bleed, excessive diuretic usage with electrolyte imbalance; patients with azotemia and other comorbid illness that can contribute to encephalopathy; patients who have consumed oral/systemic antibiotics, proton pump inhibitors and H2 antogonists within a month of study period; and patients who could not understand or follow Arabic numericals for number connection test were excluded for this study.

After obtaining an informed consent for the investigations, all the patients were advised overnight fasting. The blood samples were subjected for routine biochemical analysis including serum creatinine, serum electrolytes, serum proteins, prothrombin time, serum bilirubin, aspartate aminotranferase (AST), alanine aminitranferase (ALT) to exclude other causes of HE, and for estimation of blood ammonia levels. They were

subjected to brief neurological examination including the mental state assessment, presence of asterexis and number connection test. Electroencephalogram was performed in those who agreed for the same. Later,they underwent gastroscopy and an antral mucosa biopsy sample was obtained which was tested for H. pylori by rapid urease test (HP test by Star Tech, Calcutta). This consists of a urea rich medium with a pH sensitive dye. If urease is present in the mucosal biopsy specimen, it catalyses the hydrolysis of urea into ammonia and carbon dioxide. The resultant increase in pH of medium from ammonia generation changes the colour of the indicator. This test may take about 24 hours to show positivity particularly in the presence of a low bacterial density.

All these patients were later stratified into three classes, based on Child-Pugh scoring system in order to establish a uniform baseline liver functional status for comparison (reference).The mental state, grade of asterexis, number connection test, blood ammonia levels, and PSE index were compared between patients with H.pylori positive status and those without it using student 't' test and Chi square test. The p value <0.05 or less was considered as significant.

RESULTS

Out of 47 patients examined in this study, males (35) were more predominant in this study. The age of patients ranged between 23 and 60 years, with a mean age of 40.2 years The antral mucosa biopsy was positive in rapid urease test (indicating the presence of infection) in 23 patients while it was negative in 24 patients (no H. pylori infection). The demography data and blood investigation values of both groups are shown in Table- 1). The data in the table indicates that both groups of patients are similar in all respects. There was no statistically significant difference in the mean values of blood investigations in patients with and without H. pylori infection ($p > 0.05$). Even though the mean blood ammonia value in H. pylori negative patients (61.04 (mol/L) was slightly higher than that in H. pylori patients (56.75 (mol/L), there was no statistical sugnificant difference between the two groups ($p > 0.05$). The blood ammonia values shown in Child Plugh A, B, and C class of patients were not significantly different ($p > 0.05$) in the presence or absence of H. pylori infection (Table - 2). Blood ammonia values and other indices of portal-systemic encephalopathy showed good correlation with the functional status of the liver as indicated by Child Pugh scoring system (Table - 3).

Table 1 : Demographic data and blood investigations in H. pylori positive and H. pylori negative patients (n=47)

Parameters	H.pylori positive (n=23)	H.pylori negative (n=24)
Gender : Males	15	20
Females	8	4
Age : Mean (years)	40.13	44.4
Range (years)	23 - 55	30 - 60
Child Pugh class: A	11	12
B	8	7
C	4	5
S. Sodium (mEq/L)	140	138
S. Potassium (mEq/L)	4.30	4.03
S. Creatinine (mg/dl)	0.93	0.98
S. Albumin (gms/dl)	3.31	2.85
S. Biluribin (mg/dl)	2.49	2.43
S. Ammonia (mol/L)	56.75	61.04
Prothrombin time (sec)	18.5	18.5

Table 2 : Mean serum ammonia values in Child Pugh class A, B, and C patients.

Child Pugh class	H. pylori positive	H. pylori negative
A	38.14 (28.21 - 43.49)	37.92 (28.21 - 43.47)
B	62.0 (41.23 - 78.20)	73.0 (67.27 - 80.00)
C	96.23 (86.40 - 110.00)	99.32 (82.60 - 110.0)

Values are in mol/L; Values in parenthesis show range

Table 3 : Blood ammonia levels and various indices of portal-systemic encephalopathy (PSE) in Child Pugh class patients.

Child Pugh class	S. Ammonia (mol/L)	Mental status (arab units)	Asterexis (arab units)	Number counting test (arab units)	PSE index
A	38.03	3.00	2.085	3.12	0.365
B	68.00	3.21	2.325	3.40	0.501
C	97.77	6.00	2.800	4.00	0.693

DISCUSSION

The pathogenesis of HE is still poorly understood, but raised systemic ammonia concentration as a consequence of shunting of ammonia rich portal blood away from the liver and impaired urea genesis have long been causally implicated in its development (8). H. pylori urease activity in the cirrhotic stomach has been proposed to represent a significant source of ammonia, contributing to the development of HE (9,10). Previous reports have offered contradictory results with respect to the existence of differences in fasting blood ammonia concentration between H. pylori positive and H. pylori negative cirrhotic patients (5,9, 56, 11, 12). Rapid urease test used as a diagnostic tool for H. pylori detection has specificity and sensitivity of >90%, but false negative and false positive results do occur. This test is the least expensive, an excellent screening test, and the diagnostic test of choice when an endoscopy is performed (13). Hence, this test was used for the detection of H. pylori positivity in our study. Venous blood ammonia levels as a monitoring method (used in our study) in patients with liver dysfunction has been reported earlier by many investigators (11,12,14).

There was no statistically significant difference in the mean fasting venous ammonia samples in patients with early encephalopathy with or without H.pylori infection, which is similar to the blood ammonia values (47 ± 22 µ mol/l in patients without and 43 ± 22 µ mol/l in patients with H.pylori infection) reported by Vasconez et al (11) who also assessed H. pylori status by rapid urease test. Kini et al (12) also reported lower levels of fasting venous blood ammonia in patients with H.pylori infection (29 µ mol/l) than those without H.pylori infection (34 µ mol/l) in cirrhosis of liver disease. They also did not find any significant difference among the two groups which is similar to our observation.

The results of portal-systemic encephalopathy parameters shown in Table 3 did not show any statistically significant difference between the patients with and those without H. pylori infection in the present study. A similar observation has been reported by Vasconez et al (11) and Kini et al (12); thus suggesting no role of H.pylori in hepatic encephalopathy.

Dasani et al (15) suggested that H.pylori infection may be risk factor for hepatic encephalopathy only in individuals with advanced cirrhosis, but not in early liver disease. Our results do not rule out completely the role of H.pylori infection in the pathogenesis of hepatic encephalopathy in patients with more advanced liver disease since all our patients had relatively preserved liver function as assesses by Child Pugh scoring system. More over, patients with acute precipitating events for hepatic encephalopathy were excluded in the present study.

From the results of our study, it is concluded that in patients with portal-systemic encephalopathy, H.pylori infection is not a major contributing factor to fasting venous blood ammonia levels, there is no significant association between H.pylori infection and parameters assessing portal-systemic encephalopathy in patients with hepatic encephalopathy, fasting venous blood ammonia levels and various indicators of portal-systemic encephalopathy correlated well with the functional status of the liver as assessed by Child Pugh scoring system and there is no role of H.pylori infection in patients with early hepatic encephalopathy.

REFERENCES

1. Schenker S, Hoyumpa AM Jr. Pathophysiology of hepatic encephalopathy. Hosp Prac 1984; 19: 99-103, 107-108, 110-14.
2. Zieve L. Pathogenesis of hepatic encephalopathy. Metab Brain diseases 1987; 2: 147-65.
3. Dunn BE, Campbell GP, Perez-Perez GI, Blaser MJ. Purification and characterization of urease from Helecobacter pylori. J Biol Chem 1990; 265: 9464-9.
4. Ito S, Miyaji H, Azuma T, Li Y, Ito Y, Kato T, et al. Hyperammonemia and Helecobacter pylori. Lancet 1995; 346 (8967): 124-5.
5. Plevris, JN, Morgenstern R, Hayes PC, Bouchier IA. Hyperammonia in cirrhosis and Helecobacter pylori infection. Lancet 1995; 346 (8982): 1104.
6. Rinaldi V, Zullo A, Diana F, Capocaccia L. Helecobacter pylori, hyperammonemia and hepatic encephalopathy; is there a correlation?. Am J Gastroenterology 1997; 82: 723-4.
7. Miyaji H, Azuma T, Ito Y, Yamazaki Y, Ohtaki Y, Sato F, et al. Effects of H. pylori eradication therapy on hyperammonia in patients with liver cirrhosis. Gut 1997; 40: 726-30.
8. Jalan R, Seery J, Taylor-Robinson SD. Pathogenesis and treatment of hepatic encephalopathy. Aliment Pharmac Ther 1996; 10: 681-7.
9. Affli AF, Rinaldi V, et al. H. pylori- a major determinant of serum ammonia levels in cirrhotic patients. J Hepatol 1994; 20: 110 A.
10. Rossala M, Haag K, et al. H. pylori is not associated with increased risk of hepatic encephalopathy. J Hepatol 1994; 20: 111 A.
11. Vasconez C, Elizalde JI, Llach J, Gines A, dela Rosa C, Fernendez RM, et al. H. pylori, hyperammonia and subclinical portal-systemic encephalopathy: effects of eradication. J Hepatol 1999; 30: 260-64.

12. Kini D, Agarwal R, Saraswat Va, Naik SR. Role of Helecobacter pylori in hyperammonia and subclinical hepatic encephalopathy in cirrhosis of liver. Indian J Gastroenterol 2001; 20: 237-40.

13. Laine L, Lewin D, Naritoku W, Estrada R, Cohen H. Prospective comparison of commercially available rapid urease tests for the diagnosis of Helecobacter pylori. Gastrointestin Endosc 1996; 44: 523-6.

14. Si J, Cao Q, Gao M, Fang L, Qian G, Wang Y. Changes in serum ammonia concentration in cirrhotic patients with Helecobacter pylori infection. Chin Med J 2000; 113: 1080-81.

15. Dasani BM, Sigal SH, Lieber CS. Analysis of risk factors for chronic hepatic encephalopathy: the role of H. pylori infection. Am J Gastroenterology 1998; 93: 726-31.