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PROGRASSIVE ELEVATION OF PLASMA HOMOCYSTEINE (PHcy) AND BLOOD AMMONIA (BA) LEVELS IN LIVER CIRRHOSIS PATIENTS

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ABSTRACT Plasma Homocysteine (PHcy) and Blood Ammonia (BA) Levels are proposed to be involved in hepatic fibronogenesis and portosystemic encephapathy. Plasma Homocysteine (PHcy) and Blood Ammonia (BA) levels are increased in post absorptive patients with biopsy proven liver cirrhosis. There is also evaluating spenomegaly and hypersplnism (Thrombocytopenia) for the severity of liver cirrhosis patients. Identifying cirrhosis patients with high levels of plasma Homocysteine (PHcy) and Blood Ammonia (BA) concertration could be clinically useful.

KEYWORDS : Liver Cirrhosis, Plasma Homocysteine (PHcy) and Blood Ammonia (BA), Fibronogenesis, Portosystemic Encephapathy Spenomegaly And Hypersplnism Thrmbocytopenia

INTRODUCTION

Plasma Homocysteine (PHcy) and Blood Ammonia (BA) are proposed to be invoved in hepatic fibrogenesis and portosystemic encephapathy. Plasma Homocysteine (PHcy) and Blood Ammonia (BA) levels are increased in postaborbtive patients with biopsy proven liver cirrhosis. There is also evaluating spenomegaly and hypersplnism (Thrombocytopenia) for the severity of liver cirrhosis. Identifying cirrhotic patients with high levels of plasma Homocysteine (PHcy) and Blood Ammonia (BA) concentration could be clinically useful. Plasma Homocysteine (PHcy) is an amino acid found free in the body or in the form of disulfide and proteins. In a total homocysteine quantity, free or reduced is 1% -2%. The most prevalent form is protein bound homocysteine is about 80%. The liver has an important role in metabolism of homocyteine. The catabolism of homocysteine is impaired either due to enzyme defect or deficiency of required intracellular cofactor , Homocyteine accumulates in cells and reaches the circulation. The homocysteine values and factors are affecting the homocystenine metabolism in patients with liver cirrhosis. On other manifestation of portal hypertention include portal hypertensive gastropathy and large spontaneous shunt. The Prevalence of portal hypertensive gastropathy is high 60-80%. About 8% of the upper digestive haemorrhages in the cirrhotic patients with this there is elevation of Blood Ammonia in the patients with Cirrhosis.

MATERIAL AND METHODS

A total number of 35 patients with liver cirrhosis and 30 age and sex matched healthy controls are examined at the clinic for gastroenterology and hepatology, ESI Hospital ,ESI Medical College, Sanath Nagar, Hyderabad, Telangana state , India. Inclusion criterion was the patients diagnosis of liver Cirrhosis as an underlying disease. All the examinations were based on medical history , physical examination, laboratory tests and liver biopsy.

RESULTS

The results were expressed as ± mean. SD OR stated.The most common cause of liver was alcohol patients. The mean plasma homocyteine and blood ammonia levels were higher in the patients with cirrhosis than healthy controls. Correlation analysis showed a positive correlation between homocysteine and blood ammonia concentration $p < 0.01$.

A statistically significant difference between plasma homocysteine (PHcy) and Blood Ammonia (BA) values in patients with cirrhosis and healthy controls.

	Age/Sex	Controls (n =100)	Patients with Corrhosis (n=35)	P value
	40 – 60 ± 15 (Male)			
	30 – 50 ± 10 (Female)			< 0.001
Plasma Homocysteine (PHcy)		9.17 ± 1.99 µmol/L	14.85 ± 5.40 µmol/L	< 0.001
Blood Ammonia (BA)		73 ± 4.04 mcM/L	220 ± 12.054 mcM/L	

DISCUSSION

The liver plays a central role in the synthesis and metabolism of homocysteine, given the fact that the majority of dietary methionine is metabolized in this organ, where 85% of the whole body capacity for transmethylation resides.1-5 Accordingly, the liver displays a specific pattern of expression of genes involved in methionine and homocysteine metabolism. There are 2 genes coding for methionine adenosyltransferase (MAT), the enzyme that converts methionine into AdoMet, one (MAT1A) is expressed exclusively in the liver and a second gene (MAT2A) is expressed in all tissues.5 BHMT and CBS expression is confined mainly to the liver, whereas MS is widely expressed. Thus, it is conceivable that in situations of liver damage, alterations in Hcy may occur. In fact, hyperhomocysteinemia has been reported in chronic alcoholics and in patients with alcoholic cirrhosis, as well as in experimental models of liver damage6-10. Although there is extensive evidence about the above-mentioned genetic and nutritional determinants for hyperhomocystinemia, knowledge of the molecular basis of the alteration of Hcy metabolism in liver injury is still limited. The pathological mechanisms by which elevated Hcy promotes atherothrombotic vascular diseases are not completely known.2,3 Endothelial injury, which can lead to altered NO production and impaired platelet modulating activity, has been demonstrated11.In addition, Hcy promotes DNA synthesis and collagen production in vascular smooth muscle cells (VSMCs) cholesterol production by hepatic cells and lymphocyte DNA hypomethylation. These observations suggest a multifactorial mechanism of action for Hcy that may take place not only at the vascular level but on a variety of cellular backgrounds. In the present report, we describe our attempt to gain further insight into the mechanisms behind the hyperhomocysteinemia associated with liver damage and into the molecular basis of Hcy interference with normal cell function. Hepatic encephalopathy, the neuropsychiatric manifestation of liver disease, incorporates a spectrum of manifestations ranging from minimal derangements in neuropsychological function to confusion and coma. Over the past 10 years, studies have confirmed the strong association between hyperammonemia due to liver dysfunction and infection/inflammation in the pathogenesis of HE, in acute liver failure, cirrhosis, and more recently in acute-on-chronic liver failure. In the presence of chronic liver dysfunction, urea synthesis is impaired and the brain acts as an alternative major ammonia detoxification pathway. Astrocytes have the ability to eliminate ammonia by the synthesis of glutamine,

however, hyperammonemia leads to the accumulation of glutamine within astrocytes, which exerts an osmotic stress that causes astrocytes to take in water and swell. The determination of plasma ammonia levels is often performed in the clinical setting to support the diagnosis of HE. However, this practice has been scrutinized over the past decade with poor correlation between ammonia levels and HE.20 Many conditions unrelated to liver disease can result in elevated ammonia levels. Plasma ammonia levels are generally higher in patients with liver disease; however, the use of plasma ammonia levels as a diagnostic marker for HE presents many challenges.2 Results showed a strong correlation between blood ammonia and homocysteine levels with liver cirrhosis in the study population.

CONCLUSION

In liver cirrhosis the genesis of homocysteine and blood ammonia were multofactorial , influenced significantly by impaired catabolic liver function, renal failure and hypoalbuminermia.This prospective study showed that ammonia and homocysteine levels correlated with cirrhosis in the study population. Also, majority of patients coming to the study hospital with hepatic encephalopathy and hepatic fibrogenesis . Therefore, there is a need to focus on such population more vigilantly for blood ammonia and plasma homocysteine levels are helpful tool in this regard.

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