Serum Lithium in Hepatic Cirrhosis with and without Hepatic Encephalopathy

Thesis

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بسم الله الرحمن الرحيم

﴿وقل ربِ زدنى علماً﴾

صدق الله العظيم

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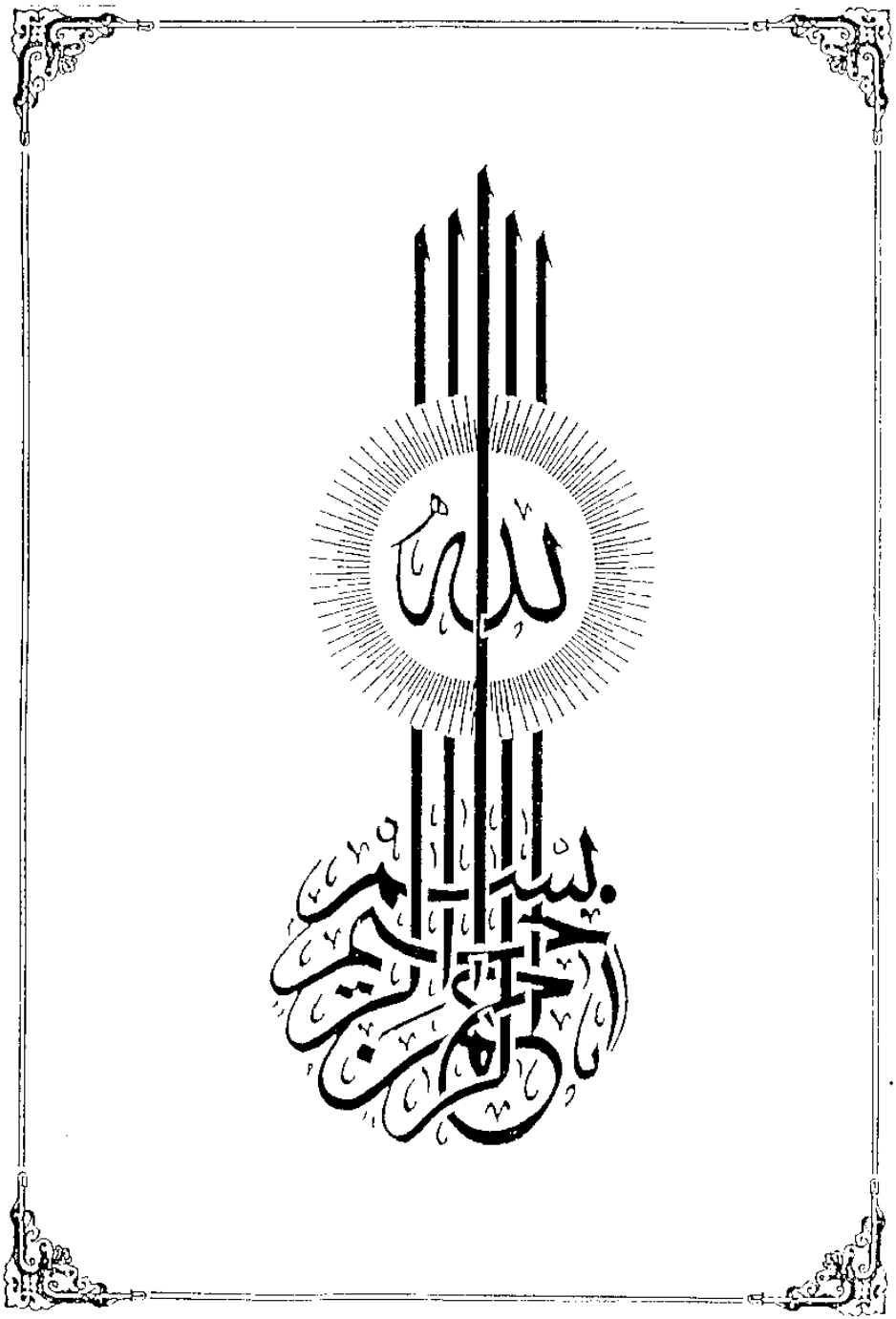

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Hepatic encephalopathy is a neuropsychiatric syndrome which may complicate liver disease of almost all types. It can culminate in coma and death (Sherlock, 1985).

The encephalopathy of cirrhosis has portal-systemic shunting as a component but hepato-cellular damage is also important (Sherlock, 1985).

In most cases of hepatic encephalopathy the neuro-pathologic alterations are insufficient to account for the clinical manifestations. It seems that the metabolic abnormalities rather than the anatomic abnormalities are the likely bases of this syndrome (Zieve, 1982).

Unlike vitamins trace elements can not be synthesized in the body. These trace elements represent an extremely small part of the total organism.

Lithium is found to be a trace element which is biologically active in many tissues especially those of neuro-endocrine system (Smith, 1988).

Although the physiological role of lithium in the human cells is still being explored and the relation of its level to some certain diseases are not found yet, the use of lithium as a drug therapy, especially in psychiatric illness is increasing.

AIM OF THE WORK

The aim of this work is to study serum lithium in cirrhotic patients with and without encephalopathy and to find out whether lithium level can contribute to the pathogenesis of neuro-psychiatric syndrome of hepatic encephalopathy.

Review of Literature

LIVER CIRRHOSIS

INTRODUCTION

In Babylonian days, the liver was endowed with such mystic powers that the priest physician would examine minutely that organ of sacrificial animals for signs of import from the gods (divination).

Throughout much of recorded history there was a belief that the liver was in the center of things which in truth it is.

Consider the theory of the four humors-buried in the teaching of Hippocrates, Empedocles and Aristole... blood is hot and moist like air, phlegm is cold and moist like water, yellow bile is hot and dry like fire and black bile is cold and dry like earth.

As one or another of these humors predominated in an individual, he was supposed to be of a sanguine, phlegmatic, chloric or melancholy temperament (Libby, 1922).

DEFINITION

Cirrhosis is a condition involving the entire liver in which the parenchyma is changed into a large number of nodules separated from one another by irregular branching

and anastomosing sheets of fibrous tissue. It results from long continued loss of liver cells with a persistent inflammatory reaction accompanied by fibrosis and compensatory hyperplasia.

The condition is irreversible and the fibrosis and architectural distortion interfere with the flow of blood through the liver (Muir's, 1982).

The features of cirrhosis which includes extensive fibrosis in association with the formation of regenerative nodules result from hepatocyte necrosis, collapse of the supporting reticulin network with subsequent connective tissue deposition, distortion of the vascular bed and nodular regeneration of remaining liver parenchyma (Jones et al., 1984).

Cirrhosis can best be defined in terms of what is patho-anatomically certain about the liver. Cirrhosis is a chronic disease of the liver in which diffuse destruction and regeneration of hepatic parenchymal cells have occurred and in which a diffuse increase in connective tissue has resulted in disorganization of the lobular architecture (Ludwig and Elveback, 1972).

Although some observers have argued about whether the scar tissue represents de novo formation of connective tissue or whether collapse and condensation of pre-existing structural tissue is responsible, all agree that the amount

of connective tissue scar is increased. In all cirrhotic patients regardless of the presence, absence or nature of the individual clinical manifestations, the triad of parenchymal necrosis, regeneration and scarring which was first emphasized by Rossle is present (Leon Schiff, 1975).

Cirrhosis is defined anatomically as a diffuse process of fibrosis and nodule formation. It has followed hepatocellular necrosis. Fibrosis is not synonymous with cirrhosis (Anthony et al., 1977).

PATHOGENESIS OF CIRRHOSIS

Cirrhosis results from long continued loss of liver cells, accompanied by compensatory liver cell hyperplasia and nodule formation and by a chronic inflammation and progressive replacement fibrosis e.g., chronic hepatitis. The irregular liver cell hyperplasia and fibrosis interfere with blood flow to such an extent that whatever the initial cause of the injury hepatocyte loss continues as a result of ischaemia. The changes become progressive leading to death from hepatocellular failure and/or portal hypertension (Muir's, 1982).

When large areas of parenchymal cells have undergone necrosis, as may occur in severe viral hepatitis, these empty necrotic areas collapse and undergo collagenization. The passive septa thus formed represent merely the

condensation of the collapsed reticular supporting framework of the hepatic parenchyma. This pattern is characteristic of sub-acute hepatic fibrosis of viral hepatitis (Boyer and Klatskin, 1970).

Alcoholic liver injury is centri-lobular but the process extends in bridge-like fashion to the portal tracts. Massive necrosis of whole lobules, however, may also occur in alcoholic hepatitis and may thus cause broad areas of collapse that accounts for the post-necrotic pattern, sometimes seen in alcoholic liver cirrhosis (Galambos, 1972).

Active fibroplasia is stimulated by alcoholic injury and inflammation of parenchymal, ductular, sinusoidal and reticulo-endothelial cells.

This fibroplasia gives rise to active septa which radiate to the parenchyma, primarily from the portal areas (Lieber, 1973).

Simultaneously, hepatic parenchymal necrosis stimulates regeneration. Parenchymal hyperplasia which occurs at the same time further distort the random fibrous pattern (Leon Schiff, 1975).

Irrespective of the etiology, the ultimate histological pattern of the liver is the same or nearly the same. Necrosis may no longer be apparent by the time, the

liver is examined. This may be piecemeal in Rappaport's zone, leading to portal-portal fibrous bridges. Confluent necrosis in zone 3 leads to centro-portal bridging and fibrosis. Spotty necrosis is followed by focal fibrosis (MacSween, Anthony, Schever, 1987).

The necrosis is followed by nodules which disturb the hepatic architecture and a full cirrhosis developed. sinusoids persist at the periphery of the regenerating nodules at the site of the portal-central bridges. Blood is diverted past-functioning liver tissue leading to vascular insufficiency at the centre of the nodules (zone 3) and even to persistence of cirrhosis after the initial causative injury has been controlled. The distribution of the fibrous septa varies with the causative agent (Sherlock, 1989).

CLASSIFICATION OF CIRRHOSIS

The major problem that complicates classification of cirrhosis is the frequent lack of correlation between the etiology and pathologic types of cirrhosis.

In Laennec's alcoholic cirrhosis, for example, which is supposedly characterized by uniform, micronodular formation and fine, almost ubiquitous strands of connective tissue, one may frequently find, large, irregularly sized nodules and brands, dense bands of scar, characteristic of

post-necrotic cirrhosis especially in later stages. Both lesions often co-exist in the same liver, the so-called mixed cirrhosis (Gall, 1960).

One may find micro-nodular Laennec-like nodules in post-hepatitis cirrhosis (Rubin et al., 1962).

Expert pathologists have frequently disagreed in differentiating Laennec's from post-necrotic and post-hepatitic cirrhosis in the blind histologic classification of cirrhosis (Goldblatt, 1947).

The gross appearance of the liver may often be more reliable than a small histologic sample (Steiner, 1960).

A. MORPHOLOGICAL

Micro-nodular:

Is characterized by thick, regular septa, by regenerating small nodules varying little in size and by involvement of every lobule. It may represents impaired capacity for regrowth as in alcoholism, malnutrition, old age or anemia.

Macro-nodular:

Is characterized by septa and nodules of variable sizes and by normal lobules in the larger nodules (sherlock, 1989).