RELATIONSHIP BETWEEN THE DOPAMINERGIC FUNCTION AND THE PROGNOSIS OF HEPATIC ENCEPHALOPATHY

THESIS

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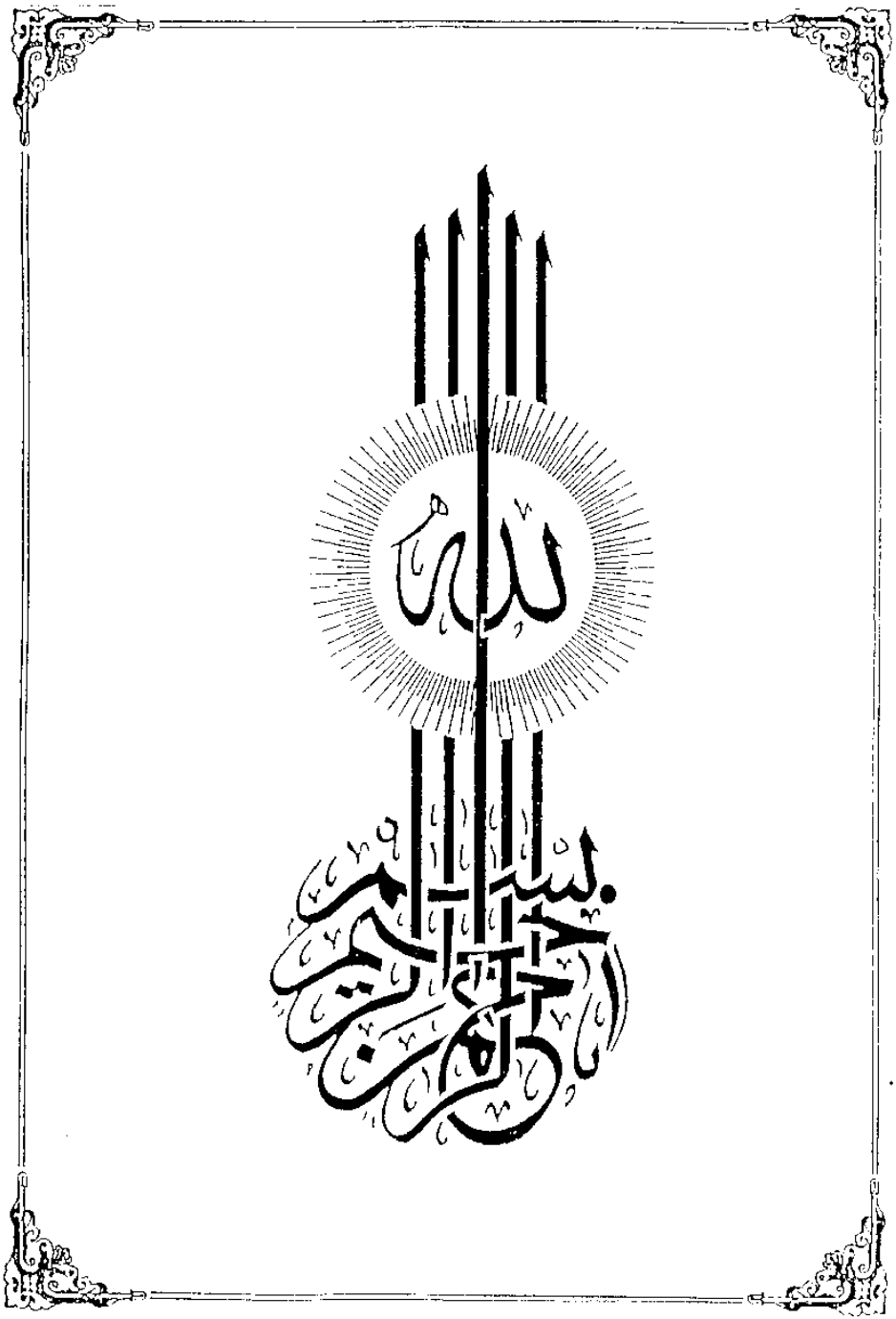

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INTRODUCTION

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Portal systemic encephalopathy (PSE), is a comlex patho-physiologic state which is probably multifactorial in origin. (Zieve, L., 1975).

One recently putative mechanism for PSE is the accumulation of false neurotransmitters, such as octopamine, and phehyleth-nolamine, occuring in association with depletion of true neu-rotransmitters, such as dopamine (Fischer, 1976), (James, et.al.1975).

Recently it has been questioned wheather the abnormalities in neurotransmitters observed in PSE play a primary causative role or wheather they merely represent correlation with PSE (Zieve, et.al., 1979).

McClain, found out that in patients with alcoholic liver disease and PSE they all had marked elevated prolactin level as compaired to controls. Also found among patients with PSE those who had a markedly higher prolactin level, (more than 3 times normal), had significantly greater derangement of serum albumin, billirubin, prothrombin time and also had a higher mortality rate, when compaired to the other group of PSE patients with plasma prolactin of less than 3 times normal. (McClain, CJ., et. al., 1981).

Prolactin is a pituitary hormone whose release is regulated in part by dopamine. (Tuomisto, J., 1978).

Moreover, agents directed at correcting neurotransmitter abnormalities such as bromocriptine, L-Dopa, and special amino-acid infusion have been used with success in treatment of PSE. (Morgan, MY., et.al., 1977).

Aim of The Work

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The aim of this work is :

1- To find out the plasma prolactin level in patients with PSE due to liver cell failure.

2- Suggest a possible role for plasma prolactin in the selection and monitoring of PSE patients who are to be treated with agents aimed at correcting neurotransmitter abnormalities.

Hepatic Encephalopathy

Hepatic encephalopathy (hepatic coma) is a commonly encountered problem in patients with liver disease.
It is defined as a neuropsychiatric syndrome characterized by, intellectual deterioration, altered state of consciousness, and neurologic abnormalities in a patient with advanced liver disease or porta - systemic shunting (Zieve, 1979).

Sherlock, states that the syndrome of hepatic ecephalpathy is difficult to synthesize into an entity, that a spectum of syndromes exists :-

(i) Chronic portal-systemic encephalopathy, with a 100% survival, the eitiological factors for this type are : Portal systemic shunting, dietary protien intake, intestinal bacteria.

(ii) Cirrhosis with precipitant, with a 70-80% survival, among the precipitating causes are :
Diuresis, haemorrhage, paracentesis, infection, diarrhoea and vomiting, surgery, alcoholic excess, sedatives, fluid and electrolyte abnormality.

(iii) A third type is acute liver failure, with 20% survival tate, among its aetiological factors are :
Viral hepatitis, alcoholic hepatitis, drugs reaction and over doses (Sherlock, 1985).

Clinical Features

The picture is complex and affects all parts of the brain. The disorder is an organic mental reaction, associated with a neurological disturbance. Variability is a marked feature, particularly in the more chronic forms. The featurs depend on the nature and intensity of aetiological and precipitating factors. Children show a particularly acute reaction, often with mania. Disturbed consciousness with disorder of sleep is usual. Hyper somina appears early and progress to inversion of the sleep rhythm. Reduction of spontaneous movements, a fixed stare, apathy, and slowness and brevity of responce are early signs, further deterioration result in reaction to intence or noxious stimuli. Personality changes are most conspicuous, with liver disease. These include : childishness, irritability and loss of concern for the family. Even in remission the patient may present similar personality features suggesting frontal lobe involvement (Sherlock, 1985).

Focal defects appearing on a setting of clear conciousness relate to disturbance in visual spatial gnosis. These are most easily elicited as construtional apraxia shown by inability to reproduce simple designs with blocks or matches. (Davidson E., et.al., 1966).

The (Reitan) trial making test, a standerd may be used serialy to assess progress. (Conn Ho , 1977).

Speech is slow and slurred and the vioce is monotonous. The most characteristic neurological abnormality is the flapping tremor (asterixis), this is due to impaired inflow of joint and other afferent information resulting in lapses in posture, gait is ataxic.

Flapping tremors are not specific for hepatic precoma it can also be seen in ureamia, respiratory failure, and in severe heart failure. (Sherlock S., 1985).

Diagnosis

Hepatic encephalopathy, is a clinical syndrome, and the diagnosis is based on the history, physical examination, and laboratory findings. The history and physical examination, will be suggestive of hepatic failure, and the neurologic examination will demonstrate ulterations in the neuro-muscular and mental status. Patients with acute hepatic failure are usually quite jaundiced and the liver failure is generally apparent.

Hyperammonemia is found in the majority of patients with hepatic encephalopathy. It is not found in all patients, however, since the blood ammonia level depends on both the rate of production and metabolism of ammonia. Because of this apparent discrepancy, the use of blood ammonia level to diagnose hepatic encephalopathy is unreliable. However, blood ammonia level does appear to be useful in following the clinical state of individual patients. (Mutchnick, MG., 1974).

Cerebrospinal fluid glutamine, which is the end product of cerebral ammonia metabolism, is usually elevated in hepatic encephalopathy. Elevated cerebrospinal glutamine levels have been alleged to be more specific than blood ammonia level and may distinguish between encephalopathy of hepatic and other causes (Mourani, et.al., 1971).

Ammonia and, hence, glutamine levels may also be elevated in hepatic encethalopathy as a consequance of ensuing renal failure, which may result in worsening the coma, or, misinterpretation of these tests. (Imler, M., et.al., 1979)

Abnormalities of amino acids, short chain fatty acids, and false neurotransmitters are known to be abnormal in hepatic encephalopathy. Although wheather this represents a cause or an effect is not well established.

Electroecephalography may also be used to diagnose hepatic encephalopathy, Laidlow, found that in patients with hepatic coma there is. Generalized slowing of cereberal electrical activity, usually accompained by high voltage, and slow wave form (Laidlow, J., et.al., 1963).

Pappas noted that triphasic waves in paroxysmal bursts are commonly found in electroencephalograms of patients with hepatic encephalopathy, as are paroxysms of delta waves (1.5 to 3 Hz). (Pappas, CS., et.al., 1983).

These abnormalities are characteristic of but not specific for the disorder, since other metabolic encephalopathies can cause similar abnormalities.

Visually-evoked potential, Cohn is an expresion of post synaptic cellular potential activity. A flash of light elicits changes in subcortical and cortical neurones, through stimulation

of cortical areas. Latency and wave forms are constant. This is a useful method for differentiating the degree of encephalopathy and identifying the pre-clinical stage (Cohn et.al., 1966).