SERUM CHOLINESTERASE IN CHRONIC LIVER DISEASE

THESIS

رسالة

Submitted to the Faculty of Medicine
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In Partial Fulfillment for the Requirements of
Master Degree in Internal Medicine

By
Mona Mostafa Kamal Ali El-Rayes
M.B.B.Ch.

Supervisors

Prof. Dr.
Ali Monis
Professor of medicine
Faculty of medicine,
Ain-Shams University.

Dr. Inas Assfour
Assistant professor of medicine
Faculty of medicine,
Ain-Shams University.

Dr. Souzan kamal El-din Hussin
Lecturer of medicine
Faculty of medicine,
Ain-Shams University.

Ain-Shams University
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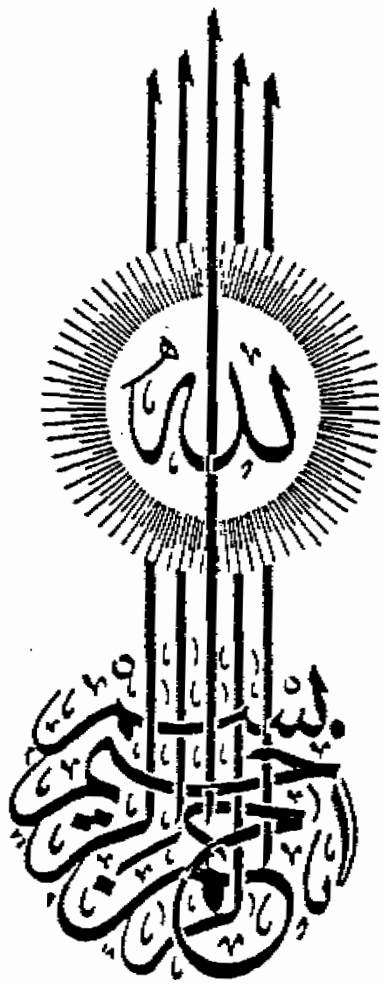

قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا
عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ.

صَدَقَ اللهُ الْعَلِيمُ
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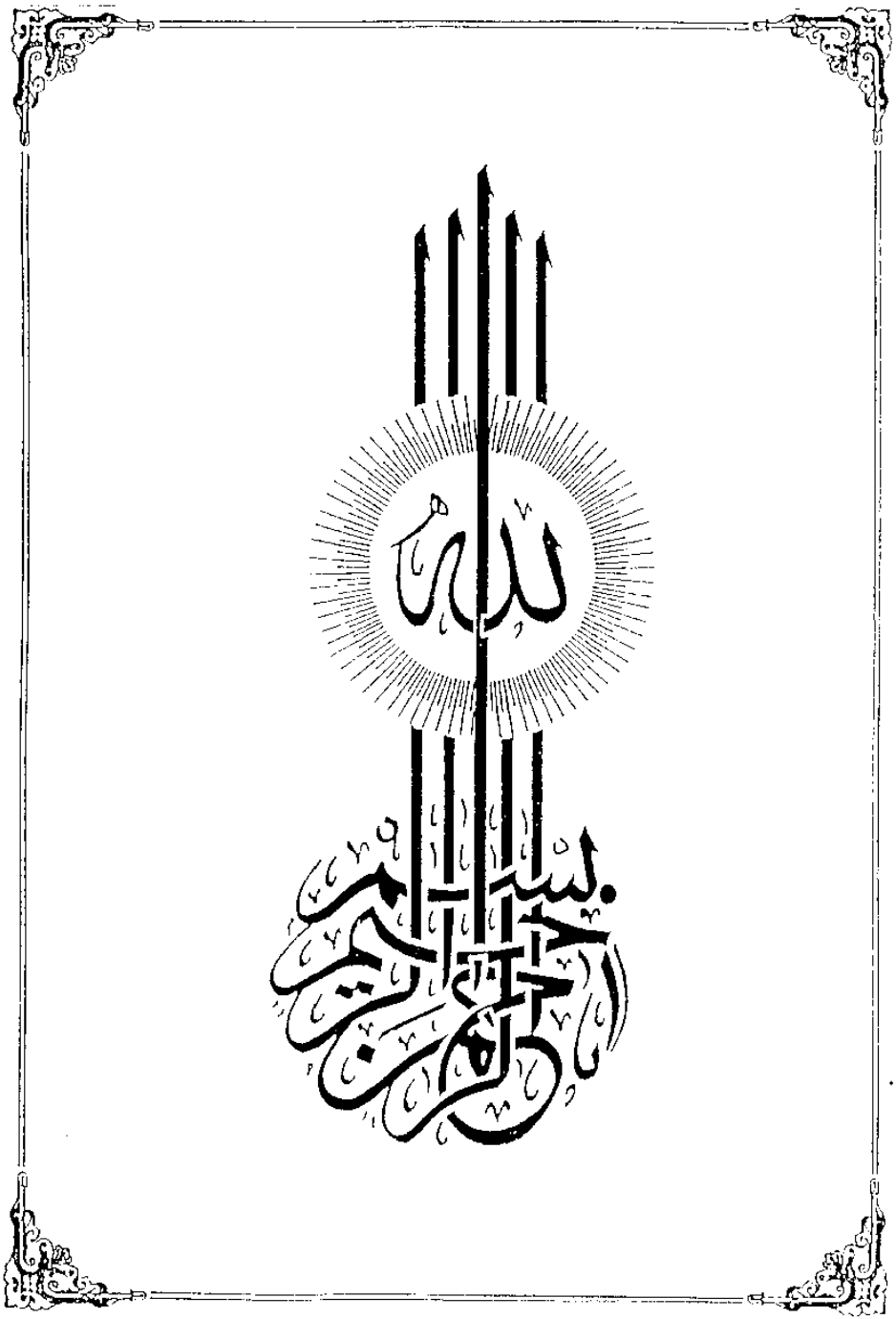

Dedication

To my mother

Who has given me
too much and received too little

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Contents

List of Abbreviations

- AAAs :Aromatic amino acids
- AEP :Auditory evoked potential
- BCAAs :Branched-chain amino acids
- Bz :Benzodiazepine
- ChE :Cholinesterase
- CSF :Cerebrospinal fluid
- DM :N-desmethyl-diazepam
- DN :Dibucaine number
- DZ :1,4-Benzodiazepines diazepam
- EEG :Electroencephalogram
- FHF :Fulminant hepatic failure
- FN :Fluoride number
- GABA :Gamma aminobutyric acid
- HE :Hepatic encephalopathy
- 5-HIAA :5-Hydroxy indolacetic acid
- 5-HT :5-Hydroxy tryptamine (serotonin)
- 5-HTP :5-Hydroxy tryptophan
- ICP :Intra cranial pressure
- PCS :Portocaval shunt
- PSE :Portosystemic encephalopathy
- QUIN :Quinolinic acid
- VEP :Visual evoked potential

INTRODUCTION AND AIM OF THE WORK

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Hepatic encephalopathy occurs in severe liver disease, whether acute (as in toxic or fulminant viral hepatitis and Reye's syndrome) or chronic (as in cirrhosis) (**Tietz *et. al.*, 1987**).

There are no diagnostic liver function test abnormalities although an elevated serum ammonia level is highly suggestive of the diagnosis and there is no predictive test to suggest the possibility of development of hepatic encephalopathy (**Podolsky and Isselbacher, 1991**).

In hepatic encephalopathy 10% of blood ammonia values are within the normal range (**Sherlock and Dooley,1993**).

The diagnosis is also most difficult when liver disease is not obvious (**Scharschmidt, 1992**).

Cholinesterase is a non specific esterase synthesized by the liver. It decreases in hepato-cellular disease, especially cirrhosis. (**Sherlock and Dooley, 1993**).

Any decrease in activity in serum reflects impaired synthesis of the enzyme by the liver. A 30-50% decrease in level is observed in acute hepatitis and in chronic hepatitis of long duration. Decreases of 50-70% occurs in advanced cirrhosis. Normal levels are seen in chronic hepatitis, mild cirrhosis and obstructive jaundice (**Tietz *et. al.*, 1987**).

In this study we try to use serum cholinesterase to assess hepatic impairment and as a predictor for the development of hepatic encephalopathy in comparison with blood ammonia.

REVIEW OF LITERATURE

HEPATIC ENCEPHALOPATHY

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Definition:

Hepatic encephalopathy (also called hepatic coma or portal-systemic encephalopathy) is a reversible neuropsychiatric syndrome which can accompany advanced, decompensated liver disease of all types and/or extensive portal systemic shunting **(Scharschmidt, 1992)**.

It is by definition reversible, and this distinguishes porto-systemic encephalopathy from acquired hepato-cerebral degeneration, an irreversible neurologic syndrome characterized by ataxia, dementia, and parkinsonian features and which may occur in the setting of prolonged porto-systemic shunting **(Pappas, 1990)**.

Myelopathy is another rare manifestation of advanced chronic liver disease and portal-systemic shunting and may be manifested by spastic paraparesis, hyperreflexia, and incontinence **(Scharschmidt, 1992)**.

Hepatic encephalopathy is the reversible decrease in the level of consciousness seen in patients with severe liver disease. Such patients characteristically have an abnormal electroencephalogram and a peculiar intermittency of sustained posture (asterixis). When the defect in the consciousness becomes sever, the syndrome deserves the name hepatic coma. Whereas early hepatic encephalopathy may be under diagnosed, this syndrome may be applied too often to any neurologic defect in a patient suspected of having liver disease. The non specificity of tests available to diagnose hepatic encephalopathy coupled with the predisposition of cirrhotics to subdural hematomas, intracranial hemorrhages, hypoglycemia, and tuberculous meningitis (to name just a few possibilities) prevent the careful clinician from hasty diagnostic judgment on a neurological defective, hepatically insufficient patient **(Schafer & Jones, 1990)**.

As with other types of metabolic encephalopathy, asymmetric neurologic findings are unusual, and brain stem reflexes such as the pupillary light response, oculovestibular response, and oculocephalic response are typically preserved. Thus asymmetric neurologic signs or abnormal brain stem reflexes may suggest a structural lesion of the central nervous system such as a subdural hematoma. Seizures are also uncommon in the absence of alcohol withdrawal and should alert the clinician to the possibility of a structural lesion or hypoglycemia. The disappearance of pupillary reactivity, of the oculocephalic or oculovestibular response, or of deep tendon reflexes is associated with a very poor prognosis in all types of metabolic encephalopathy, including hepatic encephalopathy (but excluding drug overdose) **(Scharschmidt, 1992)**.

It is a matter of debate whether or not the coma associated with fulminant hepatic failure is the same as that seen in patients with chronic liver disease. For example, the psychiatric (manic) presentation of acute disease contrast with the generally depressed and lethargic aspects of chronic encephalopathy. Also, there are pathologic differences. Cerebral oedema is more common in the acute patients, and astrocytic changes are more common in chronic cases.

The following table lists the features differentiating acute and chronic types of hepatic coma:

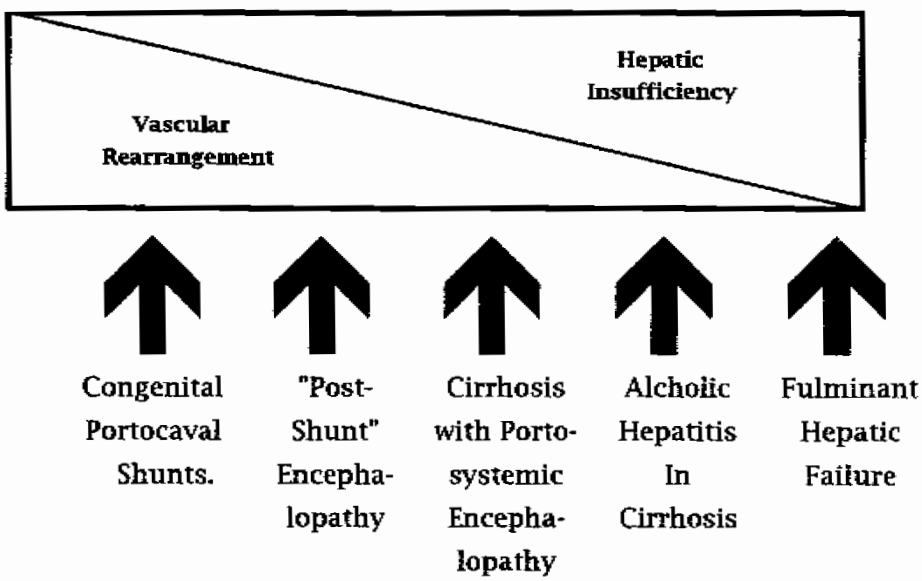
Features Distinguishing Acute From Chronic Encephalopathy

Feature	Acute	Chronic
Clinical features:		
Signs		
-Liver size	-Small or "shrinking"	-Firm, usually large
-Muscle mass	-Normal	-Reduced
-Abdominal collateral circulation	-Absent	-Present
-Ascites	-Occasional	-Usual
-Hepatic tenderness	-Present	-Absent
-Seizures	-Occasional	-Rare
-Asterixis	-Occasional	-Usual
-Mania	-Common	-Rare
Symptoms		
-Right upper quadrant pain	-Usual	-Occasional
-Rate of onset	-Abrupt	-Gradual
-Nausea & vomiting	-Usual	-Rare
Laboratory features:		
-Serum transaminases	-Very high	-Mildly elevated or normal
-Coagulopathy	-Always present	-Usually present
-Serum amino acids	-Generally increased except for branched chain amino acids	-Increased aromatic, decreased branched chain amino acids
Pathological features:		
-Central nervous system	-Cerebral oedema common -Herniation occasional	-Glial abnormalities very common (Type II astrocyte proliferation)
-Spinal myelopathy	-Absent	-Rare
-Hepatic	-Necrosis	-Cirrhosis

Because of ignorance regarding the underlying neurologic mechanisms in both of these syndromes, it is difficult to be dogmatic about their separation.

In order to unify all the types of hepatic encephalopathy encountered in practice, it is helpful to think of encephalopathy as being composed of at least two elements: hepatocellular insufficiency and vascular rearrangement (protal_systemic shunting) **(Schafer & Jones, 1990).**

The follwing figure portrays this as a spectrum of syndromes.
The spectrum of Hepatic Encephalopathy:



Hepatic encephalopathy has traditionally been divided into two syndromes: One is associated with fulminant hepatic failure; the other is protosystemic encephalopathy. However, some patients do not fit into these catigories. If encephalopathy is thought of as a mixture of hepatic insufficiency and vascular rearrangement (shunting), with one or the other predominating, a spectrum of encephalopathy can be constructed.

One end of spectrum is "pure" portal-systemic encephalopathy as seen in patients with congenital shunts and no liver disease **(Kerlan *et. al.*, 1982).**

A similar syndrome has been described in dogs and cats **(Ewing *et. al.*, 1984; Rothuizen *et. al.*, 1982).**

At the other end of spectrum is fulminant hepatic failure and acute hepatic encephalopathy. Between these extremes are the