Study Of Serum Manganese Levels In Relation To Chronic Hepatic Encephalopathy

Thesis Submitted For Partial Fulfillment Of Master Degree In Internal Medicine

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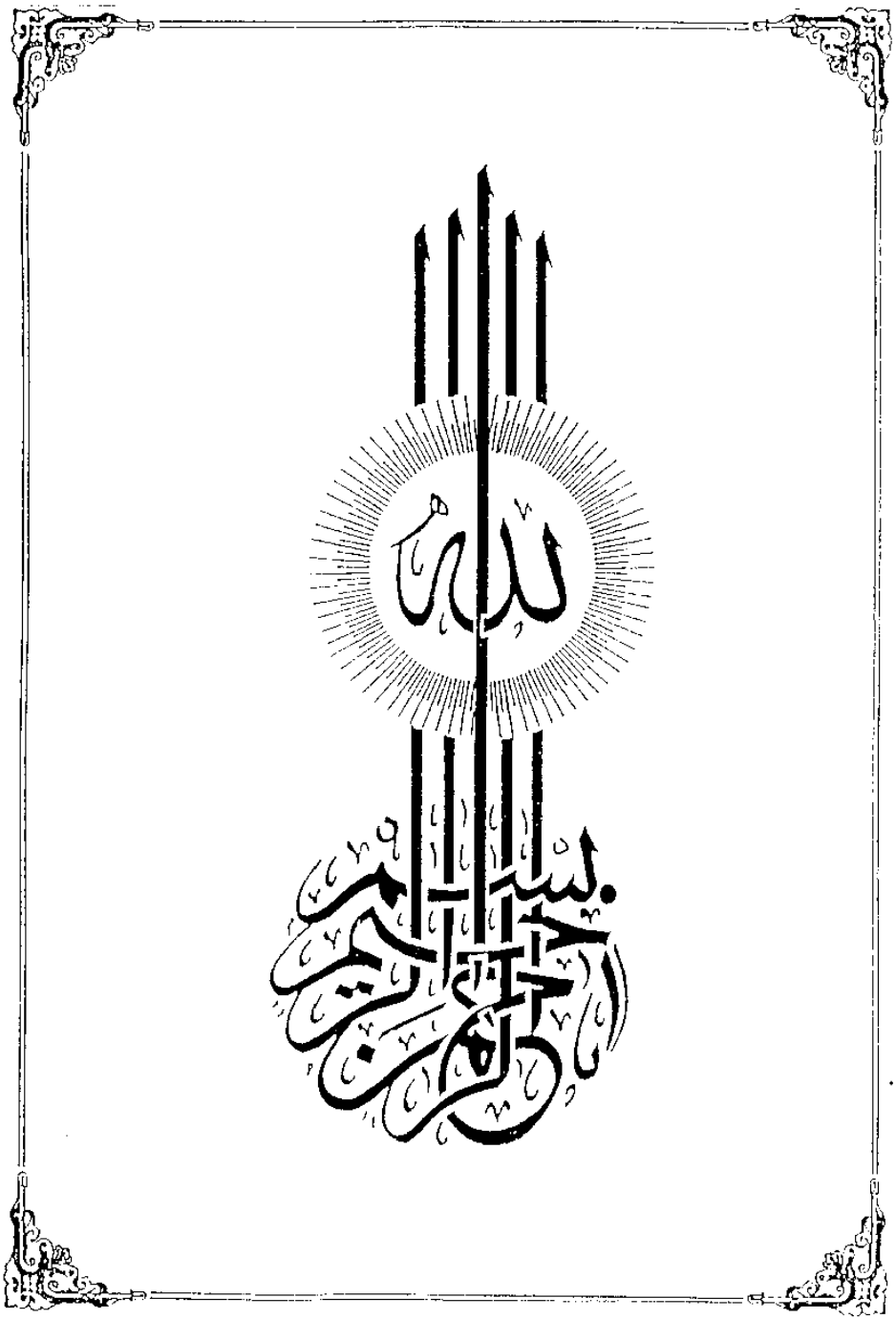
"و ما توفيقى إلا بالله عليه
توكلت و إليه أنيب"

صدق الله العظيم



DEDICATION

Dedicated To My

Mother

Husband

&

Lovely Daughters

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Introduction

INTRODUCTION

Chronic hepatic encephalopathy consists of progressive or episodic changes of personality and behaviour with blunted affect and deterioration of cognitive function. The neurological features include signs and symptoms of pyramidal and extrapyramidal dysfunction, brisk tendon reflexes and flapping tremors ***(Krieger et al., 1995).***

Manganese seems to have a special affinity for the extrapyramidal system, and was found to be neurotoxic possibly via striatal dopamine depletion, excitotoxicity or oxidative stress ***(Devenyi et al., 1994).***

Similarities between manganese neurotoxicity and the neurodegenerative features of chronic hepatic encephalopathy suggest that this metal has a role in the pathogenesis of chronic hepatic encephalopathy ***(Krieger et al., 1995).***

Both hepatocytes and astrocytes have a specific manganese transport system and in the CNS this metal is an integral component of important enzymes including superoxide dismutase and glutamine synthetase, the latter

is important for ammonia detoxification in liver failure ***(Norenberg et al., 1992).*** This enzyme accounts for about 80% of brains manganese ***(Wedler and Toms, 1986).***

Aim Of The Work

HEPATIC ENCEPHALOPATHY

Definition :

Hepatic encephalopathy is a complex neuropsychiatric syndrome that appears to be characterized predominately by augmented neural inhibition. The syndrome is a feature of acute, late onset, or chronic hepato-cellular failure ***(Sergio et al., 1989 and Krieger et al.,1996).***

Pathology:

Macroscopic:

Grossly, the brain may be normal, about half, usually the younger patients dying with prolonged, deep coma, show cerebral oedema ***(Sherlock, 1989).***

Adams and Foley, (1953) studied extensively the pathology of the brain and other nervous tissues. They found that, in some jaundiced patients, the dura seemed to have a pale greenish hue.

Microscopic :

The brain in hepatic encephalopathy shows no definite or consistent light or electron microscopic structural changes in neurons ***(Sergio et al., 1989).***

In some patients with liver cirrhosis and portal systemic shunts, there is increase in number and enlargement of astrocytes especially "AIZHEIMER" type II cells.

The characteristic finding of Al-Zheimer's type II astrocyte proliferation varies with the chronicity of the under lying liver disease ***(Butterworth et al., 1995).***

Long standing liver disease with hyperammonemia favours the development of this change. All humans with chronic liver disease show proliferation of Al-Zheimer's type II astrocytes but the relationship of this lesion to clinical neurologic defects is not clear ***(Norenberg, 1981).***

Al-Zheimer's type II change is present in the grey matter of cerebrum, cerebellum, putamen and globus pallidus (the nerve cells show relatively minor alterations) ***(Sergio et al., 1989; Sherlock and Dooley, 1997).***

These changes may be reversible and appear to be specific for liver disease and/or increased portal-systemic shunting of blood ***(Duffy and Plum, 1982 and Zieve, 1982).***

In very long standing case, the structural changes may be irreversible and the patient unresponsive to treatment. The cortex is thinned, neurons and fibers are lost ***(Victor, 1965).***

The deep layer's of cortex may show laminar necrosis. The cerebellum and basal ganglia are also involved. Demyelination in the pyramidal tracts may also occur and is associated with spastic paraplegia ***(Sherlock and Dooley, 1997).***

A more dramatic histologic lesion, hepato-cerebral degeneration, has been described in a few patients ***(Victor, 1965).***

Some authors suggest that "the degeneration follows a vascular pattern" with the most damage done in border-line areas. Such patients may also differ clinically from the usual patient with encephalopathy by manifesting dystonia, athetosis and dementia ***(Finlayson and Superville, 1981).***

Clinical manifestation :

Neurological and neuromuscular abnormalities are the predominant symptoms observed in patients with hepatic encephalopathy.

The symptoms may initially be mild but eventually progress to frank coma if the encephalopathy is not corrected. The severity of the symptoms depends on the acuteness and extent of liver failure and on the development of metabolic or infectious complications ***(Conn et al., 1977).***

There are no specific individual diagnostic features of hepatic encephalopathy that enable this syndrome to be distinguished from other encephalopathies with confidence ***(Sergio et al., 1989).***

Factors precipitating hepatic encephalopathy :

Some factors precipitate encephalopathy by increasing the availability of false neurotransmitter in addition the brain in cirrhosis may be sensitized to other factors such as drugs able to precipitate hepatic encephalopathy. Factors are uremia (spontaneous, diuretic

induced), drugs (sedatives, antidepressants, hypnotics), GIT bleeding, excess dietary protein, constipation, paracentesis (volumes > 3.5), hypokalaemia, infection, trauma ***(Finlayson and Bouchier, 1995).***

Physical findings :

Excluding the neurologic examination, the physical signs will be determined principally by the etiology, severity, and chronicity of the patient's liver disease. Patients with fulminant hepatic failure may have a normal examination except for reduced hepatic dullness by percussion. In contrast, patients with decompensated alcoholic cirrhosis manifest the familiar findings of spider angiomas, palmar erythema, scleral icterus, muscle wasting gynecomastia, testicular atrophy and protuberant fluid filled abdomen containing a firm liver. Multiple subcutaneous echymoses due to the anti-coagulated state of many such patients and a positive test for blood in the stool suggests GIT bleeding as precipitating cause of hepatic coma ***(Zakim and Boyer, 1990).***

Neurological findings:

Personality changes including childness, irritability and loss of concern for family. Intellectual deterioration

II	Drowsiness, lethargy disorientation, inappropriate behavior	Asterixis, dysarthria primitive reflexes (suck and snout). Ataxic paratonia.
III	Somnolent but arousable, marked confusion, incomprehensible speech	Hyperreflexia, extensor plantar response, incontinence, myoclonus, hyperventilation.
IV	Coma	Decerebrate posturing brisk oculocephalic reflexes, response to painful stimuli. Present early, may progress to flaccidity and absence of resonance to stimuli.

(Bruce, 1996).