Vitamin B12 deficiency in diabetes mellitus

Thesis

Submitted in partial fulfilment
for master degree in
Internal Medicine

By

Waleed Wael Ahmed Al Azhary
M.B.B.Ch.

Supervised
By

Prof.Dr. Moghazy Ali Mahgoub
Prof. of Medicine and Endocrinology.

Prof.Dr. Mohammed Fahmy Abdel Aziz.
Prof. of Medicine and Endocrinology

Dr. Baher Ali Masoud
Lecturer of Medicine and Endocrinology.

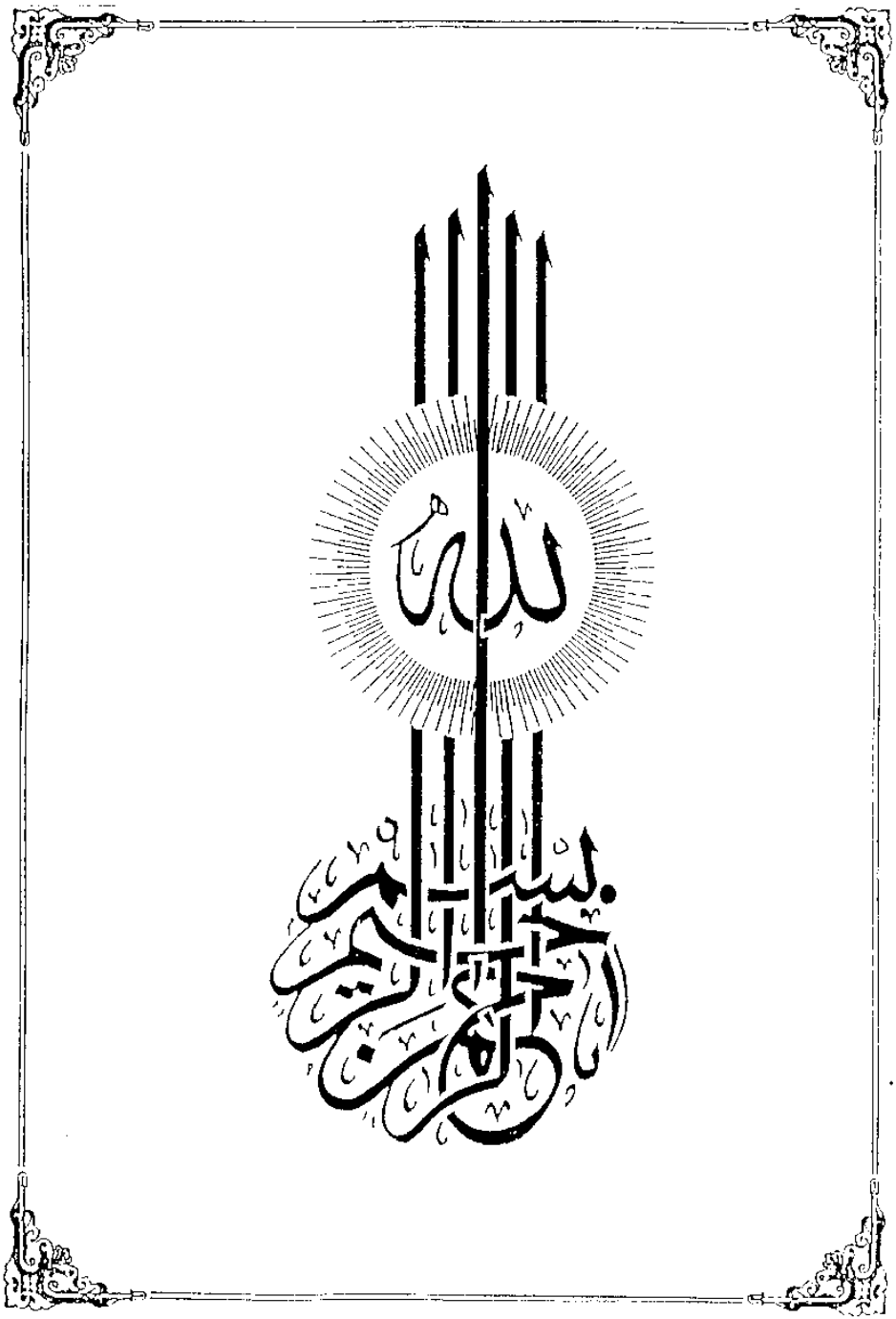
Faculty of Medicine
Ain Shams University

1994

بسم الله الرحمن الرحيم

وما أوتيتم من العلم إلا قليلاً

صدق الله العظيم



Contents

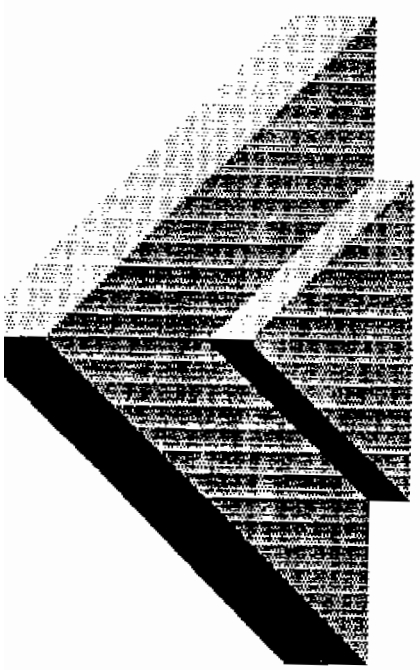
Acknowledgment

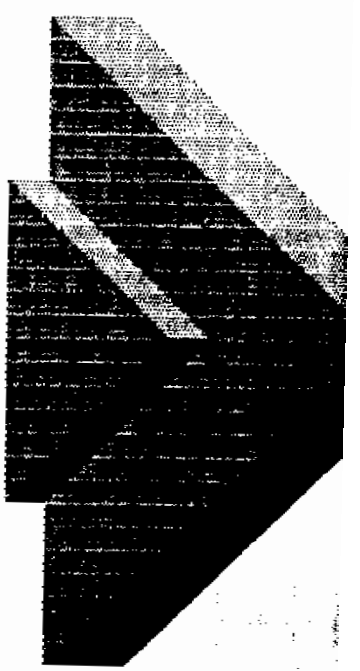
I am greatly honoured to express my deep gratitude and thanks to Professor Dr. Moghazy Mahgoub, Prof. of General Medicine and Endocrinology, Faculty of Medicine, Ain Shams University for his parently advises, continuous and sincere encouragement and for his kind supervision of this work.

I feel deeply indebted to Professor Dr. Mohammed Fahmy Abdel Aziz, professor of General Medicine and Endocrinology, Ain Shams University as he offered me a good deal of his valuable time to forward this research by continuous advice, constructive remarks, his scientific open questions, and sincere encouragement.

I am indebted to Dr. Baher Masoud, Lecturer of General Medicine, and Endocrinology, Faculty of Medicine, Ain Shams University for his supervision and constant help throughout this work.

Introduction
&
Aim of work





Introduction and Aim of the work

Nervous system diseases caused by nutritional and metabolic disorders include a large and diverse number of neurologic disabilities, which readily fall into two distinct types acquired and inherited.

In so far, no other category of disease -but nervous system diseases- so clearly exemplifies the tight connection to both nutritional and metabolic disorders.

Many nutritional deficiencies have been well known to cause neurologic disabilities, the most famous are Werneck's encephalopathy and Korsakoff's psychosis due to thiamine deficiency, alcoholic cerebellar-degeneration met with in nutritionally depleted alcoholics, pellagra as a feature of niacin deficiency, deficiency amblyopia in smokers and alcoholics deficient in B_1, B_2, and B_{12}, and biliary atresia induced vitamin E deficiency which leads to dysartheria, cerebellar ataxia, sensory polyneuropathy, and ophthalomoplegia (Sokol,1983)

Vitamin B_{12} deficiency leads to subacute combined degeneration of the spinal cord, such a deficiency being the subject of interest in this study will be discussed in details in this thesis.

On the other hand, numerous metabolic disorders are capable of inducing nervous system diseases.

These metabolic disorders may be hereditary or acquired. The hereditary metabolic disorders leading to nervous system diseases may be of early onset - which are of more interest to pediatricians-, and of late onset which include metachromatic leukodystrophy, adrenoleukodystrophy, ceroid lipofuscinosis, and adult lipid storage diseases, and these are the diseases of interest to internist.

The acquired metabolic diseases which may affect the nervous system include anoxic ischemic encephalopathy, hypercapnic encephalopathy, electrolyte disturbances, hepatic and uremic encephalopathies, hypoglycemia, hyperglycemic ketoacidosis, and hyperosmolar non ketotic hyperglycemia.

Among all these metabolic disorders, diabetes mellitus and the subsequent diabetic neuropathy are the issues of interest in this study, so, light should be shed on them which we hope to perform satisfactorily in this thesis.

Diabetic neuropathy is actually a mutlifactorial problem, It is thought to be due to :

- A vascular error, in the form of microangiopathic changes affecting the vasa nervosa (Barbosa,1980)
- Metabolic disorders involving the polyol pathway, myoinositol and lipid metabolism.

* The nutritional deficiency which has emerged in the pathogenesis of diabetic neuropathy laying stressin vitamin B12 deficiency, and being a fertile soil for research work.

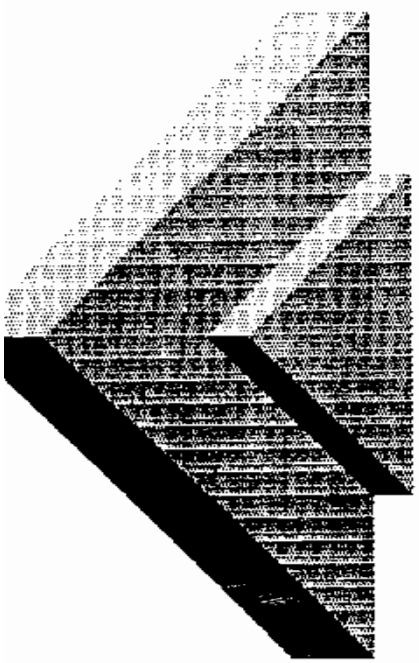
A research work showed that parathesia, burning pain, and heaviness dramatically improved within few hours to one week following intrathecial injection of 2.500 Ug of methylcobalamin in 10 mL saline, and lasting for several months up to four years (Fujia et al., 1987).

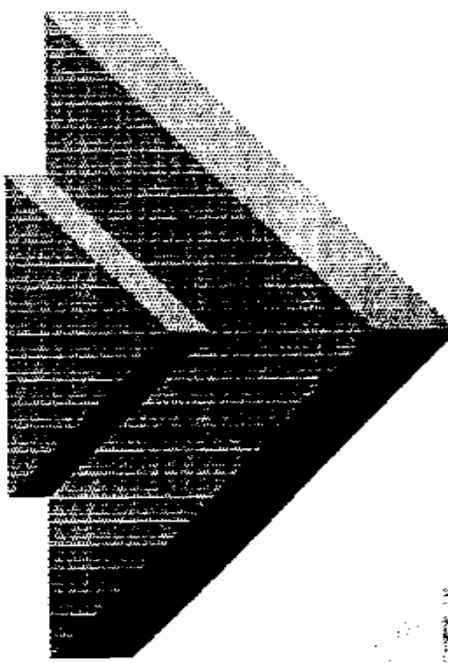
Another study showed that methylcobalamin improves nerve conduction in streptozotocin diabetic rats without affecting sorbitol or myoinositol contents of the sciatic nerve (Yasuda, et al., 1988).

Aim of the work :

Estimating the serum level of vitamin B12, in diabetic patients of both types (juvenile and mature onset), to be correlated with the severity and degree of control of diabetes, and to be also correlated with the neurological complications of diabetes mellitus, to state whether or not diabetic patients are prone to and/or more liable for vitamin B12 deficiency, and this in turn would give us an idea about the expected values of various routes of vitamin B12 administration as a hopeful therapeutic opportunity and as a prophylactic drug in the face of diabetic neuropathy.

Review of Literature





Vitamin deficiencies in diabetes mellitus

The role of vitamin in disease has changed within the past few decades.

Deficiency of a single vitamin in diabetic patients is now rarely endemic, and instead occurs either as a portion of states of malnutrition which may accompany malabsorption which is frequently observed in diabetic patients, or as a result of an error of metabolism.

Indeed, disorders of vitamin excess-even among diabetic patients may now be more common than vitamin deficiency (Herbert,1980)

Diabetes mellitus being a systemic disease, and a widespread illness, may lead to vitamin deficiencies by many means.

To outline the means by which diabetes mellitus can cause vitamin deficiencies, we can state that these means include the followings:

Although polyphagia is more common in diabetes mellitus (especially, on the initial phases of the disease), yet, anorexia, and subsequently malnutrition are not uncommon in

complicated long-standing diabetes mellitus which would inturn lead to multivitamin deficiencies (Bressler,1969).

Malabsoprtion is considered to be one of the gastrointestinal troubles met within diabetic patients, and in those patients malabsorption may participate in vitamin deficiencies (Kohner et al,1981).

Diabetic patients are liable for repeated attacks of cholecystitis, which in the long term may lead to chronic cholecystitis with subsequent interference with the functions and efficacy of the bile salts, the resul of which would be defective absorption of the fat soluble vitamins (A,D,E,and K) (Kohner et al,1981).

Gastrointestinal upset, (a problem met with diabetes mellitus frequently) may share in defective absorption, and subsequently utilization of the vitamins, for example through autonomic diabetic neuropathy in the form of intermittent diarrhoea, steatorrhoea, gastric fullness, vomiting, and gastroparesis diabeticorum (Catt,1974).

The fact that the frequency of occurrence of circulating antibodies to the gastric parietal cells, and to the intrinsic factor itself is increased among diabetic patients (particularly the juvenile onset ones) can explain the liability of diabetics, especially type I, for vitamin B_{12} deficiency (Goldstein et al,1970).

A remarkable incidence of fatty liver is demonstrated in diabetic patients, which may affect the ability of the

liver to convert carotenes into vitamin A leading to its deficiency (Smith, and Goodman,1976).

Diabetic nephropathy is a common complication of diabetes mellitus, the end result of which may be renal failure leading to vitamin D deficiency whether due to loss of the vitamin or defective hydroxylation (Jean,1992).

Diabetic patients being more susceptible and prone to different forms of infections (T.B., skin, chest,GIT, infections,...etc) are having higher incidence of using systemic antibiotics than the non diabetic individuals, and this usage of long term antibiotics may lead to some sort of bowels sterilization with subsequent deficiency of vitamin K which is normally manufactured by the intestinal flora.

1) Nicotinic Acid (Pellagra preventive factor-PPF).

Nicotinic acid deficiency leads to pellagra which is manifested by cutaneous, neurological, and gastrointestinal manifestations in the form of dermatitis, dementia, and diarrhoea respectively (Bollet,1982).

Pellagra in diabetic patients can be caused by chronic diarrhoea, malabsorption, and hepatic function impairment (Gopalan, and Rao,1975).

Pellagra can be treated by 10 mg of niacin per day (Darby,1977)

2)Vitamin B1 (Thiamine,aneurine).

This vitamin which is needed in a daily requirement of 15 mg which are supplied in seeds of cereals, yeast, meat, and vegetables (Brown,1970) can be deficient in diabetic patients due to:

- Genetic factors (Scriver,1973)
- Chronic peritoneal dialysis, and haemodialysis, as diabetic patients are in great risk of renal impairment and failure which can be caused by diabetic nephropathy and the repeated urinary tract infections (especially pyelonephritis) leading to damage of the renal tissue on the long run (Kawai,1980).

Diabetic patients with Vitamin B_1 deficiency would experience Beri Beri whether the wet type with cardiovascular affection (Kosam,1972), or the dry type with nervous system derangement in the form of Wernke's encephalopathy and Korsakoff's psychosis (Blass and Gibson,1977), and these can be treated by 50 mg per day of the vitamin intramuscularly to be reduced several days later to 2.5-5 mg daily (Harrison,1992).

3) Vitamin B_2 (Riboflavin):

Vitamin B_2 deficiency in diabetics can be caused by malabsoarption, anorexia, malnutrition, and chronic diarhoea (Printo,1981).

B_2 deficiency may be manifested by corneal vascularization, cheilosis, angular stomatiatis, anaemia (normocytic normochromic) and pitriasis alba of the face (Rivlin,1979)

Such a deficiency can be treated by 10 mg riboflavin thrice daily.

4) Pyridoxin (vitamin B_6)

This vitamin is essential for haem synthesis, as well as for conversion of tryptophan to niacin (Gershoff,1976).

Daily requirement is about 5 mg (Harrison,1992). B_6 deficiency can be caused in diabetics by Malabsorption, and malnutrition, and also during INH therapy to treat T.B. commonly met with in diabetics as it is a pyridoxin antagonist (Jaffe,1972).

Pyridoxin deficiency leads to peripheral neuropathy, psychosis and even convulsions (Frimpter,1969), dermatitis, and hypochromic sideroblastic anaemia which can be corrected by oral dose of 50 to 150 mg of the vitamin daily (Harris,1964).

5) Vitamin A (Retinol)

This vitamin which is needed in a daily dose of 5000 i.u. as a replacement therapy whenever the vitamin is deficient, this vitamin is present in egg yolk, liver, milk, and fish liver oil (Sauberlich,1974).