THE ROLE OF VITAMIN B COMPLEX AS AN ADJUVANT THERAPY FOR DIABETIC NEPHROPATHY IN PEDIATRIC PATIENTS WITH TYPE 1 DIABETES

Thesis

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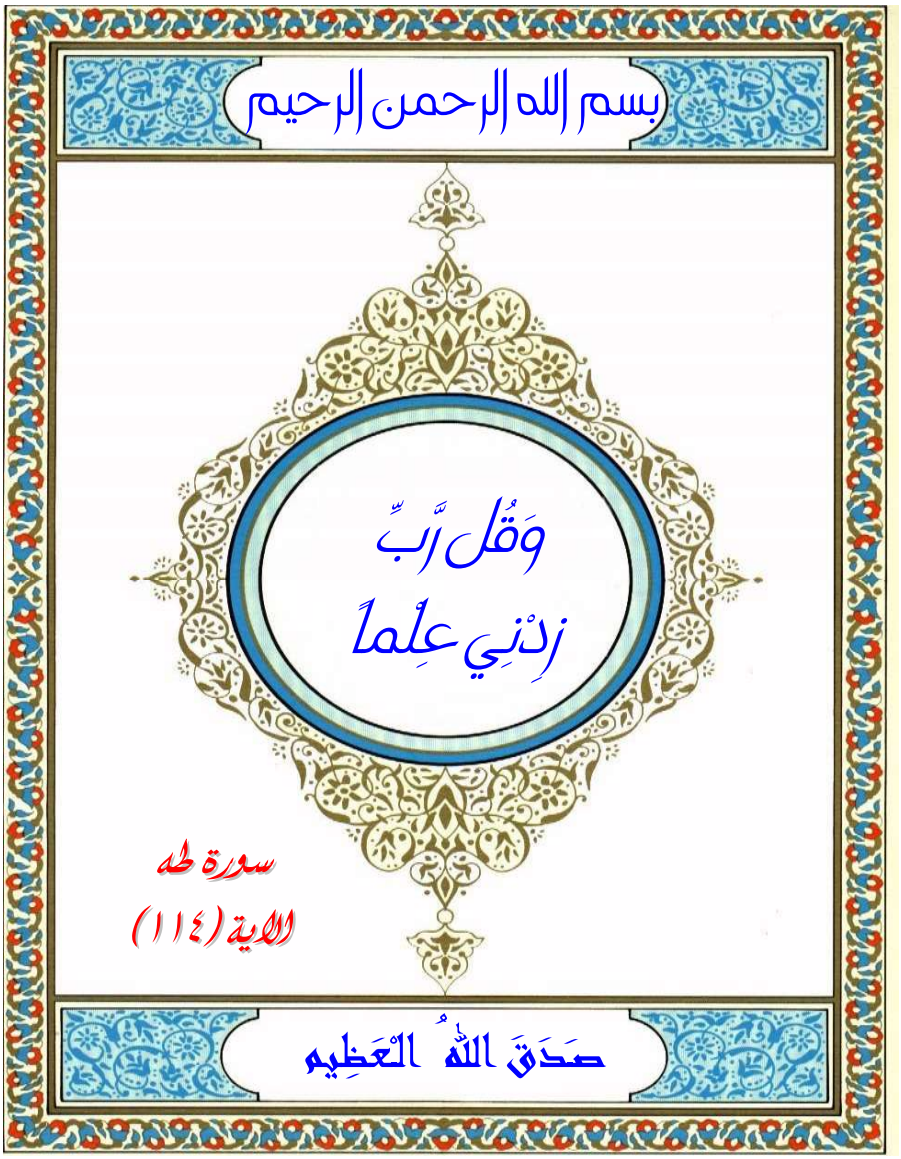
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List of Abbreviations

Abb.	Full term
ACE	*Angiotensin-converting enzyme inhibitors*
ACR	*Albumin/creatinine ratio*
ADA	*American Diabetes Association*
AER	*Albumin excretion rates*
AGEs	*Advanced glycation end products*
α-KDH	*α-ketoglutarate dehydrogenase*
ARBs	*Angiotensin II receptor blockers*
ATP	*Adenosine triphosphate*
BMI	*Body mass index*
CKD	*Chronic kidney disease*
CoA	*Conversion of methylmalonyl coenzyme A*
CVD	*Cardiovascular Disease*
CysC	*Cystatin C*
DAG	*Diacylglycerol*
DCCT	*Diabetes Control and Complications Trial*
DKA	*Diabetic ketoacidosis*
DM	*Diabetes mellitus*
DN	*Diabetic Nephropathy*
EDIC	*Epidemiology of Diabetes Interventions and Complications*
ESRD	*End stage renal disease*
GABA	*γ- aminobutyric acid*
GAD	*Glutamic acid decarboxylase*
GAD-65	*Glutamate decarboxylase-65*
GAPDH	*Glyceraldehyde-3 phosphate dehydrogenase (*
GDF-15	*growth differentiation factor-15*
GDM	*Gestational diabetes mellitus*
GFR	*Glomerular filteration rate*

List of Abbreviations (Cont...)

Abb.	Full term
GSH	*Reduced glutathione*
GSSG	*Oxidized glutathione;*
HbA1c	*Hemoglobin A1c*
HCC	*Human Cys C*
HIV	*Human immunodeficiency virus*
IDF	*International Diabetes Federation*
IF	*Intrinsic factor*
IgA	*Immunoglobulin A*
KDOQI	*Kidney Disease Outcomes Quality Initiative*
KIM	*Kidney injury molecule*
LADA	*Latent autoimmune diabetes in adults*
LDH	*Lactic dehydrogenase;*
MCV	*Mean cell volume*
MMA	*Methylmalonic acid*
MODY	*Maturity-onset diabetes of the young*
NAG	*N-acetyl-b-D-glucosaminidase*
NGAL	*Neutrophil gelatinase–associated lipocalin*
NKF	*National Kidney Foundation*
NMDA	*N-methyl-D-aspartate*
PARP	*Poly (ADP-ribose) polymerase*
PCA	*Parietal cell antibodies*
PDH	*Pyruvate-dehydrogenase;*
PKC	*Protein kinase C*
RAAS	*Renin–angiotensin–aldosterone system*
ROS	*Reactive oxygen species*
T1DM	*Type 1 diabetes mellitus*
T2DM	*Type 2 diabetes mellitus*

List of Abbreviations (Cont...)

Abb.	Full term
TC	*Transcobalamin*
TD	*Thiamine deficiency*
TGF-β1	*Transforming growth factor-beta*
TPP	*Thiamine pyrophosphate*
UAE	*Urinary albumin excretion*
WE	*Wernicke's encephalopathy*
YKL-40	*Chitinase-3-Like Protein 1*

Abstract

Background and Objectives: Diabetic nephropathy (DN) is a major microvascular complication of type 1 diabetes mellitus (T1DM). Although with established conventional therapy for glycemic and blood pressure control in patients with DN, and the use of inhibitors of the renin–angiotensin–aldosterone system (RAAS), a significant proportion of diabetic patients develop chronic kidney disease and progress to end-stage renal disease, indicating a need for additional treatments. Evidence for deficiencies of vitamins B1 and B12 in T1DM has been described in several publications. The role of vitamin B supplementation in preventing microvascular complications of diabetes has already been a focus of research for some years. Homocysteine levels are elevated in T1DM patients with DN. Supplementation of folic acid and vitamin B12 is known to reduce homocysteine levels. A combined therapy with vitamin B1 (thiamine) and vitamin B6 (pyridoxine) in patients with type 2 diabetes and nephropathy significantly decreased glycation of nuclear DNA in leukocytes. We studied the role of oral supplementation with vitamin B complex as an adjuvant therapy for diabetic nephropathy in children and adolescents with T1DM and assessed its relation to glycemic control, microalbuminuria and cystatin C as a marker of nephropathy.

Methods: This randomized controlled trial included 80 vitamin B12-deficient type 1 diabetic patients with nephropathy, despite oral angiotensin-converting enzyme inhibitors (ACE-Is). Enrolled patients aged 12-18 years with at least 5 years disease duration and glycated hemoglobin (HbA1c) $\leq$8.5%. Patients were randomly assigned into two groups; one group received oral supplementation with vitamin B complex (Neurorubine ^{TM} –Forte Lactab ^{TM} Mepha Pharma Egypt S.A.E manufactured by Medical Union Pharmaceuticals) and the other group did not. Both groups were followed-up for 12 weeks with assessment of FPG, HbA1c, urinary albumin excretion (UAE) and cystatin C.

Results: Baseline clinical and laboratory parameters were consistent between vitamin B and no vitamin B groups ($p>0.05$). After 12 weeks, supplementation with vitamin B complex resulted in significant decrease of fasting blood glucose, HbA1c, total cholesterol, triglycerides, UAE and cystatin C compared with baseline levels ($p<0.001$) and compared with patients without vitamin B treatment ($p<0.001$). No adverse reactions due to vitamin B complex were reported. Baseline vitamin B12 was negatively correlated to UAE ($r=-0.877$, $p=0.009$) and cystatin C ($r=-0.77$, $p=0.043$) among DN patients with vitamin B adjuvant therapy.

Conclusions: Oral supplementation with vitamin B complex for 12 weeks improved glycemic control and renal function. Thus, it could be a safe and effective strategy for treatment of pediatric type 1 diabetic patients with nephropathy.

Keywords: Type 1 diabetes, nephropathy, vitamin B complex, cystatin C.