BRAIN STEM AUDITORY EVOKED POTENTIAL STUDIES IN DIABETIC PATIENTS

A THESIS SUBMITTED FOR PARTIAL FULFILMENT OF MASTER DEGREE

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Abstract

Diabetic community is vast enough, giving researchers a very good reason to explore more in their world. One of their rarely probed complications is brainstem dysfunction. In this study, we investigated brainstem auditory evoked potential studies (BAEPs) in diabetic patients, as well as its associations with diabetic complications, especially diabetic microangiopathy. Our study was conducted on 40 diabetic patients having type I or type II. They were classified into two groups; group I (< 5 years duration of illness) and group II (> 5 years duration of illness). Their ages ranged from 20 to 59 years. The patients were examined clinically, neurologically and electrophysiologically. Brainstem auditory evoked potential studies, nerve conduction studies and flash electroretinography were performed to all patients. Urine analysis, instantaneous random blood sugar and funduscopy were also performed for patients. The brainstem auditory evoked potential studies of patients were compared to values of 30 normal subjects and their ages ranged, also, from 20 to 59 years. The diabetic patients experience brainstem dysfunction early in their disease course (before 5 years duration of the illness) that is increased as the disease duration increases. This dysfunction is evident by significant delay of wave V in diabetic patients as compared to normal individuals. Later, after 5 years duration of the illness, delay of wave III, further delay of wave V, prolongation of I-V IPL and decrease in amplitude of wave V occur. Diabetes type, I or II, has no different effect on BAEPs results.

Microangiopathic complications (retinopathy and nephropathy) are associated with increasing hearing threshold in diabetic patients, mainly after 5 years duration of the illness. Wave III is significantly delayed in presence of diabetic retinal affection; functionally and by funduscopy. Also, wave V is significantly delayed, in patients with abnormal skin and peripheral nervous system manifestations. In addition, wave V latency and III-V IPL are prolonged in patients having cardiovascular affection symptoms and postural hypotension. Finally, in patients with sweating abnormalities, wave I amplitude is significantly increased.

So brainstem dysfunction occurs early in the course of diabetes (type I and II similarly) and it is further affected by its duration. It starts by affection at the midbrain level (inferior colliculus) then proceeds by time to lower levels; caudal pons (cochlear nucleus). Also, as diabetic microangiopathic complications occur, hearing threshold increases. Retinopathy is accompanied with brainstem disintegration, at the caudal pons level. In three situations, we questioned the occurrence of similar pathogenesis theories, intracranially and extracranially. First, diabetic patients, with abnormal skin or peripheral nervous system manifestations, experience midbrain dysfunction (in the vicinity of the inferior colliculus) as well. The presumed theory if microvascular or, less likely, autoimmune affection. Second, diabetic patients with cardiovascular affection symptoms and postural hypotension show retrocochlear dysfunction. The doubted theory is macrovascular affection.

Finally, diabetic patients with sweating abnormalities show evidence of affection of olivocochlear bundle. The probable theory is small fiber neuropathy.

Keywords: Microangiopathic – Retinopathy – Nephropathy – Diabetic community

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TO

MY FATHER

AND

MY MOTHER

THE CAUSE OF MY EXISTANCE
and
THE REASON FOR BEING HERE TODAY

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- ABR= Auditory Brainstem Response
- ADC= Alternating-Direct current
- ADP= Adenosine Di-Phosphate
- AER= Albumin Excretion Rate
- AGEs= Advanced Glycation Endproducts
- ATP= Adenosine Tri-Phosphate
- BAEP= Brainstem Auditory Evoked Potentials
- BAEPs= Brainstem Auditory Evoked Potential studies
- BDR= Background Diabetic Retinopathy
- CAD= Coronary Artery Disease
- CIDP= Chronic Inflammatory Demylinationg Polyneuropathy
- CMAP= Compound Motor Action Potential
- CN= Cranial Nerve
- CTS= Carpal Tunnel Syndrome
- CTT= Central Transmission Time
- dB= deci-Bels
- DCCT= Diabetes Control and Complication Trial
- DKA= Diabetic Ketoacidosis
- DM= Diabetes Mellitus
- DME= Diabetic Macular Edema
- DN= Diabetic Neuropathy

- DNA= Deoxy Ribo Nucleic acid

- DR= Diabetic Retinopathy

- DSP= Diabetic peripheral Sensorimotor Polyneuropathy

- ERG= Electroretinography

- FA= Fluorescin Angiography

- FBG= Fasting Blood Glucose

- FPG= Fasting Plasma Glucose

- f-ERG= flash Electroretinography

- GAD= Glutamate Decarboxylse

- GAPDH= Glut-Amide Phosphodehydrogenase

- GDM= Gestational Diabetes Mellitus

- GHb= Glycoselated Heamoglobin

- H- reflex= Hoffman reflex

- HbA1 = Glycated Hemoglobin

- HbA1c= glycoselated Heamoglobin A1c

- Hearing Level= HL

- Hz= Hertz

- IAA= Insulin Autoantibodies

- IC= Inferior Colliculus

- ICA= Islet Cell Antibodies

- IDDM= Insulin Dependent Diabetes Mellitus

- IFG= Impaired fasting Glucose

- IGT= Impaired Glucose Tolerence

- IGF-I= Insulin Growth Factor I

- IPL= Inter Peak Latency

- LADA= Latent Autoimmune Diabetes of the Adult

- LL= Lateral Leminscus

- MGB= Medial Geniculate Body

- MI= Myocardial Infarction

- MNCS(s)= Motor Nerve Conduction Study (ies)

- MODY= Maturity Onset Diabetes of the Young

- msec= Milli second

- MTT= Meal Tolerance Test

- mV= millivolt

- m/sec= meter per second

- NAD= Nicotine-Amide Adenine Di-nucleutide

- NCG= Normal Control Group

- NDR= No evidence of Diabetic Retinopathy

- NCS(s)= Nerve Conduction Study(ies)

- NCV(s)= Nerve Conduction Velocity(ies)

- nHL= normal Hearing Level

- NIDDM= Non Insulin Dependent Diabetes Mellitus

- NO= Nitric Oxide

- NOS= Nitric Oxide synthase

- NPDR= Non Proliferative Diabetic Retinopathy

- OPs= Oscillatory Potentials

- PDR= Proliferative Diabetic Retinopathy

- PEDF= Pigment Epithelium Derived growth Factor

- PKC= Protein Kinase C

- PPDR= Pre- Proliferative Diabetic Retinopathy

- PTN= Posterior Tibial Nerve

- PTT= Peripheral Transmission Time

- RBS= Random Blood Sugar

- ROS= Reactive Oxygen Species

- SAMP= Score of Distal Amplitudes

- SD= Standard Deviation

- SNAP= Sensory Nerve Action Potential

- SNCS(s)= Sensory Nerve Conduction Study(ies)

- SNCV= Sensory Nerve Conduction Velocity

- SOC= Superior olivary complex

- SSR= Sympathetic Skin Response

- TGF-beta= Transforming Growth Factor-beta

- VEGF= Vuscular Endothelial Growth Factor

- VLDL= Very Low Density Lipoproteins

- μV= Micro-Volt

INTRODUCTION

Diabetes mellitus (DM) is a clinical syndrome characterized by hyperglycemia due to absolute or relative deficiency of insulin ***(Frier et al., 1999)***. The two major types are:-

TYPE I: Insulin Dependant Diabetes Mellitus (IDDM)

TYPE II: Non Insulin Dependant Diabetes Mellitus (NIDDM).

Among the long term complication of diabetes, is hearing impairment, and its frequency varies ***(Durmus et al., 2004)***. However, the relation between diabetes mellitus and hearing impairment is still a matter of controversy. Peripheral and central auditory dysfunctions may be in question as the cause for the hearing impairment ***(Lisowska et al., 2002).***

Previous data suggest that Brainstem Auditory Evoked Potentials (BEAP) deteriorate before the hearing impairment appears in patients with Diabetes ***(Durmus et al., 2004)***. Thus, the diagnosis of sub clinical damage of the peripheral and central auditory pathways in diabetes mellitus could be reached by the Brain stem Auditory Evoked Potential studies (BEAPs) which are an objective, clinically useful and non-invasive procedure to stress the early impairment of both auditory nerve and brainstem function **(Al-Azzawi and Mirza , 2004)**. It was concluded that changes in BEAPs in patients with diabetes should be an alarm to possible damage to the auditory nerve and close follow up is needed in these patients ***(Durmus et al., 2004).***

Small blood vessels disease (diabetic microangiopathy) is another long term complication of diabetes. It is a specific complication that contributes to mortality by causing renal failure and diabetic nephropathy. In addition, diabetic retinopathy is also one of the long term complications of diabetes ***(Frier et al., 1999)***.

It is worth of notice that there is a postulated correlation between peripheral auditory function and microangiopathy (nephropathy and retinopathy) ***(Lisowska et al., 2002)***. The first clinical evidence of nephropathy is the appearance of low, but abnormal, albumin levels in the urine i.e. microalbuminuria ***(Tarchini et al., 2005)***. On the other hand, abnormalities of the capillary bed (dilatation or closure), are the earliest lesions in retinopathy ***(Frier et al., 1999)***.

AIM OF WORK

To evaluate the efficacy of BEAP examination; as a useful method for early detection of brain stem dysfunction and therefore subclinical central nervous system damage in diabetic patients, and its correlation to the presence of microangiopathy elsewhere in the body.