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Physiology

ASSESSMENT OF COGNITIVE FUNCTION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS.

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ABSTRACT Type 2 DM is a complex metabolic disorder which can have detrimental affect on all the system of the body. This is often associated with accelerated risk of dementia.Objective of the study is to assess the cognitive function in individuals with type 2 diabetes. Twenty five type 2 diabetics attending the endocrinology outpatient department of MS Ramaiah Medical College and Hospital were recruited for the study. Twenty five age, sex and education matched normal subjects were enrolled for the study. Detailed history was taken. A thorough general physical examination and systemic examination was done. The subjects were divided into the two groups based on their serum HbA1C level. Cognitive function was assessed using Critical Flicker Frequency (CFF) and a validated questionnaire Adenbrooke's Cognitive Examination-III (ACE-III). Statistically significant reduction was found in CFF values between controls and type 2 diabetics. ACE III scores were also significantly lower in type 2 diabetics compared to controls. Decrease in CFF value and ACE-III score indicates reduction in cognitive function in type 2 diabetics. Our study shows an early onset of cognitive decline in type 2 diabetics compared to normal subjects.

KEYWORDS : Type 2 diabetes, Cognitive function, Critical Flicker Frequency (CFF), Adenbrooke's Cognitive Examination-III (ACE-III)

INTRODUCTION:

Type 2 DM previously referred to as non-insulin-dependent diabetes or adult onset diabetes includes individuals who have insulin resistance and relative insulin deficiency[1]. Overall life expectancy of type 2 diabetics is less than those without diabetes because of its complications. Estimated number of people with diabetes worldwide in 2015 is 415 million and by 2040, 642 million people will have diabetes[2]. Type 2 diabetes usually occurs in elderly people. However in recent years, it is increasingly seen in younger individuals and adolescents. DM is associated with microvascular and macrovascular complications affecting multiple organs of the body especially the eyes, kidneys, nerves, heart and brain. These complications can also lead to accelerated cognitive decline and increased risk of dementia[3]. The neurological deficits may have an early onset in type 2 diabetes but remain unnoticed due to their subtlety. Neurological defects may occur in the form of slowness of intellectual functions, lethargy, memory deficits, depression, cognitive dysfunction etc. Cognitive decline in an early age group is a matter of concern as it will have an impact on person's social, educational and professional fields.

The insulin resistance and relative insulin deficiency in type 2 diabetes lead to a higher blood glucose level and impaired fat and protein metabolism. Deranged metabolic activity leads to the production of reactive oxygen species resulting in oxidative stress[4]. Oxidative damage has been associated with deposition of amyloid and neurofibrillary tangles in the brain[5] which may lead to cognitive decline and dementia. Very few studies have been done to assess the cognitive function in diabetes. It is also unclear whether the cognitive decline is present in the early stages of diabetes. CFF is a simple, reliable and sensitive neurophysiological test that has frequently been used for assessment of cognitive function in various neurological and metabolic disorders like AD[6] and mild hepatic encephalopathy[7]. It is related to general arousal of the subject and can assess the ability of CNS to detect flickering light which is influenced by cortical activity[8]. CFF has been found to be correlated with other standard psychometric tests[7,8]. Adenbrooke's cognitive examination III (ACE III) is another brief bedside neuropsychological test for assessment of cognitive function[9,10]. This 100-item screening tool has a broad range of clinical use because it does not require any specialized equipment and needs only 10-15 minutes to complete.This test had shown to have a higher sensitivity and positive predictive value for evaluation of the progression from questionable dementia to Alzheimer's disease[9]. In our study we have assessed cognitive function using CFF and ACE-III score in early stage of type 2 DM.

METHODOLOGY:

Twenty five type 2 diabetics attending the endocrinology outpatient department of MS Ramaiah Medical College and Hospital were recruited for the study after getting the informed consent. Twenty five age, sex and education matched healthy controls were enrolled for the study. The study was conducted from January 2015 to April 2016. The study subjects were divided into 2 groups. Control group (group1) included age, sex and education matched normal subjects. The study group (group2) comprised of both male and female patients with type 2 diabetes mellitus in the age group of 20 - 50 years. Patients with past or present history of psychiatric and neurological disorder, history of eye disease, chronic alcoholics and chronic smokers, history of thyroid and renal disorder, patients on drugs which may alter the psychomotor function and patients with acute or chronic liver disease has been excluded from the study.

Ethical clearance was obtained from the authority. Testing procedures were explained and consent was obtained from the cases and controls. Detailed history was taken. A thorough general physical examination and systemic examination was done. The subjects were divided into the two groups based on their serum HbA1C level. Serum HbA1C level was estimated by High Performance Liquid Chromatography (HPLC). Cognitive function was assessed using Critical Flicker Frequency (CFF) and a validated neuropsychological questionnaire ACE-III.

The CFF was measured in a quiet, semidarkened room without distracting noises. A portable critical flicker frequency instrument and the software AudioSweepGen-version 3.7.4.36 were used. The analyser evoked a light stimulus with a wavelength of 635 nm. The stimulus or red light initially presented at a frequency of 10 Hz which gave the subject an impression of flickering light. The frequency of stimulus presentation the gradually increased towards 60 Hz until the subject had an impression that the flickering light had changed to steady light. The frequency at which the subject perceived that the flickering light had changed to steady light was noted.

ACE-III, a validated neuropsychological questionnaire was introduced after completing the neurophysiological tests. Subjects were explained about the procedure of the questionnaire. Assessment of cognitive function in ACE-III is based on attention, memory, verbal fluency, language and visuospatial ability. This test took 10-15 minutes to perform. Based on their answers to the questionnaire, scores have been given to assess the cognition.

Statistical Analysis

The parameters were tested for normal distribution. Parametric data were described in terms of mean and standard deviation (mean ± S.D.). ANOVA was used to analyze the differences in mean between the groups. Two-way ANOVA was used to adjust for the age. Post hoc comparison between the groups was done using Bonferroni test. P-values less than 0.05 were considered significant. Statistical analyses

were done using SPSS version 17.0.

RESULTS:

The study was conducted on 25 normal subjects and 25 type 2 diabetics. The participants were between the age group of 20-50 years. The mean BMI of the normal subjects and diabetics were 23.07 ± 2.19 and 28.64 ± 2.20 Kg/m^2 respectively. The mean HbA1C levels in control group and study group were 5.14 ± 0.21 and 7.74 ± 1.39 % respectively. Duration of type 2 DM people was less than 5 years. Basic parameters of the study groups are summerised in **Table 1**.

Table 1: Baseline characteristics of study groups

PARAMETERS	CONTROL MEAN ± S.D.	TYPE2 DIABETIC MEAN ± S.D.
AGE	25.88 ± 5.76	32.03 ± 4.38
SEX (M/F)	10/15	13/12
BMI	23.07 ± 2.19	28.64 ± 2.20
HbA1C%	5.14 ± 0.21	7.74 ± 1.39

The difference in CFF scores between the three groups was found to be statistically significant. The mean CFF values of control group and type 2 diabetic group were 43.56 ± 2.07 and 39.12 ± 4.29 Hz respectively as shown in **Table 2.**

Table 2. Comparison of CFF values between Group 1 & Group 2

Study group	Mean CFF value	S.D.	P-value
Control	43.56	2.07	<0.001*
Type 2 diabetic	39.12	4.29	
*Significant- P-value: P<0.05			

ACE-III scores in control group and type 2 diabetics were within normal limit (>88). However, when the scores between the groups were compared, the difference was found to be statistically significant as mentioned in Table 3 .

Table 3. Comparison of ACE-III scores between Group 1 & Group 2

Study group	Mean ACE-III	S.D.	P-value
Control	96.88	1.36	<0.001*
Type 2 diabetic	93.20	2.30	
*Significant- P-value: P<0.05			

DISCUSSION:

In the present study the cognitive function was compared between type 2 diabetics and normal subjects. Cognition was assessed by CFF and a validated neuropsychological test ACE-III. Low CFF values have been found to be associated with cognitive decline in mild hepatic encephalopathy[7,8]. Alzheimer's disease was also found to be associated with low CFF values[6,11]. In the present study efforts were made to find any early cognitive decline in type 2 DM using CFF.

In this study, difference in CFF values between the study groups were statistically significant (P=0.000). Diabetic people had lower CFF values as compared to control group. Lower CFF values in type 2 diabetics compared to normal subjects is an indicator of initiation of cognitive decline.

ACE-III scores in all the study groups were found to be within normal limit (> 88). However, when the ACE-III scores were compared between control group and diabetic group the difference was statistically significant (P=0.000). Diabetic group had lower ACE-III scores as compared to healthy subjects. Lower ACE-III scores in type 2 diabetics may indicate the initiation of cognitive decline in these groups of individuals.

Krishna Kumar S et al[12] showed in their study that type 2 diabetic people had significantly lower ACE-III score as compared to nondiabetic controls which was in affirmation with the findings of the present study. The study conducted by A. Salazar Salgado et al also showed similar findings with a lower ACE score in type 2 DM [13].

Weili Xu et al concluded in their study that diabetes accelerate the progression from mild cognitive impairment to dementia[14]. Result of the study conducted by Nazaribadie M et al showed significant differences in cognitive function in patients with type 2 DM when compared with normal subjects[15]. These results support the findings of the present study.

The findings of our study showed the presence of cognitive decline in early stage of type2 diabetes. An early onset of cognitive decline may have a negative impact on the personal and professional life of an individual. Hyperglycaemia leads to formation of advanced glycation end product (AGEs) which can cause degeneration of neurons, glial cells and myelin sheath[16,17]. AGE mediated brain injury may be a cause of cognitive decline in type 2 DM.

Type 2 DM is no longer considered to be a disease of elderly. Increasing incidence of obesity in younger age group is one of the causes of early onset type 2 DM. Cognitive decline in type 2 DM is a matter of concern as cognition is associated with goal directed behavior and helps the individual to adjust with changing environmental needs. Early onset of cognitive decline can lead to poorer performance in educational and professional fields. Self-care ability of type 2 diabetics will be affected due to cognitive impairment which can also worsen the diabetes related complications. All type 2 diabetic patients should be screened for cognitive decline along with other neurological examination at the time of diagnosis and regularly thereafter to improve the quality of life.

CONCLUSION:

Type 2 diabetics were found to be associated with lower CFF values and reduced ACE-III scores compared to the normal subjects. These findings suggests the existence of cognitive decline in early stages of disease.

Conflict Of Interest: None

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REFERENCES:

1. American diabetes association. Diabetes care 2015; 38 (Suppl.1): S8-S16.
2. IDF Diabetes Atlas. Seventh edition; 2015.
3. Saczynski JS, Jonsdottir MK, Garcia ME, Palmi V. Jonsson, Rita Peila, Gudny Eiriksdottir et al. Cognitive Impairment: An Increasingly Important Complication of Type 2 Diabetes. The age, gene/environment susceptibility- Reykjavil study. Am J Epidemiol. 2008; 168 (10): 1132-9.
4. Ceriello A, Taboga C, Tonutti L, Quagliaro L, Piconi L, Bias B et al. Evidence for an independent and cumulative effect of postprandial hypertriglyceridemia and hyperglycemia on endothelial dysfunction and oxidative stress generation: effects of short- and long-term simvastatin treatment. Circulation Sep 2002; 106(10):1211–1218.
5. Nunomura A, Perry G, Aliev G, Hirai K, Takeda A, Balraj EK et al. Oxidative damage is the earliest event in Alzheimer disease. J Neuropathol Exp Neurol. Aug 2001; 60(8):759–767.
6. Cronin-Golomb A, Corkin S, Rizzo JF, Cohen J, Growdon JH, Banks KS. Visual dysfunction in Alzheimer's disease: relation to normal aging. Ann Neurol. 1991; 29:41-52.
7. Romero-Gomez M, Cordoba J, Jover R, Del Olmo JA, Ramirez M, Rey R et al. Value of the Critical Flicker Frequency in Patients with Minimal Hepatic Encephalopathy. Hepatology 2007; 45(4).
8. Praveen Sharma, Barjesh Chander Sharma and Shiv Kumar Sarin. Critical flicker frequency for diagnosis and assessment of recovery from minimal hepatic encephalopathy in patients with cirrhosis. Hepatobiliary Pancreat Dis Int 2010; 9: 27-32.
9. Clare J. Galton, Sharon Erzinclioglu, Barbara J. Sahakian, Nagui Antoun and John R. Hodges. A Comparison of the Addenbrooke's Cognitive Examination (ACE), Conventional Neuropsychological Assessment, and Simple MRI Based Medial Temporal Lobe Evaluation in the Early Diagnosis of Alzheimer's disease. Cogn Behav Neurol 2005; 18: 144-150.
10. Hsieh S, Schubert S, Hoon C, Mioshi E, Hodges JR. Validation of the addenbrooke's cognitive examination III in frontotemporal dementia and alzheimer's disease. Dement Geriatr Cogn Disord. 2013; 36:242-250.
11. Curran S, Wattis J. Critical flicker fusion threshold: a potentially useful measure for the early detection of Alzheimer's disease. Hum Psychopharmacol 2000; 15:103-112.
12. Krishna Kumar S, Rajaram S, Rajendran P, Ismail M, Thirumalaikolundu Subramaniam. A comparative study of cognitive function and information processing ability among type 2 diabetes mellitus patients and healthy volunteers. J of Evolution of Med and Dent Sci. 2015 May 07; 37(4): 6378-6383.
13. Salazar Salgado A, K. Zavala Aguilar, J. Soria Viteri, P Salazar Lopez. Diabetes mellitus and cognition-cross sectional study. Revista Ecuatoriana de Neurologia. January 2011; 20(1): 43-49.
14. Weili Xu, Barbara Caracciolo, Hui-Xin Wang, Bengt Winblad, Lars Backman, Chengxuan Qiu and Laura Fratiglioni. Accelerated progression from mild cognitive impairment to dementia in people with diabetes. Diabetes 2010 November; 59: 2928-2935.
15. Marzieh Nazaribadie, Karim Asgari, MasoudAmini, Mohammad Ahmadpanah, Monireh Nazaribadie, Somaye Jamlipaghale. Cognitive processes and functions in patients with type 2 diabetes in comparison to prediabetic patients. J Res Health Sci 2013; 13(2): 208-213.
16. Ceriello A, Taboga C, Tonutti L, Quagliaro L, Piconi L, Bias B et al. Evidence for an independent and cumulative effect of postprandial hypertriglyceridemia and hyperglycemia on endothelial dysfunction and oxidative stress generation: effects of short- and long-term simvastatin treatment. Circulation Sep 2002; 106(10):1211–1218.
17. 1Nunomura A, Perry G, Aliev G, Hirai K, Takeda A, Balraj EK et al. Oxidative damage is the earliest event in Alzheimer disease. J Neuropathol Exp Neurol. Aug 2001; 60(8):759–767.