ORIGINAL RESEARCH PAPER

Ayurveda

COGNITIVE FUNCTIONS IN DIABETIC AND NON-DIABETIC PATIENTS- AN OBSERVATIONAL STUDY

KEY WORDS: Type 2 Diabetes mellitus, Cognitive functions, Memory

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ABSTRACT

Background: Type 2 Diabetes mellitus is a major life style metabolic disorder affects various body parts including the brain. Brain is responsible for memory, sensory and motor activities and is associated with cognitive process. Disturbance in brain physiology can cause disturbance in cognition. Type 2 Diabetes mellitus affects physiology of the body specially the brain. In Type 2 Diabetes mellitus evaluation of cognitive functions are justified as it may affect various common day to day activities.**Aims and Objectives:** Our prospective comparative observational study aimed to analyze the cognitive decline in patients with Type 2 Diabetes mellitus. **Methods:** It is a prospective, comparative, observational and non-interventional study. 50 subjects non diabetic healthy individuals served as a control and 50 subjects affected with Type 2 Diabetes mellitus who were on Antidiabetic treatment at least 5 years duration enrolled in the study based on inclusion and exclusion criteria. Cognitive functions were assessed by Addenbrooke's Cognitive Examination (ACE III) at the time of enrollment.**Result:** The analysis of results done by paired t-test. The level of all cognitive functions was lower in Diabetic patients especially memory, visuospatial ability and attention. Total ACE III was significantly reduced in diabetic patients. **Conclusion:** All Cognitive functions is significantly reduced in Diabetic patients who were on antidiabetic medication in the past 5 years. Hyperglycemia could be the possible risk factor for Cognitive decline. The understanding of pathogenesis of Diabetes and cognitive decline and its relationship can help in preventing the decline in Cognition.

Introduction:

Type 2 Diabetes mellitus(T2DM) is a chronic metabolic condition characterized by abnormalities in carbohydrate and fat metabolism, hyperglycemia, insulin resistance, and a relative insulin secretion defect. It increases the risk of developing complications.1 Many organ systems are adversely affected by diabetes, including the brain, which undergoes changes that may leads to cognitive impairment. T2DM induced cognitive decline has a complex etiology through multiple mechanisms including direct effect of chronic hyperglycemia on the brain, blood lipid, blood pressure, insulin resistance, chronic complication as micro and macro vascular complications, dysregulation of limbic-hypothalamic- pituitary-adrenal axis, Advanced glycation End Products (AGEs), inflammatory cytokines, oxidative stress etc. Diabetes mellitus patients have greater rate of Cognitive decline. Cognitive decline is the condition of having memory loss, reduced or slower thinking skills, or other impairment in mental capabilities.[2]

The status of potential epidemic grows rapidly in India with more than 62 million diabetic individuals, 415 million worldwide and forecasted to be 640 million by 2040.3 There are various cognitive assessment tests until today for the assessment of various neurocognitive functions. Out of which The Addenbrooke's Cognitive examination III (ACE III)4 is a brief cognitive test that assesses five Cognitive domains: attention, memory, verbal fluency, language and visuospatial abilities.

Previous researches have shown a connection between DM and Cognitive Decline in persons with earlier onset and greater severity of Diabetes mellitus. This study was planned to access the impact of Diabetes mellitus on Cognitive Decline, so that if any connection between DM and Cognitive Decline was found further studies can be carried out to see the impact of Diabetes control on Cognitive function.

Materials and Methods:

This study was observational; and non-interventional. The study protocol was approved by Intuitional ethical committee. The study was conducted at Kaya chikitsa Department Ayurveda Hospital, Bharti Vidyapeeth, Pune during the period of September 2019 to February 2020. Informed consent was obtained from the participants.

Participants were divided into controls and cases. Controls(n=50) consisted of age matched healthy non diabetic individuals of both genders. Cases(n=50) consisted of diabetic patients of both gender who were on antidiabetic treatment from at least 5 years. Patients were enrolled from OPD's and IPD's of Kaya chikitsa department based on inclusion criteria and exclusion criteria. DM was diagnosed by patients' symptoms of diabetes and fasting blood glucose above 126 mg/dL or 2-hour blood glucose above 200 mg/dL.

Inclusion and Exclusion Criteria

Patients of Diabetes mellitus who were on antidiabetic treatment from at least 5 years were included. Those patients who were not giving consent for enrollment in study, taking drugs that affect cognition such as Anticonvulsants, Antidepressants, Anticholinergics, Barbiturates, Benzodiazepines, Opiates etc. were excluded in study. Those patients were also excluded who has progressive neurological disorder, Head injury, Mental retardation, Drug and Alcohol abuse and Severe Psychiatric problem.

A training session on cognitive function and how to fill the Addenbrooke's Cognitive Examination III form was conducted by Dr Madhavi Mahajan madam. Cognitive function testing was done by Addenbrooke's Cognitive Examination III. The Addenbrooke's Cognitive Examination (ACE III) is one of the best cognitive tests that assesses five Cognitive domains: attention, memory, verbal fluency, language and visuospatial abilities.

After taking consent and basic details, participant is informed about the test and that he will be asked questions from Addenbrooke's Cognitive examination score sheet and scoring done accordingly as per the scoring guidelines. The subjects were given participant information number which contained details of the subject, which were kept confidential.

Statistical analysis

The data were analyzed using Microsoft Professional Plus 2010. Data were expressed as mean± standard deviation. Student's t- test was used to assess statistical differences between the groups. P< 0.05 was considered statistically significant.

RESULTS:

Fifty healthy non diabetics were taken as control. (Mean age was 51.18± 7.32; 29 males, 21 female). Fifty confirmed cases of DM who were on antidiabetic treatment from at least 5 years were enrolled in the study 49.97± 7.73, 33 males and 17 females)

Table No. 1

Variables	Control	Case
Age	51.18± 7.32	49.97± 7.73
Gender		
Male	29	33
Female	21	17
FBS(mg/dL)	98.39± 11.19	180.10± 67.11
PPBS(mg/ dL)	120.33± 10.11	230.65± 77.47

Fasting blood sugar (FBS) and Postprandial blood sugar (PPBS) were 98.39± 11.19 and 120.33± 10.11 in the control group, respectively. Fasting blood sugar (FBS) and Postprandial blood sugar (PPBS) were 180.10± 67.11 and 230.65± 77.47 in the treatment group, respectively.

Table number 2 shows the effect of DM on various domains of cognitive function.

Table No.2

Variables	Normal Value	Control	Case
Attention	18	15.74 ± 1.37	14.35± 2.34
Memory	26	21.84 ± 3.35	13.68± 4.60
Fluency	14	11.10 ± 1.58	10.77± 2.29
Language	26	23.39 ± 1.67	22.55 ± 2.34
Visuospatial ability	16	13.87 ± 1.41	12.90 ± 2.52
Total score	100	85.94 ± 9.38	74.25 ± 14.09

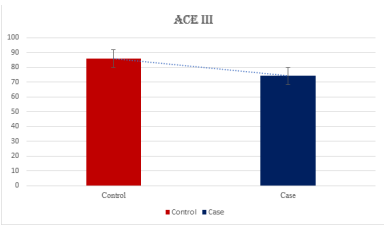

Figure 1: Effect of Diabetes on Cognitive function. Total score of ACE III was significantally reduced in case group compared to control group.

Attention:

Before treatment in case group attention was significantly reduced to 14.35± 2.34compared to 15.74 ± 1.37in control group (p< 0.05).

Memory:

In case group memory was significantly reduced to 13.68± 4.60 as compared to 21.84 ± 3.35in control group (p< 0.05).

Fluency:

In case group fluency was reduced to 10.77± 2.29as compared to 11.10 ± 1.58 in control group, but the change was not significant.

Language:

In case group language was reduced to 22.55 ± 2.34 as compared to 23.39 ± 1.67in control group, but the change was not significant (p> 0.05).

Visuospatial ability:

In case group visuospatial ability was significantly reduced to 12.90 ± 2.52 as compared to 13.87 ± 1.41 in control group (p< 0.05).

Discussion:

Diabetes mellitus Type 2 is an endocrine and metabolic disorder affecting most of the population in the world. It has many significant complications and affecting most of the vital organs in the body including the brain.[5] Cognitive decline is a less addressed complication of T2DM. Diabetic patients have a greater chance of decline in cognitive function and exhibit approx. a 1.5-fold greater risk of accelerated cognitive decline and a 1.6-fold greater risk for the development of future dementia. Also, cognitive decline in T2DM patients may complicate adherence to medical regimen.[6]

This study was conducted to assess the effect of T2DM on cognitive function. In this study testing of cognitive function of controls and T2DM patients was done by Addenbrooke's Cognitive Examination III (ACE III). Cognitive functions were assessed by Five domains (Attention, Memory, Verbal fluency, Language, and Visuospatial ability) of ACE III. At last total scoring of these five domains was done. The total score is 100 with higher scores indicating better cognitive functioning. The total ACE III score (/100) consists of the sum of the five domains scores. The cutoff scores as the ACE III are 88 and 82 out of 100 are recommended for suspicion of dementia.

In this study, there was significant decrease in Attention, Memory and Visuospatial ability as compared to healthy individual. Verbal fluency and Language was also decreased but the change was not significant. On concluding the result in this study there was significant decrease as compared to control, suggesting the role of Diabetes mellitus in decline of cognitive function.

The risk factors of cognitive decline in diabetes are Duration of diabetes, microvascular and macrovascular complication.[7] The important pathophysiological aspects considered responsible for cognitive dysfunction in DM are Hyperglycemia, Vascular disease, hypoglycemia, and insulin resistance, but still mechanisms are non-clear and further studies are needed to understand the mechanism responsible for cognitive decline so that planning can be developed for its prevention and treatment.[8]

A study showed that people with chronically elevated fasting blood sugar showed marked hippocampal atrophy after 4 years.[9] Chronic elevated Blood sugar level caused end organ damage through increases in reactive oxygen species (ROS), in particular superoxide, which could than lead to increased polyol pathway activation, then increased formation of AGEs, activation of protein kinase C, and increased glucose shunting in the hexosamine pathway.[10]

To prevent and treat all the hyperglycemia associated complication of diabetes we have to identify firstly the mechanism by which DM may impair cognitive function.

CONCLUSION

T2DM significantly causes Cognitive decline. In addition, understanding the pathophysiology of cognitive decline in patients with T2DM, its prevention and treatment will stimulate new research in this field.

REFERENCES:

1. Acee AM, Type 2 Diabetes and Vascular Dementia- Assessment and Clinical Strategies of care, Mesorg Nurs 2012; 21: 349-84.
2. Jaguseh W et.al., Cognitive function and metabolic state in elderly diabetic patients, Diabetes Nutr Metab, 1992; 5: 265-74.
3. Rawlings AM, Sharrett AR et.al., Diabetes in midlife and cognitive change over 20 years: a cohort study. Ann Intern Med. 2014; 161(11): 785-93.
4. Hodges JR., Larner AJ et al. Cognitive screening instruments: A Practical Approach. Second edition. Springer; Berlin, Alemania: 2017. Addenbrooke's Cognitive Examinations: ACE, ACE-R, ACE III, ACEapp, and M-ACE; pp.109-

137.
5. Zhang H, Hao Y, Novak V, et. al. Altered Resting- State Connectivity of Hippocampus with Default Mode Network in Type 2 Diabetes. Joint Annual Meeting ISMRM- ESMRMB; 2014.
6. Shemesh E, Rudich A, Effect of intranasal insulin on cognitive function: a systemic review. The J of Clin Endocrinal and Metabol. 2012; 97 (2): 366-76.
7. Tuma I, Diabetes mellitus and cognitive impairments. Vnitrni lekarstvi. 2007; 53(5): 486-8.
8. Kodl CT, Seaquist ER, Cognitive Dysfunction and Diabetes mellitus. Endocrine Reviews. 2008; 29(4): 494-511.
9. Goldman E. How hyperglycemia drives cognitive dysfunction. Holistic primary care News for health and healing; 2013.
10. Brownlee M. The pathobiology of diabetic complications: a unifying mechanism. Diabetes. 2005 Jun 1; 54(6): 1615-25.