

SHORT-TERM EFFECTS OF STRUCTURED EXERCISE THERAPY ON MEMORY OF ADULT PATIENTS NEWLY DIAGNOSED WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Background and Objectives: *Diabetes Mellitus is a multifaceted metabolic disease that can have devastating effects on multiple organs in the body and in the long run with micro and macro vascular complications that cause significant morbidity and mortality. Cognitive dysfunctions and impaired memory are commonly seen in patients with T2DM. The present study was to investigate cognitive function i.e. various domains of Memory of newly diagnosed patients with type 2 diabetes mellitus and to study the effects of short term structured exercise therapy of eight weeks would improve various domains of memory in diagnosed patients with type 2 diabetes mellitus of age group 20-45 years.*

Methods: *30 patients with newly diagnosed T2DM were enrolled in Diabetic control group. The structured exercise therapy was given to diabetic group after measuring baseline parameters. 30 normal healthy sex and age matched healthy control were enrolled under normal control group. HbA1c, BMI, and various domains of memory functions were measured.*

Results: *Patients on Interventional therapy showed statistically significant improvement in attention and concentration ($p < 0.001$), Immediate recall ($p < 0.05$), verbal retention for similar pairs ($p < 0.05$), and visual retention ($p < 0.05$)*

Interpretation and Conclusion: *Exercise therapy along with dietary control and anti-diabetic medication will have a positive influence on various domains of memory functions.*

Keywords: *Memory, PGIMS, Structured Exercise Therapy.*

INTRODUCTION

Diabetes Mellitus is a multifaceted metabolic disease that can have devastating effects on multiple organs in the body. The venomous effects of diabetes on the retina, renal, cardiovascular, and peripheral nervous systems are now extensively recognized.¹ A lesser amount of attention has been given to the effect of diabetes on cognitive function.

The association between Type 2 diabetes is with desecration of memory, executive functions and information-processing speed is reported in various papers.²⁻³ There have been a number of studies suggesting association of diabetes and for cognitive dysfunction and revealed that diabetes is independent risk factor for neurological disorders.⁴⁻⁵ But very less amount of literature is available to understand the stage of diabetes at which declining in the cognitive functions starts and how they progress over time. However,

type 2 diabetes classically develops insidiously and may often be undiagnosed in the early stages. Thus, cognitive decrements may start to develop years before the actual diagnosis, may be in the pre-diabetes stages. The clear and detailed neuropsychological data on the early stage of type 2 diabetes are not yet available. The enormous amount of literature is available suggesting the positive beneficial effect of physical activity on the functions of brain.⁶ However, the sedentary lifestyle that encompass modern society has taken precedence over the necessity for a physically active lifestyle. The impact of inactivity on progression of disease has been now the focus to a great extent. Evidence suggests that physical activity and exercise can to some extent lower the risk of adverse outcomes associated with advancing age.⁷⁻⁹

Physical activity augments the cognitive performance and reinforces the imperative for exercise therapy interventions with the outcome of promoting health and productivity. Despite the fact of

accumulating evidence supporting the effects of exercise therapy in T2DM elderly patients, there is limited evidence in adults to suggest that regular aerobic exercise can augment upon Memory parameters. Therefore, the aim of the present study was to investigate cognitive function i.e various domains of Memory of newly diagnosed patients with type 2 diabetes mellitus and to study the effects of short term structured exercise therapy of eight weeks would improve various domains of memory in diagnosed patients with type 2 diabetes mellitus of age group 20-45 years with cognitive decline by using memory scale of PGI battery which is conveniently applied to the Indian population.

Objectives:

1. To study the various mentioned domains of memory in diagnosed patients with type 2 diabetes mellitus
2. To study the effects of structured exercise therapy on various mentioned domains of memory in adults with T2DM.

MATERIALS AND METHODOLOGY

The study was undertaken by Dept. of Physiology, J.N Medical College, KLE University, Belgaum. Thirty patients aged 20-45 years, with newly diagnosed T2DM (Duration less than one year) attending Medicine OPD KLE's Dr Prabhakar Kore Hospital and Research Centre were enrolled as Diabetic Control group. Thirty sex, age and mean education level matched healthy subjects were enrolled as controls. All enrolled subjects were invited for in-person assessment, where informed consent was obtained, followed by a history and physical examination.

Study Design: A Pre-Post Interventional Study

Inclusion Criteria:

- I. All the patients of age group 20-45 years.
- II. Patients treated with only diet and oral anti-diabetic drugs.
- III. Subjects who, based on their medically assessed health status and

physical characteristic, will be enrolled to perform a physical training program designed with ADA guidelines.

- IV. Minimum educational qualification up to fifth year of schooling.
- V. Patients who can read and write Kannada or Marathi or Hindi or English.
- VI. Patients who will be willing to be enrolled for the study and who will give the written informed consent after receiving information about the study objective.

Exclusion Criteria:

- I. Subject with history of Diabetes more than a year.
- II. Known vascular complication of diabetes, such as coronary artery disease, stroke, nephropathy, retinopathy, and polyneuropathy which, in the investigators judgment, may have comprised the physical integrity of the patient.
- III. Other chronic diseases restricting physical activity.
- IV. With peripheral Vascular Diseases.
- V. Smokers and Alcoholics.
- VI. Any psychiatric history
- VII. Juvenile Diabetes
- VIII. Subjects with prior regimen of physical exercise

Logistics of the administration of the various memory tests to evaluate the verbal and nonverbal memory functions were organized.

Exercise Protocol: The interventional therapy was administered to the Diabetic group after obtaining baseline parameters which consists of 8 weeks of the individually designed exercise program of regular exercise consisting of aerobic and resistance exercises. The aerobic exercise is 30 min of activity 5 days/week, duration at an intensity of 70-80% of their individualized maximum heart rate and with no gap of more than 2 consecutive days without physical activity. Resistance exercise performed 3 times a week targeting all major muscle groups, progress to 3 sets of 8-10 repetitions at a weight that can't be lifted more than 8-10 times. All patients were provided with detailed instruction booklets describing

each resistance training exercise and appropriate equipment's (dumbbells) to perform resistance training. Participants were also instructed to complete weekly training diaries and were instructed to attend the research laboratory weekly once to perform the home-based training so that technique and progression could be monitored.¹⁰⁻¹¹

Parameters Assessed:

1. Height was measured by Commercial stadiometer. The participant will be made to stand erect with bare foot on the floor board of the stadiometer with his or her back to the vertical backboard of the stadiometer.
2. Weight (kg) was recorded by Digital Weighing Scale (seca), barefoot and with light clothes.
3. BMI: The BMI of each subject was calculated by dividing her body weight in kilograms by the square of her height in metres. The categorization of the BMI was done according to the BMI criteria for the Indian population.¹²
BMI ≤ 18.49 kg/m², underweight; BMI 18.5–22.99 kg/m², normal weight, BMI ≥ 23 kg/m² overweight or obese.
4. HbA1c: was measured using a commercially available test kit according to the manufacturer's recommendations and also with a laboratory method (Ion Exchange Resin method) using a semi-auto analyzer.¹³
5. Tests for memory: The PGI memory scale (PGIMS) was employed to assess memory function of patients. It provides a comprehensive scale to measure verbal and nonverbal memories on the basis of neurological theory; very short term, short term and long term memories on basis of experimental evidences and remote, recent and immediate memories on basis of clinical practice of evaluation of memory. The PGIMS consists of 10 subtests.¹⁴ Each subtest has maximum score of 6, 5, 9, 15, 10, 12, 5, 15, 13, and 10, respectively. The total score is 100. These tests measure different aspects of memory and employ different methods of recall. Scores are allotted as per the correct responses given by the patient.

The various domain of memory tests are as follows:

1. Remote memory: It comprises of six simple questions relating to personal and current information.
2. Current memory: It consists of five questions that assess the patient's ability to recall information and events in the recent past.
3. Mental balance: This test gives an idea of balance over one's mental functioning. The learned materials (alphabet and numbers) were recalled in backward and forward series.
4. Attention and concentration: This function was evaluated by the test of digit span forward and backward repetition.
5. Delayed recall: In this test, the investigator reads out the names of common objects (two series of five each) at a uniform interval. The patient was instructed to recall the same after one minute and score of correct recall recorded.
6. Immediate recall: This test included sequential reproduction of the sentence in verbatim. Patient was asked to recall the sentences immediately.
7. Verbal retention for similar pairs: A series of similar associative pairs of words were administered to the patient. Patient was asked to mention the associate words in response to the stimulus word.
8. Verbal retention for dissimilar pairs: It is similar to the previous test. However, the associate pair of words was unrelated and dissimilar. Patients were allowed up to three trials in the test.
9. Visual retention: In this test, the investigator displayed some cards containing geometrical figure. Each card was shown for 15 s and after 30 s patient instructed to reproduce the drawing from memory. No time limit was set for this test. Correct reproductions of figures were scored.
10. Recognition: In this test, the investigator showed a card containing common objects. The patient was allowed to observe this card for 30 s. Two minutes later a second card containing another set of pictures having some picture appeared in first card shown to the patient. Patient was asked to identify and name the picture that appeared in both the cards.

Correct responses were recorded and scores allotted accordingly.

mean \pm Standard Deviation values between the groups by using the Students't' test; p values < 0.05 were taken as the level of significance.

Statistical Analysis: The data was summarized to test the difference in the

RESULTS:

Table 1: Socio-demographic profile

	NC	DC (Baseline)	DC (At end of 8 weeks)	P value
Gender:				
Males:	16	12	12	NS
Females:	14	18	18	NS
Age	35.3 \pm 4.24	35.6 \pm 3.72	35.6 \pm 3.72	NS
BMI	24.6 \pm 3.05	30.1 \pm 2.67	25.8 \pm 2.44	Significant
HbA1c	4.9 \pm 3.8	5.9 \pm 4.5	5.7 \pm 0.37	Not Significant

Values are expressed as mean \pm SD and p value < 0.001 , was taken as significant.

In this study, there were 40% males and 60% females in Diabetic group with mean age of 35.6 \pm 3.72. The Basal Metabolic Index was significantly on the higher side as compared to normal control and the statistical significant improvement was

observed after interventional therapy. No statistical significant improvement has been observed between the groups but it's in normal range which shows the good control of diabetes.

Table 2: Effect of Interventional Therapy on PGI memory scale

S.no	Sub Test	NC	DC (Baseline)	At the end of 8 weeks	p value
1	Remote memory	6.0 \pm 0.0	6.0 \pm 0.0	6.0 \pm 0.0	NS
2	Recent memory	4.9 \pm 0.01	4.9 \pm 0.01	4.9 \pm 0.01	NS
3	Mental balance	8.4 \pm .50	6.3 \pm 0.96	6.3 \pm 0.96	NS
4.	Attention and concentration	13.4 \pm 1.45	8.5 \pm 1.19	10.6 \pm 1.29	Significant
5.	Immediate Recall	11.2 \pm 0.88	9.1 \pm 0.11	10.3 \pm 0.14	Significant
6.	Delayed Recall	9.5 \pm 7.7	9.4 \pm 6.42	9.4 \pm 1.0	NS
7.	Verbal retention for similar pairs	4.8 \pm 0.37	4.8 \pm 0.77	4.8 \pm 0.34	NS
8.	Verbal retention for dissimilar pairs	13.8 \pm 1.37	10.1 \pm 1.53	10.7 \pm 1.25	NS
9.	Visual retention	12.1 \pm 1.01	9.7 \pm 1.10	10.1 \pm 1.01	Significant
10.	Recognition	10 \pm 0	8.3 \pm 1.40	9.1 \pm 0.80	NS

Patients on Interventional therapy showed statistically significant improvement in attention and concentration (p < 0.001), Immediate recall (p < 0.05), verbal retention for similar pairs (p < 0.05), and visual retention (p < 0.05)

DISCUSSION

Diabetes mellitus is an endocrine disorder associated with cognitive dysfunction and literature revealed that diabetes causes detrimental effect on a range of cognitive functions which is reported in battery of papers. Cognitive functions are

defined as brain's ability to acquire, process, integrate, store, and retrieve information. Memory is a highly complex phenomenon and a subject matter of many biological and behavioral sciences. Memory is generally believed to be a function of the temporal lobe of the cortex.¹⁵ Impairment of memory is one of the significant findings reported both with hyperglycemia and hypoglycemia in series of papers. In the present study, there is a decrease in attention and concentration, immediate recall, verbal retention and visual retention in the Diabetic group as compared to the normal control group. The prime finding of our study showed statistically significant

improvement in these domains of memory after the administration of interventional therapy i.e structured exercise therapy.

The study by Stewart and Vandenberg, have reported the decrease in memory functions, executive functions, and information processing speed in diabetic population.¹⁶⁻¹⁷ Various studies have documented a negative relationship between glycated hemoglobin and cognition in both type 1 and type 2 Diabetes mellitus.¹⁸⁻¹⁹ Magnetic resonance imaging studies have establish that the declining of cognitive functions in diabetic patients are associated with modest brain atrophy and vascular lesions.²⁰

Animal studies have reported increase hippocampal levels of BDNF during exercise on a running wheel, which is very important for synaptic plasticity, learning and memory²¹ and also improved performance on Morris water maze, a task involves spatial learning and memory.²² Increase in levels of neurotrophins and growth factors, which promotes neurogenesis, synaptic plasticity, and vascular functions and enhances learning and memory, are also reported with the exercise.²¹ The beneficial effects of acute and intermediate exercises on respond speed are reported in study by Mc Morris.²³ Studies have also reported differences in cognitive functions during and after exercise between different modes of exercise and these changes could be explained by changes in cerebral blood flow.²⁴

Pagliari in his study observed the increased levels of catecholamine's in exercising rats and explained the physiological basis of enhanced cognitive functions is increase amount of release of Catecholamine's in central nervous system.²⁵ Neuroimaging studies revealed the enhanced functioning of cortical regions with exercise therapy.²⁶

The study by Krick et.al has reported that the hippocampus shrinks during the late adulthood leading to impaired memory and increased risk of dementia. The physical

activity training increases hippocampal perfusion. The authors have also demonstrated that increased hippocampal volume is associated with greater serum levels of BDNF, which is mediator of neurogenesis in the dentate gyrus and hence enhances cognition and memory.²⁷ Aerobic exercise promotes neurogenesis by increasing the production of neurotrophic factors such as brain-derived neurotrophic factor and Insulin-like growth factor 1.²⁸

CONCLUSIONS

Memory decrements can be found in early stages of type 2 diabetes mellitus and integrated approach of structured exercise therapy delays the memory deficits and also improves cognitive functions such as remote memory, mental balance, attention and concentration, delayed and immediate recall, verbal retention and recognition tests. Our findings have implication for diabetes education and self-management.

Limitation of our study:

1. The magnitude for the difference in cognition between the diabetic and control groups found in our study is small compared reflecting the moderately short duration of diabetes in our population.
2. We could not confirm relationship between glycated hemoglobin and memory impairment possibly because of relatively strict metabolic control in our diabetic population.

Strength of our study: is the measurement of various domains of memory in the early stage of the disease. Previous studies focused mainly on patients with longer diabetes duration. This study gives more information on early decrements of various domains of memory and improvement was observed with structured exercise therapy.

Recommendations: Finally, we provide recommendations for capitalize on the long-term benefits of structured exercise therapy on memory in patients with newly diagnosed type 2 diabetes mellitus.

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