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RESEARCH ARTICLE

Effect of glycemic control on short-term memory in Type 2 diabetics

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ABSTRACT

Background: The increase in diabetes among the elderly is of concern because in addition to the wide range of traditional diabetes complications, evidence has been growing that diabetes is associated with memory decline. Short-term memory plays a very important role in daily activities. **Aims and Objectives:** To find out the effect of glycemic control on short-term memory in Type 2 diabetics. **Materials and Methods**: The study was conducted in 150 individuals aged between 40 and 65 years consisting of 100 diagnosed cases of Type 2 diabetes mellitus who were further divided into Group I: Controlled diabetes with glycosylated hemoglobin (HbA_{1C}) levels < 7% and Group II: Uncontrolled diabetes with HbA_{1C} level > 7% compared with control group consisting of 50 non-diabetics HbA_{1C} < 6% from outpatient department of McGann Hospital, Shivamogga. Rye's auditory verbal learning test, verbal fluency test and Benton visual retention test to assess short-term memory. Statistical analysis was performed using SPSS 21. **Results:** Uncontrolled diabetics showed a significantly reduced score compared to non-diabetics and controlled diabetics ($P < 0.001$) and controlled diabetics showed a significantly ($P < 0.001$) reduced score compared to non-diabetics for all the three memory tests used to assess short-term memory. **Conclusion:** The main hypothesis to explain the pathophysiology of decline in short-term memory in Type 2 diabetes may be glucose dysregulation, accumulation of senile plaques, metabolic oxidation products associated with hyperglycemia, insufficient action or effect of insulin due to insufficient secretion, activity, or both.

KEY WORDS: Diabetes; Glycemic Control; Short-term Memory

INTRODUCTION

Memory is the complex function of the brain that uses several storage buffers of different capacity and duration. Memory function includes registration (encoding or acquisition), retention (storage or consolidation), stabilization, and retrieval (decoding or recall).[1]

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Memories are stored in the brain by changing the basic sensitivity of synaptic transmission between neurons as a result of the previous neural activity. The new or facilitated pathways are called memory traces. They are important because once the traces are established; they can be selectively activated by the thinking mind to reproduce the memories.[2] Short-term memory refers to the function that temporarily retains stimuli that have just been perceived and lasts for ~ 20 s.[3]

The complications of diabetes mellitus on the retinal, renal, cardiovascular, and peripheral nervous systems are widely acknowledged. Less attention has been given to the effect of diabetes on short-term memory. Neurological consequences of diabetes appear parallel to those observed in aging brain. The main hypothesis to explain the pathophysiology of

decline in short-term memory in Type 2 diabetes may be glucose dysregulation,[4] accumulation of senile plaques, metabolic oxidation products associated with hyperglycemia, insufficient action or effect of insulin due to insufficient secretion, activity, or both.[5]

Few studies have shown individuals with established Type 2 diabetes demonstrated a clear age-adjusted inverse relationship between cognitive function and the degree of chronic hyperglycemia as measured by the glycosylated hemoglobin (HbA_{1C}) level.[5] Hence, this study was conducted to evaluate the effect of glycemic control on short-term memory in Type 2 diabetics.

MATERIALS AND METHODS

The study was conducted in 150 individuals aged between 40 and 65 years consisting of 100 diagnosed cases of Type 2 diabetes mellitus who were further divided into HbA_{1C} compared with a control group consisting of 50 non-diabetics $HbA_{1C} < 6\%$ from outpatient department of McGann Hospital, Shivamogga. Rye's auditory verbal learning test (AVLT), verbal fluency test (VFT), and Benton visual retention test (VRT) to assess short-term memory. Statistical analysis was performed using SPSS 21.

Institutional Ethical Committee clearance was obtained. Details of the study protocol were explained to the subjects who volunteered for the study, and informed consent was taken. General information, present complaints, history of diabetes and hypertension if present, duration and treatment of same, any past illness, drug history and family history were noted. Pulse and blood pressure were recorded. Laboratory investigations include fasting blood sugar, postprandial blood sugar, and HbA_{1C}.

Inclusion Criteria for Both the Groups

1. Age 40-65 years who have given written consent
2. Educational status: Minimum primary school.

Exclusion Criteria for Both the Groups

1. History of any known psychiatric disorders
2. History of any other known endocrinal disorders
3. History of any sedative/narcotic abuse
4. History of any other known medical disorders causing dementia
5. History of intake of any drugs known to cause dementia.

The following tests were carried out on the subjects (study and control) in a relaxed state and privacy was given utmost importance: Rye's AVLT, VFT, and Benton VRT to assess short-term memory.[1]

Rye's AVLT

In each trial a list of 15 words that are read to the subject at a rate of one word per second. Then, the subjects are asked to recall words immediately in any order from the list. A total number of words remembered correctly was designated as the score and expressed in percentage. Five such trials were given. The total score is the sum of the scores of all five trials in percentages.

VFT

Subjects have to give a list of words (with a maximum of 10) belonging to a specific semantic category in 15 s. Four semantic categories were successively used (cities, fruits, animals, and colors).Total score was the average of all the scores of different categories expressed in percentage.

Benton VRT

In each trial, a design is presented to the subject, who is allowed to study the design for 10 s. Then design is removed, and the subject had to identify the design correctly from a list of similar designs. Score was given based on the correct answer. Five trials are given. The total score is the sum of the scores of all five designs in percentages.

Statistical analysis was performed using SPSS software version 21. Initially, data were tested for normality using Kolmogorov–Smirnov test and Shapiro wik test. Kruskal–Wallis and one-way ANOVA tests were used.

RESULTS

In this study, non-diabetics with $HbA_{1C} < 6\%$ were considered as the control group. Diabetic patients were divided into two groups according to their HbA_{1C} levels as; Group I: Controlled diabetes with HbA_{1C} levels $\leq 7\%$ and Group II: Uncontrolled diabetes with HbA_{1C} level $> 7\%$. Rye's AVLT, VFT, and Benton VRT to assess short-term memory. Statistical analysis was performed using SPSS 21.

Mean ± standard deviation of HbA_{1C} value among the control group was: $5.55 \pm 0.75\%$; In Group I (controlled diabetics) was: $6.54 \pm 0.96\%$ and in Group II (uncontrolled diabetics) was found to be: $8.15 \pm 1.05\%$ (Table 1). Median and interquartile range of all the memory test for diabetic patients of control group, Group I and II are shown in Table 2. The median scores of the tests are depicted in Figure 1. Table 2 also shows statistical analysis by Kruskal–Wallis one-way ANOVA test.

AVLT

The median memory score of the control group was found to be 55%, Group I - 42% and Group II - 26.75%. The pairwise

comparisons of AVLT memory score were found to be statistically significant ($P < 0.001$).

VFT

The median memory score of the control group was found to be 66.5%, Group I - 50.25% and Group II - 30.5%. The pairwise comparisons of VFT memory score were found to be statistically significant ($P < 0.001$).

VRT

The median memory score of the control group was found to be 93%, Group I - 88% and Group II - 67%. The pairwise comparisons of VRT memory score were found to be statistically significant ($P < 0.001$).

Inter-group significance by Kruskal–Wallis one-way ANOVA test for the memory scores of diabetics of different glycemic index showed a significant $P < 0.001$ (Table 2) during overall comparison as well as pairwise comparison between the three groups-control group (non-diabetics), Group I (controlled diabetics) and Group II (uncontrolled diabetics). Uncontrolled diabetics showed a significantly reduced score compared to non-diabetics and controlled diabetics and controlled diabetics showed a significantly ($P < 0.001$) reduced score compared to non-diabetics for all the three memory tests used to assess short-term memory.

The study revealed that an increase in HbA_{1C} worsened the short-term memory status (by Kruskal–Wallis ANOVA).

Table 1: Comparison of mean HbA_{1C} levels between control group, controlled diabetic and uncontrolled diabetic group and significance using one-way ANOVA

Groups	HbA_{1C} value (%) (mean±SD)	*P*-value
Control group	5.55±0.75	<0.001 (significant)
Group I - controlled diabetics	6.54±0.96	
Group II - uncontrolled diabetics	8.15±1.05	

SD: Standard deviation, HbA_{1C}: Glycosylated hemoglobin

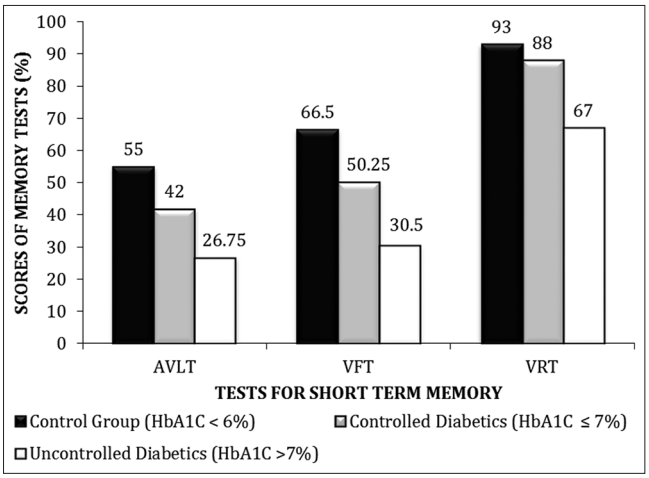

Figure 1: Glycemic index versus short-term memory status. Control group: Glycosylated hemoglobin (HbA_{1C}) <6% ($n = 50$), Group I: Controlled diabetics $HbA_{1C} \leq 7\%$, Group II: Controlled diabetics $HbA_{1C} > 7$

Table 2: Median and IQR of memory scores (%), *P* values of Kruskal–Wallis one-way ANOVA test of short-memory tests

Tests	Control and study group						Inter group significance
	Control group HbA_{1C} <6%		Group I HbA_{1C} <7%		Group II HbA_{1C} <7%		
	Median	IQR	Median	IQR	Median	IQR	
AVLT	55	5.6	42	10.7	26.75	22	Overall: *P*<0.001 (S) Pairwise: Control I: *P*<0.001 (S) Control II: *P*<0.001 (S) Group I, II: *P*<0.001 (S)
VFT	66.5	19.6	50.25	11	30.5	10.4	Overall: *P*<0.001 (S) Pairwise: Control I: *P*<0.001 (S) Control II: *P*<0.001 (S) Group I, II: *P*<0.001 (S)
VRT	93	8	88	9	67	36	Overall: *P*<0.001 (S) Pairwise: Control I: *P*<0.001 (S) Control II: *P*<0.001 (S) Group I, II: *P*<0.001 (S)

MED: Median, IQR: inter-quartile range, AVLT: Auditory verbal learning test, VFT: Verbal fluency test, VRT: Visual retention test, HbA_{1C}: Glycosylated hemoglobin

DISCUSSION

When pairwise comparison was done using Kruskal–Wallis one-way ANOVA test among control group (non-diabetics), Group I (controlled diabetics) and Group II (uncontrolled diabetics) for all three memory tests used to assess short-term memory; uncontrolled diabetics showed a significantly reduced score compared to non-diabetics and controlled diabetics and controlled diabetics showed a significantly ($P < 0.001$) reduced score compared to non-diabetics for all the three memory tests used to assess short-term memory.

Similar results have been shown in studies like the one involving 60 patients aged above 70 years with mean age 79 ± 5 years and duration of diabetes 14 ± 1.3 years of which 34% of patients had low clock in box test (≤5), and 38% of patients had low clock drawing test (≤13). Both the test scores were inversely correlated with HbA_{1C} suggesting that cognitive dysfunction is associated with poor glycemic control.[6] Yaffe et al. in a study done on 1983 postmenopausal women (mean age of 67.2 years) with the mean level of HbA_{1C} 5.8%, 86 (4.3%) women developed mild cognitive impairment (MCI) or dementia. For those with HbA_{1C} level ≥ 7% ($n = 49$), the age-adjusted risk for developing MCI was increased nearly 4-fold and was increased nearly 3-fold for developing MCI or dementia.[4]

Yaffe et al. in another study assessed the relationship of HbA_{1C} and fasting plasma glucose levels to performance on four cognitive tests was assessed, adjusting for age and other determinants of cognitive status. The tests were the digit symbol substitution test (DSST), mini–mental status examination, Rey's AVLT, and Stroop test. A statistically significant age-adjusted association was observed between the A_{1C} level and the score on all four cognitive tests. The association between the DSST score and HbA_{1C} persisted in all multiple linear regression models. Higher HbA_{1C} levels are associated with lower cognitive function in individuals with diabetes.[5]

In the present study, it was found that increase in the glycemic index worsened the short-term memory status in diabetes patients indicating poor glycemic control was associated short-term memory among diabetic individuals. The results are comparable to the works of Munshi et al.,[6] Yaffe et al.[4] and Yaffe et al.[5] This may be due to glucose dysregulation,[4] accumulation of senile plaques, metabolic oxidation products associated with hyperglycemia, insufficient action or effect of insulin due to insufficient secretion, activity, or both,[5] neuronal damage as a result of advanced glycosylated end product production and oxidative stress, damage to vascular endothelium as a result of high osmotic stress induced by hyperglycemia which disrupts the blood–brain barrier causing local leakage of vascular substances and aggravates neuronal damage.[7]

Limitations

Prospective studies are required to examine the putative link between glycemic control and short-term memory status, because only using such study designs can a causal relationship be established. Since different studies have utilized different psychological tests, there is a need to develop a standard study design that can be employed in testing short-term memory Type 2 diabetes.

CONCLUSION

This study shows that the short-term scores were decreased in diabetic patients and this decrease in memory status was statistically significant in uncontrolled diabetics when compared to controlled diabetics and non-diabetics. This may be due to glucose dysregulation, accumulation of senile plaques, metabolic oxidation products associated with hyperglycemia, insufficient action or effect of insulin due to insufficient secretion, activity, or both, neuronal damage as a result of advanced glycosylated end-product production and oxidative stress, damage to vascular endothelium as a result of high osmotic stress induced by hyperglycemia which disrupts the blood–brain barrier causing local leakage of vascular substances and aggravates neuronal damage.

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