Correlation of Blood Glucose Level with Working and Short Term Memory Status in Type 2 Diabetes Mellitus

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Research Article

Abstract: Background and Objectives: Working and short term memory loss is common in poorly controlled diabetic patients. Though cognitive deficits affect daily activities much importance is not given to assess working and short term memory at bedside. Hence this study was undertaken to correlate blood glucose level with working and short term memory in type 2 diabetics compared with age and gender matched normal subjects. Methodology: Present study was conducted in Al-Ameen Medical College and Government district Hospital, Bijapur on 114 diabetics aged (40-60 yrs.) and 119 normal subjects aged (40-60 yrs.). Cognitive function assessment was done for short term and working memory by using 5 memory tests. For short term memory- AVLT, VFT and VRT and for working memory - WDST and VST were used. The results were expressed in average total scores(%). T test and Correlationregression analysis were used for statistical analysis. Results: Significant decrease in working and short term memory was observed in diabetic patients. In diabetes patients mean FBS was found to be 146+29.2mg% compared to the mean FBS levels of normal subjects (97.9±12.6mg %). In diabetes patients mean PPBS was found to be 194±39mg % compared to the mean PPBS levels of normal subjects (133+11.1mg %). Memory scores in all 5 tests were found to be decreased correlating negatively with the FBS and PPBS levels. Interpretation and Conclusion: The short term and working memory status in the present study decreased significantly in the diabetic patients, which may be due to hyperglycemia, hypoglycemia, vascular dementia and insulin resistance. Therefore these observed effects of FBS and PPBS levels are of potential clinical importance because working and short term memory loss could interfere with day today activities.

Keywords: short term and working memory, Diabetes, hyperglycemia, hypoglycemia.

Introduction

Memory is one of the most important cognitive domains with respect to every day function and is the process of storing, encoding and retrieving information. Different forms of memory are recognized including short term, long term and working memory. Short term memory refers to the function that temporarily retains stimuli that have just been perceived and lasts for ~20 secs. Working

memory is a short term memory system that allows concurrent retention and manipulation. It is used for thinking about what is an already known and deriving conclusion on the basis of that knowledge¹. Some cross studies suggest that hypoglycemia, sectional hyperglycemia, hyperinsulinemia and vasculopathy in DM lead to decline in cognitive function. Studies of cognitive function among older persons might focus on the areas of cognition most affected by common dementing illness, including memory, attention, language, visuospatial ability and abstraction². Several studies have reported significant cognitive impairment among subjects with DM compared with non DM individuals. Hence this study is undertaken to correlate blood glucose levels with impairment in Working and Short term memory in type 2 diabetes patients in comparison with age and gender matched normal subjects in Indian population.

Materials and Methods

The present study was conducted in the department of physiology Al-Ameen Medical College, Bijapur. One Hundred and fourteen (114) diabetic patients between 40-60 years of age and One hundred and nineteen (119) normal subjects near hospital premises and from Bijapur city were volunteers for this study. Level of education, Type of Diabetes, Duration of the disease, personal history and past history were recorded. In biochemical investigations, Fasting and Post-prandial blood sugars were recorded. Different memory tests were used to assess short term and working memory. Short term memory tests used were: Auditory verbal learning test (AVLT), Visual reproduction test (VRT) and Verbal fluency test (VFT). Working memory tests used were: Working digit span test (WDST) and Validation span $test^{3}$, 1 (VST) Data was analyzed using t test and correlation-regression analysis.

Table 1: Mean and SD of memory scores (in %) of different tests in diabetes patients and normal subjects

	Diabetes Patients		Normal Subjects		T test	
Tests	Mean	SD	Mean	SD	t	P
1. AVLT	40.6	15.5	62.8	6.17	39	<0.0001 (S)
2. VFT	77.2	22.8	100	00	27.6	<0.0001 (S)
3.VRT	96.1	7.9	100	00	26.2	<0.0001 (S)
4.WDST	55.3	25.3	96.5	8.09	31.8	<0.0001 (S)
5.VST	56.1	27.1	96.1	8.7	31	<0.0001 (S)

Table 2: r and p values of correlation regression analysis for memory tests in diabetes patients

	Fasting Blood Sugar		Post Prandial Blood Sugar	
Tests	r	р	r	р
1. AVLT	0.80	<0.0001 (S)	0.69	<0.0001 (S)
2. VFT	0.81	<0.0001 (S)	0.74	<0.0001 (S)
3. VRT	0.55	<0.0001 (S)	0.58	<0.0001 (S)
4. WDST	0.78	<0.0001 (S)	0.66	<0.0001 (S)
5. VST	0.83	<0.0001 (S)	0.71	<0.0001 (S)

Table 3: Mean and SD values of Blood glucose (FBS and PPBS), Age and Duration of Diabetes

	Diabetes Patients		Normal Subjects	
	MEAN	SD	MEAN	SD
FBS (mg%)	147	29	97.9	12.6
PPBS (mg%)	194	39	131	11.3
Duration (yrs.)	6.54	3.88		
Age (yrs.)	49.2	6.79	48.2	5.51

Results and Discussion

In normal subjects mean of FBS was found to be 97.9±12.6mg% where as in diabetes patients mean FBS was 146±29.2mg%. Increase in the FBS level in the diabetes patients was statistically significant when compared to normal subjects. In normal subjects mean PPBS was found to be 133±11.1mg% where as in diabetes patients PPBS was 194±39mg%. Increase in the PPBS level in the diabetes patients was statistically significant when compared to normal subjects.

1. Auditory verbal learning test

Refer Table No.1. Table No.2 and 3.A statistically significant correlation was found between FBS levels and scores of AVLT (r=0.80, p<0.0001) indicating that as the FBS levels increased the scores of AVLT were fund to be decreased. A statistically significant correlation was found between PPBS levels and scores of AVLT (r=0.69, p<0.0001) indicating that as the FBS levels increased the scores of AVLT were found to be decreased.

2. Verbal fluency test

Refer Table No.1. Table No.2 and 3.VFT Scores were found to be decreased with the increased levels of FBS which was statistically significant with negative correlation. (r=0.81, p<0.0001). VFT Scores were found to be decreased with the increased levels of PPBS which was statistically significant with negative correlation. (r=0.74, p<0.0001)

3. Visual reproduction test

Refer Table No.1. Table No.2 and 3.The memory scores of VRT were found to be decreased as levels of FBS increased indicating negative correlation between FBS and memory status in diabetes patients which was statistically significant. (r=0.55, p<0.0001). The memory scores of VRT were found to be decreased as levels of PPBS increased indicating negative correlation between PPBS and memory status in diabetes patients which was statistically significant. (r=0.58, p<0.0001)

4. Working digit span test

Refer Table No.1. Table No.2 and 3.WDST scores were decreased with the increased levels of FBS. This decrease in the memory status was found to be statistically significant and it was negatively correlated. (r=0.78, p<0.0001). WDST scores were decreased with the increased levels of PPBS. This decrease in the memory status was found to be statistically significant and it was negatively correlated. (r=0.66, p<0.0001)

5. Validation span test

Refer Table No.1. Table No.2 and 3.A statistically significant correlation was found between the levels of FBS and memory scores of VST (r=0.83, p<0.0001) indicating that as the FBS levels increased the scores of VST were fund to be decreased. A statistically significant correlation was found between the levels of PPBS and memory scores of VST (r=0.71, p<0.0001) indicating that as the PPBS levels increased the scores of VST were

found to be decreased. In diabetes patients mean FBS was found to be 146+29.2mg% compared to the mean FBS levels of normal subjects (97.9+12.6mg %). This increase in the FBS levels in diabetes patients was found to be statistically significant. Memory scores in all 5 tests were found to be decreased correlating negatively with the FBS levels. In diabetes patients mean PPBS was found to be 194+39mg % compared to the mean PPBS levels of normal subjects (133±11.1mg %). This increase in the PPBS levels in diabetes patients was found to be statistically significant. Memory scores in all 5 tests were found to be decreased correlating negatively with the PPBS levels. R. K. Solanki, Vaibhav Dubey and Deeptimunshi in 2009, in their study entitled "Neurocognitive impairment and comorbid depression in patients of Diabetes mellitus" used digit span test, stroop test, controlled word association test, visual target cancellation test, digit symbol substitution test and visuospatial working memory cancellation matrix to assess cognitive function. They found that 48% of elderly diabetic patients showed cognitive impairment. Poor metabolic control (hyperglycemia) was associated significantly and negatively with cognitive index in diabetic patients. Hyperglycemia was significantly and negatively correlated with immediate memory and attention, verbal memory, psychomotor functioning visuospatial memory.4 (DSST) and Andrew J.Sommerfield, Vincent McAulay, Ian J. Deary and Brian M. Frier in 2002 studied 16 adults in Type 1 diabetes on two separate occasions. They found that the effect of hypoglycemia on working memory and delayed memory was more profound. Performance in the memory tests, the trial making B test and the digit symbol test also deteriorated during hypoglycemia and concluded that all of the memory systems examined in the present study were affected significantly by acute hypoglycemia, particularly working memory and delayed memory. Selftreated hypoglycemia is common in individuals with insulin treated diabetes. In the study entitled "Carbohydrate induced memory impairment in adults with Type 2 Diabetes" by Carol E. Greenwood, Stacey Hebblewaite, Randall J Kaplan and David J A Jenkins in 2003 studied impact of 50g of rapidly absorbed carbohydrate at breakfast in Type 2 Diabetes adults (n=19). Subjects were tested under fed and fasted conditions using both word list and paragraph recall test, trials test part B as a measure of general brain function and mood. Under fasting conditions, higher fasting blood glucose trended toward poorer word list recall. Carbohydrate ingestion influenced measures of delayed, but not immediate recall in a time dependent fashion such that delayed recall was improved at 15 minutes post ingestion but was impaired at 30 minutes. Neither trails

test scores nor was mood influenced by food ingestion.⁵ In this study it was observed that in diabetic patients mean + SD FBS was found to be 146+29.2 mg% compared to the mean + SD FBS levels of normal subjects (97.9+12.6 mg%). This increase in the FBS levels in diabetic patients was found to be statistically significant (P<0.0001). Memory scores in all 5 tests were found to be decreased correlating negatively with the FBS levels. These results were comparable with the works of R. K. Solanki and co-workers. ⁴This may be due to the hyperglycemia causing damage by advanced glycated products, diacyl glycerol of protein kinase C, increased glucose shunting in hexose amine pathway, elevated super oxide levels, impairment in neurotransmitter functioning, and HPA Axis dysregulation. In the present study it is observed that in diabetic patients mean + SD PPBS was found to be 194+39 mg% compared to the mean + SD PPBS of normal subjects 134+11.1 mg%. This increase in PPBS levels in diabetic patients was found to be statistically significant (P<0.0001). Memory scores in all 5 tests were found to be decreased correlating negatively with the PPBS levels. This decrease in memory scores in diabetic patients may be due to hyperglycemia which is agreeable to the works of Chui MH, ¹⁰Sherin antony ¹¹ and Carol E. ⁵This may be due to the hyperglycemia causing damage by advanced glycated products, diacyl glycerol of protein kinase C, increased glucose shunting in hexose pathway, ⁶ elevated super oxide levels, ⁷ impairment in neurotransmitter functioning,8 and **HPA** Axis dysregulation.9

Conclusion

The short term and working memory scores were decreased in all 5 memory tests in diabetic patients and this decrease in memory status was statistically significant when compared to normal subjects. Memory scores of short term and working memory by all memory tests were found to be decreased in diabetic patients with hyperglycemia. FBS and PPBS were negatively correlated with memory status. Poorly controlled diabetic patients are at greater risk of cognitive decline. The decreased memory status in diabetic patients may be due to many factors like hyperglycemia, hypoglycemia, vascular disease, insulin resistance, duration of the disease and type of therapy.

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References

- Andrew J.Sommerfield, Vincent McAulay, Ian J. Deary, Brian M. Frier. Short-Term, Delayed, and Working Memory Are Impaired During Hypoglycemia in Individuals With Type 1 Diabetes. Diabetes care 2003;26:390-396
- Martha Clare Morris, Dennis A. Evans, Liesi E. Hebert, Julia L. Bienias. Methodological issues in the study of cognitive decline. Am J Epidemiol 1999; 149:789-93.
- Celile Proast Lima, Haelena Amieva, Jean Francois Dartigues, Helene Jaquirim Gadda. Sensitivity of 4 psychometric tests to measure cognitive changes in brain aging-population based studies. Am J Epidemiol 2007; 165:344-350.
- R.K.Solanki, Vaibhav Dubey, Deepthi Munshi. Neurocognitive impairment and comorbid depression in patients of Diabetes mellitus. Int J Diabetes Dev Ctries. 2009; 29:133-138.
- Carol E. Greenwood, Stacey Hebblewaite, Randall J Kaplan, David J A Jenkins. Carbohydrate induced memory impairment in adults with Type 2 Diabetes. Diabetes care 2003; 26:1961-1966.

- Toth C, Schmidt AM, Tuor UI, Francis G, Foniok T, Brussee V, et al.. Diabetes, leukoencephalopathy and rage. Neurobiol Dis 2006; 23:445–461.
- Aragno M, Mastrocola R, Medana C, Restivo F, Catalano MG, Pons N, et al.. Up-regulation of advanced glycated products receptors in the brain of diabetic rats is prevented by antioxidant treatment. Endocrinology 2005; 146:5561–5567.
- 8. Biessels GJ, Kappelle AC, Bravenboer B, Erkelens DW, Gispen WH. Cerebral function in diabetes mellitus. Diabetologia 1994; 37:643–650.
- Lupien S, Lecours AR, Lussier I, Schwartz G, Nair NP, Meaney MJ. Basal cortisol levels and cognitive deficits in human aging. J Neurosci 1994;14:2893–2903.
- Rachel A. Whitmer, Andrew J. Karter, Kristine Yaffe, Charles P. QuesenherryJr, Joseph V. Selby. Hypoglycemic episodes and risk of dementia in older patients with Type 2 diabetes mellitus. JAMA 2009;301:1565-1572.
- Sherin Antony, Peeyushkumar T, Jobin Matthew, T R Anju, C S Palose. Hypoglycemia induced memory changes in cholinergic receptor expression in the cerebellum of diabetic rats. Journal of Biomedical Science 2010:17:7.