ORIGINAL ARTICLE

Neurocognitive impairment in patients of diabetes mellitus

R K Solanki , Vaibhav Dubey, Paramjeet Singh, Deepti Munshi, Mukesh Kr. Swami

Abstract : *This study was conducted to find out the association of diabetes mellitus with cognitive functioning. We included 50 diabetic and 3O control subjects who were screened on the basis of various inclusion and exclusion criteria. Then a history of variables under study was taken and respective laboratory investigations were noted. The cognitive function was then assessed using the Digit Span test, Stroop Test, Controlled Oral Word Association Test, Visual Target Cancellation test, Digit Symbol Substitution test, Visuospatial working memory matrix. The composite score on all tests was used to make cognitive index. The data was compiled and appropriate statistical methods were used. We found that48 % 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 (DSST) and visuospatial memory. In conclusion although genesis of cognitive deficits in diabetic patients is complex, it appears from the study that such deficits do exist and may be associated with chronic poorly controlled diabetes.*

Key words : Neurocognition, diabetes mellitus

JMHHB 2009; 14 (1) : 46-50

INTRODUCTION

The impact of diabetes on cognitive function has been of interest since investigations have suggested that both chronic hyperglycemia[1] and recurrent episodes of severe hypoglycemia[2] are associated with cognitive dysfunction in people with type 1 (insulin dependent) diabetes .It has also been widely reported that type 2 (non insulin dependent) diabetes is associated with cognitive impairment.[3,4,5] However this presumed association has recently been disputed by Strachan et al 6, who found in their review that the studies vary widely with respect to nature of diabetic population studied and psychological tests used.

Greenwood et al[7] in their study examined the association between glycaemic control and cognitive performance under fasting conditions and impact of carbohydrate consumption on cognitive functions in adults with type 2 diabetes. The results demonstrate a negative relationship between measures of glycaemic control specifically HbA1C and fasting blood glucose and fasting cognitive performance such that individual with poorer glycaemic control show poorer performance on test of verbals recall.[7]

Problematic to understanding the association between diabetes mellitus and cognitive performance is the fact that other complications typically observed with type 2 diabetes mellitus

including cardiovascular disease; hypertension and depression are also associated with cognitive deficit. The specific mechanism linking type-2 diabetes with cognitive deficits has not been identified however extraneuronal hyperglycemia, disturbed brain glucose metabolism, altered brain insulin signaling and complications secondary to potential hypercortisolemia have all been implicated.[8]

These potential effects may be even more significant from a population based perspective when one considers that diabetes is highly prevalent (particularly in older age groups), expensive and one of the leading causes of death in the world.

So ultimately we can say, if the hypothesis of association between diabetes mellitus and cognitive impairment comes true then early detection and treatment of NIDDM may mitigate its cognitive sequel.

Aim and Objectives:

The study was planned to assess the neurocognitive functioning in patients of diabetes mellitus and its correlation with the severity of diabetes mellitus.

Methodology:

This study was done on patients of diabetes mellitus taken from Diabetic Clinic OPD (a specialty clinic for diabetes mellitus run by Department of Medicine, SMS Medical College, Jaipur). Subjects preferably relatives or attendants of patients matched on age, sex, education, occupation and economical status formed the control group. 50 patients and 30 control meeting selection criteria were included in the study. The subjects were enrolled after taking written informed consent. On a specially designed pro forma their sociodemographic profile and data regarding diabetes mellitus was recorded. In our study severity of illness was assessed by fasting blood sugar. The recent blood sugar level (both fasting and PP) done on previous day was noted. After this subjects were asked to perform neuropsychological tests- Digit Span Test (DST), Stroop Test[9,10] ,Controlled Oral Word Association Test (COWA)[11], Visual Target Cancellation Test, Digit Symbol Substitution Test (DSST), and lastly Visuospatial working memory matrix.[12,13] All Findings of the study were compiled, suitable statistics was applied and results were drawn and discussed.

Selection criteria:

Subjects diagnosed as having diabetes mellitus were included in the experimental group. Subjects without diabetes mellitus were included in control group.

From both the groups illiterate patients, subjects having history of psychiatric disease , any coexisting neurological disease, severe sensory handicap, patients suffering from hypertension (diagnosed by medical records and clinical examination), any history of past / current substance abuse/ dependence, any other medical /endocrinal disorder except diabetes mellitus were excluded.

Results:

Table 1: Neuropsychological profile of subjects (mean ± standard deviation)

	Neuropsych-ological test	Experimental group	Control group
1	Digit Span Test		
	Forward	4.7±0.70	5.4±0.84
	Backward	3.18±0.68	4.1±0.69
2	Stroop Test	105.8±39.9	106±44.5
3	COWA Test	20.18±5.79	23.03±6.3
4	Visual Target cancellation test	6.86±2.83	7.11±2.92
5	Digit symbol Substitution test	32.26±15.39	44.1±4.9
6	Visuospatial working memory matrix	8.24±3.07	11.13±2.86

Table 2: Distribution of diabetic patients according to cognitive performance

(n=50)	
Diabetic patient showing poor cognitive performance	24 (48%)
Diabetic patients showing average or above average cognitive performance	26 (52%)

Cut off value for poor cognitive performance was cognitive index of 1.108 (based on 1st quartile value of control population.

Table3:

Data of status of diabetic patients

	Poor cognitive performers	Avg. & above Avg. cognitive performers
Blood sugar level (in mg %)	153±30.5	123.1±30.7

Above table shows the mean and range of fasting blood sugar level .Range is calculated by adding or subtracting one standard deviation from the mean.

Table 4:

Correlation of fasting blood sugar level with cognitive index

Variable	Beta	Standard error	P Level
Cognitive index	-0.374	1.327	0.007

The fasting blood sugar had negative correlation with cognitive index. For each unit increment in fasting blood glucose, the score on cognitive index declined by 0.37 and it was significant.

Each unit increment in fasting glucose levels caused decline in DST (forward) score of test by 0.41 and it was significant.

A positive correlation was found with Digit Span test Backward which was however not significant.

There was positive but insignificant correlation between fasting blood sugar level and Stroop test scores.

A significant negative correlation was found between fasting blood sugar level and COWA Test scores.

Table 5:

Correlation of Fasting Blood Sugar Level with Neuropsychological Tests

Variable	Beta	Standard error	P Level
Digit Span Test Forward	-0.41	6.44	0.002
Digit Span Test Backward	0.089	7.24	0.53
Stroop Test	0.181	0.1207	0.20
COWA test	-0.390	0.795	0.005
Visual target cancellation test scores	-0.416	1.58	0.0026
DSST	-0.340	0.29	0.01
Visuo- spatial working memory matrix	-0.17	1.61	0.45

Each unit increment in fasting blood sugar caused decline in scores of visual target cancellation test by 0.41 and it was significant.

Each unit increment in Blood Glucose level caused decline in DSST scores by 0.34 and this correlation was found to be significant.

Patient's performance on visuospatial memory matrix had insignificant negative correlation with fasting blood glucose level.

Discussion:

We found that 48% of total diabetic patients were showing poor cognitive performance on different neuropsychological tests. Ryan et al[14] reported magnitude of psychomotor slowing on specific tests ranging from 12% to 23%. The high prevalence in our study may be due to high cut off point for cognitive impairment. Most of the studies defined a low score as the bottom 10th percentile and compared low score with top 90th percentile. We used 25th percentile as cut off point because we were interested in characterizing performance that was well below average i.e. well below the 50th percentile but not necessarily indicative of severe dysfunction (cut off point at 10th percentile).Considering this finding, further studies are needed in our set up to look for the validity of our results.

Correlation of blood sugar level and

performance on different neuropsychological tests:

1) Immediate memory and attention: Digit forward test is a measure of immediate auditory memory span and attention. Digit backward measures working memory. The mean score of digit span forward test was found 4.7±0.70 whereas mean score of digit span backward test was 3.18±0.68. In our study the fasting blood glucose level was significantly and negatively correlated with digit span forward test scores whereas digit backward score had insignificant positive correlation. U Ren et al[15] and Jagusch[16] et al also showed in their study that forward digit span was impaired significantly in diabetic patients. Impairment in performance on digit span backward test was shown by Perlmuter et al.[17]

2) Psychomotor efficiency:

I. Stroop test

II. Digit Symbol Substitution test

Mean Score on Stroop test was 105.8±39.9 and mean score on DSST was 32.26±15.39. Stroop test in our study had insignificant positive correlation with fasting blood glucose level, but DSST was correlated negatively and significantly with fasting blood glucose level. Each unit increment in fasting blood glucose level caused decline in DSST score by 0.34. The DSST requires attention, rapid responding, visual scanning and associative learning because subjects substituted number of symbols according to pre- established code. Changes in psychomotor efficiency in diabetic patients was also shown by Reaven et al.[19] Ryan et al[14] suggested that mental slowing may be a common manifestation of central neuropathy induced by chronic hyperglycemia.

3) Verbal fluency

The controlled oral word association test (COWAT) is a measure of verbal fluency/concept formation and the ability to shift set and inhibit incorrect responses .In our study the fasting blood glucose level was significantly correlated with COWA test scores. For each unit increment in fasting blood glucose level, score on COWA test declined by 0.39.

Nilsson[20] found that letter fluency is more sensitive to diabetes related impairment than category fluency & it can be interpreted to indicate that frontal structures are selectively impaired in diabetes.

4) Visuo - spatial functioning: It was tested in our study by two tests : I. Visual target cancellation test II. Visuospatial working memory matrix

The visual target cancellation test scores were significantly and negatively correlated with fasting blood glucose level while visuospatial working memory test was correlated negatively although insignificant.

Mooradian et al[3] also showed significantly poorer performance on visual spatial memory in diabetic patients. Strachan6 et al showed that chronic hyperglycemia appeared to compromise organizational strategy use and new learning/ consolidation across both visual and verbal modalities.

In our study correlation between cognitive index and fasting blood glucose level was significantly negative .For each unit increment in fasting blood glucose level, the scores on cognitive index declined by 0.37. Kalmijn et al[21] showed that poorer glycaemic control was associated with poorer cognitive function in diabetic patients.

Conclusion: 1) 48 % diabetic patients showed cognitive impairment. 2) Poor metabolic control (hyperglycemia) was associated significantly and negatively with cognitive index in diabetic patients. 3) Hyperglycemia had significant and negative correlation with immediate memory and attention, verbal memory, psychomotor functioning (DSST) and visuospatial functioning.

In conclusion genesis of cognitive deficits in diabetic patients is complex. However it appears that from the study that such deficits do exist and may be associated with chronic poorly controlled diabetes. Whether poorly controlled diabetes causes cognitive deficit through some metabolic derangement or micro-vascular disease

is unknown. It is possible that diabetic patients with worse cognitive deficit are unable to care for themselves and thus have worse metabolic control .In either case practitioner should recognize that diabetes in population is associated with cognitive impairment that may affect self care and the treatment strategies should be altered accordingly.

Limitations: The results of this study need to be viewed in context of its limitations: 1) Due to the limited resources and time, a larger sample size was not taken. 2) Due to Cross sectional study design we were not able to measure whether chronically disturbed metabolic control or few peaks of uncontrolled hyperglycemia cause more damage. Nonetheless this study though does not establish a cause and effect relationship between diabetes and cognitive functions; however it does establish a correlation between them.

References:

1. Ryan CM, Williams TM et al. Cognitive function in adults with type 1 (insulin dependent) diabetes mellitus of long duration: effect of recurrent hypoglycemia and other chronic complications. Diabetologia 1993; 36:329-334.
2. Wredling R, Levander S et al. Permanent neuropsychological impairment after recurrent episodes of severe hypoglycaemia in man. Diabetologia 1990; 33:152-157.
3. Mooradian AD. Diabetic complication of central nervous system. Endocr Rev 1988; 9:346-356.
4. Richardson JTE. Cognitive function in diabetes mellitus, Neurological Bio Behav. Rev 1990; 14:385-388.
5. Biessels GJ, Kappelle AC et al. Cerebral function in DM. Diabetologia 1994; 37:643-650.
6. Strachan MWJ, Deary IJ et al. Is type 2 (non insulin dependent) DM associated with an increased risk of cognitive dysfunction. Diabetes Care 1997; 20: 438-445.
7. Greenwood CE, Hebblethwaite S et al. Carbohydrate-induced memory impairment in adults with type -2 diabetes. Diabetes care 2003; 26:1961-1966.
8. Stewart R, Lio Litsa D. Type 2 diabetes mellitus, cognitive impairment and dementia. Diabet Med 1999; 16:93-112.
9. Comalli PJ, Wapner S and Werner H. Interference effect of color word test in childhood, adulthood and aging. J Genet Psychol; 1962; 100:47-53.
10. Stroop J. Studies of interference in serial verbal reactions. J Exp Psychol 1935; 18:643.
11. Spreen O& Brenton AL. Neurosensory Center Comprehensive Examination For Aphasia (NCCEA), Victoria:Univ of Victoria Neuropsychology Laboratory.
12. Roopesh BN. The role of central executive in encoding of organizational strategy and in working memory. Mphil Dissertation, NIMHANS, Bangalore 2000.
13. Vecchi T, Montecellai ML. Visuospatial working memory: structures and variables affecting a capacity measure. Neurology; 1995; 33 (1): 1549-1564. Med 1999; 16:93-112.
14. Ryan CM, Geckle MO .Circumscribed cognitive dysfunction in middle age adults with type 2 diabetes. Diabetes Care 2000; 23:1486-1493.
15. U Ren RC, Riddle MC et al. The mental efficiency of the elderly person with type 2 diabetes mellitus. J Am. Geriztr Soc. 1990; 38:505-510.
16. Jagusch H, Puranen M et al. Cognitive function and metabolic state in elderly diabetic patients. Diabetes Nutr Metab 1992; 5:265-274.
17. Perlmuter LC, Hakami MK et al. Decreased cognitive function in aging non insulin dependent diabetic patient. Am J Med 1984; 77: 1043-48.
18. Lezak MD : Neuropsychological assessment 3rd ed. Newgarle Oxford Univ. Press.1995
19. Reaven GM, Thompson LW et al. Relationship between hyperglycemia and cognitive function in older NIDDM patients. Diabetes Care 1990; 13:16-21.
20. Nilsson E. diabetes and cognitive functioning: the role of age and comorbidity. Dissertation 2006. Aging research center, karolinska institute, Stockholm, Sweden.
21. Kalmijn S, Feskens EJM et al. Glucose intolerance hyperinsulinemia and cognitive function in general population of elderly men. Diabetologia 1995; 38: 1096-1102.

R K Solanki , Professor
Vaibhav Dubey, Assistant Professor
Paramjeet Singh, Associate Professor
Deepti Munshi, Resident
Mukesh Kr. Swami, Resident,
Department of Psychiatry S.M.S. Medical College, Jaipur

Corresponding author
R K Solanki
D-840, Malviya nagar, Jaipur, India
E Mail ID: solanki_ramk@yahoo.com