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Research Paper

Morning Cortisol Level and Cognitive Abilities in People with Type 2 Diabetes Mellitus

Medical Science

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ABSTRACT

Objetives: *Relation between morning cortisol level and cognitive abilities in people of Type 2 diabetes were accessed .*

Design: *Cross-sectional epidemiological study*

Material and method : *100 Participants, aged 60-75 years were recruited randomly of type 2 diabetes, living in North-west Rajasthan. A fasting venous blood sample was taken for measurement of plasma cortisol. Cortisol levels were measured by radioimmunoassay. Cognitive ability was assessed by a battery of psychometric tests*

Results : *This study showed significant relationship between cortisol levels and cognitive dysfunctions. Odds ratio of morning cortisol levels with mini-mental state examination (MMSE), mental flexibility-trail making test (TMT) and executive function- verbal fluency test (VFT) were 4.407 , 2.647 and 0.195 respectively.*

Conclusion: *There is highly significant causal correlation between cortisol level and cognitive dysfunctions in diabetic patients . Increased age and other complications of diabetes also have impact on cognitive function spectrum.*

Introduction

Type 2 diabetes is associated with cognitive impairments, including deficits in processing speed, executive function, declarative memory and with structural changes in the brain including reductions in hippocampal and amygdalar volumes, which are key areas influencing learning and long term memory[1,2]. Various studies have illustrated that cognitive dysfunctions are early predictors of dementia.

Hyperglycemia, cerebral micro-vascular disease and recurrent severe hypoglycaemic episodes are important causative factors[3], but these factors are unlikely to explain entire effect of diabetes on cognition .

It has been already seen that exogenous glucocorticoid administration and elevated endogenous glucocorticoids (as occurs in Cushing syndrome) are associated with cognitive impairment in animals and humans . More subtle alterations in hypothalamic-pituitary-adrenal (HPA) axis function have also been linked with cognitive function, with higher morning plasma cortisol level being associated with poor age related cognitive abilities in a small group of elderly, healthy male volunteers[4]. Conversely, manipulations that reduce plasma glucocorticoid concentrations or their effects on target tissues can attenuate cognitive decline with ageing in rodents[5,6].

In relation to memory, hippocampus is an important part, that is highly susceptible to elevated levels of cortisol. Elevated glucocorticoid levels have widespread effects within the central nervous system including directly inhibition of long term synaptic potentiation; cause neuronal damage and sensitize neurons to metabolic and neurochemical challenges. They have also effects on structure and function of the hippocampus, a key locus for cognitive function and memory, which also highly expresses glucocorticoid receptor[7,8] and highly susceptible to elevated cortisol levels . Hence this study was reception to determine association of fasting cortisol levels with other complications with cognitive ability in diabetes .

Study design

A cross-sectional hospital based study including 100 participants, aged 60-75 years, recruited at random from a comprehensive database of all subjects with established type 2 diabetes, living in North-West Rajasthan

Inclusion criteria

1. Patients with established type 2 diabetes mellitus .
2. Age between 60-75 yrs.
3. HbA_1C <10%.
4. Blood sugar >70 mg/dl

Exclusion criteria

1. History of head trauma.
2. Old or new cerebrovascular accident.
3. Patients taking glucocorticoids by any route within last 3 months.
4. Mentally retarded individuals.
5. HbA_1C >10%.
6. Blood sugar <70mg/dl.
7. Patient is chronic alcoholic.
8. Patient is chronic smoker.

A fasting venous blood sample was taken between 0800 h to 0830 h, for measurement of cortisol and other biochemical parameters. Plasma cortisol levels were measured by chemi-luminescent immunoassay (CLIA) with intra-assay coefficient of variation (CV) 5.1-7.0% and inter-assay CV 6.0-7.9 %. Value of Cortisol level was measured in nmol/L.

BMI (Body Mass Index): It is the index of total body fat content. It was calculated as-

BMI= Weight /height^2 (Kg/m^2)

Blood glucose level: fasting blood sugar levels were obtained for all the participants. It was estimated by glucose oxidase method.

HbA1c: it was measured by ion exchange chromatography.

Serum lipid profile was obtained by auto-analyser and included HDL, LDL, VLDL, triglycerides and total cholesterol level

A battery of psychometric tests, providing a comprehensive and validated assessment of cognitive function and mood state were used[9] . Tools of the battery were -

1.Mini-Mental State Examination (MMSE)[10] - Variables were

orientation , registration, attention and calculation, recall and language

Maximum score was 30 and a score of 25 or more was considered as normal .

2.Executive function- Verbal Fluency Test (VFT)
Semantic / Category Subtest and Phonetic / Letter Subtest

To score VFT, the total number of animals or words that the individual was able to produce were counted in 60 seconds . A score of under 17 was concerned abnormal.

3.Mental flexibility-Trail Making Test(TMT)

Trail Making Test (TMT) Parts A and B

	AVERAGE (A)	DEFICIENT (D)
Trail A	29 seconds	> 78 seconds
Trail B	75 seconds	> 273 seconds

Statistical Analysis
Data were assessed using statistical program SPSS version 15.0. Scores from the three cognitive tests were used to test the

presence of a general

cognitive ability factor, via a principal- components analysis.

Results

Demographic profile – In our study, mean age was 70.08±4.45 years, mean BMI was 30.67±6.98, mean WHR was 0.9±0.11, mean FBS was 101.06±8.18gm%, mean HbA_1C was 7.02±0.61%, mean total cholesterol was 173.77±35.24 mg%, mean triglyceride was 168.49±52.46mg%, mean HDL was 38.70±52.46, mean ABPI was 0.83±0.15 were found while male to female ratio was 5.66:1 (85 males; 15 females), **(Table 1)** .

In relation to cortisol –

In Cortisol level <23 nmol/L, total 62 patients were found and out of them 17 and 45 belonged to MMSE group <25 and 25-30 respectively while 45 and 17 patients belonged to TMT group A and D respectively while 7 and 55 patients belonged to VFT group <17 and ≥17 respectively.

In Cortisol level ≥23 nmol/L total 38 patients were found and out of them 3 and 35 patients belonged to MMSE group <25 and 25-30 respectively 19 patients belonged to each TMT group A and D respectively while 15 and 23 patients belonged to VFT group <17 and ≥17 respectively.

On statistical comparison, odds ratio of MMSE and cortisol level was 4.407 (95% CI 1.196-16.244) while Odds ratio of TMT was 2.647 (95% CI 1.136-6.168) while in VFT odds ratio was 0.195(95% CI 0.070-0.542) **(Table 2)** .

Discussion

There are numerous studies to support the premise that high cortisol levels have deleterious effects on cognitive functions but only few studies are available to support that in relation to diabetes . Present study was planned with this purpose and included full spectrum of type 2 diabetes patients.

In this study, only elderly people were included and found that higher fasting morning cortisol levels were significantly associated with cognitive dysfunctions . It was observed that poor glycemic control , increased waist hip ratio , deranged lipid profile also exert impact on cognitive functions. All the results were almost consistent with the study done by Reynolds et al[10] to determine whether fasting cortisol levels are associated with cognitive ability and estimated lifetime cognitive change in an elderly population with type 2 diabetes. They observed that in age-adjusted analyses, higher fasting cortisol levels were not associated with current g (a general cognitive ability factor) or with performance in individual cognitive domains. However, higher fasting cortisol levels were associated with greater estimated cognitive decline in g and in tests of working memory and processing speed, independent of mood, education, metabolic variables, and cardiovascular disease ($P < 0.05$). Some differences were observed which might be due to small pool of participants and small tools in battery for cognitive function tests in our study.

Our study is also comparable to study done by Lupien et al[11] in the year 1994. They described that a group of 19 healthy elderly subjects previously shown to differ in terms of their cortisol levels over a 4 year period were administered a neuropsychological test battery assessing memory, attention, and language. Correlational analyses performed on various corticosteroid measures showed that the slope of the change in cortisol levels over time predicted cognitive deficits in this elderly population. Aged subjects showing a significant increase in cortisol levels with years and with high current basal cortisol levels were impaired on tasks measuring explicit memory and selective attention when compared to aged subjects presenting with decreasing cortisol levels . As compared to this study a more number of patients was enrolled who showed more consistency with the results.

Personal history of smoking and alcohol was also found to affect cognitive functions. By these points of view, this study is also comparable with the study done by Hudetz and Warltier[12], they described that either diabetes or alcohol abuse can impair cognitive function .

Present study also supported the Edinburg Type 2 Diabetes Study [ET2DS], done to examine the relationship between fasting cortisol and both late-life cognitive ability and estimated lifetime cognitive change in a large, representative population of people with type 2 diabetes[13].

If future studies succeed to establish causative correlation between cortisol level and cognitive dysfunctions in diabetic patients that will lead to development of therapeutic manipulations to improve the cognitive functions. 11- hydroxysteroid dehyrogenase enzymes (11 HSDs) catalyze the interconversion of active steroid cortisol and inactive form cortisone. In the recent years some studies have shown that carbenoxolone, 11- HSD inhibitor improved verbal fluency and memory.

In summary, this study shows significant causal relationship between cortisol levels and cognitive dysfunctions. In the coming years we need to determine the exact relation between cortisol levels and cognitive dysfunctions, if causal then that will help in development of the therapeutic menuvers to lower the cortisol levels for ameliorating cognitive decline in human race affected with diabetes.

Table 1
Demographic Profile of study population

Parameters	Mean	SD
Age	70.08	4.45
BMI	30.67	6.98
WHR	0.91	0.11
FBS	101.06	8.18
HbA_1C	7.02	0.61
TC	173.77	35.24
TG	168.49	52.46
HDL	38.70	6.11
LDL	80.60	25.69
VLDL	37.04	11.45
ABPI	0.83	0.15

SD-standard deviation.

Table 2
Distribution of cases according to Cortisol level in relation to MMSE, TMT and VFT

Cortisol Level	Total Cases	MMSE				TMT				VFT			
		<25		25-30		A		D		<17		≥17	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
<23	62	17	85.0	45	56.3	45	70.3	17	47.2	7	31.8	55	70.5
>23	38	3	15.0	35	43.8	19	29.7	19	52.8	15	68.2	23	29.5
Total	100	20	100	80	100	64	100	36	100	22	100	78	100
Odds Ratio		4.407				2.647				0.195			
95% CI		1.196-16.244				1.136-6.168				0.070-0.542			

REFERENCE

1. Bruehl H, Wolf OT, Sweat V, Tirsi A, Richardson S, Convit A. Modifiers of cognitive function and brain structure in middle-aged and elderly individuals with type 2 diabetes.Brain Res 2009; 1280 : 186-194. 2. Gold SM, Dziobek I, Sweat V, Tirsi A, Rogers K, Bruehl H, Tsui W, Richardson S, Javier E, Convit A. Hippocampal damage and memory impairements as possible early brain complications of type 2 diabetes.Diabetologia 2007; 50 : 711-719. 3. Strachan MW, Reynolds RM, Frier BM, Mtchell RJ, Price JF. The role of metabolic derangements and glucocorticoid excess in the aetiology of cognitive impairement in type 2 diabetes Implications for future therapeutic strategies. Diabetes Obes Metab 2009; 11 : 407-417. 4. MacLullich AM, Deary IJ, Starr JM, Ferguson KJ, Wardlaw JM, Seckl JR. Plasma cortisol levels, brain volumes and cognition in healthy elderly men. Psychoneuroendocrinology 2005; 30 : 505-515. 5. Vallee M, Maccari S, Dellu F, Simon H, Le MM, Mayo W. Long-term effects of prenatal stress and postnatal handling on age related glucocorticoid secretion and cognitive performance: a longitudinal study in rat. Eur J Neurosci 1999;11 : 2906-2916. 6. Yau JL, Noble J, Hibberd C, Rowe WB, Meany MJ, Morris RG, Seckl JR. Chronic treatment with the antidepressant amitriptyline prevents impairements in watermaze learning in ageing rats. J Neurosci 2002; 22 : 1436-1442. 7. McEwen BS. Stress and hippocampus. Front Neuroendocrinol 1999; 20 : 49-57. 8. Seckl JR, Dickson KL, Ytes C, Fink G. Distribution of glucocorticoids and mineralococorticoid receptor messanger RNA expression in human postmortem hippocampus. Brain Res 1991; 561 : 332-337. 9. Seeley WW, Miller BL. Dementia. In : Harrison's Principles of Internal Medicine. Longo, Kasper, Jamson, Fauci, Hauser, Lascalzo (eds) 2012; 2 : pp 371-5. 10. Reynolds RM, Strachan MW, Labad J, Lee AJ, Frier BM, Morning cortisol levels and cognitive abilities in people with type 2 diabetes: the Edinburgh type 2 diabetes study. Diabetes Care. 2010; 33(4) : 714-20. 11. 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(5 Pt 1) : 2893-903. 12. Hudetz JA, Warltier DC. Cognitive function in older diabetic subjects with a history of alcohol abuse. Psychol Rep. 2007; 101(3 Pt 2) : 1125-32. 13. Rebacca M. Reynolds, MarkW.J.Strachan, Javier Labad, Amanda J. Lee, Brian M.Frier, F.Gerald Fowkes, Rory Mitchell, Jonathan R.Seckl, Ian J.Deary, Brian R.Walker, Jackie F.Price on behalf of the Edinburg Type 2 Diabetes Study Investigators (ET2DS)—Diabetes care 2010; 33 : 714-720.