SUBCLINICAL COGNITIVE IMPAIRMENT IN MIDDLE-AGED PATIENTS WITH TYPE II DIABETES MELLITUS

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ABSTRACT

Background. Diabetes mellitus (DM) is a major risk factor for vascular disease (including the cerebrovascular disease). One of the major consequences of cerebral microangiopathic disease is the cognitive decline. This study's objective is to assess cognitive abilities of a selected group of 23 type II diabetic patients.
Materials and methods. The trial enroled 48 patients aged between 40 and 68 years old. None of the patients had a personal history of cerebrovascular disease or a history of cognitive impairment. Cognitive status was assessed using current tests such as IQ, MMSE, the clock-drawing test, Hamilton Scale for depression and each patient was given a set of specific psychometric tests in order to accurately evaluate a specific area of cognition (memory, attention, visual and spatial orientation, executive function). The results were statistically processed by SPSS.
Results. The global cognitive score for diabetic patients was significantly lower -60,3/100 points compared to that of the control group -69.08/100 points (p = 0.048). The cognitive field most affected in these patients was the evecutive function 7.30/20 points in diabetic patients compared to that of the control group – 11.04/20 points (p = 0.008). There were no statistically signifiant differences between the two groups related to the presence of symptoms of depression or cognitive capacity level evaluated by standard tests (IQ, MMSE, clock-drawing test).
Conclusions. Patients with type II DM have a lower overall cognitive score, even at middle-age, when compared with patients without this type of metabolical impairment. The most affected domain is the executive function.

Key words: type II diabetes mellitus, cognition, executive dysfunction

INTRODUCTION

Diabetes mellitus is a major risk factor for vascular disease (including the cerebrovascular disease) mainly the type II. Diabetes, along with arterial hypertension, smoking and dyslipidemia, is a specific risk factor for cerebral microangiopathy (1,2), and its incidence varies in several studies between 5-25% (3). The main consequence of small cerebral vessels disease might be a decrease in individual cognitive capacity.

The presence of these risk factors during "middle life" is intimately correlated with increased incidence of cognitive impairment during "late life". This aspect was highlighted in numerous epidemiological studies (4,5) but these analyzed mainly the cognitive capacity in older patients (over 65 years) and by now, this is well established (6,7,8). "Brain at risk" is a term introduced in current medical literature (5) reffering to cognitive impairment that occurs in a patient who in "middle life" was diagnosed with arterial hypertension, dyslipidemia, diabetes, obesity, atherosclerotic disease..

We do not know exactly the dimension of cognitive impairment determined by a metabolic disease in "middle life". The objective of this study is to analyze the cognitive capacity of a group of middle-aged, type II diabetic patients as well as highlighting a certain field of cognition that is mostly affected in the presence of this risk factors, knowing that the evolution towards a certain type of dementia is in acordance to impairment of a certain cognitive domains (memory, attention, executive function, visual and spatial orientation).

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MATERIALS AND METHODS

We studied a group of middle-age patients (40 to 68 years old) adressed to Neurology and Endocrinology, Diabetes and Metabolical Disorders Departments from Elias Emergency Hospital between August 2009 and December 2011. None of these patients had a personal history of cerebrovascular disease or a history of cognitive impairment or any neurological symptoms possibly related to a central nervous system lesion.

Initially, we evaluated the cognitive capacity of the patients in order to exclude a possible form of cognitive impairment with clinical manifestation. We used an intelligence test (IQ) – the most common used in Romania – Raven Matrix – SPM (standard matrix for general population). This is a non-verbal IQ evaluation test based on completing a serie of pictograms with increased difficulty (ABCDEseries with 60 items). The results were afterwards correlated with the examined subject's age. The most common tests of cognitive evaluation are: MMSE (with a total score of 30 points) and the clock-drawing test (with a total score of 10 points).

A false cognitive impairment due to depression was excluded by Hamilton Depression Scale 17 questions form (chosen due the abcence of psychiatric manifestation in interview). The results (along with the clinical evaluation of the subjects) excluded a possible cognitive impairment with clinical correspondence.

This evaluation was necessary in order to make possible a further comparison of the results obtained after the set of cognitive tests were performed.

Cognitive ability was evaluated by running each patient a set of psychometric tests adressed predominantly to a certain cognitive area (memory, way of thinking, visual and spatial orientation, attention). The set consisted in 5 tests with a maximum score for each test of 20 points.

Short term memory was examined using Morse test. The subject was given 10 lines of Morse signals with increased difficulty (containing 3 to 7 signs) which he had to rewrite right away. This test evaluates the short term information storage capacity of the subject, as well as the attention and concentration capacity.

Long term memory was assessed using generic names test. The subject was given 2 series of names, correlated with generic names (trees, dogs) which he had to store and recall after 15-20 minutes. This test is usefull for the evaluation of delayed storage capacity and is less influenced by the vocabulary.

Attention and concentration were evaluated using the double barrier test. The subject was given 10 series of 32 numbers and he had to highlight separately 2 numbers that were repeating (encircle one, bar the other) and this task had to be performed rapidly. The way of thinking and cultural level of the subject did not interfere with completing this test, but other elements such as presbyopia or physical incapacity could interfere the subject's real performance.

Visual and spatial orientation was examined by rulers test. The subject had to observe a ruler with 10 white squares from which a few were marked progressively (between one to five black squares). The subject had to reconstruct afterwards the image he had seen before. This test evaluates visual and spatial orientation and the short term storage capacity and is not influenced by individual physical ability.

Executive function (thinking, reasoning, concentration) was studied using the geometrical forms test. The subject was asked to complete series of forms that were connected through symmetry, correspondence, difference, rotation. Each of the 5 series is independent.

The patients were clinically and metabolically examined (including BMI estimation- considered pathological when is over 30; abdominal circumference measurement – parameters used in – NCEP:ATPIII 2001). Laboratory evaluation included blood tests, with lipid and glycemic profile, neck and brain arteries ultrasonography with measurement of IMT-CCA, atheromatous plaques, TCD and cerebral vasoreactivity.

The obtained results were statistically processed. An analysis of the studied groups was possible using ANOVA(ANalysis Of VAriance). – simple or factorial when existing 2 or more independent variables. The statistical analysis program used was SPSS Statistics 17.0.(10)

RESULTS

48 patients were examined, 23 in the studied group and 25 in the control group. Distribution by gender was aproximately the same – female/male percentage: 56/44. Medium age of the diabetic patiens was higher – 53.52 years old compared to that of the control group – 48.88 years old.

Clinical and paraclinical features are displayed in Table 1.

TABLE 1. *Clinical and paraclinical features*

	Diabetic patients (n = 23)	Control (n = 25)	p value
Female	13 (56.5%)	14 (56%)	0.953
Average age (years old)	53.52	48,88	0.712
Smoking	11 (47.8%)	14 (56%)	0,571
Hypertension	21 (91.3%)	4 (16%)	< 0.001
Dyslipidemia	20 (87%)	14 (56%)	0.018
Obesity	21 (91.3%)	12 (48%)	0.001
Increased abdominal circumference	20 (87%)	15 (60%)	0.036
Cervical atheromatous plaques	9 (39.1)	5 (20%)	0.145
Average IMT (mm)	0,59	0.54	0.638
Impaired cerebrovascular reactivity	11 (47.8%)	13 (52%)	0.773

Associated pathology such as arterial hypertension, dyslipidemia, obesity or increased abdominal circumference in diabetic patients was significantly more frequent when compared to control group, contrary, the abnormal vascular parameters (IMT, atheromatous plaques, vascular reactivity) did not shown substantial differences between the two groups.

Cognitive capacity evaluation revealed the following:

- Average IQ in diabetic patients was 111.70 points and 120.0 points in control group subjects.
- MMSE had similar values in the two groups: 29.39 compared to 29.80
- When clock-drawing test performed, the diabetic patients obtained a score of 9.35/10 points compared to control group's score – 8.88/10 points.

Hamilton score for diabetic patients was 6.65 while for subjects from control group was 4.68. There were no statistically significant differences between cognitive tests results of the two groups (Table 2).

Considerring the homogeneity of cognitive capacity that include the two groups, a detailed analysis of cognitive capacity was performed.

Global cognitive score of diabetic patients was significantly lower, the studied group had 60.30/100 points while patients from control group had an medium score of 69.08/100 points (p = 0.048). Of the five tests that were performed, the one that evaluates the executive function – the geometric forms test, was the one that highlighted important differences between the two groups as follows – diabetic patients obtained an average score of 7.30/20 points compared to that of the control group, of 11.04/20 points (p = 0.008). Results are presented in Table 3.

DISCUSSION

Cognitive performance of diabetic patients is lower compared to that of subjects that do not suffer from this kind of metabolic impairment. Considering the results, the "brain at risk" stage (risk for dementia) is not asymptomatic, manifests subclinically as cognitive performance impairment. (5) Of the cognitive areas that were assessed, the main field which was affected appeared to be the executive function. This is consistent with the existing data in medical literature. Prospective, multicentric and multinational studies like LADIS or randomized studies such as PROSPER highlighted diabetes as an independent risk factor for cognitive impairment in elderly individuals (over 70 years old). Cognitive fields that are mainly affected are executive function, attention and short term memory (11,12). This aspect was proven in our study, as well. Considering the age of the patients that were included and evaluated throughout LADIS and PROSPER studies, memory impairment in these cases may be due to degenerative pathology as

TABLE 2. *Cognitive capacity evaluation*

	Diabetic patients (n = 23)	(95% CI)	Control (n = 25)	(95% CI)	p value
IQ (age)	111.70	102.06-121.33	120.08	113.62-126.54	0.515
MMSE	29.39	29.01-29.78	29.80	29.63-29.93	0.213
Watch test	9.35	8.87-9.83	8.88	7.75-10.01	0.615
Hamilton score	6.65	4.44-8.43	4.68	2.70-6.66	0.467

TABLE 3. *Cognitive performance evaluation*

	Patient with DZ (n = 23)	(95% CI)	Control (n = 25)	(95% CI)	p value
Double barrier test	13.39	12.13-14.65	14.04	12.57-15.51	1.00
Rulers test	13.57	11.31-15.82	14.56	12.78-16.34	1.00
Morse test	16.61	15.24-17.97	18.00	16.93-19.07	0.280
Geometric forms test	**7.30**	**5.52-9.08**	**11.04**	**9.30-12.78**	**0.008**
Generic names test	9.43	7.72-11.15	11.44	10.12-12.76	0.218
Global cognitive score	**60.30**	**54.30-66.30**	**69.08**	**64.25-73.91**	**0.048**

well, but we consider that the cognitive impairment begins at middle-age.

Compiling studied groups is difficult and if the demographic features such as sex, age are relatively easy to balance, we must say that to identify a group of individuals that have no risk factors (smoking) or an associated pathology (arterial hypertension, dyslipidemia, obesity) is much more difficult, considering the increased frequency of these elements in general population.

An ideal sample of healthy individuals is unrealistic for the same reasons. It is also difficult to identify those patients in whom the presence of type II diabetes mellitus is a singular pathology.

The limits of our study were represented by the size of the studied group of patients and the set of psychometric tests performed. The group included a relatively small number of patients. But even under these circumstances, the high statistical significance achieved, especially in investigating executive function, allows us to extract some conclusions. Validation of these conclusions needs a larger group of subjects. In our study we have chosen a set of tests used by psychologists in psychiatric clinics. Of the tests most commonly used for the European and North American populations, none has been validated for Romania's population.

Presence of risk factors for cognitive impairment determines not only an increased incidence of dementia in late-life but also an individual cognitive impairment in middle-life. An ideal assessment of cognitive performance implies the existence of a set of standard tests considering the demographic characteristics of the evaluated population.

With few exceptions (Mayo Clinic), this set of tests does not exist (13) and its existence would imply large population studies, dedicated, but that has not been performed so far.

At this moment there are only standardized tests designed to diagnose dementia but the certain transition area between normal and pathological status is yet evaluated somewhat in an empirical manner. (14) Although mild cognitive impairment concept (MCI) has been introduced and used in clinical practice for over a decade (Petersen, 1995), nowadays there is still no consensus regarding its definition. (15)

CONCLUSIONS

1. Cognitive ability of diabetic patients is decreased when compared to that of subjects with no metabolic impairment.
2. Executive function was the most affected from all cognitive fields amoung those assessed in our study.
3. The risk factors for cognitive impairment determine not only an increased risk for dementia in "late life" but a cognitive ability impairment during "middle-life", as well.

Disclosure

The authors report no disclosures.

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