Study of Cognitive Functions and Cerebral Blood Flow in Elderly

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Abstract: Background and Aim: Little information is available about cognitive functions and changes in cerebral blood flow in elderly people with or without cognitive dysfunction, despite the great influence of this problem on patient, family and society. Our study aimed at evaluating the cerebral blood flow (CBF) in elderly patient with cognitive dysfunction, either primary (Alzheimer Dementia), or secondary (vascular Dementia). **Methods:** assessment of the cognitive function and CBF of a group of 20 patients aged > 65 years old, 10 patients with vascular dementia while the other 10 patients with Alzheimer dementia and the results compared to a group of healthy volunteers. **Results:** all patients had significantly decreased Mini Mental State Examination (MMSE), Set test scores compared to that of healthy volunteers while there is significant difference regarding the Geriatric Depression Scale (GDS). Patients with vascular dementia had significantly diminished CBF compared to the healthy volunteers which doesn't go for those with Alzheimer dementia. There is significant positive relationship between MMSE scores and CBF in patients with vascular dementia (r=0.77, *p*-value=0.009). Patients with vascular dementia had significantly high percent of hypertension and diabetes than do Alzheimer group. **Conclusion:** Brain ischemia was suggested to be the main factor responsible for decline of cognitive functions. The role of cerebral ischemia in Alzheimer dementia was insignificant. Cardiovascular risk factors are more related to vascular dementia.
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1. Introduction

Mental dysfunction usually leads to impairment in the quality of life, increase dependence, social and financial burden and caregiver stress, it is most of the time more hazardous than the original co-morbidity.[1] So, early detection, intervention and prevention can help to relieve both personal and community burden of this problem.

The main objective of the present study is to evaluate cerebral blood flow (CBF) in elderly patient with cognitive dysfunction, either primary (Alzheimer Dementia), or secondary (vascular Dementia).

2. Patients and methods:

After approval of the institutional ethical committee 10 healthy volunteers (group I) and 20 patients aged ≥ 65 years old attending to Kasr Al-Aini outpatient clinic were included in our study , patients with end organ disease , anemia or endocrinal disease (other than DM) were excluded from our study. The studied group of patients were categorized into two groups, 10 patients with vascular dementia (group II), and 10 patients with Alzheimer dementia (group III). All the studied groups were subjected to Assessment of daily living activities, evaluation of psychic status using geriatric depression scale, detailed clinical examination, biological tests, and assessment of cognitive functions by MMSE, Set test. Non-contrast enhanced computed tomography (CT scan) of the brain, Duplex ultrasonography using HDI-5000 Doppler machine with high frequency transducer 7-10 MHZ of extracranial internal carotid artery and vertebral artery was performed to measure cerebral blood flow using timed average velocity and diameter of vessels studied.

Interpretation of MMSE:

A total maximal score on the MMSE is 30 points. A score of less than 24 points is suggestive of dementia. Using a cutoff of 24 points, the MMSE had a sensitivity of 87% and a specificity of 82% in a large population based sample[2]

However, the test is not sensitive for mild dementia, and scores may be influenced by education, as well as language, motor, and visual impairments[3]

Interpretation of Set test:

The Set test is referred to also as the category Fluency test, is particularly helpful in assessing patients with low formal education levels that the MMSE cannot reliably be used to test.

To administer the Set test, the older person is asked to name as many items as they can in each focus Sets are categories. The four sets are (fruits, animals, colors and towns). The test examines a number of cognitive domains including language, executive functions and memory. The test best score

is 10 in each set, for a maximum score of 40. A Set test score less than 15 is considered abnormal.[4]

Statistical analysis:

Statistical analysis was done using Minitab, version 16. Descriptive statistics were expressed as mean ± standard deviation for quantitative variables and frequency ± percent for qualitative variables. The Student's t-test and Mann- Whitney test were used to compare between the quantitative variable while the chi-square test was used to compare between the qualitative variable in the study group. *P*-value was considered significant if less than 0.05.

3. Results:

Characteristics of participants and their laboratory data are represented in table (1). The results of our study showed that there is no statistically significant difference between the three studied groups regarding the mean triglycerides (TG) levels or the percent of ischemic heart disease patients, while the vascular dementia group showed a statistically significant increase in the percent of hypertensive and diabetic patients than do other studied groups , while patients of Alzheimer dementia group have statistically significant elevated levels of total cholesterol than do patients of other groups.

By assessing the cognitive function for all studied groups, it was reported that patients of both vascular and Alzheimer dementia groups have significantly decreased mean MMSE scores than do those of the control group, the same goes for mean set test scores and mean MMSE + Set test scores, while there is no statistically significant difference between the studied groups regarding the mean GDS. Regarding the mean total cerebral blood flow it was reported that patients of Vascular dementia group have significantly decreased levels than that of the control group and this doesn't go with patients of Alzheimer dementia group.

There is a statistically significant positive relationship detected between MMSE and CBF in vascular dementia group with r = 0.77 and *p*-value = 0.009, while this relationship becomes statistically insignificant week negative relationship in Alzheimer dementia group (r = -0.09 and *p*-value = 0.8). Also a statistically significant positive relationship detected between the mean CBF levels and the scores of set test + MMSE test in vascular dementia group with r=0.83 and *p*-value=0.003.

Regarding the mean serum blood glucose levels, it showed a statistically insignificant negative relationship with the mean MMSE scores with r = -0.37 and *p*-value = 0.29 in vascular dementia group, while this relationship becomes statistically insignificant positive with r=0.31and *p*-value=0.39 in Alzheimer dementia group. It doesn't show any statistically significant relationship with the mean CBF levels in both vascular and Alzheimer dementia groups.

Comparison of laboratory findings, cognitive functions, cerebral blood flow, imaging finings of three groups

4. Discussion:

Cerebral blood flow (CBF), is the blood supply to the brain in a given time[4].In our studied group it was reported that Mean total CBF in vascular dementia group was significantly lower than that of healthy volunteers group. This finding supports the idea that dementia in those patients is explained by loss of part of brain tissue, either single large part or multiple small parts. On the other hand the mean total CBF in Alzheimer group was insignificantly different from that of the healthy volunteers group and this comes in concordance with the suggestion that the role of ischemia in the development of Alzheimer's disease is not an important etiological factor. Also we found no major vessel disease in Alzheimer group with controversy to vascular dementia which shows diminution of CBF and major vessels affection in most of patients. This doesn't go with what was concluded with other studies[5-6]

In our study having a considerable percent of patients with hypertension, diabetes mellitus and ischemic heart disease in patients with vascular ischemia suggests that cardiovascular risk factors played an important role in development of vascular dementia where it is known that patients with small vessel and large artery disease (SLAD) had poorer cognitive and functional outcomes when compared to patients without SLAD[7]. While having significantly higher values of serum cholesterol in patients with Alzheimer dementia suggest that the high cholesterol level was the only cardiovascular risk factor in Alzheimer dementia group, which doesn't go with other studies[8]. Other studies had studied the relationship between vascular comorbidity and Alzheimer dementia, where many individuals with Alzheimer dementia, especially those beyond 85 years of age, show significant vascular comorbidity, to the extent that they are more accurately characterized as having mixed vascular- Alzheimer dementia.[9] In one large autopsy series, 'pure' vascular dementia was seen in 9.4% of 900 individuals with dementia, but in only 2.9% of patients with the clinical diagnosis of probable or possible Alzheimer dementia. [11] Vascular disease has also been reported to accelerate atrophy and result in white matter abnormalities, asymptomatic infarct, inflammation and reduced glucose metabolism, cerebral blood flow and vascular density.[12] While other studies reported

that determining the neurobehavioral and neuroimaging correlates of ischemic brain lesions occurring in the context of significant Alzheimer dementia alterations can be a very difficult task, and the usefulness of the traditional strict differentiation between Alzheimer dementia and vascular dementia has been challenged.[14] Even though a mixed etiology is likely to be more common than either pure Alzheimer dementia or vascular dementia among older patients, there are no current clinical criteria for ante-mortem diagnosis of mixed dementia.[11] Pathological changes have been associated with not only dementia of the vascular type but also Alzheimer disease.[15-16], In conclusion: Tissue infarction was suggested to be the main factor responsible for decline of cognitive functions in vascular group. The role of cerebral ischemia in Alzheimer dementia group was mostly insignificant. Cardiovascular risk factors were more related in vascular dementia group than Alzheimer dementia and this support the idea that correction of cerebrovascular risk factors is essential to prevent secondary dementia in these groups of patients. Further large scale study is recommended to combine both duplex ultrasound to measure CBF in major cerebral vessels and SPECT to evaluate micro vascular disease and neuron metabolism, as this will be more informative about effective CBF. Data obtained can be analyzed in comparison to MRI angiography that is considered an accurate tool for CBF measurement.

Table (1): laboratory findings, cognitive functions, cerebral blood flow, imaging findings of three groups:

	Group I	Group II	Group III
Age Mean±SD Min/Max	67.8±3.85 65-77	71.2±6.58 65-85	71.4±5.02 65-79
Sex Male/Female	8/2	4/6	4/6
HTN	0 (0%)	7 (70%)	2 (20%)
DM	0 (0%)	6 (60%)	1 (10%)
IHD	0 (0%)	4 (40%)	1 (10%)
HB (gm %)	13.54 ± 1.51	12.77 ± 1.90	12.23 ± 1.6
GLU(mg/dl)	89.4 ± 13.18	147.5 ± 74.96	95.4 ± 20.24
AST (IU/dl)	24.9 ± 7.49	29.7 ± 17.15	29.2 ± 14.85
ALT(IU/dl)	31.8 ± 20.25	19.16 ± 11.08	24.9 ± 14.91
BIL-T(mg/dl)	0.709 ± 0.29	0.56 ± 0.38	0.592 ± 0.33
GGT(U/L)	63.4 ± 24.80	32.9 ± 33.27	26 ± 10.27
TP(g/dl)	7.35 ± 0.68	7.09 ± 1.33	6.63 ± 0.50
ALB(g/dl)	4.05 ± 0.26	3.34 ± 0.77	3.49 ± 0.41
ALP(U/L)	81.5 ± 19.52	75.1 ± 15.01	86.1 ± 31.34
UREA(mg/dl)	35.3 ± 6.67	46.9 ± 18.28	51.4 ± 30.39
CRE(mg/dl)	1.04 ± 0.23	1.038 ± 0.32	1.005 ± 0.22
Total CHOL(mg/dl)	179.6 ± 33.07	168.7 ± 58.03	235.8 ± 72.74
TG(mg/dl)	145.7 ± 39.92	95.4 ± 36.62	96 ± 26.35
LDH	249.4 ± 48.10	290 ± 142.63	342.3 ± 162.6
CA(mg/dl)	8.81 ± 0.4.	8.22 ± 0.85	8.9 ± 0.75
PHOS(mg/dl)	3.78 ± 0.53	3.76 ± 0.55	3.54 ± 0.55
Na(meq/L)	139.1 ± 3.84	136.7 ± 4.42	141.7 ± 4.14
K(meq/L)	4.28 ± 0.49	4.25 ± 0.57	4.29 ± 0.62
Assessment of cognitive functions			
MMSE	26.6 ± 3.66	9.6 ± 4.55	10.1 ± 2.47
Geriatric Depression Scale	11.9 ± 10.42	11.6 ± 9.77	9.5 ± 5.91
Set test	39.4 ± 0.97	9.2 ± 6.18	12.2 ± 1.99
MMSE+ Set test	66 ± 4.52	18.8 ± 9.78	22.3 ± 3.62
Assessment of cerebral blood flow			
RT ICA(ml/min)	255.05 ± 39.36	263.06 ± 117.79	---
LT ICA(ml/min)	199.48 ± 46.10	176.196 ± 145.03	---
Total internal carotid flow(ml/min)	454.53 ± 79.08	439.26 ± 123.48	---
LT VA(ml/min)	83.81 ± 33.22	69.766 ± 50.04	---
RT VA(ml/min)	88.59 ± 34.95	52.606 ± 24.29	---
Total vertebral flow(ml/min)	172.40 ± 63.17	122.37 ± 64.97	---
Total CBF(ml/min)	628.83± 87.3	520.88 ± 132.22	579.17 ± 72.84
CT brain findings:			
CT Brain showing Infarction	0	10 (100%)	0
CT Brain with involutional Changes	0	0	6 (60%)
Normal CT	10(100%)	0	4(40)

Table (2): Comparison of the clinical and investigational techniques in studied groups:

	Group I	Group II	Group III	p-value	
				Group I vs. II	Group I vs. III
HTN	0 (0%)	7 (70%)	2 (20%)	0.003	0.474
DM	0 (0%)	6 (60%)	1 (10%)	0.011	1
IHD	0 (0%)	4 (40%)	1 (10%)	0.087	1
Total CHOL(mg/dl)	179.6 ± 33.07	168.7 ± 58.03	235.8 ± 72.74	0.336	0.008
TG(mg/dl)	145.7 ± 39.92	95.4 ± 36.62	96 ± 26.35	0.78	0.89
Assessment of cognitive functions					
MMSE	26.6 ± 3.66	9.6 ± 4.55	10.1 ± 2.47	0.000	0.000
Geriatric Depression Scale	11.9 ± 10.42	11.6 ± 9.77	9.5 ± 5.91	0.94	0.53
Set test	39.4 ± 0.97	9.2 ± 6.18	12.2 ± 1.99	0.000	0.000
MMSE+ Set test	66 ± 4.52	18.8 ± 9.78	22.3 ± 3.62	0.000	0.000
Assessment of cerebral blood flow					
Total CBF(ml/min)	628.83± 87.3	520.88 ± 132.22	579.17 ± 72.84	0.047	0.185

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