Myeloperoxidase activity, lipid profile and thyroid function in patients who suffer from Alzheimer´s disease

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ABSTRACT

Alzheimer´s disease increases its global incidence and prevalence, the WHO includes the disease among the main problems in public health today. Cuba is not apart from this reality. Biochemical markers pretends to enhance its early diagnosis. Objective: to determine myeloperoxidase activity (MPO), lipid profile and thyroid function, in patients who suffer from Alzheimer´s disease. Methods: it was a case and control analytic observational study, in patients from the Santa Clara polyclinic. The MPO activity, total cholesterol, LDL-c, HDL-c, total triglycerides, VLDL, total T_3 and T_4, and TSH were determined in serum of both groups. Results: no association was found between MPO activity and the presence of the disease (p = 0.348). There was an almost absolute predominance of low levels of HDL-c, more evident in cases (0.43mmol/L), the levels of T_3 tended to be close to the lower limit of the physiological range (1.46nmol/L), a relevant finding was a general presence of subclinical hypothyroidism (23.75 %), with no significant differences between groups. Conclusions: The Alzheimer´s disease keeps showing its increasing with age and it is more common in females. High levels of LDL-c and low of HDL-c are frequent in the elderly. Higher levels of HDL-c and T_3, this last one into the physiological range, act as protectors against the disease. The subclinical hypothyroidism is present and remains hidden in many of the elder with Alzheimer or not. In a high number of patients, coexist Alzheimer´s disease and some diseases from the metabolic syndrome, as dyslipidemias.

Key words: Alzheimer´s disease, myeloperoxidase activity, oxidative stress, lipid profile, dyslipidemias, thyroid function.

METHODS

Universe and study group definition:

The study universe was composed by all the individuals (44 patients), who suffered from Alzheimer´s disease (AD) in the population of the Santa Clara Policlinic.

The case group was compose by all AD diagnosed individuals as the only inclusion criteria. It was not stated any exclusion criteria. Only four patients were not included due their deteriorated health status.

The control group was composed by 40 individuals with the following inclusion criteria: Not to be diagnosing of any dementia, being supposedly healthy, and be a 60-year's minimum limited aged.

Method: an analytical and observational case-control study during 2017.

Information sources.

- Individual clinical history of all persons including in the study.

- Individual interview to parents or tutors from Alzheimer´s patients.

- Individual interview to control group members.

- Results from the lab exams.

Variable: study groups, age, sex, color of the skin and biochemical parameters.

Biological sample

It was take ten ml of venous blood in starvation from cases and controls, with previous consent from the individuals of control group and parents or tutors of the Alzheimer´s patients.

Technics and biological samples processing

Myeloperoxidase (MPO) activity was determined by the Krawisz JE method.

Total cholesterol (TC), total triglycerides (TG)and HDL-c, were all determined in serum and processed in a Hitachi 902 chemical autoanalyzer for each lab exam analytical phase. For this, were used HELFA diagnosis reactive kits made at "Carlos J. Finlay" Biological Production Factory. VLDL and LDL-c levels were measured mathematically; VLDL levels through the own chemical autoanalyzer and LDL-c using the Friedewald formula.

TSH, T_3 and T_4 were determined by radio immune analysis and their respective results were evaluated by the radio immune analysis laboratory from Celestino Hernández Robau´s Hospital in

Santa Clara city, using reactive kits from CENTIS factory taking into account a previous adjust for these parameters.

Statistical analysis

The laboratory personal was prepared enough, and all the used laboratory equipment was correctly calibrate.

Statistical test

- T Student parametrical test to compare a continuous variable distribution between study groups, with quantitative results and normal distribution.
- Chi square for qualitative variable.
- U Mann Whitney no parametrical test for not normal distribution.
- Fisher test for little sample.
- Logistical regression analysis for the more significant data.

The confidence interval were estimate in 95 % level to determine if results in cases were into the normal range.

Significant ranges:

Significant differences if $p < 0.05$

Very significant differences, if $p < 0.01$

Highly significant differences, if $p < 0.001$

RESULTS

In relation to MPO activity, a slightly high medium value was found in cases, with no significant differences, compared to the control group ($p = 0.348$).

Serum TC levels were all into the physiological range in both groups, with no significant differences, but near to the signification limit (0.086). It was a slightly high medium value in control group (5.36), in relation to cases (4.84).

The LDL-c levels were homogeneous in both groups, so there were not significant differences (0.119). In control, the medium value was higher (4.22) (up to the physiological limit), compared to cases (3.76). The confidence interval upper limit surpassed the physiological range in case and controls.

Serum levels of HDL-c in both groups were under the physiological limit, with a medium value higher in controls (0.69), than in cases (0.43). It lead to highly significant differences (0.000).

TG results didn´t show significant differences between cases and controls (p = 0.37), although the medium value was higher in controls (1.51), than in cases (1.30). The confidence interval upper limit in controls (1.81) was superior to the upper limit of the physiological range (1.6 mmol/L).

The VLDL results didn´t included any pathological value in case nor in control, but there were very significant differences between both groups (0.002), with a superior medium value in cases (0.59) even near to the pathological limit, compared to the control group (0.43).

In relation to the thyroid function, the T_3 values showed highly significant differences between both groups (0.000). Although the medium value in cases was into the physiological range, it was much close to the lower limit (1.46nmol/L).

The T_4 values were normal in both groups, but much close to the signification range (0.055).

TSH serum levels, didn´t showed significant differences between cases and controls (0.117), although the medium value in cases was the same than the upper limit of the physiological range (3.5), and the confidence interval limits in both groups surpassed the upper limit of the physiological range.

We found the presence of individuals with subclinical hypothyroidism (SCH) in both groups. In specific 11 cases and 8 controls; such a difference was not statistically significant (p = 0.602).

The multivariable analysis, included only the variable which contributed, in a significant way, to stated the statistically differences between groups: T_3, HDL-c and T_4; the first two with odds ratio (Exp of B) lower than one, so considered as protector factors.

Lipid profile

Parameter	Normal values	Groups	Media	SD	95 % CI	p
TC	3.87 – 6.71 mmol/L	Cases	4,84	1,12	4,48 – 5,20	*0,086
		Controls	5,36	1,54	4,87 – 5,86	
LDL-c	< 3.84 mmol/L	Cases	3,76	1,18	3,38 – 4,14	*0,119
		Controls	4,22	1,41	3,77 – 4,67	
HDL-c	> 1.1 mmol/L	Cases	0,43	0,30	0,33 – 0,52	**0,000
		Controls	0,69	0,41	0,56 – 0,82	

Source: Lab exams.
*Signification associated to T Student test.
**Signification associated to U Mann Whitney no parametrical test.

Thyroid function

Parameter	Normal values	Groups	Media	SD	95 % CI	p
T3	1 – 4 nmol/L	Cases	1,46	0,54	1,29 – 1,63	**0,000
		Controls	2,19	1,24	1,81 – 2,71	
T4	55 – 167 nmol/L	Cases	111,38	25,88	103,1 – 119,65	*0,055
		Controls	96,1	42,06	81,32 – 111,83	
TSH	0,3 – 3,5 mUI/L	Cases	3,5	4,35	2,1 – 4,89	**0,117
		Controls	2,98	6,32	0,7 – 5,33	

Source: Lab exams.
*Signification associated to T Student test.
**Signification associated to U Mann Whitney no parametrical test.

DISCUSSION

The MPO activity level is consider as a quantitative and sensitive marker of the neutrophils infiltration in the inflammatory process and oxidative stress. The oxidative stress is in relation to neuroinflammation in patients with AD, because redox status modulates inflammatory factors, which are, at the same time, oxidative stress and inflammation critical mediators, causing neurodegeneration.[1]

The homogeneous results from MPO activity in both groups, denies it´s association to the AD. It was not an objective in our study, to relate the MPO activity level to the presence and degree of the oxidative stress in the studied individuals.

In relation to TC, prevails the criteria about high levels associated to an increasing risk to suffer AD or cognitive impairment, however, our findings are agree to the report of advanced AD patients with lower lipid level than controls.[2]

Regalado et al.[3] said the hypercholesterolemia, in the middle age, is a risk factor for AD in the last decades of life. Moreover, the disease itself, as well as an aged associated process of progressive reduction of lipid levels, still not explained at all, could cause the low TC levels observed in patients who suffers from the disease or detected few years before it´s onset.

Mielke et al.[4] reported high TC levels in the elder associated to a lower risk of dementia. That´s why they referred those high values of TC could protect against dementia for contributing to the structural integrity and fluidity modulation of the cellular membrane, and it´s participation in the basic synaptic integrity and neurotransmission. They added that high TC values in the late life could be an indicative of a better health status, so those who reach an advanced age with high TC

levels would be stronger individuals and could be relatively invulnerable to the negative side effects of hypercholesterolemia, including dementia.

The low HDL-c levels in both groups seems to be in relation to its decreasing in the late aged. There is an evidence, in the elder, between low HDL-c levels, poor memory and AD. In the other hand, higher HDL-c levels has been associated to longevity, enhance cognition and a longer surviving free of dementia.[5]

Our TG and VLDL results, denies its association to AD. Although VLDL values didn´t surpassed its physiological range, delivered very significant differences between both groups.

It is recognized high TG levels, along lowHDL-c levels, as risk factors for atherosclerosis, which partially explains the vascular changes in brains from patients with AD. It has been suggested a possible relation between high TG levels and a worst cognitive function in diabetic, but keeps still unknown why hypertriglyceridemia could leads to the increasing of the risk of dementia.[6]

Our T_3 results, although these are into the physiological range, were significantly lower in patients with AD, than in controls. Quinlan et al.[7] found a reverse association between total T_3 values under the lower limit of the physiological range and cognitive function, in patients with mild cognitive impairment.

T_3 regulates the expression of LDL receptors, and at the same time, has been associated to a protector effect against LDL oxidation. Hippocampus is very sensitive to T_3, so a relative increasing could aggravate the affection in the episodic memory.[7]

Our T_4 results were not associated to AD. The Honolulu-Asia Aging study[8] found higher levels of total and free T_4 in association to dementia, AD and neuropathology.

About TSH levels, although its tendencies to an increasing values in cases and controls, the homogeneous behavior in both groups denies its association to AD. De Jong et al.[8] suggested that an increased thyroid function, even into the physiological range, could be involved in dementia and AD neuropathology. They remarked as well, that the insidious onset and the slow natural progression of AD could indicates, that the high thyroid function could be more a marker of the subclinical disease, than a triggering factor in the AD development.

In relation to our SCH finding, there was a superior amount (even higher in AD patients), compared to other studies. It has been reported a positive relation between TSH and LDL-c, and a negative one between TSH and HDL-c.[9]

The TC values in our study were not excessive in case nor in controls. It´s increasing in LDL-c fraction seems to be in relation to its low level in the HDL-c fraction. The increasing in LDL-c levels, along its decreasing in HDL-c, could increase the oxidative stress and its negative influence in the brain tissue.

The tendency of higher or near the physiological limit values of TSH in both group, were in relation to high LDL-c levels and, in a reverse way, to low values of HDL-c. Kexi Zha et al.[10] found an increasing of LDL-c levels and lipid peroxidation, more accentuated in patients with significant SCH, compared to individuals with normal thyroid function.

The multivariable analysis in our study confirmed the protector behavior of closer T_3 values to the medium point of the physiological range, and the closer HDL-c values to the physiological limit. Support this resultin relation to T_3, the AD association to a low or close to the lower limit of the physiological range as low thyroid function indicative, even more in relation to SCH. About HDL-c, taking into account its positive effect over memory, cognition and in fact, as a protector against dementia when its serum levels are adequate.

CONCLUSIONS

The determined biochemical parameters could be acting, combined or not, in the AD development of the studied individuals. However, knowing the AD multifactorial genesis, some other genetic or acquired factors (not including in our study design), could be acting too in a higher or a lower degree, in relation to the presence of the AD.

In summary, in our study, the MPO activity didn´t impressed to be associated to suffering from AD. The SCH is present in the elderly with AD or not and tends generally to pass undercover. In an important number of patients with AD, coexist SCH and dyslipidemia. In relation to the last one, the more common in the elder is the presence of high levels of LDL-c and low levels of HDL-c. Closer values of T3 to the medium point of the physiological range, as well as higher HDL-c levels, acts as protectors against the disease.

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