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Full length research paper

Comparison of Cognitive Functions between patients with thyroid dysfunction with and without astheno-emotional syndrome

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In elderly, clinical status of hyperthyroidism is very similar to hypothyroidism. Only 25% of patients above 65 years present typical symptoms of hyperthyroidism. As age increases, the typical hyperthyroidism symptoms become less frequent. The objective of this study was to compare the symptomatology and cognitive performance of older adults with thyroid dysfunction with and without astheno-emotional syndrome. Methods: 57 patients were divided into 2 groups, 31 patients with diagnostic of thyroid dysfunction presenting astheno-emotional syndrome (AES), aged 60-87 years; and 26 patients with thyroid dysfunction without AES symptoms. Results: The AES group were more depressed (GDS p = 0.039) when compared to group without AES. There are significant cognitive changes between the two groups. Considers: It is suggested a longitudinal follow-up of these cases in order to uncover the reason for this difference.

Keywords: astheno-emotional syndrome; cognitive functions; thyroid dysfunction

Introduction

Astheno-emotional syndrome (AES) is one of six basic syndromes of organic psychiatry classification of the Lindqvist and Malmgren (1993) system. This system is based on a psycho physiological theory and assumes that the brain reacts through limited answers to different insults. The AES is the most common among them and can be graded as mild, moderate and severe. The mild and moderate forms are characterized by decreased ability to concentrate, poor memory, increased mental fatigability, irritability, emotional labiality, insomnia and nervousness. The difference between the mild and moderate forms depends on the degree of the symptoms (Rödholm, 2001). In severe forms the mentioned symptoms become more pronounced and others arise, such as slowness of thought, loss of summary and reduction capacity and abstraction capacity (Lindqvist and Malmgren 1990, 1993).

The psicorganics syndromes are mental changes associated with somatic diseases. According to Damasceno (2002) the somatic causes can be divided into two big groups, one of intracranial location (trauma, CVA, degenerative diseases and hydrocephalus) and other extra-cranial (systemic infections, cardio-respiratory failure, and endocrine diseases toxic-metabolic). Thyroid dysfunction in elderly is often developed insidiously and is dominated by clinical findings and nonspecific symptoms, many times related to normal aging or age-related diseases. Hypothyroidism is strongly associated with memory impairment, psychomotor slowing, decreased attention, fatigability, decreased visuospatial organization and depression. The clinical manifestations of hyperthyroidism during aging are very similar to hypothyroidism, especially in apathetic form, and are discreet and can be obscured by coexistent diseases. Neuropsychological symptoms observed in thyroid dysfunction are directly related to increasing age, so that

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should be searched in the presence of dementia, depression and astenoemocional (AES) syndrome in elderly patients.During the evaluation procedures to identify a AES case, the professional is facing a symptomatologic set that can be produced by various diseases and/or manifestations. In this sense one can attribute that AES is the prodromal phase of illness that have not yet expressed their clinical status. As a result of such investigations, prodromal AES can be found in cerebrovascular accidents, normal pressure hydrocephalus, Alzheimer's disease, traumatic brain injuries, hypothyroidism and hyperthyroidism.Since this is not specific to elderly and / or related to age, can be found in younger patients, as well as with other diseases such as multiple sclerosis, lupus erythematosus and subarachnoid hemorrhage after ruptured aneurysm. Despite these studies, the relationship between endocrine diseases, especially thyroid dysfunction (hypothyroidism and hyperthyroidism), and AES is little explored in the literature as a result of numerous factors, such as lack of assessment tools, diagnostic difficulties cohesion, among others. Thyroid dysfunction may be an increase in hormone production, which characterizes hyperthyroidism, or a decrease, which causes hypothyroidism. Although less frequent, clinically hyperthyroidism is usually richer in symptoms such as palpitations, sweating, insomnia and weight loss. However, in older people, can be expressed only as apathy, often being mistakenly diagnosed as depression or just a harbinger of Alzheimer's disease. Thus, as a result of lack of studies that explain the manifestations of AES, this study sought to publicize findings in Brazilian population. In this way, this study aimed to analyze the neuropsychological deficits in elderly patients with thyroid dysfunction manifesting as AES and compare them with a control group with thyroid dysfunction without AES.

Methods

Participants

57 patients attended to this study, 31 with thyroid dysfunction and AES, aged 60-87 years (78.61 ± 6.70) with 19 women and 12 men (21 with hyperthyroidism and 10 with hyperthyroidism) all outpatients from the Geriatrics Clinic from Jundiai Medical School (JMS). The patients with hypothyroidism had TSH levels ranging from 0.01 IU / ml to 0.23 IU / ml (0.06 ± 0.07) whereas FT4 levels ranged from 0.58 to 2.06 ng / dl (1.43 ± 0.42). Those with hyperthyroidism had serum levels of TSH between 9.1 to 269.25 IU / ml while the T4L undetectable to 3.7 ng / dl. The tests were confirmed at least 3 times, with a 3 month sample interval. The second group called "control" comprised of 10 hyperthyroidism and 16 hypothyroidism patients without AES symptoms matched for age, sex, schooling, medical conditions and medications. The control group was diagnosed in the same period all other patients. All study participants were asked and consented to participate in the study by signing the informed consent term. Hence, the group selection was made by convenience. The selection criteria was having any kind of thyroid dysfunction; then, AES symptoms were assessed by clinical interview. The research was approved by the Jundiai Medical School hospital ethics committee.

Procedures

All patients undergone: a) detailed medical history, general physical examination and neurological tests b) neuropsychological assessment using the Mim-Mental State Examination (Folstein *et. Al.,* 1975), the battery from the CAMDEX (Roth, 1982), the Clock Drawing Test (CDT) under the scale of Clock Drawing Interpretation scale (*Mendez et al.,* 1982; Shulman, 1986) and the Geriatric Depression Scale (GDS abbreviated Yessavage, 1993); c) laboratory TSH which was measured with a chemiluminescent method using a commercial kit (Immulite, Diagnostic Products Co.) with a sensitivity of 0.05 mU / l and FT4 was determined through a method of a fluorimetric enzyme (Stratus System II, Baxter Diagnostics Inc. Deerfiel, IL) with a sensitivity of 0.2 ng / dl. To graduate the symptoms of thyroid dysfunction we used the Psychopathological Comprehensive Rating Scale (CPRS) scale of Asberg *et. al.* (1978). In CPRS each symptom was prepared in a categorical scale, with discretion of levels 0, 1, 2 and 3. CPRS items were selected according to AES symptoms. For patients using lithium, antidepressants, fentoína, amiodarone, high doses of salicylates and steroids or any medication that could interfere with thyroid function were excluded.

Results

Based on this study objectives the results can be seen in Table 1 in which we grouped clinical symptoms of patients with thyroid dysfunction with AES, compared with the control group. All symptoms were significantly higher in AES patients with thyroid dysfunction. Only the symptom insomnia showed no statistical difference between the two groups. Table 2 showed the values of global MEEM, CAMCOG and its subtests, the EDG and the depression scale of CAMDEX, TDR (second Mendez and Shulman) as well as the CAMCOG subtests in the two groups.

According to the results we ascertain that patients with thyroid dysfunction and AES have underperformed in the scores of MMSE, CAMCOG and TDR (Mendez and

Table 1. Comparison of clinical symptoms between groups with and without AES

Thyreoid dysfunction without AES							Thyreoid dysfunction with AES							
VARIÁble	**N**	**Mean**	**S.D.**	**MÍN**	**MEDIAN**	**MÁX**	**VARIÁble**	**N**	**Mean**	**S.D.**	**MÍN**	**MEDIAN**	**MÁX**	**P***
Fatigability..	26	0.12	0.33	0.00	0.00	1.00	Fatigability..	31	2.10	0.79	1.00	2.00	3.00	P<0.001
DifConcentr	26	0.04	0.20	0.00	0.00	1.00	DifConcentr	31	1.06	0.51	0.00	1.00	2.00	P<0.001
DeficitMemo	26	0.19	0.40	0.00	0.00	1.00	DeficitMemo	31	1.19	0.65	0.00	1.00	2.00	P<0.001
Insomnia	26	1.00	0.89	0.00	1.00	2.00	Insomnia	31	1.39	0.95	0.00	2.00	3.00	P=0.140
Irritability..	26	0.23	0.59	0.00	0.00	2.00	Irritability..	31	0.74	0.58	0.00	1.00	2.00	P<0.001
LentPensam	26	0.08	0.27	0.00	0.00	1.00	LentPensam	31	1.32	0.60	0.00	1.00	2.00	P<0.001
InstabEmot	26	0.04	0.20	0.00	0.00	1.00	InstabEmot	31	0.42	0.50	0.00	0.00	1.00	P=0.001

*p value refers to Mann-Whitney test to compare variables between groups (without AES vs with AES)

Table 2. Comparison of clinical findings and cognitive test scores between patients with and without AES

Thyreoid dysfunction without AES							**Thyreoid dysfunction with AES**							
VARIÁble	**N**	**Mean**	**S.D.**	**MÍN**	**MEDIAN**	**MÁX**	**VARIÁble**	**N**	**Mean**	**S.D.**	**MÍN**	**MEDIAN**	**MÁX**	**-P***
TSH	26	24.43	32.62	0.01	11.50	122.00	TSH	31	55.46	67.32	0.01	35.35	269.25	P=0.189
T4L	26	1.02	0.81	0.22	0.93	3.60	T4L	31	1.01	0.78	0.00	0.80	3.70	P=0.761
AGE .	26	77.12	6.50	65.00	76.00	93.00	AGE	31	78.61	6.70	60.00	82.00	87.00	P=0.087
MEEM	26	27.85	1.64	24.00	28.00	30.00	MEEM	31	23.68	4.56	11.00	25.00	29.00	P<0.001
CAMCOG	26	94.15	5.63	81.00	94.50	103.00	CAMCOG	31	77.71	16.28	44.00	80.00	101.00	P<0.001
Language	26	26.42	1.14	24.00	27.00	28.00	Language	31	23.94	3.23	18.00	25.00	28.00	P=0.004
Resp Motor.	26	3.88	0.33	3.00	4.00	4.00	Resp Motor	31	3.32	0.87	1.00	4.00	4.00	P<0.001
Resp Verbal	26	3.00	0.00	3.00	3.00	3.00	Resp Verbal	31	2.94	0.25	2.00	3.00	3.00	P=0.191
Lecture	26	2.00	0.00	2.00	2.00	2.00	Lecture	31	1.90	0.30	1.00	2.00	2.00	P=0.106
Definitions	26	5.54	0.76	4.00	6.00	6.00	Definitions	31	5.13	1.06	3.00	5.00	6.00	P=0.113
Noun Figures	26	5.69	0.55	4.00	6.00	6.00	Noun Figures	31	5.45	0.99	2.00	6.00	6.00	P=0.530
Fluenc Verbal	26	3.31	0.47	3.00	3.00	4.00	Fluenc Verbal	31	2.65	0.80	1.00	3.00	4.00	P<0.001
RepetAdress..	26	3.08	0.39	3.00	3.00	5.00	Repet Address.	31	2.55	1.03	0.00	3.00	5.00	P=0.013
Memory.	26	23.77	2.01	19.00	24.00	27.00	Memory.	31	19.23	5.28	7.00	20.00	26.00	P<0.001
Remote	26	4.77	1.42	1.00	5.00	6.00	Remote	31	3.58	1.78	0.00	4.00	6.00	P=0.006
Recent.	26	3.50	0.65	2.00	4.00	4.00	Recent.	31	2.68	1.19	0.00	3.00	4.00	P=0.005
Evocation	26	5.23	0.76	4.00	5.00	6.00	Evocation	31	4.55	1.29	1.00	5.00	6.00	P=0.038
Recognizing...	26	5.50	0.51	5.00	5.50	6.00	Recognizing	31	5.13	1.02	2.00	5.00	6.00	P=0.252
Fixation	26	4.77	0.65	2.00	5.00	5.00	Fixation	31	3.29	1.60	0.00	3.00	5.00	P<0.001
Atention	26	6.54	0.86	4.00	7.00	7.00	Attention	31	4.03	2.40	0.00	4.00	7.00	P<0.001
Praxis	26	11.15	1.08	9.00	12.00	12.00	Praxis	31	9.42	2.20	4.00	10.00	12.00	P<0.001
Abstract	26	6.62	1.94	0.00	7.00	8.00	Abstract	31	4.23	2.85	0.00	4.00	8.00	P=0.001
OrTemporal	26	4.81	0.49	3.00	5.00	5.00	Or Temporal	31	4.10	1.27	0.00	5.00	5.00	P=0.007
OrSpacial .	26	5.00	0.00	5.00	5.00	5.00	Or Special	31	4.74	0.68	2.00	5.00	5.00	P=0.034
Perception	26	7.77	1.75	4.00	7.50	11.00	Perception	31	6.39	1.80	2.00	7.00	10.00	P=0.010
Mendez	26	18.77	2.20	9.00	19.00	20.00	Mendez	31	14.52	6.54	1.00	18.00	20.00	P=0.006
Shulman	26	4.54	0.71	2.00	5.00	5.00	Shulman	31	3.45	1.55	0.00	4.00	5.00	P=0.007
GDS	26	3.58	2.69	0.00	3.50	11.00	GDS	31	5.68	2.59	1.00	6.00	13.00	P=0.004
CAMDEX_DEPR	26	4.50	2.52	0.00	5.00	10.00	CAMDEX_DEPR	31	7.32	3.61	3.00	7.00	25.00	P<0.001

Shulman) while in the EDG scores and the CAMDEX depression scale a superior performance were observed. Considering the low number of patients with hyper and hypothyroidism, no comparisons of the measures within and between the groups could be made but new investigations with larger samples should compare and control this effects, once this can affect the relations between thyroid dysfunction and AES. This limits the data interpretation in this research and invites for further investigations.

Discussion

Regarding the previously described results, the AES diagnosis is not tied to a specific etiology or a causal factor which would initiate the pathogenic process eventually triggering the symptoms, where a set symptomatology was similar to several diseases, varying only the intensity of these symptoms (Malmgren and Lindqvist, 1993). Among the cases of thyroid dysfunction, patients with hyperthyroidism presented very similar AES symptoms to those with hypothyroidism with a strong presence of fatigue. According to Lishman (1998) the most common psychological symptoms found in patients with hypothyroidism are the slowness of cognitive function, general blunting of personality, mental lethargy, fatigue and memory impairment, latter becoming a very important symptom. Memory is often affected since the early stages of the disease with difficulty to record events and happenings of the day-to-day. Evolutionarily, there is a marked inability to sustain mental exercise and increased slowness of understanding and control. The profound loss of interest and initiative leads to a delay in the search for medical care. The change of mood is typical for apathy rather than depression, but this differentiation is difficult to establish. Irritability is a common characteristic and some patients become agitated and aggressive.

Hypothyroidism is invariably listed as a cause of potentially reversible dementia in elderly, but the frequency, severity and characteristics of mental changes induced hypothyroidism of varying severity levels are unknown. The myxedema can cause neurological and psychiatric diseases, including myopathy, ataxia, psychosis and dementia. Asher described confusion, disorientation and psychosis as mixedematosa madness. The neurobehavioral and psychological changes associated to hyperthyroidism are varied, multiple and the most frequent symptoms are anxiety, dysphasia, insomnia, and emotional liability. With the start of thyrotoxicosis may occur delirium, agitation and impatience of sudden onset that is not present in elderly patients (Lishman). In contrast to these findings is the mental state of patients with apathetic thyrotoxicosis, an unusual form of thyrotoxicosis that imitates depressive illness. About 20 to 40% of elderly patients with hyperthyroidism are marked by apathy, depressed mood, inactivity, lethargy, disinterest and pseudo dementia. As shown, the symptomatology set of AES may be present in both, hypothyroidism and hyperthyroidism, that confirms our results. Many patients with AES are brought into the clinic labeled by their families or care takers, as suffering from depression. Perhaps this "diagnostic" is a reflection of the clinical symptoms of the syndrome, especially the fatigability that can be expressed as disinterest, exhaustion and fatigue. Manifest their condition demonstrating indifference regarding the tasks at your fingertips, difficulty initiating activities and also take them on. This symptom usually accompanied by other manifestations such as altered sleep patterns, irritability and decreased capacity of attention and concentration are interpreted by the family as expressions of depression. The results of the present research showed a higher prevalence of depressive symptoms measured by the GDS and the CAMDEX depression scale for patients with thyroid dysfunction and AES is due to the characteristics of the syndrome that can influence the result of the tests (GDS average 5.68 ± 2 , 59 and the depression scale CAMDEX average of 7.30 ± 3.61). A range of dysphonic symptoms, such as feelings of sadness, hopelessness and helplessness, anguish or ideas of guilt and death, are not always present what differentiates depression.

Final Considers

When used the classification system of the DSM-IV mental disorders resulting from thyroid dysfunction is classified as Mental Disorder Due to a General Medical Condition on Axis I, but do not lets you specify that it triggers mental disorder, which is closer and mood disorder to the side depressive. On Axis III we code the thyroid dysfunction (hyper or hypothyroidism) as the cause of the mental disorder. Why use the classification system of Lindqvist and Malmgren (1993) and not operating the symptoms of DSM-IV and ICD-10? The first system does not form a diagnosis of a pathology, but a symptomatic complex that has almost always organic etiology and is often the first manifestation of somatic diseases brain and extra-cerebral of all types. In its milder forms, it is difficult to differentiate from neurasthenia that is seen in cases of work overload. In its more severe forms, manifests as frank dementia. The second system makes the diagnosis of a specific entity (neurasthenic syndrome) and do not open the possibility to investigate the nature of organic or inorganic (Damasceno, 2002). Based on the described above, we suggest new studies in order to confirm the findings described before and systematize such characteristics, to aid clinicians in both procedures: evaluation and

intervention. But specifically, it is suggested that in a longitudinal follow-up of these cases will reveal why such differences exist.

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