HORMONAL DYNAMICS STUDY OF THE THYROID AND ADRENAL AXIS IN ELDERLY PATIENTS

ABSTRACT

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CRAIOVA
2011
INTRODUCTION

The current worldwide trend is a rise in elderly population and therefore we should pay attention to this numerous category involving many important social and health problems. This paper aims to bring a modest contribution to the study of hormonal dynamics in this population and to provide some means to improve the quality of life of elderly.

PURPOSE AND OBJECTIVES

The purpose of this paper is to specify the characteristics of the thyroid and adrenal axis in elderly patients. These patients have atypical presentations and coexisting medical problems. The study has the following objectives:

- analysis of variability in specific laboratory investigations in elderly;
- evaluation of anthropometric, hematological, biochemical, hormonal and cardiovascular parameters in a group of healthy elderly versus elderly patients with cardiovascular disease;
- the study of hormonal dynamics of the thyroid and adrenal axis in elderly patients without endocrine diseases;
- to link hormonal parameters to risk factors and cardiovascular pathology in elderly patients;
- to develop a project of endocrine assistance in elderly patients.

MATERIAL AND METHODS

The study was conducted in the Municipal Filantropia Hospital and County Emergency Hospital Craiova in the 2003-2010 period, with a prospective and a retrospective component.
The cases presented are based on a total of 135 patients aged over 65 who were divided into two groups: the control group composed of healthy elderly and the study group with elderly patients diagnosed with various cardiovascular diseases, without endocrine problems.

The patients were investigated by clinical examination carried out based on a protocol and laboratory tests (hematologic, biochemical, enzymatic, hormonal, immunological, imagistic), with cardiovascular assessment. The results were processed by statistical methods for obtaining clear conclusions on the data studied.

Hormone reference values in elderly were as follows:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Reference value</th>
</tr>
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<tbody>
<tr>
<td>TSH (µU/ml)</td>
<td>0,27 - 4,2</td>
</tr>
<tr>
<td>ACTH (pg/ml)</td>
<td>&lt; 46</td>
</tr>
<tr>
<td>Serum Cortisol (nmol/L)</td>
<td></td>
</tr>
<tr>
<td>- morning between 7-10</td>
<td>171 – 536</td>
</tr>
<tr>
<td>- afternoon between 16-20</td>
<td>64 – 327</td>
</tr>
<tr>
<td>DHEA-S (µg/dl)</td>
<td></td>
</tr>
<tr>
<td>- men 65 – 74 years</td>
<td>33,6 – 249</td>
</tr>
<tr>
<td>- women 65 – 74 years</td>
<td>9,4 – 246</td>
</tr>
<tr>
<td>- men ≥ 75 years</td>
<td>16,2 – 123</td>
</tr>
<tr>
<td>- women ≥ 75 years</td>
<td>12 – 154</td>
</tr>
<tr>
<td>FT4 (pmol/L)</td>
<td>12,0 – 22,0</td>
</tr>
</tbody>
</table>

**DISCUSSION AND INTERPRETATION OF RESULTS**

Aging is characterized by a decline in the functional reserve of the body, resulting in an inability to restore the balance after environmental stresses. This inability of homeostatic control related to age is evident on several endocrine axes and may become clinically evident only during an acute stress or during a significant long term stress. As significant long-term stress, we introduced the study of cardiovascular disease about which we mentioned characteristics and dynamics of the thyroid and adrenal hormonal axis and we linked hormonal parameters with cardiovascular risk factors in geriatric patients.

In this study we analyzed two groups of patients for hormonal dynamics observation of the thyroid and adrenal axis in elderly patients: a control group (group 1) consisting of 66 healthy elderly and the study group (group 2) consisting of 69 elderly patients diagnosed with various cardiovascular diseases.

Both groups were matched for chronological age, sex, area of origin, habits (smoking, alcohol). The prevalence of smoking and alcohol consumption was low in both groups.

Mean body mass index (BMI) was close to both groups: 23.73 kg/m2 in group 1, 24.55 kg/m2 respectively in group 2. Among the risk factors studied, only alcohol had a possible influence on BMI in subjects from the control group.

Mean biochemical and hematological parameters were generally within the normal range in both groups, except for some values of lipid fractions or blood sugar levels.

We chose to study for group 2 patients with the most common heart disease encountered in clinical medicine, and these were in order of frequency: hypertension (41 patients - 59%), ischemic heart disease (40 patients - 58%), heart failure (20 patients - 29%) and atrial fibrillation (19 patients - 28%). Patients with hypertension (HTN) were divided according to hypertension levels: grade 1 in 13 patients, grade 2 in 16 patients and grade 3 hypertension had 12 elderly. Of the 20 patients with heart failure (CHF), 50% were diagnosed with CHF NYHA class II, class III CHF 30% and 20% with CHF NYHA class IV heart failure. There were no patients with CHF NYHA Class I.

Serum hormone values were located in the normal range for age, with intra- and interindividual variability close to the normal distribution of values for these hormones, and, sometimes, reference intervals were smaller or wider.

**ACTH** had a mean of 17.55 pg/ml in group 1 and for lot 2 the mean ACTH was 18.74 pg/ml. Compared with normal ACTH values (below 46 pg/ml), we noticed lower average values in both groups.
In patients diagnosed with hypertension ACTH mean values (20.24 pg/ml) were higher compared with normal BP individuals of lot 1 (17.55 pg/ml). Mean ACTH decreased with increasing severity of hypertension.

There were no statistically significant differences between mean values of ACTH in patients diagnosed with CAD (16.08 pg/ml) compared to the patients in group 1.

Patients diagnosed with CHF had higher average values of ACTH than those in group 1, in all age groups, without a statistically significant difference.

Mean ACTH in cases of atrial fibrillation was almost equal (17.37 pg/ml) with that of the people in group 1, with a slight decrease in values with increasing age.

Specialized studies revealed no significant differences between ACTH levels in the elderly compared to those in young people.

The average **morning cortisol (cortisol 1)** was higher (392.93 nmol/l) in group 2 patients compared with group 1(336.92 nmol/l). There was a downward trend for morning cortisol values in group 2 patients with increased age.

In group 1, mean cortisol 1 was about 100 nmol/l higher in women (396.38 nmol/l) than in males (298.27 nmol/l) and consumers of alcohol had much higher mean values of cortisol 1, 502.54 nmol/l compared to those who did not drink alcohol, 296.3 nmol/l. Significant statistical correlations were obtained between cortisol 1 levels in healthy elderly and BMI, lipid levels and glucose: the high values of morning cortisol corresponded to high levels of BMI, total cholesterol, LDL-cholesterol and blood glucose and low levels of HDL cholesterol.

Patients with hypertension from group 2, regardless of severity, had average values of cortisol 1 higher (483.73 nmol/l) than that of the control group: the more severe was the hypertension, mean cortisol 1 was higher.

Mean cortisol 1 in patients with chronic ischemic heart disease, was 363.8 nmol/l, higher than control group.

In patients with CHF, regardless of heart failure NYHA class, mean cortisol 1 was 60 nmol/l higher than that obtained in the control group but the difference was not statistically significant. In these patients, mean cortisol levels tend to decrease with age with more than 100 nmol/l.

Mean cortisol 1 in patients with atrial fibrillation (316.89 nmol/l) was slightly smaller than the control group, without statistical significance. Analyzing gender distribution of patients with AF, it appears that women have lower levels of cortisol 1 (277.29 nmol/l) compared with men (340 nmol/l). Analyzing the effect of risk factors on the mean cortisol values collected in the morning in patients with atrial fibrillation did not reveal any significant statistical difference, although alcohol consumers were found to have higher average value of cortisol 1 (361.25 nmol/l) than those recorded in patients who did not drink alcohol (305.07 nmol/l).

Mean **evening cortisol (cortisol 2)** were slightly higher in cases with cardiovascular disease (228.55 nmol/l) compared to values obtained in the control group (205.58 nmol/l).

As with cortisol 1, mean cortisol 2 levels in group 1 were higher in women (238.81 nmol/l) than in males (183.97 nmol/l), with high statistical significance. Alcohol consumers had higher mean values of cortisol 2, 303.23 nmol/l than those who did not drink alcohol, 181.62 nmol/l. Statistical significant correlations were obtained between cortisol levels in healthy elderly and BMI, lipid levels and glucose: high levels of evening cortisol correlated to high levels of BMI, total cholesterol, LDL-cholesterol and blood glucose and low levels of HDL-cholesterol.

Highly statistically significant differences were observed when comparing the mean value of cortisol 2 in hypertensive patients (281.42 nmol/l) with the average evening cortisol collected in the control group. Mean cortisol 2 levels increased with increasing severity of hypertension, the difference being highly statistically significant.

Mean cortisol 2 levels in patients with chronic CAD (211.03 nmol/l) were slightly higher than that of the control group, without statistical significance.

Although mean cortisol 2 was around 30 nmol/l higher in patients with CHF than that obtained in the control group, the difference was not statistically significant.

Patients diagnosed with atrial fibrillation had a mean cortisol 2 level of 185.42 nmol/l, lower by about 20 nmol/l compared to the average control group. Mean cortisol 2 levels in patients with atrial fibrillation decreased with increasing age.
We have not noticed significant differences in evening vs. morning cortisol levels tied to a particular cardiovascular disease. Average decrease was around 40% for all four conditions studied. There were differences in the rate of decrease in cortisol collected at 20:00, compared with that collected at 8 am, depending on age group, in patients with HTN, CAD, AF, but not in patients with CHF, where the percentage decrease in evening cortisol was similar in all three age groups.

Related medical references revealed cortisol levels were normal in the elderly, but with decreasing amplitude of daily variations, as well as slightly elevated levels especially in men with cardiovascular disease.

In group 2 patients diagnosed with cardiovascular disease there was a 50% decrease in mean values for DHEA-S (49.16 µg/dl) compared to control group values (98.18 µg/dl). This decrease was highly statistically significant.

In the control group, we noticed a tendency for decrease in DHEA-S average values with increased age. No statistically significant difference was noted between DHEA-S mean values based on gender, although DHEA-S values were lower in women (90.31 µg/dl) compared to men (103.3 µg/dl).

With regard to alcohol consumption there were highly statistically significant differences: people who drank alcohol had mean values of DHEA-S with more than 50% lower (39.38 µg/dl) than those who did not drink alcohol (112.6 µg/dl).

Hypertensive patients in group 2 had a mean DHEA-S by about 40% lower (57.27 µg/dl) than the control group subjects, regardless of severity of hypertension. There is a tendency for a decrease in DHEA-S mean values with increased age in patients diagnosed with hypertension and a significant downward trend in mean DHEA-S with increasing blood pressure. In hypertensive smokers, mean DHEA-S was 99.4 µg/dl, almost double then in nonsmokers - 51.41 µg/dl, the difference being statistically significant.

A decrease by about 80% of the average values of DHEA-S (highly statistically significant) occurred in patients diagnosed with CAD (18.78 µg/dl) compared with group 2. As with hypertensive patients, there is a tendency for a decrease in DHEA-S mean values with increased age in patients diagnosed with chronic CAD.

There was a significant decline in DHEA-S mean values compared with the control group in patients with heart failure (16.05 µg/dl), respective of NYHA class of CHF (about 80%, highly statistically significant). Analysis of gender distribution in CHF patients revealed statistically significant differences: men had average values of DHEA-S 40% higher (20 µg/dl) than women (11.22 µg/dl).

Atrial fibrillation patients in group 2 had mean levels of DHEA-S around 40% lower (61.47 µg/dl) compared with DHEA-S mean values in the control group, which was highly statistically significant. Mean levels of DHEA-S in AF patients decreased by 50% with increased age of subjects (90.67 to 45.25 µg/dl). This decrease was also present in the control group, but not as significant (from 116.1 to 86.84 µg/dl).

Related medical references showed up to 70% decreases in DHEA-S values in people over 70 compared to young people, with research arguing that the low DHEA-S levels in elderly men would be involved in their increased mortality, especially in smokers and drinkers. Some studies have shown that patients with low serum levels of DHEA-S had an increase in the prevalence of chronic CAD, the authors claiming that low DHEA-S may predispose to CAD. A decrease in DHEA-S values was also found in patients diagnosed with heart failure: DHEA-S level were decreased in patients with CHF, directly related to it's severity. Other studies have suggested that low DHEA-S levels are a nonspecific indicator of aging.

Mean TSH value in group 1 patients was 1.24 µUI/ml, and for group 2 patients it was about 60% higher - 2.07 µUI/ml.

There was a downward trend in TSH levels with increasing age in healthy subjects in group 1, statistically significant. A direct link, highly statistically significant, was found between TSH, BMI, total cholesterol, LDL-cholesterol, triglycerides and glucose: high levels of TSH correlated with high levels of BMI, total cholesterol, LDL-cholesterol, triglycerides and glucose. HDL cholesterol was inversely related to TSH: low TSH levels corelated to high levels of HDL-cholesterol.
In hypertensive patients from group 2, regardless of HTN severity, mean TSH was almost double (2.39 µUI/ml) than that determined in control group subjects. TSH mean values were higher in patients with CAD from group 2 compared to the control group - 2.06 µUI/ml.

Mean TSH in patients diagnosed with heart failure in group 2 was 1.96 µUI/ml, greater than that of the control group. We noticed a decrease in mean TSH values with increasing severity of CHF.

TSH in atrial fibrillation patients was approximately 50% lower compared to control group - 0.54 µUI/ml.

In related medical sources there has been described a decrease in TSH levels in people over 70 years by about 20% compared to young people; some authors have reported normal or even elevated TSH levels in the elderly, and other studies have shown low TSH values in elderly patients with atrial fibrillation. In another study, low levels of TSH in the elderly have been considered a predictive factor for increased mortality in these patients.

**Free T4** mean values for patients in group 1 was 16.54 pmol/l, similar to that found in patients with cardiovascular diseases - 16.48 pmol/l.

The same mean values for Free T4 were seen in patients diagnosed with HTN (15.93 pmol/l), CAD (15.98 pmol/l) or CHF (15.85 pmol/l).

Free T4 values increased slightly with advanced age in hypertensive patient, without statistical significance.

Gender distribution of the mean Free T4 values in CHF patients revealed statistically significant differences: mean values of Free T4 were higher in men (17 pmol/l) compared to women (14.44 pmol/l). There is a statistically significant increase in mean Free T4 values with increasing severity of CHF: the higher the CHF class, the higher the Free T4 value.

Mean Free T4 values in patients with atrial fibrillation from group 2 was 20.63 pmol/l, about 20% higher than that of the control group, highly statistically significant.

In previous studies, some authors have not experienced significant changes in Free T4 values in the elderly, while others have found lower Free T4 values.

As a summary of the discussion above, it appears that the hormonal dynamics of the thyroid and adrenal axis in the elderly correlated to previous research, and diseases such as hypertension, coronary artery disease, chronic heart failure and atrial fibrillation influenced the secretion of hormones, or altered serum levels of these hormones could be predictors for cardiovascular pathology.

**CONCLUSIONS**

- Serum hormone levels studied in this paper were within normal values for age, with intra- and inter-individual variability close to normal distribution of values for these hormones, and sometimes the reference intervals were smaller or wider.
- Compared with normal values for ACTH, in elderly patients ACTH mean values are closer to the lower limit for both the healthy elderly and those with cardiovascular disease.
- Mean morning cortisol levels in both groups were within normal limits, approaching the upper limit of reference. In patients with cardiovascular diseases mean morning cortisol levels were higher then in healthy subjects.
- In both groups, mean evening cortisol levels were within normal limits, reaching towards the upper limit of reference. Patients with cardiovascular diseases had higher mean values of evening cortisol than patients in the control group.
- DHEA-S average values in both groups were within normal limits, approaching the lower limit of reference range. Healthy subjects in the control group showed a downward trend in average values of DHEA-S with increasing age. In patients diagnosed with cardiovascular diseases DHEA-S levels decreased by 50% compared to the control group.
The mean TSH levels in the two groups studied were located in the mid-normal reference range. In healthy subjects in group 1, there was a downward trend in TSH levels with increased age and for patients with cardiovascular diseases mean TSH levels increased by approximately 60% compared to healthy subjects.

Mean Free T4 levels in the two groups studied were located in the mid-normal reference range. In patients with cardiovascular diseases the mean value of Free T4 was similar to that recorded in healthy elderly.

Diseases such as hypertension, coronary artery disease, chronic heart failure and atrial fibrillation could influence the secretion of some hormones.

It should be necessary to introduce hormonal determinations as routine investigations in elderly, because abnormal hormonal levels could be predictors for the development and prognosis of cardiovascular diseases.

REFERENCES


Europass

Curriculum Vitae

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Teaching assistant (2004 – present) „Medical Semiology” Department

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Education

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Specialist in Internal Medicine (2007 - present)

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2008 - 2010 Master studies in “Management of Health Units”, University of Medicine and Pharmacy Craiova

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2000 - 2006 Internal Medicine Resident

1999 - 2000 Internship, Emergency County Hospital Craiova

1998 - Graduated from Faculty of Medicine - University of Medicine and Pharmacy Craiova

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Personal skills and competences

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2007 Certificate in General Ultrasonography

2006 Specialist in Internal Medicine

Postgraduating courses attended: 14

Mother tongue(s)
Romanian

Other language(s)
English, French

Self-assessment

<table>
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<tr>
<th></th>
<th>Understanding</th>
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<th>Writing</th>
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<td>Listening</td>
<td>Reading</td>
<td>Spoken interaction</td>
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and competences Operating systems: Windows, MS-DOS. Editing software: Microsoft Office, FoxPro 2.6, Dbase IV
Others: Internet user, Computer architecture
Driving licence B since 1996
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- The Romanian Association of Clinical Endocrinology
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PERSONAL PAPER WORKS IN PHD THESIS THEME
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Abstracts: