IMPORTANCE OF DEHYDROEPIANDROSTERONE SULFATE ASSESSMENT WITH SPECIAL ATTENTION FOR ADRENAL TUMOURS AND ARTERIAL HYPERTENSION

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Abstract

Objective. To investigate the significance of DHEAS assessment in males of different ages.

Methods. Retrospective cohort study of patients investigated in two large academic centres.

Results. The data of DHEAS assessment of 3533 patients (3013 females and 520 males) was analysed. DHEAS was 1.6 – 13.5 times more frequently investigated in women than in men. A peak of DHEAS evaluation test for women was at 25 years old and distribution was uniform in males over decades, excepting being lower in 0-9 and 75+ages. In the age group 10-24 years, DHEAS levels were higher in females. After 45 years, DHEAS was higher in men than in women. Analysis of 510 case records showed low DHEAS levels in boys (0-9 years) and in men aged 65 – 84+. Higher DHEAS levels were detected as a peak at 30 years old, but never after 55 years. In individuals with low DHEAS levels prevailed congenital adrenal hyperplasia (32%), adrenal tumours (30%) and primary or secondary adrenal insufficiency (19%). High DHEAS levels prevailed in patients with arterial hypertension (26%), overweight-obesity – (19%), non-toxic goiter (17%) and alopecia (9%). In the normal DHEAS miscellaneous diagnoses were met most frequently – 40%. Disorders exceeding 5% were non-toxic goiter (19%), adrenal tumours – 17%, overweight/obesity – 16% and arterial hypertension – 8%. In 71 women and 124 men adrenal neoplasms were detected. Higher frequency of these was observed in women in their 30s. A peak of adrenal neoplasms in men was at their 70s. This gender difference was not conditioned by earlier attempts to seek medical care by women. A significant correlation of DHEAS, weight, body mass index and systolic blood pressure with diastolic blood pressure was found.

Conclusion. Our study permits to determine which DHEAS secretion and clinical pattern might be associated in males of different ages.

Keywords: DHEAS, adrenal tumors, hypertension.

INTRODUCTION

Time of hopes, that the most abundantly found steroid hormones in the human body dehydroepiandrosterone (DHEA) and its sulfated form DHEAS are rejuvenating hormones (1-3), has past. In clinical practice DHEA had no adverse side effects (4), but no positive health effects were found except that it improves ovulation in older women undergoing assisted reproductive techniques (5).

Currently, research on DHEAS is reactualized. From epidemiological studies it is known that DHEAS deficiency in men (6) and women (7) can lead to increased cardiovascular morbidity and mortality.

Another important field in DHEAS research is linked to the fact that DHEA/DHEAS are neurosteroids (8). Alterations of DHEAS secretion may be related to bipolar II disorder (9) and Alzheimer's disease (10).

Initial DHEAS studies in patients with adrenocortical tumours led to the expectation that DHEAS increase is a sign of tumour malignancy and normal DHEAS levels indicate benignity (11, 12) but no recent data on this topic emerged since this hypothesis was reported in 2000s. Significance of DHEAS levels is also rarely mentioned when assessing patients with adrenal incidentalomas (13) even though large amounts of DHEAS are occasionally secreted by adrenocortical carcinomas (14).

DHEAS pathology in women is routinely investigated when presenting with hyperandrogenemia (and hypersecretion of DHEAS) commonly related to polycystic ovary syndrome (15, 16). In our own practice we reported similar findings of frequent DHEAS measurement in women with mild virilization (17). The current investigation was triggered by our recent case report of a patient with functional adrenal oncocytoma who presented with a 2.4-fold DHEAS

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increase (18). In this context, the aim of the study was to review the indications and results of DHEAS measurements performed in a large cohort of patients referred to two national referral centres (Kaunas and Vilnius) in Lithuania.

MATERIALS AND METHODS

Patient identification

Medical records of patients investigated in Lithuanian University of Health Sciences, Hospital Kaunas Clinics and Vilnius University Santaros Clinics during 2014- 2016 were reviewed. Analysis of referral data of 3533 patients (3013 women and 520 men) was performed.

All available clinical, laboratory and imaging information data were collected from clinical records of 590 women and from 510 men.

Calculation of “normality” of DHEAS was done using the ratio of patient’s DHEAS and the highest concentration indicated in DHEAS radioimmunoassay kit instructions (F-ULN-fold higher than the upper limit of DHEAS) and patient’s concentration of DHEAS and the lowest concentration at respective age (F-LLN-fold lower than the lower limit of DHEAS).

High DHEAS concentration (F-UPN) exceeded 1. Low DHEAS concentration (F-LLN) was less than 1. Normal concentration was defined as F-ULN <1 and F-LLN >1.

The study was performed with permission of the regional ethical committee.

Abdominal CT examinations

As a parallel investigation, results of 3700 individuals who had abdominal CT assays for various pathologies were analysed. This was considered important to search if AT peaks of females and males

are conditioned by earlier referral for CT in women.

Two groups of patients were identified: one group only with abdominal CT and a second group – patients who performed multiple regions CT (chest, abdominal and pelvic region). These groups were separately analysed because majority of patients with multiple regions CT were known as oncologic patients, assessed for extension of malignant process, or polytrauma.

Definition of adrenal neoplasms

The group of adrenal neoplasms (AN) included all the patients with changes visible in any of adrenal imaging assessment - ultrasound, CT or magnetic resonance imaging (MRI). Presumed extra-adrenal tumours or metastases were not separated into a distinct group.

Follow-up

During 2018 January – June we attempted to contact patients, which case records were analyzed in 2014 – 2016. Some of them were finally hospitalized for diagnosis and subsequent management. Adverse events and death circumstances were analysed.

Statistical analysis

Normal distributed data are presented as mean STD and compared using t- test. Data with non-normal distribution is presented as median (range) and compared with ANOVA test. Statistical processing was performed using SPSS 22.0 software package.

RESULTS

Referrals for DHEAS assessment. High female/male ratio

Referrals for DHEAS assessments in different

Figure 1 A. Referrals for DHEAS assessments in different age groups.

Figure 1 B. Mean DHEAS concentration in different age groups.

age groups are shown in Figure 1A. These results include consecutive unselected patients referred by the specialists (mainly endocrinologists) for the DHEAS assay. Overall mean value of female/male ratio was 5.66, ranging from 1.59 at 10-19 years age group to 13 at 20-24 years. More males than females (% of different age groups) were referred from birth to 19 years and from 45 to 84 years.

DHEAS concentration in different age groups in referred males and females

Mean DHEAS concentration in different age groups is presented in Figure 1B.

Referred males had a statistically significantly higher DHEAS concentration compared with women in early childhood (birth – 9 years) and in later life (over 45 years).

Concentration of DHEAS in females was higher than in males from 10 to 24 years. In a next 2 decades DHEAS concentration in females and males did not differ significantly, but later (45+ years) DHEAS levels in men were significantly higher than in women.

The highest concentration of DHEAS was found in 20 - 44 years for men (peak at 30 years), while in women it was between 10 - 34 years (peak at 22 years).

Distribution of DHEAS concentration in males

Results of analysis of DHEAS findings (low, normal or high) at different ages are shown in Figure

Figure 2. Mean DHEAS concentration in different age groups in males. F-LLN-fold lower limit of normal, F-ULN-fold upper limit of normal.

2. In whole the group of 510 males 11.7% had low DHEAS (F-LLN<1), 78.3 % - normal (F- ULN <1 and F-LLN >1) and 10 % - high DHEAS (F-ULN > 1).

Low DHEAS concentration was found in all ages, and had a flat form with high prevalence in boys from birth to 9 years, the level lower than 10 % until the age of 64 years, and increase of prevalence again after 65 years.

High values of DHEAS had a form of bell: increasing prevalence from birth to peak at 25 – 34 years, very small at 45-54 years and undetectable after 55 years.

It is also important to know at what age there are normal DHEAS values most likely (i.e. the lowest chances to find pathological values). Double peak distribution was apparent, with one peak at 10-19 years and a second large peak at 45-64 years (Fig. 2).

Our data suggest that assessment of DHEAS will result in more pathologic results in investigation of 0-9 boys and 65 + men (hyposecretion suspected), and in 25-35 years young men (hypersecretion suspected) groups.

Main pathologies in respect to DHEAS concentrations in males

Main pathologies in respect to DHEAS concentrations in 510 males are shown in Figure 3.

In the group of low DHEAS predominant pathologies in males were congenital adrenal hyperplasia (CAH - 32%), adrenal tumours (AT – 30 %) and primary or secondary adrenal insufficiency (P/S-AI, 19%). Miscellaneous diagnoses (i.e. diagnoses

Figure 3. Main pathologies in different DHEAS concentration groups of males.

that do not exceed 5% of total investigated population) were found in 19%.

In the group of high DHEAS predominant pathologies in males were arterial hypertension (HT+26%) and overweight/obesity (O/O -19%), followed by non-toxic goiter (NTG - 17 %) and alopecia (ALP-9%). Twenty nine percent of cases had miscellaneous diagnoses.

In the largest group of normal DHEAS miscellaneous diagnoses were met most frequently – 40%. Pathologies exceeding 5% were NTG -19%, AT – 17%, O/O – 15.6% and HT+– 8% (Fig. 3). New findings for DHEAS pathology search were:

1. High frequency of adrenal tumours in low DHEAS group. They appear in older than 65 years men and have a peak for men in their 70s, which is very late in comparison with women (peak of AT around their 30s).

2. High frequency of arterial hypertension and overweight/obesity in patients with high DHEAS.

Distribution of adrenal tumours in females/males in different age groups

The distribution of AT in females/males in different age groups is shown in Figure 4. Peak prevalence of AT was found at age 25-34 years in women and at 65-74 years in men.

In men, AT are found for the first time at the age of 25-34 years, and its incidence increases up to the peak at 65-74 years and later decreases.

In females AT were documented for the first time earlier- at 10-19 years old. In the subsequent age groups percent of patients with AT was 10 – 14 %, with incidence peak at 25-34 years and decline after 84 years old.

Figure 4. Individuals with adrenal tumors in different age groups.

Combination of AT and high DHEAS was 0.2% of all the males investigated and 0.8% of patients with adrenal neoplasms (AN).

Combination of AT and high DHEAS was 0.34% of all females investigated and 2.8% of patients with AN.

Earlier it has been published that the age of diagnosis is lower in women with functional tumors (including Cushing's syndrome) than in men, while the age was similar in men and women with adrenal incidentaloma (19).

Analysis of the cohort of 3700 consecutive abdominal only and complex abdominal, chest and pelvic computer tomographies (CT) for the age and gender

Analysis of the cohort of 3700 consecutive abdominal only and complex abdominal, chest and pelvic computer tomography (CT) for the age and gender of examination was performed. Peak performance of CT in men and women was the same - between 65 and 74 years of age (Fig. 5). Earlier attempts to seek medical care in women was not shown to be a cause of peak percent of AN at their 30-ties.

The data of patients with complex CT performed were very similar to earlier mentioned patients (data not shown).

Essential findings in different male groups

Essential findings in different patient groups are shown in Table 1.

One hundred twenty four patients with adrenal neoplasms were analysed. Nine groups of patients were distinguished: 1. Bilateral adrenal tumours (n=18, B-AT); 2. Left side adrenal tumours (n=43,

Figure 5. Abdominal CT scans in different age groups.

L-AT); 3. Right side adrenal tumours (n=45, R-AT); 4. Hyperplasia, thickened part of adrenal, nodular and multinodular changes of adrenals (n = 7, A-NEO); 5. Patients after adrenal surgery (n=11, A-PS); 6. Patients aged >55 years with hypertension (n=43, HT+). 7. Patients aged >55 years without hypertension (n=22, HT-). 8. Dead patients (n=6, DEATHS) and 9. All the patients with adrenal neoplasms (n=124, AN).

A-NEO and A-PS patients were younger, and statistically oldest men were those who died. Patients who died also had the lowest DHEAS concentrations, lowest calculated DHEAS parameters (F-ULN and F-LLN) and multimorbidity.

Tumor size higher than 5 cm was rare in B-AT – 0, R-AT – 1, L-AT-3 patients.

Duration with actual diagnosis (DAD, years) was from 3 to 5 years, without statistically significant

differences between groups. In 9 patients DAD was less than 1: in B-AT – 1, L-AT – 2, R-AT – 2 and patients with HT – 4.

DHEAS concentration negatively correlated with age ($r = -0.43$, $p < 0.0001$) and age at diagnosis ($r = -0.44$, $p < 0.0001$). DHEAS concentration positively correlated with height ($r = 0.21$, $p < 0.027$) and weight ($r = 0.18$, $p < 0.017$). Similar correlations were found in DHEAS-related calculated parameters.

Positive correlation was found of F-ULN with DBP ($r = 0.159$, $p < 0.044$) and of F-LLN with DBP ($r = 0.185$, $p < 0.019$). Significant correlation of DBP was found also with weight ($r = 0.31$, $p < 0.002$), BMI ($r = 0.230$, $p < 0.023$) and SBP ($r = 0.716$, $p < 0.0001$). These correlations are probably significant because most of the patients had normal DHEAS values and therefore reflect the correlations found in normal people.

Table 1. Essential findings in different male groups

Variables/ Groups	B-AT n=18	L-AT n=43	R-AT n=45	A-NEO n=7	A-PS n=11	AN n=124	HT+ n=43	HT- n=22	Deaths n=6
Age (years)	63.16 ±10.42	64.46 ±14.79	66.22 ±12.65	58.42 ±16.47	51.72 ±23.07	63.44 ±14.84	64.38 ±7.77	65.80 ±8.65	78.90 ±6.32
Age at dgn. (years)	58.66 ±10.72	59.41 ±14.34	61.93 ±12.24	55.42 ±16.27	47.63 ±23.46	58.95 ±14.59	60.30 ±7.76	62.10 ±8.22	76.00 ±5.48
Height (cm)	174.70 ±6.38	176.3 ±8.35	173.20 ±7.08	183.50 ±10.60	181.30 ±9.39	175.80 ±8.15	179.20 ±7.82	177.00 ±8.16	170.00 ±5.71
Weight (kg)	95.50 ±21.04	91.22 ±21.93	90.10 ±18.00	110.00 ±28.28	88.35 ±23.99	91.67 ±20.61	91.90 ±18.41	84.20 ±19.24	84.67 ±26.19
BMI (kg/m ²)	32.00 ±6.87	29.36 ±6.82	30.00 ±5.19	32.50 ±4.94	26.60 ±6.19	29.70 ±6.17	27.80 ±4.96	26.90 ±20.40	28.78 ±7.09
DHEAS (µkmol/L)	3.13 ±1.76	5.18 ±3.92	3.96 ±2.66	5.55 ±3.83	5.30 ±3.10	4.47 ±3.22	4.48 ±2.83	3.47 ±2.65	0.54 ±0.39
F-ULN	0.24 ±0.14	0.40 ±0.30	0.31 ±0.20	0.43 ±0.30	0.35 ±0.17	0.34 ±0.24	0.35 ±0.22	0.27 ±0.20	0.04 ±0.03
F-LLN	2.20 ±1.27	5.40 ±5.07	2.73 ±1.77	3.72 ±2.74	2.79 ±1.40	3.64 ±1.01	3.25 ±2.04	2.49 ±1.79	0.44 ±0.30
SBP (mm/Hg)	139.40 ±21.88	136.00 ±18.65	147.90 ±20.07	161.70 ±16.66	136.30 ±13.31	142.00 ±20.00	161.40 ±22.23	132.40 ±7.16	147.20 ±13.75
DBP (mm/Hg)	86.25 ±10.80	82.34 ±11.00	88.70 ±10.08	95.00 ±17.32	84.45 ±14.30	86.09 ±11.47	95.00 ±13.24	80.00 ±5.85	80.00 ±7.07
Pulse/min	75.93 ±8.53	77.00 ±7.26	76.40 ±10.30		72.45 ±13.17	75.84 ±9.74	70.50 ±8.70	76.20 ±9.27	74.60 ±6.00
DAD (years)	4.50 ±3.58	5.00 ±3.58	4.16 ±2.54	3.00 ±1.29	4.00 ±1.84	4.42 ±3.02	4.07 ±2.16	3.64 ±2.18	1.60 ±0.90
Size R-AT (cm)			2.31 ±0.72			2.22 ±0.75			5.13 ±4.30
Size L-AT (cm)		2.21 ±1.18				2.51 ±1.13			2.53 ±1.26
Size B-AT R (cm)	1.99 ±0.81								
Size B-AT L (cm)	1.75 ±0.56								

B-AT: Bilateral adrenal tumors, L-AT: Left adrenal tumor, R-AT: Right adrenal tumor, A-NEO: Minor visual changes of adrenals, A-PS: post-surgery adrenals, AN: Adrenal neoplasms, HT+: Arterial hypertension present, HT-: Arterial hypertension absent, BMI: Body mass index, DHEAS: Dehydroepiandrosterone sulfate, F-ULN: fold upper limit of normal, F-LLN: fold lower limit of normal, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, DAD: Difference of time of actual consultation and time of diagnosis establishment, R: Right, L: Left. Results: mean ± standard deviation. n – number of patients.

Deaths

Six men died. Diagnosis at endocrinology department in men was documented at 79 years(mean), death – at 81 years, tumour size on CT – 3.8 cm, DHEAS concentration – 0.5 $\mu\text{mol/L}$, F-ULN (fold higher than upper limit of DHEAS)- – 0.04, F-LLN (fold lower than lower limit of DHEAS) - – 0.33, and comorbidities were characteristic. In decreasing order there were 3 persons with type 2 diabetes, hypertension and possible metastases. Two patients had lung cancer, 1 patient had both kidney carcinoma and stroke. One patient had lung metastases of malignant melanoma. Therefore in men death occurred in older patients with median size of AT, low DHEAS concentration and multiple comorbidities.

DISCUSSION

This article reopens the scene of adrenal research for an old, forgotten and neglected player in males – dehydroepiandrosterone sulfate.

Referrals for DHEAS test

Referral criteria for DHEAS assessment in males are ill-defined. Because men are never “too masculine” it is easy to explain why men’s referrals for DHEAS investigation was much less frequent than women’s. As a consequence, our study demonstrated a high female/male ratio for referrals for DHEAS assessment.

DHEAS test in males of our centers was 1.59 – 13 times lower than in females. Males were referred for androgen diagnostic work-up in childhood and in young years because of signs of congenital adrenal hyperplasia (CAH) and primary or secondary adrenal insufficiency (P/S-AI). Adult men are referred for DHEAS test in findings of adrenal tumours (AT), hypertension (HT) and rarely – alopecia.

DHEAS concentrations

DHEAS peaks in youth and then begins to decline evenly (20, 21). A new result of our research is that DHEAS in referred young females (10-24 years), was statistically higher than in the respective age group of males. This probably because young women are frequently referred for DHEAS assessment, having signs of hirsutism or PCOS. Also it can be explained by double source (adrenal and ovary) of DHEA in pubertal adolescents and young women in comparison with predominantly adrenal secretion of DHEA in males.

Assessment of DHEAS and AT in women

is only a clinical start point for much more complex investigations. Genetic markers for polycystic ovary syndrome are studied today even between ethnic populations, as in famous MEDIGENE program (22).

Distribution of low, normal and high DHEAS in males

In this clinical study we distinguished 80 % patients with normal DHEAS and 20 % patients with pathology of DHEAS: 11% had low and 9% - high DHEAS concentrations.

There is a controversy in explaining DHEAS concentrations in CAH. Classically, in the most frequent form of CAH, steroid 21-hydroxylase deficiency, patients should have higher than normal DHEAS. Our results show an increased frequency of lower but not higher DHEAS levels in patients with CAH. This could be explained by the incomplete defect of enzyme or another enzymatic defect, or decrease of DHEAS as a result of hormonal management of CAH.

Adrenal tumours and DHEAS

As concerning AT, our study differs from earlier research of Terzolo *et al.* in 2000 (12) because of a higher number of men with adrenal neoplasms (124 vs. 39), larger age span of DHEAS test (0-85+ vs. 66) and inclusion of extra-adrenal tumours in our study. In contrast to conclusion that normal or low levels means benignity of adrenal tumours (12), our results show that in 65+ men with AT low DHEAS may be a sign of unfavourable life prognosis.

Trying to explain the gender discrepancy of age at diagnosis of AT, we proposed that early detection of AT in females is due to higher addressability of females to medical institutions. Both male and female maximal number of CT was the same – at age of 55-64 years.

Another, more attractive, data explanation is that higher DHEAS levels in men in late decades slows down the development of AT. This is a speculation which requires further investigation.

Pathology with low DHEAS

In endocrinological clinical practice low DHEAS is used as a marker of primary, secondary or tertiary adrenal insufficiency (23).

In epidemiological studies low DHEAS was associated with different health and pathology conditions. To mention only a few, low DHEAS was associated with decreased physical vitality and function (24), all-cause and cardiovascular mortality (25), higher risk of type 2 diabetes (26), increased fracture risk in older men

(27) and pulmonary arterial hypertension (28).

A consequence of finding low DHEAS would be DHEA replacement in DHEAS-deficient patients. Attempts of such replacement with 25-50 mg DHEAS for 6 months were performed and finally resulted in clinical practice guideline for diagnosis and treatment of primary adrenal insufficiency (29).

Very few men with adrenal insufficiency were treated with DHEA. Some positive effects were shown on wellbeing and mood in patients with primary or secondary adrenal insufficiency (30).

Pathology with high DHEAS

In males, the significance of high DHEAS is rarely addressed. DHEAS test is mandatory in diagnostic work-up of patients with suspicion of adrenocortical cancer (31). If high, it serves as tumour marker and is useful for follow-up of patients after surgery (32). Increased DHEAS is also found in some forms of congenital adrenal hyperplasia {steroid 21-hydroxylase deficiency and 11 β -hydroxylase deficiency (33)}, and in pure androgen secreting adrenal tumours {PASAT – (34)}.

We found high DHEAS in childhood and in young men with peak at their 30s. High DHEAS was extremely rare during 45-54 years and never appeared after 55 years. Predominant pathology in these patients was hypertension (HT) – 26%, overweight/obesity (O/O) – 19% and non-toxic goiter – 17%. Rarely, alopecia was found – 9%.

Young male patients with hypertension and obesity are more frequently tested for adrenal hyperfunction (including DHEA) than older ones and this bias of patients selection may have influenced the results.

High DHEAS and arterial hypertension

Association of high DHEAS with arterial hypertension was noted. Typical patients of this group are patients with O/O.

More detailed assessment of this correlation was tentatively done, looking for possible differences of DHEAS and HT in men 55+ with HT (HT+) and men 55+ without hypertension (HT-). No statistical difference was found between these 2 groups. On the other hand, a positive correlation of diastolic blood pressure with DHEAS was found.

Recently, a significant positive association of DHEAS and seated diastolic blood pressure was found in normotensive men of 55+years, but not in women (35). Earlier, a relation between DHEAS and

blood pressure was also found (36) in population-based studies. In our study, hypertension and high DHEAS were described mainly in young men with overweight/obesity. We could not exclude that this relationship is only accidental, and genetic or epigenetic conditions are of importance here. As a rule, high DHEAS finding in these patients had no consequences for further investigation or treatment. We suggest at least one imaging method for adrenal pathology search to be applied for this particular group of patients with high DHEAS. Discussion on treatment of young men with high DHEAS and hypertension is open now.

Deaths

Six men died. All 6 were of advanced age and had, very low DHEAS and multimorbidities. The group of patients who died are the elderly, whose natural concentration of DHEAS is low although an additional effect of multimorbidity by inducing low DHEAS or vice versa could be considered as well. Recent study of physiological markers in multimorbidity conclude, that DHEAS is the first line physiological marker of multimorbidity (37).

Strengths and limitations

The strength of this study is a systemic approach of males who were referred for DHEAS assessment in respect to DHEAS concentration and different pathologies appearing in groups of different ages from birth to 85+ years.

An unavoidable limitation of this study is the absence of a control group. Furthermore, one can argue with the use of patient's DHEAS ratio with the maximal (F-ULN) and minimal (F-LLN) values indicated in DHEAS assessment kit. F-ULN is used also in recent publications to estimate how elevated was DHEAS in patients, investigated for different androgen-related pathologies in children (38) and adult women (39). Instead of leaving overlapping low normal and low values of DHEAS, we used F-LLN as criterion which enables to estimate how low was DHEAS in patients. A further unavoidable limitation of the study is related to the fact that we analysed only patients who had at least one DHEAS assessment. Patients with adrenal tumours with radiological features of malignancy rarely have DHEAS measurements before being offered treatment (40) and therefore it is likely that the study failed to capture data on patients with the most aggressive adrenal tumours.

In conclusion, referrals of males for DHEAS test are several times lower than in females in all age

groups. DHEAS concentration in referred adolescents and young women was higher in females, but after 45 years old DHEAS concentration was higher in referred men. Low and high levels of DHEAS are found in around 10% each. Low DHEAS has two peaks – 0-9 years old and 65-74 years old. Main pathologies found in low DHEAS group were congenital adrenal hyperplasia (in children), adrenal tumors (in adults) and primary or secondary adrenal insufficiency (in both).

High DHEAS was found in tested young men with peak at 30s and rapid fall, never found after 55 years old. Main pathologies found in high DHEAS group were hypertension, overweight/obesity, non-toxic goiter and alopecia.

Our study demonstrates the importance of DHEAS assessment in males of different ages and adds additional information about the use of DHEAS results for clinical decisions making. As a consequence, males of different ages should be referred much more frequently for DHEAS testing.

Conflict of interest

The authors declare that they have no conflict of interest.

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