The analysis of dehydroepiandrosterone sulphate concentration in elderly age women depending on coexisting disease states

Kędziora-Kornatowska K[1], Beszczyńska-Oleś R[1], Kornatowski T[2], Szadujkis-Szadurski L[2]*

[1] Department of Geriatrics, Collegium Medicum of Nicolaus Copernicus University, Toruń, Poland
[2] Department of Pharmacology and Therapy, Collegium Medicum of Nicolaus Copernicus University, Toruń, Poland

Abstract

Purpose: The aim of the study was evaluation of dehydroepiandrosterone sulphate (DHEA-S) serum concentration in elderly women and determining interdependence between DHEA-S levels and occurrence of diseases typical for this period of life.

Material and methods: The study was conducted on 103 elderly women (mean age 70.7±7.3 years). The control group consisted of 25 young and healthy women (mean age 33.5±1.7 years). The elderly patients were fully functional, well nourished, and only periodically required medical care due to chronic illnesses such as coronary heart disease, arterial hypertension, type 2 diabetes, osteoporosis, depression. DHEA-S serum concentration was determined by Spectria DHEA(S) RIA radioimmunological kit. Statistically significantly important decrease of DHEA-S serum concentration was determined in elderly women compared with the control group.

Results: Mean blood serum DHEA-S concentration in elderly group was significantly lower compared to controls. Mean blood serum DHEA-S concentration was statistically significantly lower in the group of patients suffering from coronary heart disease, osteoporosis, and depression. Statistically significantly lower DHEA-S concentration was observed in patients with benign disorders of cognitive functions and depression compared with patients with correct MMSE and GDS results.

Conclusions: In elderly women DHEA-S concentration can turn out to be useful aging biomarker. Concentration of this hormone significantly decreases together with age, especially with coexisting diseases typical for this period of life.

* CORRESPONDING AUTHOR:
Katedra i Klinika Geriatrii Collegium Medicum UMK
85-094 Bydgoszcz, ul. M. Skłodowskiej-Curie 9, Poland
Tel: +48 52 5854021
e-mail: kasiakor@interia.pl (Kornelia Kędziora-Kornatowska)

Received 01.04.2007 Accepted 16.04.2007

Key words: dehydroepiandrosterone sulphate, aging, elderly age illnesses.

Introduction

Aging leads to progressive involutional changes concerning structure and functioning of multiple systems and organs including endocrine system.

Mentioned changes differ in amplitude as far as different endocrine glands are concerned.

Secretion of some hormones does not change, can be handicapped or increased [1]. However, together with age we can observe significant decrease of concentration of the main adrenal androgen – dehydroepiandrosterone (DHEA) [2].

Dehydroepiandrosterone and its sulphate (DHEA-S) are endogenic hormones synthesized in adrenal cortex, gonads and central nervous system. DHEA secretion is stimulated by adreno-corticotropin (ACTH). ACTH secretion does not change together with age, so the reasons for decreasing DHEA secretion in elderly age remain unexplained [3]. The open question as well is the participation of this hormone deficiency in aging process and influence on occurrence of elderly age diseases. It was proved that low DHEA concentration increases intensification of atherosclerosis. It was also determined that low DHEA concentration increases the risk of myocardial infarction in men [4]. At present, it is thought that the relation between DHEA concentration and cardiovascular diseases is different depending on age where menopause is the borderline [5]. It was demonstrated that DHEA deficiency in premenopausal women can be the risk factor for coronary heart disease development or may be the indicator of early stage of atherosclerosis development [6]. Other authors claim that high DHEA concentration protects against cardiovascular diseases in men, but not in women [7]. There is no agreement concerning DHEA concentration influence on carbohydrate and lipid metabolism. Some authors claim that DHEA decreases glycaemia and it is

Table 1. **Illnesses occurring in groups of patients in early and late elderly age**

Illness		YES		NO		P
		N	%	N	%	
Hypertension	early old age	48	67.6	23	32.4	
	late old age	23	71.9	9	28.1	p=ns
Coronary heart disease	early old age	56	78.9	15	21.1	
	late old age	30	93.8	2	6.2	p<0.05
Osteoporosis	early old age	42	59.2	29	40.8	
	late old age	28	87.5	4	12.5	p<0.01
Depression	early old age	39	54.9	32	45.1	
	late old age	25	78.1	7	21.9	p<0.05
Diabetes	early old age	6	8.5	65	91.5	
	late old age	3	9.4	29	90.6	p=ns

advantageous for lipid concentration, others negate this positive influence [8,9]. DHEA belongs to the group of so-called neurosteroids, which are locally produced in central nervous system and modulate neural conduction [1]. It was also observed that above mentioned hormone shows antidepressive properties [10]. Decreased concentration of DHEA was observed in patients suffering from Alzheimer's disease [11].

Another important aspect of DHEA action is its advantageous influence on bone mass increase and lowering bone tissue resorption markers [12]. DHEA influence in the immune system was also observed. Some advantageous changes in some immunological parameters were observed in DHEA treated elderly patients [13]. Another important factor of DHEA activity is its anti-neoplastic action, which might be connected with antioxidative properties of this hormone [5]. On the other hand, DHEA may activate development of estrogen and androgen dependent neoplasms, as it is the precursor for these hormones. Despite many advantageous effects of DHEA action in human body it is still not certain what the connection between the concentration of this hormone and occurrence of old age diseases is. What remains controversial problem is supplementation of DHEA in elderly patients. For that reason the aim of the study was evaluation of blood serum dehydroepiandrosterone sulphate (DHEA-S) concentration in elderly women and determining interdependence between DHEA-S levels and occurrence of diseases typical for this period of life.

Material and methods

103 women aged 60 to 83 (mean 70.7±7.3 years) were included in the study. Among included there were patients in good condition, physically fit, service-independent, only periodically requiring ambulatory treatment due to chronic diseases such as: coronary heart disease, primary arterial hypertension, type 2 diabetes, osteoporosis without fractures, depression. In the selected group 2 sub age groups were isolated – 71 women in early elderly age (aged 60 to 70 years) and 32 women in late elderly age (aged 75 to 89 years). Control group consisted of 25 healthy women aged 30 to 36 (mean 33.5±1.7 years).

All the patients underwent subjective and objective study. Elderly women were subjected to complex geriatric assessment. In order to do this, standardized measurements such as: functional efficiency, ADL scale (Activities of Daily Living) and IADL scale (Instrumental Activities of Daily Living) were applied. To evaluate cognitive functions MMSE scale (Mini-Mental State Examination) [14], and for emotional functions GDS scale (Geriatric Depression Scale) [15] were used.

7 ml of blood from basilic vein was taken from all the included in the study in order to determine dehydroepiandrosterone sulphate (DHEA-S) blood serum concentration. The concentration was determined by Spectria DHEA(S) RIA radioimmunological kit. Coated sample technology by Orion Diagnostica (Finland) was used in the study. The kit is used to *in vitro* quantitative determining whole blood serum DHEA-S concentration. All the samples were detected in gamma radiation detector, Wallac (Finland). Statistical analysis was conducted with one-way ANOVA. The statistically significant level of significance was set at $p<0.05$.

Results

The results of 6 point ADL scale showed that all the examined patients got 6 points which means that they all were efficient. On the basis of IADL scale it was determined that most of the examined elderly patients functioned in their environment without any help (97.1%) or with a little help (2.9%). On the basis of MMSE test it was observed that 93 patients (90.3%) had mild disorders of cognitive functions and 10 patients (9.7%) had correct MMSE results. According to GDS it was observed that 62 patients (60.2%) suffered from mild depression, 5 patients (4.9%) suffered from profound depression and 36 patients (35%) had no depression. Illnesses in early and late elderly patients are shown in *Tab. 1*.

Mean blood serum DHEA-S concentration in elderly group (0) was significantly lower compared with controls (K) ($p<0.001$).

Mean blood serum DHEA-S concentration in late elderly group (00) was significantly lower than in the early elderly group (Y0) ($p<0.05$). The results are presented in *Tab. 2*.

Mean blood serum DHEA-S concentration was statistically significantly lower in the group of patients suffering from coronary heart disease, osteoporosis, and depression ($p<0.05$).

Table 2. **Mean values of serum dehydroepiandrosterone sulphate (DHEA-S) concentration in elderly women (0) in early old age (Y0) and late old age (00) compared with controls (K)**

	N	DHEA-S [ng/ml]			p
		mean ± SD	Minimum	Maximum	
O	103	655±261	49	1 264	p<0.001
OY	71	691±273	49	1 264	p<0.05
OO	32	574±214	112	988	p<0.05
K	25	2 526±796	1 148	3 887	p<0.001

Table 3. **Occurrence of illnesses in elderly women vs mean dehydroepiandrosterone sulphate (DHEA-S) concentration values**

Illness		N	DHEA-S [ng/ml]			p
			Mean ±SD	Minimum	Maximum	
Arterial hypertension	YES	71	648±260	49	1 186	p=ns
	NO	32	671±267	112	1 264	
Coronary heart disease	YES	86	632±247	49	1 171	p<0.05
	NO	17	772±304	268	1 264	
Osteoporosis	YES	70	614±253	49	1 186	p<0.05
	NO	33	742± 261	96	1 264	
Depression	YES	64	611±258	49	1 186	p<0.05
	NO	39	727±254	138	1 264	
Diabetes	YES	9	502±241	96	922	p=ns
	NO	94	669±259	49	1 264	

Table 4. **Mean dehydroepiandrosterone sulphate (DHEA-S) concentration vs Geriatric Depression Scale (GDS) results**

	DHEA-S [ng/ml]				
	N	Mean	SD deviation	Minimum	Maximum
No depression	36	752*	246	138	1 264
Mild depression	62	612	255	49.21	1 186
Profound depression	5	482*	265	274	922

* statistically significant difference (p<0.01)

However, there was no statistically significant difference in the group of people suffering from primary arterial hypertension, and type 2 diabetes compared with the patients free from these diseases (*Tab. 3*).

Statistically significantly lower DHEA-S concentration (628±252 ng/ml) was observed in patients with benign disorders of cognitive functions compared with patients with correct MMSE result (902±219 ng/ml) (p<0.01).

Mean blood serum DHEA-S concentration depending on GDS result is presented in *Tab. 4*. It was shown that together with intensification of depression, the concentration of the hormone was lower. The difference of the mean DHEA-S concentration in the group of women suffering from profound depression compared with the group free from depression was statistically significantly lower (p<0.01).

Discussion

Dehydroepiandrosterone as well as growth hormone or melatonin belongs to the group of so-called youth hormones. By now there has not been any universal concept which could explain pathomechanism of the changes in secretion of these hormones in senile age. Characteristic lifelong DHEA secretion profile, and especially its age related gradually lowering levels caused naming it the biomarker of aging [16].

In own research it was determined that blood serum DHEA-S concentration in elderly women was lower compared with younger controls. Moreover, mean DHEA-S concentration in early elderly group was significantly higher than in late senile group of women. Age related DHEA-S concentration decrease is also confirmed by other authors [17].

In own research significant decrease of DHEA-S concentration was also observed in some of the elderly women in some coexisting illnesses. Lower DHEA-S concentration was observed in patients suffering from primary arterial hypertension and type 2 diabetes, however, the differences were not statistically significant. Moreover, statistically significant lower mean DHEA-S values were observed in patients suffering from coronary heart disease, osteoporosis, and depression.

Literature confirms decreased DHEA-S concentration in patients suffering from arterial hypertension, coronary heart

disease, and diabetes [18]. It was proved that the decreased DHEA-S concentration and hyperinsulinaemia can be risk factors for development of atheromatic changes in coronary arteries area. Moreover, it was proved that total mortality caused by ischaemic heart disease in women after menopause correlates negatively with DHEA-S concentration [4]. Other researchers have not determined correlation between low DHEA-S concentration and progression of atheromatic changes in coronary arteries in women after menopause [4,19].

The interesting finding was determining such relationship in middle aged men group, which enabled the researchers to conclude that the DHEA metabolism in men and women is regulated differently. It was proved that DHEA may protect men against cardiovascular diseases, however, this does not concern women. It is confirmed by Rancho Bernardo Study [20]. In the course of research concerning prevention and complications of dyslipidaemia and chronic hyperglycemia in badly monitored diabetes it was found out that the aimed benefits can be achieved after administering overphysiological doses. The explanation of this phenomenon can be the fact that DHEA is characterized by short half life period (about 15 to 30 minutes). It seems that administering preparations with longer half life period and free metabolism in physiological doses in the future would be more justified and safer [5]. In own research decreased DHEA-S concentration in women's osteoporosis was shown. It is also confirmed by other authors [21]. Beneficial DHEA tissue action in bone tissue may be connected with a few mechanisms. One of them is direct DHEA influence on testicular receptors, which was determined in lymphocytes and osteoblasts. Through these receptors the hormone produces anabolic and anti-glycocorticoid action. Research conducted by many authors has proved bone mass hypertrophy, decrease in bone resorption markers and increase in osteocalcine level in IGF-1 in women after menopause [12].

In own research significantly decreased DHEA-S concentration was observed in elderly women with depression and mild cognitive function disorders. The relation between DHEA-S levels and function of central nervous system may result from the fact that DHEA within this system plays role of the neurotransmitter. Wolkowitz [10] observed antidepressive DHEA action. Nasman et al. [22] showed lower concentration of this hormone in patients suffering from Alzheimer's disease. Beside direct DHEA action of neurosteroid modulating neuronal functions, there is significant antagonistic action against cortisol in central nervous system. It was proved that long-lasting maintenance of increased blood glucocorticoid concentration (cortisol in human) in stress may have neurotoxic effect in neurons in hippocampus and other brain areas. As it is widely known, cortisol level on contrary to DHEA and DHEA-S does not decrease together with age, which may lead to so-called relative hypercortisolemia.

Kalmijn et al. [23] showed significant interdependence between relation of DHEA/cortisol and the level of cognitive function disorders in elderly people.

Summing up, our own research confirms decreased blood serum dehydroepiandrosterone sulphate concentration in elderly women, especially in case of coexisting illnesses typical of this period of life. Blood DHEA level can be recognized as the important aging biomarker. In this situation DHEA substitution in elderly women seems to be reasonable. However, at present there is no convincing evidence proving that such therapy would positively influence modification of aging process, protecting against accelerated development of many illnesses.

References

1. Karasek M, Pawlikowski M. Hormones and aging. Folia Med Lodz, 2003; 30: 11-38.
2. Lane MA, Ingram DK, Ball SS, Roth GS. Dehydroepiandrosterone sulfate: a biomarker of primate aging slowed by calorie restriction. J Clin Endocrinol Metab, 1997; 82: 2093-6.
3. Dodt C, Dittman J, Hruby J, Späth-Schwalbe E, Born J, Schuttler R. Different regulation of adrenocorticotropin and cortisol secretion in young, mentally healthy elderly and patients with senile dementia of Alzheimer`s type. J Clin Endocrin Metab, 1991; 72: 272-6.
4. Barret-Connor E, Khaw K-T, Yen S. A prospective study of dehydroepiandrosterone sulfate, mortality and cardiovascular disease. N Engl J Med, 1986; 315:1519-24.
5. Halecki M, Sewerynek E, Lewiński A. Dehydroepiandrosterone as an antioxidant-possibilities of application in medicine. Pol J Endocrinol, 2001; 52(1): 117-28.
6. Malczewska B, Słowińska-Srzednicka J, Szwed H, Chotkowska E, Kowalik I, Wiernikowski A, Sadowski Z. Niedobór siarczanu dehydroepiandrosteronu u premenopauzalnych kobiet z przedwczesną miażdżycą. Pol Przegl Kardiol, 2000; 2: 117-25.
7. Mortala JF, Yen SSC. The effect of oral dehydroepiandrosterone on endocrine metabolic parameters in postmenopausal women. J Clin Metab, 1999; 71: 696-704.
8. Zgliszczyński S, Bednarek-Papierska L. Application of dehydroepiandrosterone (DHEA) in clinical practice. Does DHEA prevents from premature ageing? Pol J Endocrinol, 2002; 53: 585-95.
9. Bednarek-Tupikowska G, Milewicz A, Kosowska B, Bohdanowicz-Pawlak A, Ściborski R. The influence of DHEA on serum lipids, insulin and sex hormone levels in rabbits with induced hypercholesterolemia. Gynecol Endocrinol, 1995; 9: 23-8.
10. Wolkowitz OM, Reus VI, Keebler A, Nelson N, Friedland M, Brizendine L, Roberts E. Double-blind treatment of major depression with dehydroepiandrosterone. Am J Psychiatry, 1999; 156: 646-9.
11. Moffat SD, Zonderman AB, Harman SM, Blackman MR, Kawas C, Resnick SM. The relationship between longitudinal declines in dehydroepiandrosterone sulfate concentrations and cognitive performance in older men. Arch Intern Med, 2000; 160: 2193-8.
12. Smith BJ, Buxton JR, Dickeson J, Heller RF. Does beclomethasone dipropionate suppress dehydroepiandrosterone sulphate in postmenopausal women? Aust NZJ Med, 1994; 24: 396-401.
13. Khorram O, Vu L, Yenn SS, Activation of immune function by dehydroepiandrosterone (DHEA) in age advanced men. J Gerontol A Biol Sci Med Sci 1997; 52: M 1-7.
14. Folstein MF, Folstein SE, Mc Hugh PR. "Mini Mental State" a practical method for grading the cognitive state of the patients for the clinician. J Psychiatr Res, 1975; 12: 189-98.
15. Yesevage JA, Brink TL. Development and validation of geriatric depression screening scale: a preliminary report. J Psychiatr Res, 1983; 17: 37-49.
16. Thomas G, Frenoy N, Legrain S, Sebag-Lanoe R, Baulieu E-E, Debuire B. Serum dehydroepiandrosterone sulfate levels as an individual marker. J Clin Endocrinol Metab, 1994; 79: 1273-6.
17. Sulcova J, Hill M, Hampl R, Starka L. Age and sex related differences in serum levels of unconjugated dehydroepiandrosterone and its sulphate in normal subjects. J Endocrinol, 1997; 154: 57-62.
18. Zdrojewicz Z, Kęsik S. Dehydroepiandrosteron (DHEA) – hormon młodości? Wiad Lek, 2001; 54: 693-703.
19. Mitchell LE, Sprecher DL, Borecki IB, Rice T, Laskorzewski PM, Rao DC. Evidence for an association between dehydroepiandrosterone sulfate and non fatal, premature myocardial infarction in males. Circulation, 1994; 71: 696-704.
20. Barret-Connor E, Goodman-Gruen D. Dehydroepiandrosterone sulfate does not predict cardiovascular death in postmenopausal women. The Rancho Bernardo Study. Circulation, 1995; 91: 1757-60.

21. Barret-Connor E, Kritz-Silverstein D, Edelstein SL. A prospective study of dehydroepiandrosterone sulfate (DHEAS) and bone mineral deusity in older men and women. Am J Epidemiol, 1993; 137: 201-6.

22. Nasman B, Olsson T, Backstom T. Serum dehydroepiandrosteron sulfate in Alzheimer`s disease and in multi-infarct dementia. Biol Psychiatry, 1991; 30: 684-90.

23. Kalmijn S, Launer LJ, Stolk RP. A prospective study on cortisol, dehydroepiandrosterone sulfate, and cognitive function in the elderly. J Clin Endocrinol Metab, 1998; 83: 3487-92.