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Dehydroepiandrosterone sulphate and androstenedione concentration in the serum of male patients with chronic hepatitis C

Chronic hepatitis C (CHC) infection is a significant health problem in Poland and worldwide. The clinical course of chronic CHC infection is usually asymptomatic but may lead to more aggressive liver diseases such as cirrhosis or hepatocellular carcinoma. The serum concentration of suprarenal androgens in patients with CHC infection has not been reported in medical literature, yet. Previous data concern estimation of the serum concentration of steroids in patients with acute hepatitis and liver cirrhosis caused by different etiologic agents. The aim of this study was to assess the serum concentration of suprarenal androgens in men suffering from CHC infection and the correlation between dehydroepiandrosterone sulfate (DHEAS) and androstenedione concentration in this group of patients.

MATERIAL AND METHODS

52 men were included in the study 26 of them being the control group of healthy men and the other 26 being a group of patients with CHC. The control group consisted of 26 healthy blood donors aged 21 to 37 years old. In those men all laboratory results were within normal limits. In order to eliminate the influence of age on DHEAS and androstenedione serum concentration we chose the control group in such a way that each of the examined patients had his age-appropriate healthy individual. The examined group consisted of patients aged 21 to 37 years old, hospitalized with CHC at the Department of Infectious Diseases of Medical University of Lublin. The diagnosis of CHC was based on the presence of HCV-RNA and anti-HCV antibodies in the serum, the histological examination of liver and biochemical results. In order to exclude infection with HAV and HBV, the single serum tests of anti-HAV IgM Ab, anti-HBc IgM Ab and HBsAg were done. The DHEAS and androstenedione concentrations were determined in the serum of patients twice, i.e.: on the 2nd day of hospitalization (test I) and following 4 weeks of hospitalization (test II). None of the examined men was diagnosed with any co-existing disease. Nor were infection markers of HAV and HBV found. The studied men did not undergo any pharmacological

treatment, either before the diagnosis of the disease or during the course of examinations. Standard serum investigations: bilirubin level, total protein level, ALAT, ASPAT and alkaline phosphatase (AP) activities were done at the same time as the hormone concentration tests. 26 patients underwent the liver biopsy during which the Menghini method and one-use Hepafix sets were used. No complications were observed. The histological examinations were done at the Department of Pathology of Medical University of Lublin. Each of the examined persons was informed about the aim of our research and gave his written consent for the study.

The blood for examination was obtained from ulnar veins at 7.30–8.00 a.m. with patients being with an empty stomach. It was collected in glass tubes for configuration. Some of the obtained serum was used for biochemical analysis, the rest was kept in plastic tubes, type Eppendorf, from the company Medlab, in the temperature of –200C, until the radioimmunological assay (RIA) examinations were done, but no longer than 4 months. We examined in the serum: total protein level with the use of prepared sets of reagents "Bili-T" (Bio Merieux, France); ALAT and ASPAT activities with the use of prepared sets of reagents "Enzyline ALAT/GTP 50 monoreactif" (Bio Merieux, France) and "Enzyline ASAT/GOT 50 monoreactif (Bio Merieux, France); alkaline phosphatase activity with the use of prepared sets of reagents "Enzyline PAL optimize" (Bio Merieux, France); HCV-RNA with RT-PCR method and with the use of prepared diagnostic sets "Digene Sharp Signal System" (Murex Diagnostics); anti-HCV antibodies with immunoenzymatic (EIA) method and with the use of prepared sets of reagents UBI HCV EIA (Organon Teknika, the Netherlands). The determination of HAV and HBV markers was done with the use of commercial tests of the 3rd generation, with immunoenzymatic method (EIA) and sets from the Abbot Company. The stored serum were defrosen all at the same time and used for determination of serum DHEAS and androstenedione levels. This was done by means of radioimmunological method (RIA) with the use of prepared set of reagents RIA-DHEA-S direct (Biotect, USA) and RIA – 4 androstendione, direct (Immunotech, France). The results were statistically analyzed (5,9). The analysis was made in 26 sick patients who had examinations done twice during their hospitalization time (tests I and II). The control group of 26 healthy men was also statistically analyzed. The levels of the studied features were characterized by the range of values (min-max), the arithmetical mean (M), standard deviation (SD), standard variation (S2) and the variation coefficient (V%). The statistical difference between the obtained values in both the patients and the control group was calculated with the appropriate Student-Neuman-Keuls test or c-Cochran and Cox test. We assumed 5% risk of conclusion error.

RESULTS

In all men included in the study, also in patients with CHC infection, serologic markers of HAV and HBV were not found in tested serums. The histopathological assessment of the liver bioptates revealed a low grade intralobular inflammatory-necrotic changes in 7 cases and moderate ones in 19 cases. Intralobular fibrosis was found in 21 men and features of fibrosis involving portal-biliary space were found in 5 cases. In 2 cases features of liver cells steatosis were found. In the examined group no cirrhosis features were found.

DHEAS CONCENTRATION IN THE SERUM OF THE EXAMINED GROUP

The results obtained from the analysis of DHEAS concentration in the serum of sick men and in the control group are summarized in table 1. In the control group the serum concentration of DHEAS ranged from 1400 ng/ml to 2700 ng/ml, mean 2042± 390 ng/ml. DHEAS concentration in the serum of patients suffering from CHC infection obtained from the first test ranged from 1100 ng/ml to 2700 ng/ml, mean 1946 ± 538 ng/ml. The results of DHEAS concentration in the serum of sick men obtained from tests I and II were compared to the controls, and no statistically significant differences were observed. The differences between mean values obtained from both

Table 1. Dehydroepiandrosterone sulfate (DHEAS) in serum of male patients with chronic hepatitis C

	Investi-gation	n	DHEAS ng /ml					V %	Comparison to the control group		
			min	max	M	S^2	SD		mean values differences	t	p
Control group	-	26	1400	2700	2042	152139	390.05	19.47	-	-	-
Examined group	I	26	1100	2700	1946	274209	523.65	27.12	-96	0.733	p>0.05
	II	26	1200	3100	1946	289785	538.32	28.21	-96	0.722	P>0.05

Min – minimum value, Max – maximum value, M – arithmetical mean, S^2–variation, SD – standard deviation, V% – variation coefficient, T – value of t-student test function, P – level of statistical importance

tests (I and II) and the control group was -96 and no statistical significance was observed. The variation coefficients (V%) for investigations I and II were similar and represented 27% and 28%, respectively. The serum concentration of DHEAS of patients with CHC infection was compared to the normal range calculated in the group of healthy men. We observed values lower than the mentioned normal range, which were 16% lower in test I and 20% lower in test II. The values higher than the normal range were not observed.

ANDROSTENEDIONE CONCENTRATION IN THE SERUM OF THE EXAMINED GROUP

The results obtained from the analysis of the androstenedione serum concentration of sick men and in the control group are summarized in table 2. The serum concentration of androstenedione in the control group ranged from 1.3 ng/ml to 3.0 ng/ml, mean 2.19 ± 0.537 ng/ml. Androstenedione serum concentration obtained in test I, in men with CHC infection, ranged from 1.0 ng/ml to 2.8 ng/ml, mean 2.15±0.549 ng/ml. In test II values ranging from 1.0 ng/ml to 2.8 ng/ml (mean 2.1 ± 0.536 ng/ml) were observed. There were no statistically significant

Table 2. Androstendione (A) in serum of male patients with chronic hepatitis C

	Investi-gation	n	A ng /ml					V %	Comparison to the control group		
			min	max	M	S^2	SD		mean values differences	t	p
Control group	-	26	1.3	3.0	2.19	0.288	0.537	24.92	-	-	-
Examined group	I	26	1.0	2.8	2.15	0.301	0.549	26.04	-0.04	0.274	p > 0.05
	II	26	1.0	2.8	2.1	0.288	0.536	26.27	-0.09	0.593	p > 0.05

Explanations as in table 1

ces between andro-stenedione serum concentration observed in both tests (I, II) in the sick men group, nor in the controls. The difference between mean values represented –0.04 in test I and – 0.09 in test II. These differences compared with the control group were incidental.The variation coefficients (V%) for both tests were similar and represented 26% and 25% for the control group. The serum concentration of androstenedione in the group of patients with CHC infection were compared to the normal range calculated in the control group. The values lower than minimum values in the group of healthy individuals were lower in 8% of patients in test I, and in 12% of patients in test II. The values higher than maximum values in the group of healthy individuals were not observed.

THE COMPARISON BETWEEN SERUM CONCENTRATION OF DHEAS AND ANDROSTENEDIONE

The results of the analysis of the correlation between serum concentration of the DHEAS and androstenedione in patients with CHC infection are presented in Table 3. As shown in table 3, there was no correlation in both investigations between serum concentration of DHEAS and androstenedione in the examined group (results not statistically significant).

Table 3. Correlation between dehydroepiandrosterone sulfate and androstendione in serum of examined patients

Compared investigations	s_{xy}	r_{xy}	n	t	P
I	85.154	-0.132	26	-0.654	P >0.05
II	82.249	-0.086	26	-0.42	P >0.05

s_{xy} – covariance, r_{xy} – correlation coefficient, t – value of t-student test function, p – level of statistical importance

DISCUSSION

The results of our study indicate that the serum concentration of DHEAS in men with CHC infection during hospitalization were not statistically different from the values obtained in the control group, and the observed differences were incidental. The values of DHEAS lower than the normal range were observed at the beginning of hospitalization in 16 % and after 4 weeks in 20% of patients. Bannister et al. observed low dehydroepiandrosterone serum concentration in patients with alcoholic liver cirrhosis, cirrhosis caused by unknown agents in primary biliary cirrhosis and in active chronic hepatitis (1). There were no statistically significant differences between andro-stenedione concentration in the serum of the examined men with CHC infection during hospitalization compared to the control group. The differences we observed were incidental. The androstenedione serum concentration lower than the normal range was observed at the beginning of hospitalization only in 8% and after 4 weeks in 12% of the examined men. The published data concerning androstenedione serum concentrations are controversial. Some authors point the elevation of androstenedione serum concentration in men and women with alcoholic cirrhosis, primary biliary cirrhosis, cirrhosis caused by unknown agents and also with active chronic hepatitis (1, 2, 6). Guechot et al. demonstrated in their report that the elevated androstenedione serum concentration returns to its normal values in male patients with alcohol induced or post viral hepatitis and with advanced liver disease subjected to liver transplantation (7). The data published in literature indicate that in male patients with liver cirrhosis the serum concentration of testosterone, both free and bounded, is elevated and is accompanied by the elevation of "week"

androgen – androstenedione (4,6,8). In our own study we did not observe a relationship between dehydroepiandrosterone and androstenedione serum concentration in male patients with CHC infection. The elevation of both dehydroepiandrosterone and androstenedione serum concentration were observed in men with acute hepatitis A infection (3). In conclusion, the results presented in this report demonstrated no changes in serum concentration of suprarenal steroids and the observed lower values were only incidental. The serum concentration of both tested hormones in patients with acute hepatitis and liver cirrhosis caused by hepatitis C virus remain to be elucidated.

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SUMMARY

In this study the dynamics of DHEAS and androstenedione serum concentration in male patients with CHC infection were analyzed. The study group consisted of 52 men, 26 of them being the control group of healthy men. The DHEAS and androstenedione serum concentration was determined twice with radioimmunological method (RIA). 1. Mean values of suprarenal androgens serum concentration in male patients with CHC infection were lower than in healthy men and the observed differences were incidental, 2. There was no correlation between dehydroepiandrosterone and androstenedione serum concentration in male patients with CHC infection.

Stężenie siarczanu dehydroepiandrosteronu (DHEAS) i androstendionu w surowicy krwi mężczyzn chorych na przewlekłe wirusowe zapalenie wątroby typu C (pzw C)

W pracy analizie poddano dynamikę stężenia DHEAS i androstendionu w surowicy krwi mężczyzn chorych na przewlekłe wirusowe zapalenie wątroby typu C. Badaniami objęto 52 mężczyzn, w tym 26 osób stanowiło grupę kontrolną. Stężenia DHEAS i androstendionu w surowicy krwi oznaczano dwukrotnie metodą radioimmunologiczną (RIA). 1. Średnie wartości stężenia androgenów nadnerczowych w surowicy krwi mężczyzn chorych na pzw C były niższe niż u mężczyzn zdrowych, przy czym różnice miały charakter losowy. 2. Nie wykazano współzależności pomiędzy stężeniem siarczanu dehydroepiandrosteronu a stężeniem androstendionu w surowicy krwi mężczyzn z pzw C.