



## Original Articles

# Pituitary reactivity, androgens and catecholamines in obstructive sleep apnoea. Effects of continuous positive airway pressure treatment (CPAP)

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We studied the effects of chronic nocturnal hypoxaemia due to obstructive sleep apnoea syndrome (OSAS) on the hypothalamic-pituitary-thyroid and hypothalamic-pituitary-testicular axes and on catecholamine and cortisol secretion. We investigated whether hormones other than catecholamines may serve as markers for chronic hypoxic stress and the possible effects of nasal continuous positive airway pressure (nCPAP) treatment on endocrine status.

Nocturnal oximetry was performed in 16 male patients with OSAS diagnosed by polysomnography, immediately before nCPAP treatment and in 11 of the patients the oximetry was repeated after 7 months of nCPAP therapy. Plasma and urinary catecholamines, luteinizing hormone (LH), testosterone, cortisol, thyroid stimulating hormone (TSH), prolactin (PRL), and the response of TSH and PRL to a thyroid releasing hormone (TRH) challenge test were measured immediately before and after 7 months of nCPAP treatment.

Subnormal LH and TSH and elevated serum cortisol as well as increased nocturnal urinary norepinephrine levels were found in patients prior to treatment; otherwise endocrine values were normal. There was a significant correlation between low pretreatment nocturnal arterial oxygen saturation and high plasma and urinary norepinephrine levels. The nCPAP treatment caused significant reduction in serum prolactin and TSH, and significant reduction in plasma epinephrine and urinary norepinephrine. The reduction in serum TSH and urinary norepinephrine was most pronounced in the subjects with the worst pretreatment nocturnal hypoxaemia. No other significant changes were found in basal hormone levels. The response to TRH challenge was normal before and after treatment and was not influenced by CPAP therapy.

OSAS is associated with elevated catecholamine and cortisol and decreased TSH and LH levels but a normal response to TRH challenge and a normal androgen status. Apart from catecholamines, none of the hormones studied is likely to serve as a specific marker for chronic hypoxic stress.

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## Introduction

There are often striking clinical resemblances between obstructive sleep apnoea syndrome (OSAS) and hypothyroidism (1). Elevated thyroid stimulating hormone (TSH) levels have also been found in patients suffering from other acute non-fatal non-thyroidal illnesses (2). In contrast, reduced secretion of basal TSH has been found in fatal non-thyroidal diseases (3,4). The effects of critical illness on stimulated TSH levels are varied (3,4). However, whether OSAS is accompanied by disturbances to the

hypothalamic-pituitary-thyroid axis has, to our knowledge, not been previously studied. Furthermore, treatment of hypothyroidism without discovery and treatment of any possible concomitant OSAS may lead to dangerous cardiac complications (5). Early detection of hypothyroidism is therefore probably of clinical importance in OSAS. Stimulation of TSH by thyroid releasing hormone (TRH) challenge may be a means of detection of subclinical defects in thyroid function (6). Subclinical hypothyroidism is defined as supranormal TSH increase in conjunction with normal levels of thyroid hormones (7).

Reduced secretion of testosterone (T) has been noted in men with OSAS and indeed severe (OSAS) is frequently associated with sexual and emotional disturbances such as decreased libido and depression (8,9). However, it is not known whether the hypothalamic-pituitary-thyroid axis and hypothalamic-pituitary-testicular axis are affected by

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the same mechanisms in OSAS. Therefore gonadotropins and sex hormones were also measured in the present study.

Increased excretion of catecholamines in OSAS has been noted in previous studies (10,11) and has been found to be primarily related to nocturnal hypoxaemia rather than to the frequency of apnoeas (10,12). The catecholamine levels may thus be regarded as markers of the chronic hypoxic stress induced by OSAS. Acutely augmented catecholamine secretion is associated with increased TSH secretion in healthy human subjects (13,14). However, it has not been elucidated whether a long-term elevation of catecholamine secretion due to OSAS is accompanied by increases in TSH secretion or in any other pituitary hormone.

Long-term nCPAP treatment effectively restores normal nocturnal breathing, nocturnal oxygenation and sleep patterns and most probably increases life expectancy even in severe OSAS (15). Our knowledge is, however, limited with regard to the effects of long-term nCPAP therapy on pituitary function.

The present investigation was undertaken to study the possible effects of nocturnal hypoxaemia on catecholamines and cortisol secretion as well as the hypothalamic-pituitary-thyroid and hypothalamic-pituitary-testicular axes and the effects of nCPAP treatment on endocrine status. Furthermore, we wanted to find out which hormones could serve as specific markers of chronic hypoxic stress.

## Patients and Methods

### SUBJECTS

Sixteen men with moderate to severe OSAS were included in the study. Anthropometric data are given in Table 1. All patients were heavy snorers and suffered from moderate to severe daytime somnolence. Three were treated for hypertension with diuretics or vasodilators. None suffered from labile diabetes mellitus, overt liver disease, severe alcohol abuse or unstable psychiatric disorder. No patient received any hormonal treatment. All patients gave their informed consent and the study was performed in accordance with the guidelines of the ethical committee of the Huddinge University Hospital. Data on serum and plasma hormones were compared with those obtained from 22 healthy men matched for age and as far as possible for body mass index (BMI). Urinary catecholamines were related to our routine clinical reference limits.

### SLEEP STUDIES

All patients were subjected to a daytime polysomnography after one night's sleep deprivation. Standard sleep variables, including an electroencephalogram ( $P_z$ - $F_z$ / $T_3$ - $C_2$ ), electro-oculogram and a submental electromyogram were recorded with surface electrodes (16). Respiratory movements of the thorax and the abdomen were monitored with pneumobelts connected to pressure transducers (Respirace Corp., UFI. Morro Bay, CA, U.S.A.). Nasal and oral airflow was determined by thermistors. The arterial oxygen

TABLE 1. Anthropometric, lung function and sleep study data in 16 patients

	Mean	± SEM	Range
Age (years)	51.3	3.7	26-74
BMI kg (m <sup>2</sup> ) <sup>-1</sup>	32.0	1.6	25.0-46.7
Syst. BP mmHg	143.8	4.3	110-170
Diast. BP mmHg	87.5	2.5	65-105
FEV <sub>1</sub> %P	84.6	5.9	48-111
FVC %P	81.6	5.4	47-104
PaO <sub>2</sub> kPa	10.9	0.4	7.4-13.4
PaCO <sub>2</sub> kPa	5.6	0.1	5.0-6.8
Apnoea index	43.3	4.7	20-65
ODI	39.2	7.0	8.6-93.3
MSaO <sub>2</sub> (%)	91.4	0.9	85.6-95.1
MminSaO <sub>2</sub> (%)	85.2	1.6	75.0-91.6
NNOS (%)	69.0	3.7	50.0-86.0

BMI=body mass index: 20-25 kg (m<sup>2</sup>)<sup>-1</sup>=normal; 25-30 kg (m<sup>2</sup>)<sup>-1</sup>=overweight; >30 kg (m<sup>2</sup>)<sup>-1</sup>=obese; FEV<sub>1</sub> %P=forced expiratory volume in 1 s in % predicted; FVC %P=forced vital capacity in % predicted; ODI=oxygen desaturation index; NNOS=nadir nocturnal arterial oxygen saturation; MSaO<sub>2</sub>=mean nocturnal arterial oxygen saturation; MminSaO<sub>2</sub>=mean minimal nocturnal arterial oxygen saturation.

saturation (SaO<sub>2</sub>) was traced by a finger pulse oximeter (Radiometer A/S, Copenhagen, Denmark). All variables were recorded by means of a polygraph. Apnoeas with a duration of at least 10 s were recorded and the number of apnoeas per sleep hour (apnoea index) was determined. In this way the patients' OSAS diagnosis was confirmed but data collected in conjunction with the daytime polysomnography were not utilized for statistical analysis.

After 6-12 months, the patients were subjected to a full night's pulse oximetry (Radiometer A/S). An arterial oxygen desaturation of at least 4% below the stable supine baseline level was considered significant. The oxygen desaturation index (ODI) was defined as the number of significant desaturations per hour of nocturnal recording. The mean arterial oxygen saturation (MSaO<sub>2</sub>) for the whole night was estimated. The minimal SaO<sub>2</sub> during each desaturation episode was recorded, and mean minimal arterial oxygen saturation (MminSaO<sub>2</sub>) for the whole night was calculated. The nadir nocturnal SaO<sub>2</sub> (NNOS) was recorded. All oximetry tracings were analysed by the same observer (T.B.).

### PHYSIOLOGICAL AND LABORATORY INVESTIGATIONS

The patients underwent a clinical examination including a supine blood pressure measurement on the day before the nocturnal oximetry. A 12-h nocturnal urinary collection for catecholamine assay was performed simultaneously with the pulse oximetry. Arterial blood gases were drawn on the

TABLE 2. Basal serum levels of steroid and pituitary hormones, plasma (P) and urinary (U) catecholamines in 16 untreated OSAS patients and 32 healthy controls matched for age and BMI

	Patients	Controls
Age (years)	51.3 ± 2.7	51.5 ± 2.5
BMI (kg (m <sup>2</sup> ) <sup>-1</sup> )	32.0 ± 1.4	29.6 ± 1.4
T (nmol l <sup>-1</sup> )	18.3 ± 1.3	18.5 ± 1.1
SHBG (nmol l <sup>-1</sup> )	15.0 ± 1.9 (n=4)	33.1 ± 2.7
Free T (nmol l <sup>-1</sup> )	0.51 ± 0.05 (n=4)	0.37 ± 0.03
LH (U l <sup>-1</sup> )	3.0 (1-5) <sup>‡</sup>	6.7 (2-13)
Cortisol (nmol l <sup>-1</sup> )	489 ± 39*	391 ± 22
PRL (μg l <sup>-1</sup> )	6.5 (5.0-18.0)	6.0 (2.8-27.9)
TSH (U l <sup>-1</sup> )	1.5 (0.7-3.0)*	2.0 (1.0-3.1)
P-E (nmol l <sup>-1</sup> )	0.16 (0.05-0.59)	0.10 (0.05-0.20)
P-NE (nmol l <sup>-1</sup> )	2.10 (0.80-5.50)*	1.25 (0.80-1.70)
U-E (nmol l <sup>-1</sup> )	10 (7-46)	<30 <sup>§</sup>
U-NE (nmol l <sup>-1</sup> )	160 (68-447)	<178 <sup>§</sup>

Significant differences between patients and controls are denoted by \* =  $P < 0.05$ ; † =  $P < 0.001$ .

<sup>§</sup>Clinical reference limits.

For abbreviations, see text.

following morning (ABL 520, Radiometer A/S). Venous blood samples for hormone analysis were drawn at about 0800 h after an overnight fast. Serum and plasma were separated after centrifugation and stored at -20°C until analysis. A thyroid releasing hormone (TRH) stimulation test was performed after breakfast with i.v. injection of 200 μg of TRH (Thyrefact<sup>®</sup>, Hoechst A.G., Frankfurt, Germany). Venous blood samples for analysis of thyroid stimulating hormones (TSH) and prolactin (PRL) in serum were drawn immediately before and 20 and 60 min after injection of TRH. A normal TRH response in males above 40 years of age is characterized by an increase of ≥ 100% in TSH and PRL 20 min after injection of TRH (17,18). The response to the TRH stimulation is indicated as the maximum increase in hormone concentration above the basal level (the delta value).

Patients started their nasal CPAP treatment the night following the first night's oximetry. The CPAP pressure was increased stepwise over 2-4 nights until the oximetry tracing was free from desaturations. After 6-10 months of regular nocturnal nCPAP treatment, the patients underwent a second nocturnal oximetry, taken during ongoing nCPAP treatment, and all the above mentioned measurements were repeated. All statistical analysis was based solely on hormonal measurements and other data obtained in conjunction with the oximetries immediately before and after an average 7 months of therapy. Adherence to the treatment regime was ascertained by open questioning and clinical assessment of increased daytime alertness.

## HORMONE ASSAYS

Serum concentrations of PRL, luteinizing hormone (LH), testosterone (T) and cortisol were detected by radioimmunological methods and sex hormone-binding globulin

(SHBG) by an immunoradiometric method using commercial kits obtained from Diagnostic Products Corp., Los Angeles, CA (PRL, LH, T) and Orion OY, Turku, Finland (SHBG, cortisol). TSH was measured by a fluoroimmunoassay using a commercial kit from Wallac OY, Turku, Finland. Catecholamines in plasma and urine were determined by a modified high pressure liquid chromatography technique (19,20).

Practical detection limits and within and between assay coefficients of variation were: TSH 0.4 U l<sup>-1</sup>, 5.0% and 7.2%; PRL 1.4 μg l<sup>-1</sup>, 7% and 11%; LH 1.2 U l<sup>-1</sup>, 7% and 10%; T 0.1 nmol l<sup>-1</sup>, 6% and 10%; SHBG 6 nmol l<sup>-1</sup>, 5% and 11%; cortisol 11 nmol l<sup>-1</sup>, 5% and 7%. For plasma catecholamines, the total coefficient of variation (CV) was 18% at about 2.5 nmol l<sup>-1</sup> and for urinary catecholamines total CV was about 5% at the upper reference level (Table 2). Values below the practical detection limit were set to 1.0 U l<sup>-1</sup> for LH.

Apparent concentrations of free testosterone were calculated from values for total T and SHBG and a fixed albumin concentration of 42 g l<sup>-1</sup> by successive approximation using a computer program based upon an equation system derived from the law of mass action (21).

## STATISTICAL ANALYSIS

Normally distributed variables are expressed as arithmetic means and SEM; otherwise as median and range. Results before and after nCPAP treatment were compared by paired *t*-test or Wilcoxon's signed-rank test according to distribution. Correlations between variables were assessed by Spearman's rank correlation test or simple linear regression according to distribution. A *P*-value of below 0.05 was considered significant.

TABLE 3. Basal serum levels of steroid and pituitary hormones, increments in pituitary hormones following TRH challenge (delta-values), plasma (P) and urinary (U) catecholamines, in 11 patients with OSAS before and after 7 months of CPAP treatment

	Before treatment	After treatment
T (nmol l <sup>-1</sup> )	17.7 ± 1.8	16.7 ± 2.1
SHBG (nmol l <sup>-1</sup> )	13.7 ± 1.9 (n=3)	27.1 ± 6.5 (n=7)
Free T (nmol l <sup>-1</sup> )	0.50 ± 0.07 (n=3)	0.43 ± 0.04 (n=7)
LH (U l <sup>-1</sup> )	3.0 (1-5) <sup>‡</sup>	4.0 (1-7) <sup>†</sup>
Cortisol (nmol l <sup>-1</sup> )	510 ± 38*	431 ± 36
P-E (nmol l <sup>-1</sup> )	0.21 (0.07-0.59)	0.11 (0.05-0.36) <sup>§</sup>
U-E (nmol l <sup>-1</sup> )	10.0 (7-46.0)	10.0 (4.0-20.0)
P-NE (nmol l <sup>-1</sup> )	2.15 (1.1-5.5) <sup>†</sup>	2.00 (1.30-4.40) <sup>†</sup>
U-NE (nmol l <sup>-1</sup> )	236 (119-447)	136 (66-281) <sup>§</sup>
TSH (U l <sup>-1</sup> )	1.4 (0.7-2.6)*	1.1 (0.7-2.2) <sup>†§</sup>
Delta TSH (U l <sup>-1</sup> )	6.4 (2.8-11.3)	6.3 (2.9-13.6)
PRL (μg l <sup>-1</sup> )	6.7 ± 0.5	5.1 ± 0.3 <sup>§</sup>
Delta PRL (μg l <sup>-1</sup> )	18.0 (7.0-34.0)	16.1 (7.0-35.0)

Significant differences between pre- and post-treatment values are denoted by <sup>§</sup>=*P*<0.05. Significant differences between patients and controls are denoted by \*=*P*<0.05; †=*P*<0.01; ‡=*P*<0.001. For abbreviations, see text.

## Results

The 16 patients had a diastolic blood pressure close to the upper limit of normal. In eight subjects the diastolic blood pressure was at or above 90 mmHg. Daytime polysomnography showed a mean apnoea index of 43.3 ± 3.6 h<sup>-1</sup>. The nocturnal oximetry immediately before nCPAP treatment showed a mean oxygen desaturation index of 39.3 ± 5.3 h<sup>-1</sup>. Four patients suffered from a moderately restrictive impairment of ventilation exhibiting a forced vital capacity of less than 80% of predicted value (FVC %P). However, the group as a whole had a FVC %P within the normal range (Table 1). Daytime blood gases were within the normal range (Table 1). However, three patients were slightly to moderately hypoxaemic (*Pa*O<sub>2</sub> range: 7.4-9.9 kPa) and one had an increased *Pa*CO<sub>2</sub> (6.8 kPa).

After an average interval of 7 months, 10 patients treated with a mean CPAP pressure of 8.25 (range: 5-12.5) cm of H<sub>2</sub>O were restudied. Nocturnal oximetry during CPAP treatment showed that in most of the patients there were no significant desaturations and all patients had an ODI of less than 5 h<sup>-1</sup>. Another patient underwent uvulo-pharyngo-palato-plastic (UPPP) surgery. Assessment at about 6 weeks after the operation with a static-charge-sensitive bed showed that this apnoea index was less than 5 h<sup>-1</sup>. His hormonal measurements, performed about 2 months post-operatively, were included within the study. Eleven subjects were thus restudied.

The mean blood pressure, forced expiratory volume in 1 s (FEV<sub>1</sub>), forced vital capacity (FVC), and body mass index (BMI) remained unaltered after 7 months of CPAP treatment. For technical reasons these variables were measured in only eight individuals after treatment. All patients

experienced a reduction in their daytime somnolence due to the CPAP treatment.

Endocrine data for all 16 patients before treatment and in matched controls, data on urinary catecholamines and clinical reference values are given in Table 2. The patients had significantly elevated pretreatment levels of serum cortisol and significantly decreased TSH levels compared to the controls. The hormonal response to TRH challenge was normal. The patients had significantly elevated plasma NE levels compared to the controls and their median urinary NE excretion was close to the upper clinical reference limit. Normal T but decreased LH values were found before treatment. For technical reasons SHBG could only be determined in four patients before and in seven after nCPAP treatment. Low SHBG-values and free T within the upper range of normal were observed before treatment.

Endocrine data for the 11 patients subjected to treatment are given in Table 3. The treatment caused significant suppression in plasma E and in urinary NE and in basal TSH and PRL. No other significant effects of the treatment on pituitary hormones were noted. Median values for LH were still significantly lower in the patients following treatment than in healthy subjects. There was no significant difference in SHBG between treated patients and controls. However, in the few patients where SHBG levels before and after treatment were available (*n*=3), these low values were not changed by the treatment. The treatment reduced s-cortisol in 75% of the patients. Although this change failed to attain significance, the level of cortisol was now normal, compared to controls. The median plasma NE was still close to the upper clinical reference limit, while the corresponding value for urinary NE was now clearly below this limit.

TABLE 4. Correlations between indices of pretreatment nocturnal respiratory disturbances on the one hand and pretreatment physiological and hormonal variables as well as the treatment induced change in hormonal levels on the other

	NNOS ( <i>r</i> )	Mmin.SaO <sub>2</sub> ( <i>r</i> )	ODI ( <i>r</i> )
BMI 1	-0.71*	-0.66*	0.76 <sup>†</sup>
Diastol. BP	-0.67 <sup>†</sup>	-0.66*	0.72 <sup>†</sup>
FEV <sub>1</sub> %P	0.63*	0.66*	-0.68*
P-norepinephrine	-0.60*	-0.71*	0.58*
P-epinephrine	-0.55	-0.63*	0.57*
U-norepinephrine	-0.75*	-0.72*	0.62(*)
% ch. TSH	0.47	0.70*	-0.36
% ch. U-norepin.	-0.93	1.00*	-0.83

BMI 1=body mass index before treatment; NNOS=nadir nocturnal arterial oxygen saturation; Mmin.SaO<sub>2</sub>=mean minimal arterial oxygen saturation; ODI=oxygen desaturation index; FEV<sub>1</sub> %P=forced expiratory volume in 1 s in % predicted; % ch.=the percentage change of a variable induced by 7 months of CPAP treatment; TSH=thyroid stimulating hormone.

(\*)*P*<0.05; \**P*<0.05; <sup>†</sup>*P*<0.01.

Correlations between pretreatment indices of nocturnal hypoxaemia on the one hand and BMI, blood pressure and endocrine data on the other are given in Table 4. Before treatment, indices of severe nocturnal hypoxaemia (low Mmin.SaO<sub>2</sub>, reduced NNOS and high ODI) were associated with high catecholamine levels, augmented BMI and high diastolic blood pressure. A low NNOS tended to correlate with a low total serum testosterone level (*r*=0.52, *P*=0.06). High pretreatment serum TSH values correlated with increased pretreatment P-NE levels (*r*=0.59, *P*<0.05).

The largest post-treatment reduction in urinary NE and in serum TSH was noted in the patients with the worst pretreatment nocturnal hypoxaemia (Table 4) and these changes correlated with each other (*r*=0.85, *P*<0.05). Serum T and SHBG values were positively correlated in the patients when pre- and post-treatment values were combined (*r*=0.70, *P*<0.05; *n*=11) and also in controls (*r*=0.53, *P*<0.01).

## Discussion

Elevated serum cortisol and plasma NE values in the presence of low serum TSH and LH levels were the main endocrine findings in untreated OSAS patients compared to control; however, the levels of pituitary hormones were still within normal range.

The increased nocturnal catecholamine secretion in OSAS is related to the degree of nocturnal hypoxia caused by this disease (10,12). In the present study correlations between pretreatment nocturnal respiratory disturbances and pretreatment endocrine variables were found only for

plasma and urinary catecholamines. Thus, it is rather unlikely that hormones other than catecholamines serve as specific markers for chronic hypoxic stress. Reduced nocturnal epinephrine but not norepinephrine levels following 8 days of nCPAP treatment have been reported previously (11,22). Such short-term treatment may be insufficient to regulate sleep patterns completely in OSAS (23,24) and thereby stabilize the central mechanisms regulating catecholamine secretion. Long-term nCPAP therapy has been found to reduce the level of plasma and urinary metabolites of norepinephrine (25). Significantly reduced levels of both catecholamines following nCPAP treatment were found in our study. The changes in nocturnal urinary norepinephrine were most pronounced in the subjects who were most severely affected by their disease. The reduction in norepinephrine which, to a certain extent, was paralleled by reduction in TSH in the present study, may reflect reduced chronic hypoxic stress following long-term nCPAP treatment. The post-treatment normalization of serum cortisol in our study group may be due to a long-term reduction of the level of stress in general.

Previous large cross-sectional studies have not shown an increased incidence of overt hypothyroidism in OSAS (8,26). However, thyroid status was assessed by thyroxin and thyroxin-binding globulin in only one of these two studies (8) and in the other the sensitivity of the radioimmunoassay for TSH was not indicated (26). Despite the high sensitivity for low levels of TSH of the immunoassay employed in the present study (3), no case of overt or subclinical hypothyroidism was found. Rather than being elevated, the TSH levels in our patients were lower than in the controls and the response to TRH challenge was perfectly normal before and after treatment (17). This may reflect an altered setting of the thyreostat in these patients. In the current study CPAP treatment caused a further small reduction in basal TSH. There may be possible factors contributing to this effect of long-term CPAP therapy. Firstly, it may imply that a subclinical thyroid malfunction at the hypothalamic level was present, at least in the subjects with the worst pretreatment nocturnal hypoxaemia (8,9). Secondly, the normal nocturnal increase in TSH and PRL secretion (27,28) is probably disturbed in OSAS. Disturbances of the normal sleep-related hormonal surge may result in increased TSH secretion during wakefulness (28). CPAP treatment in many cases restores normal sleep architecture and circadian rhythms (29), probably resulting in increased nocturnal PRL and TSH secretion, which in turn may contribute to the reduced daytime basal levels of these hormones found after treatment in our study. Thirdly, the reduction in catecholamine secretion after nCPAP-treatment may directly influence pituitary function or may indirectly cause reduced TSH production via its effects on the thyroid gland (13,14).

Normal LH levels have previously been demonstrated in patients with OSAS or chronic obstructive lung disease, but usually together with low levels of T (8,9,30,31). However, in contrast to previous studies, normal total and free T levels combined with subnormal LH concentrations were found in our patients, although the lowest total T levels were noted in subjects with the worst nocturnal

hypoxaemia. The findings of low LH levels in the presence of a normal T:SHBG ratio in the patients after treatment excludes an increased testicular negative feedback as the cause of the low LH levels.

Contrary to previous reports (8,9), nCPAP treatment did not significantly change total T levels. However, similar to earlier findings (8), free testosterone levels remained unaltered after nCPAP treatment. In the three subjects where both pre- and post-treatment SHBG values were available, almost identical values were found before and after treatment. Serum T and SHBG were positively correlated in the patients as well as in the controls. Circulating T and SHBG concentrations usually covariate in adult men, probably reflecting efforts to maintain a constant anabolic activity in the presence of changes in SHBG levels caused by, for example, alterations in nutritional state (32). Obesity is an extremely strong negative determinant of SHBG levels and consequently T levels are low in obese men (33). The discrepancy between our and other studies in pretreatment T levels may be explained by the inclusion of more severely diseased (8) OSAS patients in previous studies. BMI remained unaltered following nCPAP treatment in our patients. From this and from the unchanged SHBG levels in those where it was measured before and after treatment, it is reasonable to assume unchanged SHBG levels in the entire patient group. This is the probable reason for the unchanged total and free T levels in our study. The combination of subnormal LH levels in the presence of the normal androgen status found in our patients may suggest a resetting of the gonadostat, possibly at the hypothalamic level (8,9,34).

There was no correlation between LH or total T on the one hand and basal or stimulated TSH on the other. This may indicate that OSAS affects the hypothalamic-pituitary-thyroid and hypothalamic-pituitary-testicular axes by different mechanisms.

In conclusion, elevated catecholamine and cortisol levels were found in our group of OSAS patients in accordance with previous studies. In contrast to earlier investigations our patients had decreased TSH and LH levels but a normal response to TRH challenge and a normal androgen status. The decreased levels of catecholamines and reduced basal levels of TSH and prolactin following long-term nCPAP treatment probably reflect reduced chronic hypoxic stress as well as improved sleep quality. However, apart from catecholamines, it is less probable that any of the hormones studied serve as specific markers for chronic hypoxic stress.

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