Oral-appliance therapy obstructive sleep apnea-hypopnea syndrome
Hoekema, Aarnoud

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2007

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.
Chapter 4.4

Sexual function and obstructive sleep apnea-hypopnea: a randomized parallel trial evaluating the effects of oral-appliance and continuous positive airway pressure therapy

This chapter is based on the following publication:
Summary

Background  The obstructive sleep apnea-hypopnea syndrome (OSAHS) is associated with sexual dysfunction. Although treatment with continuous positive airway pressure (CPAP) has been demonstrated to improve sexual function, the effects of oral-appliance therapy are unknown. The aims of this study were to determine to what extent untreated male OSAHS patients experience sexual dysfunctions compared with control subjects, and secondly to evaluate the effects of oral-appliance and CPAP therapy.

Methods  Sexual functioning was determined in 48 OSAHS patients with the Golombok Rust inventory of sexual satisfaction (GRISS) and a testosterone measurement. GRISS outcomes were compared with 48 age matched male controls without any sexual problems. Patients were randomized for either oral-appliance or CPAP therapy. After a treatment of two to three months, the GRISS and testosterone measurement were repeated.

Results  Compared with controls, OSAHS patients had significantly more erectile dysfunction (mean: OSAHS patients 8.7 versus controls 6.8) and sexual dissatisfaction (mean: OSAHS patients 9.7 versus controls 8.1) as indicated by the GRISS. Significant changes in the GRISS or testosterone levels were not observed following oral-appliance or CPAP therapy. A correlation was demonstrated between the extent of erectile dysfunction at baseline and improvements in erectile function following treatment ($r=-0.547$, $p=0.000$).

Conclusions  This study confirms that male OSAHS patients show more sexual dysfunctions compared with aged matched control subjects. Although significant improvements in sexual functioning in neither the oral-appliance nor CPAP treated group could be established, our findings suggest that untreated OSAHS patients with pronounced erectile dysfunction experience some improvement following treatment.


Introduction

The obstructive sleep apnea-hypopnea syndrome (OSAHS) is a highly prevalent sleep-related breathing disorder affecting approximately 4% of the male and 2% of the female adults in the North-American population. The condition is characterized by disruptive snoring and repetitive upper airway collapse during sleep. In addition to various neurobehavioral and cardiovascular sequelae OSAHS is associated with sexual dysfunction. Several studies have demonstrated erectile dysfunction and decreased libido in substantial proportions of male patients diagnosed with OSAHS. In addition, up to 44% of patients with erectile dysfunction may be diagnosed with OSAHS.

The pathophysiology of sexual dysfunction in OSAHS patients is largely unknown. Besides psychosocial factors, sexual functioning is probably affected by several disease related factors including obesity, sleep fragmentation, nocturnal hypoxemia, and hypertension. Androgen deficiency has also been suggested as a mediator for sexual dysfunction in OSAHS patients. Both hypothalamic abnormality and dysfunction of the pituitary-gonadal axis have been implicated in the suppression of testosterone secretion in these patients.

Erectile dysfunction has been demonstrated to improve after successful treatment of OSAHS with continuous positive airway pressure (CPAP) or uvulopalato-pharyngoplasty. Moreover, several studies have shown improvements in testosterone levels as a result of these treatments. An increasingly popular treatment alternative for OSAHS is oral-appliance therapy. These intra-oral devices aim at relieving upper airway collapse during sleep by modifying the position of the mandible, the tongue and other pharyngeal structures. However, the effects of oral-appliance therapy on sexual function in OSAHS patients are unknown.

The aims of this study were to determine to what extent untreated male OSAHS patients experience sexual dysfunctions compared with control subjects, and secondly to evaluate the effects of oral-appliance and CPAP therapy on sexual functioning.

Methods

Patient selection

Patients were recruited through the Department of Home Mechanical Ventilation of the University Medical Center Groningen, The Netherlands. Male patients over age 20 who underwent polysomnography and were diagnosed as having OSAHS with at least five apneas or hypopneas per hour sleep (i.e., apnea-hypopnea index >5) were eligible.
Patients were selected based on medical and psychological, dental and sexual function related criteria. With respect to the medical and psychological criteria, patients were excluded in case of previous treatment of OSAHS, clearly reversible morphological airway abnormalities, endocrine dysfunction, a reported or documented history of severe cardiac or pulmonary disease, moderate or severe periodic limb movement disorder, or a psychological condition that precluded informed consent. Also excluded were patients with a dental status that could complicate oral-appliance therapy. With respect to criteria related to sexual function, patients were excluded if they did not have a heterosexual relationship, had diabetes mellitus, used beta-blocker medication, or in case of a condition other than OSAHS that could affect testosterone secretion (e.g., orchidectomy). A control group consisting of 48 subjects matched for age and gender, without any sexual problems, was recruited from a previous study. The control subjects were partners of gynecologist patients who consulted the outpatient Clinic for Gynecology of the Leiden University Medical Center (The Netherlands). The present study was approved by the Groningen University Medical Center’s ethics committee (METc 2002/032). Written informed consent was obtained from each patient before enrollment.

**Study design**

Patients were allocated to groups treated with oral-appliance or CPAP therapy by using block randomization. It was not possible to blind patients or clinicians to treatment assignment. At baseline, sexual function was determined by administering all OSAHS patients the Golombok Rust inventory of sexual satisfaction (GRISS). The control subjects had completed the GRISS in the previous study. In the OSAHS group testosterone levels were also measured and patients completed the Epworth sleepiness scale. Severity of disease was assessed based on the baseline polysomnographic study by using the apnea-hypopnea index (AHI). Patients were classified as having non-severe (AHI 5–30) or severe (AHI >30) OSAHS.

The oral appliance used in this study (Thornton Adjustable Positioner, Airway Management Inc., Dallas, TX, USA) positioned the patient’s mandible in a forward and downward position. By turning a propulsion screw incorporated anteriorly in the appliance, patients could adjust the mandibular advancement in 0.2-mm increments. When commencing oral-appliance therapy the mandible was set at approximately 50% of the patient’s maximum advancement. After having been accustomed to this protrusive position during a two-week period, patients were allowed to further adjust their appliance during a six-week period. To do so, patients were instructed to advance the mandible each night with one to two increments (i.e., 0.2 to 0.4 mm) whenever OSAHS-symptomatology persisted (e.g., snoring, apneas, hypopneas, or excessive sleepiness). This titration of the appliance was continued until symptoms abated or until further advancement caused discomfort.
CPAP-titration was performed during an afternoon nap. This technique, aimed at abolishing: all signs of apneas, hypopneas, and snoring—has been shown to be an appropriate procedure for the effective titration of CPAP. Following titration an eight-week follow-up period was arranged that allowed for habituation and, if necessary, adjustments of CPAP therapy.

After patients had used an oral appliance or CPAP for eight weeks, the treatment effect was assessed with a second polysomnographic study. For patients whose AHI was still ≥5, treatment was adjusted, if possible, to improve effectiveness. For this purpose, patients treated with an oral appliance were instructed to maximally protrude their mandible with the appliance. In patients treated with CPAP, the pressure was raised with 1 or 2 cm H₂O (depending on the severity of residual OSAHS with CPAP). In these patients, the follow-up period was extended with another four weeks. The effect was then assessed with a third polysomnographic study. This adjustment sequence was continued until the AHI was <5 or until the adjustments became uncomfortable for the patient. Follow-up review ended with a patient’s final polysomnographic evaluation or when a patient discontinued treatment because of poor tolerance or another reason. At their final follow-up review, patients were again administered the GRISS and Epworth sleepiness scale and underwent the testosterone measurement. In addition, treatment usage was evaluated at this stage by asking patients how many nights per week and how many hours per night they used their treatment.

Treatment was considered effective when the AHI either was <5 or showed “substantial reduction”, defined as reduction in the index of at least 50% from the baseline value to a value of <20 in a patient who had no symptoms while using therapy. Patients not meeting these criteria at their final review were considered “nonresponsive” to treatment. Patients who discontinued treatment for any reason were considered “nonadherent” to treatment.

**Polysomnography**

Polysomnography (Embla® A10 digital recorder, Medcare, Reykjavik, Iceland) for baseline and follow-up evaluations was conducted ambulatory in the patient’s home situation. Each study started 11 AM and stopped 9 AM the next morning. Outcomes were limited to the time in bed part of the study. Standardized criteria were used to score apneas and hypopneas, arousals, sleep stages, and periodic limb movements. All polysomnographic studies were evaluated and scored by one neurophysiologist (J.H. van der Hoeven) who was unaware of the patient’s treatment assignment.

**GRISS**

The GRISS is a self-report questionnaire that measures the most common psychosexual complaints. It has separate forms for men and women, each consisting of
Of the 48 patients included one patient, who was allocated to oral-appliance therapy, did not return for the follow-up examination (lost to follow-up review).

Abbreviations: CPAP = continuous positive airway pressure, OSAHS = obstructive sleep apnea-hypopnea syndrome.
28 items. The male questionnaire yields seven subscale scores reflecting sexual function in the following areas: impotence (i.e., erectile dysfunction), premature ejaculation, sensuality, avoidance, satisfaction, frequency and communication. The reliability of the GRISS and its predictive validity for the identification of sexual dysfunction within a sexualological population have been found to be satisfactory in English and Dutch samples. In addition, the subscales were found to be independent of social desirability. Each questionnaire was anonymized to guarantee the patients’ privacy.

Testosterone measurements
Testosterone, albumin and sex hormone-binding globuline (SHBG) levels were determined from venous blood samples that were drawn after an overnight fast between 8 and 10 AM. The total serum testosterone was measured using a radioimmunoassay (Packard 1500/1600/2700, Perkin-Elmer, Groningen, The Netherlands). Serum concentrations of SHBG were measured using a binding assay. Free and bioavailable testosterone, which more accurately reflect the levels of bioactive testosterone, were calculated using the formula by Vermeulen et al., in which the total serum testosterone concentration is corrected for both SHBG and albumin levels.

Total serum, free and bioavailable testosterone levels were compared with the lower normal limits as suggested by Vermeulen. Accordingly, subjects with a total serum testosterone level <11 nmol/l or free testosterone level <0.225 nmol/l or bioavailable testosterone level <5.3 nmol/l were considered to have a partial androgen deficiency.

Analysis
Statistical analyses were performed using the Statistical Package for the Social Sciences (version 12.0, SPSS Inc, Chicago, IL, USA). Means and standard deviations, or medians and interquartile ranges in skewed distributions, are reported. The outcomes on the GRISS were used as primary outcome measure. To determine the sexual function at baseline we compared the GRISS scores between OSAHS patients and the control subjects. At baseline, the number of patients with a partial androgen deficiency in the OSAHS group was determined. The degree of sexual dysfunction in OSAHS patients has been suggested to relate to disease severity. Pearson correlation coefficients were calculated to measure correlations between the AHI, lowest oxyhemoglobin saturation during sleep (minSaO2), Epworth sleepiness scale and the GRISS scores and testosterone levels. To evaluate the effects of oral-appliance and CPAP therapy on sexual function we evaluated changes in the GRISS scores and testosterone levels. To compare outcomes between the groups independent sample t-tests (Mann-Whitney U tests for variables with skewed distributions) were used. Differences between baseline
Sexual function

172

and follow-up outcomes in the oral-appliance and CPAP groups were compared with paired Student’s t-tests (Wilcoxon’s signed ranks tests for variables with skewed distributions). A significance level of \( p<0.05 \) was predefined in all cases.

**Results**

**OSAHS patients versus control subjects**

Between August 2003 and May 2005, a total of 48 male OSAHS patients were enrolled of whom 26 had non-severe and 22 had severe OSAHS (Figure 1, Table 1). Most of the 48 patients included were middle-aged and moderately obese. Both the mean systolic and diastolic blood pressures were elevated and 34 patients were classified as hypertensive.\(^{30}\) The Epworth sleepiness scale indicated mild to moderate excessive daytime sleepiness in most of the patients.

**TABLE 1.** Baseline characteristics of OSAHS patients and control subjects.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OSAHS patients(^*) (n = 48)</th>
<th>Control subjects(^*) (n = 48)</th>
<th>Difference(^†)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-severe OSAHS (no. patients)</td>
<td>26</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Severe OSAHS (no. patients)</td>
<td>22</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Age (years)</td>
<td>49 ± 9</td>
<td>48 ± 8</td>
<td>NS</td>
</tr>
<tr>
<td>Body-mass index (kg/m(^2))</td>
<td>31 ± 4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Neck circumference (cm)</td>
<td>43 ± 3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Consumption of alcohol (no. patients)</td>
<td>36</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Smoking (no. patients)</td>
<td>14</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Antihypertensive medication (no. patients)(^‡)</td>
<td>12</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hypertension (no. patients)(^‡)</td>
<td>34</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Blood pressure (mm Hg): - systolic</td>
<td>153 ± 21</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>- diastolic</td>
<td>93 ± 13</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Epworth sleepiness scale</td>
<td>13 ± 6</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Apnea-hypopnea index (no/hour)</td>
<td>27 (10–59)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>minSaO(_2) (%)</td>
<td>79 ± 9</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

\(^*\) Plus-minus values are means ± standard deviations, values with additives in parentheses are medians with interquartile ranges.

\(^†\) Significance for the difference in baseline characteristics between OSAHS patients and control subjects.

\(^‡\) Hypertension was defined as either the use of antihypertensive medication or a systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg.\(^{30}\)

Abbreviations: NS = not significant, minSaO\(_2\) = lowest oxyhemoglobin saturation during sleep, OSAHS = obstructive sleep apnea-hypopnea syndrome.
At baseline, the GRISS was completed by 24 and 19 patients with non-severe and severe OSAHS, respectively. OSAHS patients had a significantly higher score on the “erectile dysfunction” and “sexual dissatisfaction” subscale of the GRISS when compared with control subjects (Table 2). At baseline, a partial androgen deficiency was observed in one patient with non-severe OSAHS and in five patients with severe OSAHS. Significant correlations were demonstrated between the AHI and the “nonsensuality” subscale of the GRISS ($r=0.311$, $p=0.04$) and total serum testosterone levels ($r=-0.300$, $p=0.04$), respectively.

**Effects of oral-appliance and CPAP therapy**

Randomization yielded an oral-appliance group of 21 patients and a CPAP group of 27 patients (Figure 1). Follow-up outcomes were available in 20 and 27 patients in the oral-appliance and CPAP group, respectively (one patient lost to follow-up review). At final follow-up review, the mean advancement of the mandible with the oral appliance was 81 ± 20% of the maximum advancement. The mean CPAP pressure was 8.1 ± 1.7 cm H$_2$O at final review. The median period to final review was 82 (interquartile range 69–103) days in the oral-appliance group and 76 (interquartile range 63–109) days in the CPAP group ($p>0.05$).

### Table 2. Baseline sexual function of OSAHS patients and control subjects.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Range</th>
<th>Direction of improvement</th>
<th>OSAHS patients* (n = 48)</th>
<th>Control subjects* (n = 48)</th>
<th>Difference†</th>
</tr>
</thead>
<tbody>
<tr>
<td>GRISS‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- erectile dysfunction</td>
<td>4–20</td>
<td>-</td>
<td>8.7 ± 3.8</td>
<td>6.8 ± 2.6</td>
<td>$p=0.01$</td>
</tr>
<tr>
<td>- premature ejaculation</td>
<td>4–20</td>
<td>-</td>
<td>9.3 ± 2.9</td>
<td>8.3 ± 2.5</td>
<td>NS</td>
</tr>
<tr>
<td>- nonsensuality</td>
<td>4–20</td>
<td>-</td>
<td>5.7 ± 2.0</td>
<td>5.2 ± 2.1</td>
<td>NS</td>
</tr>
<tr>
<td>- avoidance</td>
<td>4–20</td>
<td>-</td>
<td>4.9 ± 1.6</td>
<td>4.4 ± 0.9</td>
<td>NS</td>
</tr>
<tr>
<td>- sexual dissatisfaction</td>
<td>4–20</td>
<td>-</td>
<td>9.7 ± 4.2</td>
<td>8.1 ± 2.6</td>
<td>$p=0.03$</td>
</tr>
<tr>
<td>- infrequency</td>
<td>2–10</td>
<td>-</td>
<td>6.6 ± 1.9</td>
<td>6.0 ± 1.4</td>
<td>NS</td>
</tr>
<tr>
<td>- noncommunication</td>
<td>2–10</td>
<td>-</td>
<td>4.4 ± 1.9</td>
<td>4.6 ± 1.9</td>
<td>NS</td>
</tr>
<tr>
<td>Total serum testosterone (nmol/l)</td>
<td></td>
<td></td>
<td>17 ± 6</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Free testosterone (nmol/l)</td>
<td></td>
<td></td>
<td>0.39 ± 0.14</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Bioavailable testosterone (nmol/l)</td>
<td></td>
<td></td>
<td>9.6 ± 3.3</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

* Plus-minus values are means ± standard deviations.
† Significance for the difference in baseline outcomes between OSAHS patients and control subjects.
‡ At baseline the GRISS was completed by 43 OSAHS patients.

Abbreviations: GRISS = Golombok Rust inventory of sexual satisfaction, NS = not significant, OSAHS = obstructive sleep apnea-hypopnea syndrome.
TABLE 3. Baseline and follow-up characteristics of oral appliance and CPAP treated patients.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Oral appliance (n = 20)*</th>
<th>CPAP (n = 27)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Follow-up review†</td>
</tr>
<tr>
<td>Non-severe OSAHS (no. patients)</td>
<td>13</td>
<td>-</td>
</tr>
<tr>
<td>Severe OSAHS (no. patients)</td>
<td>7</td>
<td>-</td>
</tr>
<tr>
<td>Age (years)</td>
<td>48 ± 8</td>
<td>-</td>
</tr>
<tr>
<td>Body-mass index (kg/m²)</td>
<td>28 ± 3</td>
<td>-</td>
</tr>
<tr>
<td>Neck circumference (cm)</td>
<td>43 ± 3</td>
<td>-</td>
</tr>
<tr>
<td>Epworth sleepiness scale</td>
<td>11 (5–16)</td>
<td>5 (2–7)</td>
</tr>
<tr>
<td>Apnea-hypopnea index (no/hour)</td>
<td>21 (10–31)</td>
<td>2 (0–9)</td>
</tr>
<tr>
<td>minSaO₂ (%)</td>
<td>82 ± 5</td>
<td>90 ± 4</td>
</tr>
<tr>
<td>Treatment usage</td>
<td>-</td>
<td>7.0 ± 0.2</td>
</tr>
<tr>
<td>- treatment use: nights per week</td>
<td>-</td>
<td>7.1 ± 1.1</td>
</tr>
</tbody>
</table>

* Plus-minus values are means ± standard deviations, values with additives in parentheses are medians with interquartile ranges.
† The median period to final follow-up review was 82 (interquartile range 69–103) days in the oral-appliance group and 76 (interquartile range 63–109) days in the CPAP group (p>0.05).
‡ Significance for the difference between baseline and follow-up values within treatment group.
§ p=0.000 for the difference in baseline or follow-up outcomes between the oral-appliance and CPAP group.
|| p=0.01 for the difference in baseline or follow-up outcomes between the oral-appliance and CPAP group.
¶ p=0.04 for the difference in baseline or follow-up outcomes between the oral-appliance and CPAP group.
Abbreviations: CPAP = continuous positive airway pressure, minSaO₂ = lowest oxyhemoglobin saturation during sleep, OSAHS = obstructive sleep apnea-hypopnea syndrome.
Oral-appliance therapy was effective for 18 of the 20 patients completing the final follow-up review (90%). The remaining two patients were “nonresponsive” to treatment. In the CPAP group, treatment was effective for 25 of the 27 patients completing the final review (92.6%). Of the remaining two patients, one was “nonresponsive” and one “nonadherent” to treatment. Both groups showed significant improvements in the Epworth sleepiness scale, AHI and minSaO₂ (Table 3). At baseline, the Epworth sleepiness scale and body-mass index were significantly higher and the minSaO₂ significantly lower in the CPAP group. Changes in the Epworth sleepiness scale and minSaO₂ were more pronounced with CPAP therapy. However, significant differences between both groups were not observed at final follow-up review. Patients in the oral-appliance group reported using treatment significantly more hours per night when compared with the CPAP group (Table 3).

Complete baseline and follow-up measurements of the GRISS were obtained in 14 and 24 patients in the oral-appliance and CPAP group, respectively. As a result of treatment, no significant changes in the GRISS or testosterone levels were observed in both treatment groups (Table 4). In addition, no significant differences in the baseline and follow-up outcomes were noted between the oral-appliance and CPAP group. A significant correlation was demonstrated between the extent of erectile dysfunction at baseline and improvements in erectile function following treatment according to the GRISS ($r=-0.547, p=0.000$).

**Discussion**

This study confirms that male OSAHS patients show more sexual dysfunction when compared with control subjects. We could not establish significant improvements in sexual function or testosterone levels in either the oral-appliance or CPAP group. However, the extent of erectile dysfunction at baseline correlated significantly with the improvements in erectile dysfunction following treatment. These findings suggest that patients with pronounced complaints of erectile dysfunction experience some improvement following OSAHS treatment.

The presence of sexual dysfunction in untreated male OSAHS patients is supported by the results from this study. Although several previous studies have demonstrated erectile dysfunction in these patients, the nature of sexual complaints other than impotence generally remains unexplored. As indicated by the GRISS, it appears that sexual dysfunction in OSAHS patients is related to erectile dysfunction and sexual dissatisfaction. Other areas of sexual function, including premature ejaculation, avoidance, infrequency of sexual contact or noncommunication did not differ substantially between OSAHS patients and control subjects. Erectile dysfunction has been shown to be associated primarily with more severe disease. This observation, however, could not be corroborated...
### TABLE 4. Sexual function at baseline and follow-up review of oral appliance and CPAP treated patients.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Range</th>
<th>Direction of improvement</th>
<th>Oral appliance (n = 20)*</th>
<th>CPAP (n = 27)*</th>
<th>Difference†</th>
<th>Baseline</th>
<th>Follow-up review‡</th>
<th>Difference‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Baseline</td>
<td>Baseline</td>
<td></td>
<td></td>
<td>Follow-up review</td>
<td></td>
</tr>
<tr>
<td>GRISS§</td>
<td>4–20</td>
<td>-</td>
<td>7.9 ± 3.5</td>
<td>7.9 ± 4.0</td>
<td>NS</td>
<td>9.5 ± 4.2</td>
<td>8.6 ± 3.0</td>
<td>NS</td>
</tr>
<tr>
<td>- erectile dysfunction</td>
<td>4–20</td>
<td>-</td>
<td>9.5 ± 3.5</td>
<td>9.1 ± 2.5</td>
<td>NS</td>
<td>9.0 ± 2.7</td>
<td>9.2 ± 2.5</td>
<td>NS</td>
</tr>
<tr>
<td>- premature ejaculation</td>
<td>4–20</td>
<td>-</td>
<td>5.4 ± 2.0</td>
<td>5.6 ± 1.9</td>
<td>NS</td>
<td>5.8 ± 2.1</td>
<td>5.9 ± 2.1</td>
<td>NS</td>
</tr>
<tr>
<td>- nonsensuality</td>
<td>4–20</td>
<td>-</td>
<td>4.0 (4.0–5.0)</td>
<td>4.0 (4.0–5.0)</td>
<td>NS</td>
<td>4.0 (4.0–5.5)</td>
<td>4.0 (4.0–5.5)</td>
<td>NS</td>
</tr>
<tr>
<td>- avoidance</td>
<td>4–20</td>
<td>-</td>
<td>8.5 ± 3.9</td>
<td>8.8 ± 4.0</td>
<td>NS</td>
<td>10.2 ± 4.3</td>
<td>10.5 ± 4.3</td>
<td>NS</td>
</tr>
<tr>
<td>- sexual dissatisfaction</td>
<td>4–20</td>
<td>-</td>
<td>5.9 ± 2.0</td>
<td>6.0 ± 2.5</td>
<td>NS</td>
<td>7.0 ± 1.7</td>
<td>6.5 ± 1.7</td>
<td>NS</td>
</tr>
<tr>
<td>- infrequency</td>
<td>2–10</td>
<td>-</td>
<td>4.0 ± 1.9</td>
<td>4.2 ± 2.3</td>
<td>NS</td>
<td>4.6 ± 1.8</td>
<td>4.5 ± 1.8</td>
<td>NS</td>
</tr>
<tr>
<td>- noncommunication</td>
<td>2–10</td>
<td>-</td>
<td>19 ± 7</td>
<td>18 ± 6</td>
<td>NS</td>
<td>16 ± 5</td>
<td>16 ± 5</td>
<td>NS</td>
</tr>
<tr>
<td>Total serum testosterone (nmol/l)</td>
<td></td>
<td></td>
<td>0.43 ± 0.18</td>
<td>0.43 ± 0.13</td>
<td>NS</td>
<td>0.37 ± 0.11</td>
<td>0.39 ± 0.13</td>
<td>NS</td>
</tr>
<tr>
<td>Free testosterone (nmol/l)</td>
<td></td>
<td></td>
<td>10.8 ± 4.0</td>
<td>10.3 ± 3.3</td>
<td>NS</td>
<td>8.9 ± 2.5</td>
<td>9.2 ± 3.0</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Plus-minus values are means ± standard deviations, values with additives in parentheses are medians with interquartile ranges.
† The median period to final follow-up review was 82 (interquartile range 69–103) days in the oral-appliance group and 76 (interquartile range 63–109) days in the CPAP group (p>0.05).
‡ Significance for the difference between baseline and follow-up values within treatment group.
§ Complete baseline and follow-up measurements of the GRISS were obtained in 14 and 24 patients in the oral-appliance and CPAP group, respectively.
Abbreviations: CPAP = continuous positive airway pressure, GRISS = Golombok Rust inventory of sexual satisfaction, NS = not significant, OSAHS = obstructive sleep apnea-hypopnea syndrome.
by our findings, as significant correlations at baseline were only demonstrated between the AH1 and the nonsensuality subscale of the GRISS. Based on our results and those from previous studies it appears that sexual dysfunction in OSAHS patients primarily concerns erectile dysfunction.

Several mechanisms have been proposed that may explain the erectile dysfunction observed in OSAHS patients. Organic causes include nerve involvement caused by hypoxemia, vascular abnormalities as a result of nocturnal hypertension or increased sympathetic activity, and low levels of testosterone. The lowest oxyhemoglobin saturation during sleep and systolic and diastolic blood pressures in the OSAHS patients support the former two mechanisms for erectile dysfunction. As six patients were also considered to have a partial androgen deficiency, erectile dysfunction may be explained by low testosterone levels as well in some of our patients. However, when compared with the estimated prevalence in middle aged males, these numbers do not suggest an increased prevalence of androgen deficiency in our OSAHS patients. In addition to an organic cause, erectile dysfunction may also result from psychological causes, including excessive daytime sleepiness or depression. The Epworth sleepiness scale indicated mild to moderate excessive daytime sleepiness in most of the included patients. This factor may, therefore, offer a logical explanation as well. As causality was not addressed in this study, we cannot conclude whether the erectile dysfunction reported by our OSAHS patients had a predominant organic or psychological cause.

The total serum testosterone levels at baseline inversely correlated with OSAHS severity (i.e., AH1). Similar correlations have been demonstrated in previous studies and are thought to result from increased sleep fragmentation and reduced oxygenation, both of which are known to inhibit testosterone production. A greater testosterone deficiency in patients with more severe disease is also supported by the fact that we observed a partial androgen deficiency in only one patient with non-severe OSAHS whereas it was observed in five patients with severe OSAHS. However, it should be noted that obesity and aging may account for the lower testosterone levels in OSAHS patients with severe disease as well. It remains unclear to what extent testosterone levels played a role in the sexual dysfunction reported by the OSAHS patients in this study. The precise effect of testosterone in the sexual response cycle and on erectile function is complex and full of controversies.

The extent of erectile dysfunction at baseline correlated significantly with the improvements in erectile dysfunction following treatment. These findings suggest that patients with more pronounced complaints may experience an improvement in erectile dysfunction following OSAHS treatment. This concurs with the results from previous studies that demonstrated improvements in erectile dysfunction.
following OSAHS treatment with CPAP therapy or uvulopalatopharyngoplasty. However, we could not demonstrate significant improvements in sexual function following treatment in either the oral-appliance or the CPAP group. Contrary to the results indicated by previous studies, we could not demonstrate significant changes either in testosterone levels following OSAHS treatment. At baseline, the majority of OSAHS patients had similar GRISS values compared with control subjects and testosterone levels within normal limits. The expectation of these “normal” baseline values improving following treatment would have been unrealistic. However, two other factors may also account for the non-significant changes in sexual function and testosterone levels following treatment. First, despite the fact that questionnaires were anonymized, approximately 20% of the patients refused to complete the GRISS at the final follow-up review. This may have resulted in a biased estimate of the effect of oral-appliance and CPAP therapy on sexual function. In addition, our study was of an explorative character and not based on a power calculation. Therefore, it is possible that a larger study sample would have yielded significant changes in testosterone levels or some aspects of sexual function. Secondly, we excluded patients in whom sexual function could be influenced by diabetes mellitus, beta-blocker medication or a condition other than OSAHS affecting testosterone secretion. Despite these precautions, sexual function in many of our OSAHS patients could still have been affected by the use of antihypertensive medication or an elevated blood pressure. A combination of the factors described above probably contributed to sexual function and testosterone levels not improving following treatment.

Compared with our control group, OSAHS patients displayed more sexual dysfunction on two of the GRISS subscales. The control subjects were partners of patients consulting an outpatient clinic for gynecology with some of these gynecology patients reporting sexual problems on presentation. Although, none of the male control subjects reported any sexual problems, it could be argued that both partners of a couple suffer when one of them is sexually dysfunctional. Consequently, sexual function in our control subjects may have been an underestimate of a true population “standard.” Another potential limitation of our study was the fact that control subjects could only be matched for age. Although age is probably the most important factor in a healthy male population, it is not the only variable affecting sexual function. Obesity, sleep fragmentation, hypertension and antihypertensive medication are some of the confounding factors that may also contribute to sexual dysfunction. Therefore, other disease related factors may also have affected sexual function in our group of OSAHS patients. Finally, the randomization resulted in dissimilar baseline characteristics in the oral-appliance and CPAP group. This impedes a reliable comparison of oral-appliance with CPAP therapy.
This randomized parallel trial showed that OSAHS patients show more sexual dysfunction compared with aged matched control subjects. Sexual dysfunction in OSAHS patients appears to be related primarily to erectile dysfunction; however, it may also involve complaints of sexual dissatisfaction. As causality was not addressed, the precise origin for sexual dysfunction in our group of OSAHS patients remains unclear. Our findings suggest that patients with pronounced complaints of erectile dysfunction experience some improvement following OSAHS treatment. However, significant improvements of sexual functioning in either the oral-appliance or CPAP treated group could not be established in this study. These results warrant additional studies on the specific effects of oral-appliance and CPAP therapy in OSAHS patients suffering from sexual dysfunction.

Acknowledgement The authors wish to thank Dr. J.D.M. van Lankveld from the Department of Medical, Clinical and Experimental Psychology of the University of Maastricht (The Netherlands) and Dr. M. ter Kuile from the Department of Gynecology of the Leiden University Medical Center (The Netherlands) for their assistance and disposing of the relevant data regarding the control group.
REFERENCES

37. Fahmy AK, Mitra S, Blockack AR, Desai KM. Is the measurement of serum testosterone