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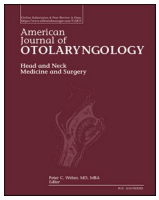

Assessment of sexual functions in male patients with obstructive sleep apnea

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ABSTRACT

Purpose: Obstructive sleep apnea is characterized by repetitive cessation of breathing during sleep. It affects different aspects of sexuality. We aimed to assess male sexual function & risk factors in obstructive sleep apnea patients.

Methods: This case control study included 2 groups, 45 healthy volunteers as control group and 45 patients with confirmed diagnosis of obstructive sleep apnea. All the participants were subjected to measurement of Body Mass Index, Full night polysomnography (only for patients group) and serum total testosterone, FSH and LH. The International Index of Erectile Function-5 and Hamilton Depression Scale questionnaires were filed out for all participants.

Results: The mean scores for all sexual domains were significantly lower among the patients group compared to the control group ($p<0.01$). The Hamilton score was significantly higher among the patients group compared to the control group ($p<0.0001$). The mean levels of Testosterone and LH were significantly lower among the patients group compared to controls ($p<0.0001$), There were significant correlations between disease severity and age ($r=0.48$, $p=0.001$), Body mass index (r=0.48, p=0.001), Hamilton score ($r=0.34$, $p=0.014$) International Index of Erectile Function 5 domain score ($r= -0.29$, $p=0.045$)Testosterone level (r= -0.29, $p=0.046$) and LH levels ($r= -0.104$, $p=0.049$).

Conclusion: We found that all domains of sexual function have been affected in patients group than controls. Their score was inversely related to the disease severity; which in turn has a complex interaction with other factors like age, obesity, hormones and psychological status. So when evaluating those patients, sexual dysfunction should be considered and assessed along with these factors.

1. Introduction

The main components of male sexual function include libido, erection, ejaculation and orgasm. Numerous physical and psychological disorders affect sexual functions such as libido, erectile dysfunction, inability to ejaculate, inability to achieve an orgasm [1].

Obstructive sleep apnea (OSA) is characterized by repeated breath cessation during sleep as a result of upper airway collapse. It is characterized by repeated upper airway obstruction, consequent blood oxygen desaturation and sleep fragmentation [2].

OSA prevalence ranged from 3% to 7%, with certain subgroups of the population bearing higher risk. Risk factors like age, gender, obesity, family history are important variables [3].

Previous studies have demonstrated male sexual dysfunction in OSA but mostly mentioning only erection problems. A study on Caucasian men with age range from 40 to79 years, was from the little researches who addressed the whole aspects of sexual dysfunction. But it assessed slightly aged patients [4].

We therefore found a need to design this study to assess all the sexual functions in male patients with OSA with different age group from 20 to 70 years old.

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1.1. Aim of the work

To assess Sexual Functions in Male Patients with Obstructive Sleep Apnea.

2. Subjects and methods

2.1. Study design and patient selection

This was a case control, descriptive study. Data were collected from 90 male who were divided in to two groups: Group (1) 45 patients; recruited from chest unit, with confirmed diagnosis of OSA who were referred to the sleep laboratory and did polysomnography. Group (2) 45 healthy volunteers as control group. Written informed consent obtained from patients enrolled in this study, which conducted according to the ethical standards of the Ethics Committee of the Suez Canal University. Patients were chosen according to the following inclusion and exclusion criteria: Inclusion criteria: Male Patients age from 20 to 70 year. Married (sexually active).Confirmed diagnosis of obstructive sleep apnea (except control group) Exclusion criteria: The patients using endocrinal diseases. Patients with Neuropathy. Patients with prostatic diseases. Patients with a history of pelvic trauma or spinal cord injury. Patients with Penile abnormalities. Alcohol dependence. Metabolic and neurological diseases. Chronic illness (e.g. liver disease, renal failure). Patient Use of any other drugs known to affect erection. All the participants were subjected to: Detailed history taking, clinical examination, full night polysomnography (except control group), assessment of sexual function by international index of erectile function (IIEF) (Appendix A [5], assessment of psychological state by Hamilton depression rating scale (HDS) (Appendix B) [6] & laboratory investigations as all participants underwent a morning venous blood draw after 12 h overnight fasting. The following were measured in Suez Canal university hospital laboratory: Total testosterone (Tt) using fully automated electrochemiluminescent immunoanalyzer Cobas 400 (Normal value: 1.88–8.8 ng/ml), Luteinizing hormone (LH) using fully automated electrochemiluminescent immunoanalyzer Cobas 4000(Normal value: 1.8–12.0 mIU/L) & Follicle-stimulating hormone (FSH) using electrochemiluminescent immunoanalyzer Cobas 4000 (Normal value: 1.3–19.3 mIU/ml). Assessment of OSA by full night polysomnography: All patients in group (1) were referred to sleep laboratory & underwent full-night polysomnography (SOMNO medics America) [7]. Apnea hypo-apnea index (***AHI***); a measurement of disease severity, was calculated (**AHI** equals total count of apnea and hypopnea events divided by the total sleep time). According to the level of (***AHI***), the patients were graded as having mild 5< (***AHI***) ≤15), moderate (15<(***AHI***) ≤30), or severe ((***AHI***) >30) OSA [8].

The sample size was calculated using the following equation [9]:

$$n = \frac{(Z_\alpha)^2 \times p \times q}{(d)^2}$$

where: Z_α=1.96.

P is expected prevalence of erectile dysfunction among OSA patients (70.6%) [10] q= 1-p d= is the accepted margin of error (d= p × β) (β= 0.2). Accordingly the calculated sample size was 40 patients. And by adding 10% of expected drop out, so n were 45 patients.

2.2. Statistical analysis

Collected data was coded, entered and analyzed using Microsoft Excel software. Data was then imported into statistical package for the social sciences (SPSS) version 21 software program for analysis. First we used one-sample Kolmogorov-Smirnov test for data normality. Qualitative data were described using number and percentage. Continuous variables were presented as mean ± SD (standard deviation). Chi-square test for association between categorical variables was used. Student *t*-test was used for comparing between the two groups. Analysis Of Variance (ANOVA test) was used for comparison of means of more than two groups. Pearson correlation was used for correlation between continuous data. For all above mentioned statistical tests done, the threshold of significance is fixed at 5% level (*p*-value).

3. Results

This case-control study included two groups (n=90); Group (1) 45 male patients with OSA attending Andrology and Infertility clinic, and Chest Unit of Internal Medicine Department, Suez Canal University Hospitals, and Group (2) 45 healthy controls. Each subject underwent thorough history taking, polysomnography for OSA diagnosis (except group 2), IIEF-5 and HDS. Tt, LH and FSH levels were also measured.

3.1. Descriptive data

The age in both groups where comparable as that of the patients group ranged from 32 to 69 years & the range in control group was 28–68. BMI measurements revealed that only 4.4% of patients have normal weight versus 20% of controls (Table 1). The mean score of AHI in patients group was 43.3±26.8 with a range of 5.2–130; with the majority of cases have severe OSA (62.2%)(Table 2). Regarding the prevalence of ED majority (86.7%) of the control group have normal erection, versus 37.8% of the OSA group(Table 3).

3.2. Analytic data

The mean scores of erectile function, orgasmic, sexual desire, intercourse satisfaction and overall satisfaction were statistically significantly lower among the OSA group compared to the control group (p<0.01)(Table 4). Depression was evident in patients group as the mean HDS was statistically significantly higher among the OSA group compared to the control group (p<0.0001)(Table 5). By analyzing laboratory findings the mean level of Tt was 3.3±0.9 and that of LH was 5.7±1.2 in OSA group and both were statistically significantly lower compared to the control group (p<0.0001), while there was statistically insignificant difference in FSH level between both groups (p>0.05) (Table 6). Many correlations were found between AHI and some of the studied factors. There were statistically significant positive correlations between AHI and age (r=0.48, p=0.001), BMI (r=0.48, p=0.001) and HDS (r=0.34, p=0.014). Meanwhile, there were statistically significant negative correlations between AHI and IIEF-5 score (r=−0.29, p=0.045), Tt levels (r=−0.29, p=0.046), LH levels (r=−0.104, p=0.049), while the level of FSH was insignificant (r=0.31, p=0.73) (Table 7).

4. Discussion

OSA is defined as repetitive breath cessation during sleep due to upper airway obstruction. It affects 5–20% of adults and has a deleterious effect on health [11].

In our study the age in both groups was comparable and this is beneficial to exclude the probable bias resulting from its negative effect

Table 1
Demographic characteristics of the two studied groups (n=90).

Variables	OSA (n=45)	Controls (n=45)
Age (years)	56.4±9.0 (32–69)	52.9±8.8(28–68)
BMI (kg/m^2):	32.5±5.6	27.6±3.3
Normal	2 (4.4%)	9 (20.0%)
Overweight	14 (31.1%)	24 (53.3%)
Obese I	12 (26.7%)	10 (22.2%)
Obese II	14 (31.1%)	2 (4.4%)
Obese III	3 (6.7%)	0 (0.0%)

Data were presented as mean ±SD, (Range) and number (percentage).

Table 2
Apnea hypo-apnea index (AHI) among the OSA group (n=45).

	AHI	OSA
Mean ±SD (Range)	43.3±26.8 (5.2–130)	
Mild OSA	6 (13.3%)	
Moderate OSA	11 (24.4%)	
Severe OSA	28 (62.2%)	

Data were presented as mean ±SD(Range) and number (percentage).

Table 3
The prevalence of erectile dysfunction (ED) in the two studied groups .

Variables	OSA n(%)	Controls n(%)
Normal erectile function	17 (37.8)	39 (86.7)
Mild ED	13(28.9)	6 (13.4)
Mild–moderate ED	6 (13.4)	0 (0.0)
Moderate ED	5 (11.1)	0 (0.0)
Severe ED	4 (8.8)	0 (0.0)
Total	45(100)	45(100)

Table 4
Comparison between the two studied groups according to IIEF-5 (n=90).

Variables	OSA (n=45)	Controls (n=45)	Mean diff.	p-Value
Erectile function	12.1±5.8	22.4±2.4	8.0	<0.0001**
Orgasmic	4.5±2.4	6.6±1.4	3.9	<0.0001**
Sexual desire	4.1±1.9	6.2±2.1	4.2	0.001**
Intercourse satisfaction	4.0±2.8	10.4±2.3	9.1	<0.0001**
Overall satisfaction	4.9±2.7	6.9±1.3	3.7	0.001**

** Significant *P*-Value <0.01.

Table 5
Comparison between the two studied groups according to HDS (n=90).

Variables	OSA(n=45)	Controls (n=45)	Mean diff.	p-Value
Mean HDS score	12.9±4.5	5.0±3.4	8.0	<0.0001**

HDS=Hamilton depression scale.
** Significant *P*-Value <0.01.

Table 6
Comparison between the two studied groups regarding to the laboratory findings.

Variables	OSA (n=45)	Controls (n=45)	Mean diff.	p-Value
Tt	3.3±0.9	6.0±1.5	2.7	<0.0001**
LH	5.7±1.2	8.7±0.6	3.0	<0.0001**
FSH	6.7±0.8	7.0±0.7	1.9	0.1

Tt=total testosterone (ng/ml), LH=luteinizing hormone (mIU/ml), FSH=follicular stimulating hormone (mIU/ml).
** Significant *P*-Value <0.01.

on the prevalence of ED in the study groups.

The prevalence of ED was much higher in patients group compare to controls.

Hanak and his colleagues used Brief Male Sexual Function Inventory (BMSFI) to study the association between obstructive sleep apnea (using snoring severity) and sexual dysfunction in 827 men and found that sexual satisfaction domain score; as assessed by BMSFI, was statistically significant lower in heavy snorer group (*P* value = 0.01) [4]. This agrees with our study, when OSA and control groups were compared according to their IIEF-5 domains scores. The mean score of satisfaction was significantly lower when compared to the control group. In addition we found that erectile function, orgasmic, sexual desire, intercourse and overall satisfaction were significantly lower among the OSA group. OSA patients usually suffer insomnia, headache, and fatigue which have a negative impact on patients quality of life including sexuality.

Table 7
Correlations between AHI and the studied variables according to Pearson correlation coefficient test.

Variables	Correlation coefficient (r)	p-Value
Age	0.478	0.001**
BMI	0.480	0.001**
HDS	0.342	0.014*
IIEF-5	- 0.290	0.045*
Tt	- 0.287	0.046*
LH	- 0.104	0.049*
FSH	0.311	0.73

r= Pearson correlation coefficient.
* Significant p-value <0.05.
** Singnificant *P*-Value <0.01.

The results of our study disagree with Seftel and his colleagues who assessed risk factors for OSA in 285 male with erection problems, and revealed that there was no association between OSA and ED [12]. We can explain that as the short self-reporting questionnaire used by Seftel and his colleagues to assess OSA was unsuitable tool for the definite diagnosis of OSA to ensure the correlation between sexual function and OSA meanwhile the patients in our study underwent full night polysomnography for definite diagnosis and assessment of the severity of OSA which explains the controversy with our results.

In our study depression among the two studied groups was evaluated by the mean of HDS score. It was statistically significant higher among the OSA group compared to the control group. And these results agree with smith and his colleagues who found that patients with OSA may also experience symptoms relating to the depression, anxiety, and stress [13].

Concerning the hormone level in our study the mean levels of Tt and LH were statistically significant lower among the OSA group compared to the control group ($p<0.0001$), while there was statistically insignificant difference between both groups regarding FSH levels ($p>0.05$). These results agree with the study of Luboshitzky and his colleagues in which they assessed the relation between sleep and diurnal testosterone level. They found a negative relationship between testosterone levels and sleep and that both testosterone and LH were significantly lower in patients group than controls [14].

Testosterone is important in the regulation of the expression of NO synthase (NOS) and PDE5 inside the penis which explains the sexual dysfunction in OSA patients.

In our study we assessed the correlation between the severity of OSA evaluated by Apnea Hypo-apnea Index (AHI) and different variables. We found that regarding age there was statistically significant positive correlation with AHI which agrees with Bliwise who had proposed a model that can account for these apparently competing age distributions. He speculates that sleep apnea is both an age-related and an age-dependent disorder [15].

Analyzing BMI measurements of our patients showed a statistically significant positive correlation with AHI. This agrees with Romero and his colleagues in their review on the interactions between body weight and OSA. They mentioned that obesity is a major factor for the development and progression of OSA [16].

By evaluation of the psychological status Habukawa and his colleagues assessed 17 males suffering from both OSA and depression that was resistant to treatment; using HDS, at the outset and after two months of CPAP treatment. HDS scores significantly decreased from 16.7 to 8.0 ($p<0.01$), two months after treatment and improvement of AHI. This goes with our results which revealed a statistically significant positive correlation between AHI and HDS (r =0.342 p=0014) [17].This is a cofactor in the negative impact of OSA on sexual functions.

So AHI in OSA patients have statistically significant correlation with different variables age, BMI, testosterone and psychological status

which all have a well-known effects on sexual function. This is in turn can explain our finding as there was a statistically significant negative correlation between sexual function; evaluated by IIEF-5 and AHI in our patients. Our results is consistent with Andersen and his colleagues study who investigated the prevalence of ED complaints associated with sleep disturbances and found that sleep apnea have a strong impact on erection and negatively affects sexual activity. They revealed that OSA syndrome were also significantly associated with a higher risk of ED complaints (OR=2.13) [18].

Our results were inconsistent with the results of Tokgoz and his colleagues who investigated the frequency and degree of ED in OSA patients and found that there was a decrease in their IIEF-5 scores. However, it was a non-significant decrease compared to the control group. This inconsistency with our results may due to in equality in numbers of controls & patients in their study (28 men as controls vs. 63 as patients) which wasn't the case in our study [19].

An important limitation of this study is the small sample size as correlation between OSA and male sexual functions should be done on larger scales and larger sample size. We suggest the usage of other tools for the assessment of ED including nocturnal penile rigidity and color Doppler ultrasonography.

In conclusion, we found that all domains of sexual function as assessed by IIEF-5 have been affected in patients with OSA more than normal controls and IIEF-5 score is inversely related to the severity of OSA; as measured by AHI, which in turn has a complex interaction with other factors like hormones, obesity, age and psychological status. So in OSA patients, sexual dysfunction should be considered and assessed by IIEF-5 along with these factors.

Data availability statement

Research data are not shared.

Funding source

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CRediT authorship contribution statement

All authors contributed significantly to the completion of this work. Details of each individual contribution are listed below.

Rashad M. Mostafa MD –Study design, application, data analysis revision, manuscript, final approval, senior author.

Noha M. Kamel MD, laboratory assessment of hormones.

Eman M. Elsayed - subject recruitment, data collection &analysis,

Hany M, Saad, MD - Study design, data analysis, manuscript, final approval, corresponding author.

Declaration of competing interest

The authors have no conflict of interests to disclose. This work has not been submitted for publication elsewhere.

Appendix A

INTERNATIONAL INDEX OF ERECTILE FUNCTION (IIEF)

Patient Questionnaire

HOSPITAL NUMBER (IF KNOWN) ☐☐☐☐☐☐☐

NAME .....

DATE OF BIRTH ☐☐/☐☐/☐☐ AGE ☐☐

ADDRESS .....

.....

.....

TELEPHONE .....

These questions ask about the effects that your erection problems have had on your sex life over the last four weeks. Please try to answer the questions as honestly and as clearly as you are able. Your answers will help your doctor to choose the most effective treatment suited to your condition. In answering the questions, the following definitions apply:

- sexual activity includes intercourse, caressing, foreplay & masturbation
- sexual intercourse is defined as sexual penetration of your partner
- sexual stimulation includes situation such as foreplay, erotic pictures etc.
- ejaculation is the ejection of semen from the penis (or the feeling of this)
- orgasm is the fulfilment or climax following sexual stimulation or intercourse

	Over the past 4 weeks:	*Please check **one** box only*
☐ Q1	How often were you able to get an erection during sexual activity?	0 No sexual activity 1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always
☐ Q2	When you had erections with sexual stimulation, how often were your erections hard enough for penetration?	0 No sexual activity 1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always
☐ Q3	When you attempted intercourse, how often were you able to penetrate (enter) your partner?	0 Did not attempt intercourse 1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always
☐ Q4	During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?	0 Did not attempt intercourse 1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always
☐ Q5	During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	0 Did not attempt intercourse 1 Extremely difficult 2 Very difficult 3 Difficult 4 Slightly difficult 5 Not difficult

Appendix B

HAMILTON DEPRESSION RATING SCALE (HAM-D)

(To be administered by a health care professional)

Patient Name _____ Today's Date _____

The HAM-D is designed to rate the severity of depression in patients. Although it contains 21 areas, calculate the patient's score on the first 17 answers.

1. DEPRESSED MOOD ☐ (Gloomy attitude, pessimism about the future, feeling of sadness, tendency to weep) 0 = Absent 1 = Sadness, etc. 2 = Occasional weeping 3 = Frequent weeping 4 = Extreme symptoms	**6. INSOMNIA - Delayed** ☐ (Waking in early hours of the morning and unable to fall asleep again) 0 = Absent 1 = Occasional 2 = Frequent
2. FEELINGS OF GUILT ☐ 0 = Absent 1 = Self-reproach, feels he/she has let people down 2 = Ideas of guilt 3 = Present illness is a punishment; delusions of guilt 4 = Hallucinations of guilt	**7. WORK AND INTERESTS** ☐ 0 = No difficulty 1 = Feelings of incapacity, listlessness, indecision and vacillation 2 = Loss of interest in hobbies, decreased social activities 3 = Productivity decreased 4 = Unable to work. Stopped working because of present illness only. (Absence from work after treatment or recovery may rate a lower score).
3.SUICIDE ☐ 0 = Absent 1 = Feels life is not worth living 2 = Wishes he/she were dead 3 = Suicidal ideas or gestures 4 = Attempts at suicide	**8. RETARDATION** ☐ (Slowness of thought, speech, and activity; apathy; stupor.) 0 = Absent 1 = Slight retardation at interview 2 = Obvious retardation at interview 3 = Interview difficult 4 = Complete stupor
4. INSOMNIA - Initial ☐ (Difficulty in falling asleep) 0 = Absent 1 = Occasional	**9. AGITATION** ☐ (Restlessness associated with anxiety.) 0 = Absent 1 = Occasional

2 = Frequent	2 = Frequent
5.INSOMNIA - Middle (Complains of being restless and disturbed during the night. Waking during the night.) 0 = Absent 1 = Occasional 2 = Frequent	**10. ANXIETY - PSYCHIC** 0 = No difficulty 1 = Tension and irritability 2 = Worrying about minor matters 3 = Apprehensive attitude 4 = Fears
11. ANXIETY - SOMATIC Gastrointestinal, indigestion Cardiovascular, palpitation, Headaches Respiratory, Genito-urinary, etc. 0 = Absent 1 = Mild 2 = Moderate 3 = Severe 4 = Incapacitatin	**7. INSIGHT** (Insight must be interpreted in terms of patient's understanding and background.) 0 = No loss 1 = Partial or doubtfull loss 2 = Loss of insig
12. SOMATIC SYMPTOMS - GASTROINTESTINAL (Loss of appetite , heavy feeling in abdomen; constipation) 0 = Absent 1 = Mild 2 = Severe	TOTAL ITEMS 1 TO 17: _____ 0 - 7 = Normal 8 - 13 = Mild Depression 14-18 = Moderate Depression 19 - 22 = Severe Depression > 23 = Very Severe Depression
13. SOMATIC SYMPTOMS - GENERAL (Heaviness in limbs, back or head; diffuse backache; loss of energy and fatiguability) 0 = Absent 1 = Mild 2 = Severe	**18. DIURNAL VARIATION** (Symptoms worse in morning or evening. Note which it is.) 0 = No variation 1 = Mild variation; AM ( ) PM ( ) 2 = Severe variation; AM ( ) PM ( )

. (*continued*).

14. GENITAL SYMPTOMS (Loss of libido, menstrual disturbances) 0 = Absent 1 = Mild 2 = Severe	**19. DEPERSONALIZATION AND** DEREALIZATION (feelings of unreality, nihilistic ideas) 0 = Absent 1 = Mild 2 = Moderate 3 = Severe 4 = Incapacitating
15. HYPOCHONDRIASIS 0 = Not present 1 = Self-absorption (bodily) 2 = Preoccupation with health 3 = Querulous attitude 4 = Hypochondriacal delusions	**20. PARANOID SYMPTOMS** (Not with a depressive quality) 0 = None 1 = Suspicious 2 = Ideas of reference 3 = Delusions of reference and persecution 4 = Hallucinations, persecutory
16. WEIGHT LOSS 0 = No weight loss 1 = Slight 2 = Obvious or severe	**21. OBSESSIONAL SYMPTOMS** (Obsessive thoughts and compulsions against which the patient struggles) 0 = Absent 1 = Mild

. (*continued*).

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