Main Article

A Prospective Study on Effect of Reproductive Hormones on Obstructive Sleep Apnoea in Women

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ABSTRACT

Introduction

Obstructive sleep apnoea patients are more likely to develop certain metabolic and endocrine conditions. During pregnancy, progesterone is linked to hyperventilation. These findings imply that progesterone improves airways. An increase in stage N2 sleep seen in the Luteal phase maybe responsible due to Progesterone. An improvement in sleep is seen in postmenopausal women due to oestrogen as demonstrated in a study.

Materials and Methods

The study aims to correlate the levels of Oestrogen and Progesterone in Pre and Post menopausal women with OSA, performed in a tertiary care centre for a duration of 2 years, wherein the patients were divided into 2 groups and the STOP BANG score and Anthropometry and hormonal levels measured and correlated with appropriate statistical method.

Results

There was a statistically significant correlation between the mean weight, neck circumference, nasopharyngeal, oropharyngeal airway diameters and levels of Oestrogen and Progesterone.

Conclusion

It is their synergistic action of progesterone and oestrogen which is responsible for the definitive improvement in patients with symptoms of OSA as identified and demonstrated in the study.

Keywords

Obstructive Sleep Apnoea; Oestrogen levels; Progesterone levels; Pre and Post menopausal

OAbout 4% of middle-aged men and 2% of women suffer from obstructive sleep apnoea (OSA), a disease marked by recurrent collapse of the upper respiratory tract during sleep. As the population ages and obesity rates rise, the disorder's prevalence is also rising. Obstructive sleep apnoea patients are more likely to develop certain metabolic and endocrine conditions, which can have major repercussions, such as a shortened life expectancy.[1] Breathing and sex hormones have an inverse effect. Progesterone, androgens, and oestrogens are all strongly suggested in the process, although it is unclear which hormone is most important. On the other hand, hormonal homeostasis is altered by sleep disorders like OSA.[2] During pregnancy, progesterone is linked to hyperventilation. According to Driver et al., women's upper respiratory tract resistance is lower during the luteal than follicular phases of the menstrual cycle.[3] These findings imply that progesterone improves airways. Sleep-related breathing difficulties are less common in postmenopausal women receiving oestrogen therapy than in women who have never had treatment. In patients receiving oestrogen-progesterone medication, the relationship is much more pronounced, suggesting that the hormones work in coordination.

More recently, studies were carried out on women

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who had gone through menopause as well as those who had not. In addition to SD, the investigators evaluated hormonal alterations in women with OSA. The FSFI score was lower in both groups than in the controls. Even after controlling for BMI, there was still a relationship between SD and OSA severity. Furthermore, there was a negative correlation between progesterone levels and FSFI scores in the premenopausal group. Severe OSA patients had lower levels of progesterone and oestradiol than controls. The scientists came to the conclusion that compared to healthy women, those with severe OSA have lower sexual function.[4] However, the hormonal condition of women was unaffected by either short-term or long-term CPAP therapy.[5]

Progesterone is a known GABA A receptor agonist.[6] An increase in stage N2 sleep seen in the Luteal phase maybe responsible due to Progesterone.[7,10] An improvement in sleep is seen in postmenopausal women due to oestrogen as demonstrated in a study.[8,9]

Progesterone increases the sensitivity of the respiratory centre to carbon dioxide, leading to hyperventilation and decreased arterial CO_2 levels. Hence during the luteal phase of the menstrual cycle the progesterone levels are elevated which cause an increase in minute ventilation and reduction in end-tidal CO_2.[14]

Oestrogen provides protection against Oxidative stress and upregulation of Hypoxic Inducible Factor 1 Alpha and hence decrease the Upper Airway Muscle Dysfunction; also, Oestrogen decreases chronic inflammation in upper airway tissues and decreases upper airway collapsibility associated with sleep apnoea. Oestrogen and progesterone improves the carotid body's ability to detect and respond to hypoxic conditions. Both hormones enhance genioglossus contractility through Oestrogen receptor α (ERα) pathways and also Oestrogen influences genioglossus muscle fibre composition, promoting Type I muscle fibres which are more fatigue-resistant.[15]

Materials and Methods

The study aims to correlate between the levels of Oestrogen and Progesterone levels in Pre and Post Menopausal women and Obstructive Sleep Apnoea.The study was done in a Tertiary Care centre wherein 40 subjects with symptoms of Obstructive Sleep Apnoea, 20 of whom were pre-menopausal and 20 of whom had attained menopause, post-menopausal. Patients presenting with symptoms of OSA to the OPD were considered for the study, appropriate history and examination were done following which patients giving consent for the study were taken as subjects. Those patients who had not consent for the study or not having any symptoms of OSA, diagnosed with endocrine disorders were excluded from the study. The pre-menopausal subjects were taken as Group A and post-menopausal subjects as Group B. The duration of study was from June 2023 to May 2025. Oestrogen and Progesterone levels are compared in Pre and Post Menopausal women with symptoms of Obstructive Sleep Apnoea and their BMI, Neck Circumference (measured at level of Laryngeal prominence/Adams Apple) and Anthropometry measures taken, X ray Nasopharynx and neck were taken for all subjects to measure Antero posterior diameters of Oropharyngeal and Nasopharyngeal Airways and correlated using STOP BANG Questionnaire (Scoring 1 for each of the following Loud Snoring, Often fatigue or sleepiness during the daytime, Observed to stop breathing during sleep, High Blood Pressure or current treatment on Hypertension, BMI - >35 kg/m^2, Age - >50 years, Neck Circumference - >40 cm, Male) and Apnoea Hypopnea index data obtained from sleep studies. Sleep studies (PolySomnography) were performed in the subjects of the study and their severity and symptoms of Obstructive Sleep Apnoea were correlated with their Body Mass Index and the levels of Oestradiol and Progesterone in Pre-menopausal and post-menopausal women.Apnoea Hypopnea Index (AHI)–measured in sleep studies conducted on all the subjects in the study.AHI <5 – Normal, AHI 5-14.9 – Mild Sleep Apnoea, AHI 15-29.9 – Moderate Sleep Apnoea, AHI ≥30 – Severe Sleep Apnoea.The data is categorized and appropriate statistical analysis done and results are obtained.

Results

The study was done on 40 subjects (20- premenopausal and 20- postmenopausal) and the appropriate anthropometric parameters compared and correlated with oestrogen and progesterone levels and results obtained.

Table I: Demographic details of age

GROUP	N	MINI-MUM	MAXI-MUM	MEAN	SD
Group A	20	33	39	35.7	1.9493
Group B	20	44	52	47.15	2.6611

Table II: Mean comparison of height and weight

PARAMETERS	GROUP	N	MEAN	SD	TEST STATISTIC	P VALUE
Height (ft)	Group A	20	5.4250	0.09105	-0.935	0.383
	Group B	20	5.4000	0.10260		
Weight (kg)	Group A	20	60.6000	7.21402	-5.176	<0.001*
	Group B	20	89.9000	5.44736		

Mann Whitney U test; pd≥0.05 considered statistically significant

The minimum age of the subjects in group A and B is 33 years and 44 years respectively and the maximum age is 39 years and 52 years respectively. Group A has a mean age of 35.7 and Group B has a mean age of 47.15.

The mean height (in feet) in Group A is 5.42ft and Group B is 5.40ft which did not show a significant statistical correlation, but the mean weight (in kg) which in Group A is 60.60kg and Group B is 89.90kg showed a significant statistical positive correlation.

Table III: Mean comparison of neck circumference

GROUP	N	MEAN (cm)	SD	t VALUE	P VALUE
Group A	20	31.9500	1.84890	–10.768	<0.001*
Group B	20	37.8000	1.57614		

Independent t-test; pd≥0.05 considered statistically significant

The neck circumference was measured at the level of Laryngeal prominence in the subjects using a measuring tape

The mean neck circumference in Group A is 31.95cm and in Group B is 37.80cm showed a statistically significant positive correlation with the symptoms and severity of OSA.

Table IV: Mean comparison of hormone level

PARA-METERS	GROUP	N	MEAN (pg/ml)	SD	TEST STATIS-TIC	P VALUE
Estradiol (pg/ml)	Group A	20	240.1250	191.53774	–5.410	<0.001*
	Group B	20	10.9610	5.43896		
Proges-terone (ng/ml)	Group A	20	7.8216	9.82813	–4.737	<0.001*
	Group B	20	0.1610	0.17038		

Mann Whitney U test; pd≥0.05 considered statistically significant

The mean levels of Oestradiol in Group A is 240.12pg/ml and in Group B is 10.96pg/ml showing a significant statistical positive correlation and the mean levels of Progesterone in Group A is 7.82ng/ml and Group B is 0.16ng/ml showing a statistically significant positive correlation suggesting both Oestradiol and Progesterone have an association with the symptoms and severity of OSA.

Table V: Mean comparison of airway parameters

PARAMETERS	GROUP	N	MEAN	SD	TEST STATISTIC	P VALUE
Nasopharyngeal (mm)	Group A	20	11.6200	1.84551	5.922	<0.001*
	Group B	20	7.9150	2.10270		
Oropharyngeal (mm)	Group A	20	10.2600	2.27813	-4.252	<0.001*
	Group B	20	6.8600	1.21759		

Nasopharyngeal - Independent t-test; pd≥0.05 considered statistically significant

Oropharyngeal - Mann Whitney U test; pd≥0.05 considered statistically significant

Nasopharyngeal airway and Oropharyngeal airway of subjects were measured using X ray cephalometry of subjects at the level of soft palate and hyoid bone.

The mean levels of Oropharyngeal and Nasopharyngeal airways are 11mm and 7.9mm in Group A, 10mm and 6.8mm in Group B respectively, with a negative correlation to the symptoms of OSA which are more in Group A subjects as compared to Group B subjects.

Table VI : Assesing Severity by using STOP BANG QUESTIONNAIRE

GROUP	MEAN STOP BANG SCORE
Group A (pre-menopausal)	4.2
Group B (post-menopausal)	6.6

Score <3 - Low risk of OSA

Score ≥3 - High risk of OSA

In our study the mean Stop Bang score of Group A (pre-menopausal) was around 4.2, mean Stop Bang score of Group B (post-menopausal) was around 6.6.

Among the 20 subjects in pre-menopausal group, 14 subjects had mild OSA with a Mean AHI of 8.6, 5 subjects had moderate OSA with a Mean AHI of 17.8, 1 subject had Severe OSA with a Mean AHI of 31.6.

Among the 20 subjects in post-menopausal group, 3 subjects had mild OSA with a Mean AHI of 12.8, 12 subjects had moderate OSA with a Mean AHI of 24.6, 5 subjects had severe OSA with a Mean AHI of 36.5.

The data shows a higher value of Mean AHI in Post-menopausal women when compared to pre-menopausal women in the study irrespective of the severity of OSA.

The values of Mean AHI when correlated with Mean levels of Oestradiol and Mean levels of Progesterone in both Pre-menopausal and in post-menopausal subjects with OSA shows a negative statistically significant correlation suggesting that severity of Obstructive Sleep Apnoea in the studied subjects is inversely proportional to the levels of Oestradiol and Progesterone.

Table VI: Severity of OSA and comparison of mean BMI and mean AHI in Pre-menopausal and post-menopausal women

	MILD OSA	MODERATE OSA	SEVERE OSA
Premenopausal women (Group A)	N = 14 Mean BMI = 21.8 Mean AHI = 8.6	N = 5 Mean BMI = 23.3 Mean AHI = 17.8	N = 1 Mean BMI = 32.4 Mean AHI = 31.6
Postmenopausal women (Group B)	N = 3 Mean BMI = 30.7 Mean AHI = 12.8	N = 12 Mean BMI = 33.4 Mean AHI = 24.6	N = 5 Mean BMI = 37.6 Mean AHI = 36.5

Table VII: Comparison of Mean AHI with levels of Oestradiol and Progesterone in Pre-menopausal and post-menopausal women

GROUP	MEAN AHI	MEAN LEVELS OF OESTRADIOL	MEAN LEVELS OF PROGESTERONE	STANDARD DEVIATION	CLINICAL SIGNIFICANCE
Premenopausal women	**13.5**	**240.12pg/ml**	**7.82ng/ml**	**7.1**	**Mild OSA**
Postmenopausal women	**24.6**	**10.96pg/ml**	**0.16ng/ml**	**7.9**	**Moderate OSA**

Discussion

The values showed a significant positive correlation between weight of the patient and symptoms of OSA, this is in correlation with study done by Carneiro-Barrera A et al.[12] Also, a similar significant negative correlation was obtained between the diameter of the nasal and oropharyngeal airway, neck circumference and symptoms of OSA and also its severity similar to study conducted by Pahkala R et al.[13] Similar results were seen in the study conducted by Sigurðardóttir ES et al[16] with regards to the levels of sex hormones and severity of AHI. A significant negative correlation was also found between the hormonal levels of progesterone, oestrogen and the anthropometric values and the symptoms of OSA suggesting that low levels of Oestrogen and Progesterone as seen in post-menopausal women is associated with an increase in the AHI levels, demonstrated in Sleep studies and hence an increase in the symptoms and severity of Obstructive Sleep Apnoea similar to studies conducted by Behan et al,[1] Stavaras C[4] and Sellix Et al.[7] A significant positive correlation is seen with Fattal D et al[17] study where BMI and Mean AHI scores are compared. Similar conclusion was made by Jehan S.et al[18] where they concluded that sleep pattern will be disturbed in post menopausal women due to hormonal deficiency and will increase the symptoms of OSA. In the study conducted by Wilhoit SC[19] et al, OSA in pre menopausal women is rare and symptoms of OSA in premenopausal is mainly due to individual anatomical variation of upper respiratory tract and obesity.In the study conducted by Qiu et al[20] a different mechanism was anticipated by which reductions in estrogen and/or progesterone hormones might cause instability in the ventilatory control system, leading to an overall increased risk for OSA and a degraded response to apneic events.Similar to our study this study also shows AHI is more in post menopausal women when compared to pre menopausal women. Similar results are seen in study conducted by Bixler et al [21] where the prevalence of sleep apnea was quite low in premenopausal women (0.6%) as well as postmenopausal women with hormone replacement therapy (HRT) (0.5%). Further, in these women the presence of sleep apnea appeared to be associated exclusively with obesity (BMI > or = 32.3 kg/ m2).

Conclusion

The study conducted on 40 female subjects of which 20 were premenopausal and 20 postmenopausal suggest that Obstructive sleep apnoea is more in the post-menopausal group, a possible reason could be the deficiency of the hormones Oestrogen and Progesterone after attaining menopause. While both Oestrogen and progesterone tend to improve the sleep as demonstrated in the study wherein a decrease in both levels of Oestrogen and Progesterone increases the Apnoea-Hypopnea Index and also the symptoms and severity of OSA. The negative correlation between hormone levels and AHI severity confirms that higher estrogen and progesterone levels are protective against OSA development and progression.

Further Longitudinal studies and Randomized Control Trials with HRT, preferably with large sample size may help understand the relation between Oestrogen and Progesterone and its effects on decreasing the Severity of OSA and if possible understand the Genetics of the hormonal influence and hence the different susceptibility of each individual to OSA.

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