Prevalence of obstructive sleep apnea in polycystic ovary syndrome

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Abstract

Background: There are many risk factors for obstructive sleep apnea syndrome (OSAS) which is a relatively widespread and chronic sleep problem that is recognized by recurrent partial or total obstruction in upper airway during sleep leading to interrupted hypoxia, arousals, excessive daytime sleepiness and increased sympathetic activity. One of these risk factors is polycystic ovary syndrome (PCOS) which is one of the commonest endocrine diseases at females' reproductive age, multiple questionnaires were used to estimate the prevalence of obstructive sleep apnea syndrome in polycystic ovary syndrome patients as Stop Bang questionnaire and Epworth sleepiness scale that used to estimate excessive daytime sleepiness in those patients.

Aim of the review is to screen for obstructive sleep apnea syndrome in patients with PCOS, prompt evaluation of both diseases and therefore decrease their serious cardio-metabolic complications.

Conclusion: There is significant association between OSAS and PCOS. Therapeutic complete interventions of PCOS may reduce the seriousness of OSA.

Keywords: Obstructive sleep apnea syndrome; Polycystic ovary syndrome; Stop Bang questionnaire; Epworth sleepiness scale.

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Introduction

Sleep is necessary and universal part of human existence. The physiologic and psychologic drive to sleep can overwhelm all other needs **(Aldrich et al, 1999)**. Obstructive sleep apnea (OSA) is a relatively widespread sleep disease that occurs due to Structural or anatomical causes that narrow space around the pharyngeal lumen, enlargement of soft tissues enfolding the pharynx, involving enlarged tongue, adenoids, and tonsils, a small bony compartment in which the airway is enclosed **(Haponik et al., 1983).**

The prevalence of Obstructive sleep apnea (OSA) is about2 to 5% for adult women and 3 to 7% for adult men **(Punjabi, 2008).**

Diagnosis of OSAS

Diagnosis of OSA begins with a sleep history. Stop-Bang questionnaire was especially appeared to meet the requirement for a trusted and simple tool for assessment of OSA, include a history of snoring, fatigue, or tiredness, observed apnea at night, treatment from high Bl/Pr, BMI>35kg/m^2, age>50yr, neck circumference>40cm, and male gender. The whole score ranges from 0 to 8. Subjects with a score of 0 to 2 according to STOP-Bang categorized as low risk for OSA, those with a score of 3 or more categorized as moderate to high risk for OSA **(Chung et al., 2008)**. While the Epworth sleepiness scale (ESS) is a group of questions which aims to estimate the grade of sleepiness during eight popular circumstances (sitting quietly in a public site (like a theater or a conference), taking a rest in the afternoon when situations allow, sitting and reading, sitting and speaking, as a passenger in a car for an hour without rest, watching television, in a car while waiting in the traffic for a few minutes, sitting after a lunch without alcohol) where patients are asked to rate on a scale of 0 to 3 if they would sleep in these eight situations, depend on their usual life in recent times. The whole score, thus, can vary from 0 to 24 in which a lower score means less sleepiness **(Johns, 1991).** The scale is interpreted as follows:

- >10 considered to be sleepy patients.
- ≤ 10 considered to be non-sleepy patients.

The physical examination should include estimation of BMI, manifestations of narrowing of upper airway, or existence of other diseases that may consider risk factors or complications for OSAS. Manifestations of OSAS that involve BMI≥ 30 kg/m2, increased neck circumference(> 16 inches in females,> 17 inches in males), Modified Mallampati score of 4 or 3 **(Friedman et al., 1999)**, the existence of lateral peritonsillar narrowing, retrognathia, enlarged tongue, enlarged tonsils, high arched palate, elongated uvula, nasal abnormalities (deviation, polyps, hypertrophied turbinate, valve abnormalities).After taking history and examination, subjects can be classified according to their risk for OSA. Those subjects with high risk should detect severity and sure diagnosis with (polysomnography)PSG, the severity of OSA must be determined to be treated appropriately **(Almeida et al., 2009)**.

Treatment of OSAS

Weight loss, improve apnea hypopnea index (AHI) with body mass index ≤25 kg/m²,avoid sedatives before sleep **(Morgenthaler et al., 2006)**.

Positive airway pressure (PAP) is the gold standard treatment for OSA (especially moderate to severe cases) and should be advised to all patients with OSA, First described by Sullivan in 1981, its action depends on producing pneumatic pressure splinting

the upper airway, so it is effective in reducing AHI **(Sullivan et al., 1981)**. PAP could be provided in different modes, continuous (CPAP), bilevel (BPAP), or auto-titrating (APAP) **(Gay et al., 2006)**.

Surgical treatment

Tonsillectomy, adenoidectomy, tongue reduction and tracheotomy.

Polycystic ovary syndrome is characterized by excess androgen, anovulation or oligo-ovulation and picture of polycystic ovaries. (5–20%) of women are affected by this disorder worldwide **(Azziz et al., 2005)**.

Diagnostic criteria for PCOS:

Diagnosis of PCOS needs at least existence of 2 of the following: (Clinical or laboratory hyperandrogenism or both - Oligo-ovulation or anovulation - picture of polycystic ovaries, after exclusion of other causes of hyperandrogenism) according to Rotterdam's criteria **(Fauser et al., 2004)**.

Management strategies for PCOS

Management of PCOS includes:

1- For irregular menstruation, hirsutism and acne: oral contraceptives **(Badawy et al., 2011).**

2- For excess androgen: spironolactone and finasteride are used to treat manifestations of hyperandrogenism and metformin can reduce serum androgen levels, improve insulin sensitivity and therefore insulin effects, and also cause weight loss **(Badawy et al., 2011)**.

3- For infertility: Weight loss, clomiphene citrate, gonadotropins, laparoscopic ovarian drilling, and in-vitro fertilization (IVF). Last studies said that letrozole and metformin have a significant effect in induction of ovulation.

Relationship between OSAS and PCOS

Last studies showed an unexpectedly high incidence of OSA in females with PCOS. Changes in sex steroids and obesity could be the main causes for increased incidence of OSA in this disease, and there may be strong relations between the existence and severity of OSA and the cardiometabolic disturbances that associated with PCOS. PCOS is distinguished by obesity, irregular menstruation and hyperandrogenism. These manifestations propose that PCOS patients may be at elevated risk for OSA **(Fogel et al., 2001)**.There are several studies discussed the relation between OSAS and PCOS as Vgontzas et al study that found the real prevalence of OSA according to polysomnography was 17% (9 of 53 PCOS patients were advised treatment for OSA) **(Vgontzas et al., 2001)**, while Fogel et al study where comparison between 18 overweight patients and 18 weight and age-matched controls, found that 66.7% of PCOS patients had OSAS in comparison with 16.7% of control **(Fogel et al., 2001)**.

Relation between hormonal changes and incidence of OSA in females with PCOS: There are many researches showing introduction of androgens to males or females can cause apnea in unaffected person previously **(Cistulli et al., 1994)**. There is also preliminary data said that OSA females have elevated levels of androgens than weight and age - matched controls **(Schwartz et al., 1989)**. Finally, we discovered that administration of short-term testosterone as replacement to hypogonadal men led to a statistically significant rising in the AHI **(Schneider et al., 1986)**. Biochemical manifestations of PCOS involve chronic anovulation and increased serum androgen. Increased serum androgen could predispose to OSA by several ways. First, we know that

testosterone can affect body composition, increased soft tissue deposition in the pharynx **(Whittle et al., 1999)**. This can reduce the lumen of the pharyngeal airway and affect its compliance, consequently, increase susceptibility to collapse. It is probable that increased levels of androgen may affect function of dilator muscles of the pharynx, we have found changes in these muscles between males and females, that maybe because of testosterone **(Popovic et al., 1995)**. Fogel and coworkers study found that AHI of overweight PCOS patients correlated with free and total testosterone levels **(Fogel et al., 2001)**. Yang and coworkers showed that total levels of testosterone were positively correlated with AHI in thin PCOS females without OSA manifestations, **(Yang et al., 2009)**.Tock and coworkers study showed relation between excess androgen and presence of OSA where 38 premenopausal women with PCOS were included, this study found that 50% of patients affected by OSA, levels of free testosterone were high, compared with just 15% of others without increased levels of testosterone **(Tock et al., 2014)**. Even after modify obesity, there is a clear and positive correlation between AHI or severity of sleep disordered breathing and free levels of testosterone **(Chatterjee et al., 2014)**. According to all these studies, it's obvious that excess androgens can affect the incidence of OSA in subjects with PCOS.

Relation between obesity and prevalence of OSA in PCOS women

Obesity is a common finding in both OSA and PCOS. Obesity may precipitate to OSA by increasing deposition of parapharyngeal fat leading to upper airway, reduced compliance of the thorax and decreased FRC because of deposition of fat in abdomen and thorax, and changes in respiratory control and neural compensatory mechanisms **(Punjabi, 2008)**. Obesity is commonly associated with PCOS **(Salehi et al., 2004)**, In PCOS women, there is typically central obesity (elevated waist-to-hip ratio) and it is discovered that central obesity carry a higher risk for OSA than general obesity **(Simpson et al., 2010)**. This also was illustrated in a Fogel and coworkers study where, there was remarkable consistence between central obesity and AHI **(Fogel et al., 2001)**. Accordant with all these data, Chatterjee and coworkers study demonstrated that waist circumference was higher in patients with PCOS and OSA than the others with PCOS only, and also positively correlated with the OSA severity **(Chatterjee et al., 2014)**. These researches together mostly involved obese patients, but in Yang and coworkers study, which only involving non-obese patients, found that in spite of the AHI in PCOS cases was not high enough to diagnose OSA, but patients with PCOS recorded AH events during sleep more than BMI and age-matched control group, so the risk of OSA is high in PCOS patients away from presence of obesity **(Yang et al., 2009)**.

OSA and metabolic dysfunction in PCOS

OSA consider an important cause for pathogenesis of metabolic complications in PCOS. Last reports say that there might be 2 sub-forms of PCOS,PCOS with or without OSA, and these 2 sub-forms might be accompanied with definite endocrine and cardiometabolic changes, but the group with PCOS and OSA together carry higher risk for CVS diseases and DM than the group without OSA and may take benefit from treatment reduce the severity of OSA **(Nitsche et al.,**

2010).OSA is separately a well-known risk for cardiovascular disease, insulin resistance and type 2 DM. Insulin resistance is also a common finding in both disorders and hence increased incidence of type 2 DM **(Dunaif et al., 1985)** and lipid abnormalities **(Wild et al., 1988)**. Insulin resistant is significantly higher in PCOS cases than weight-matched controls **(Dunaif et al., 1989)**. PCOS cases have an unexpectedly high prevalence of early-onset type 2 DM **(Ehrmann et al., 1999)** and consider an essential risk for HTN, coronary vascular disorders and dyslipidemia **(Ehrmann, 2005)**.

Conclusion:

High prevalence of OSAS in PCOS, so patients with PCOS, especially those with increased central obesity, should be accurately asked about symptoms suggestive of sleep apnea (**Fig.1**).

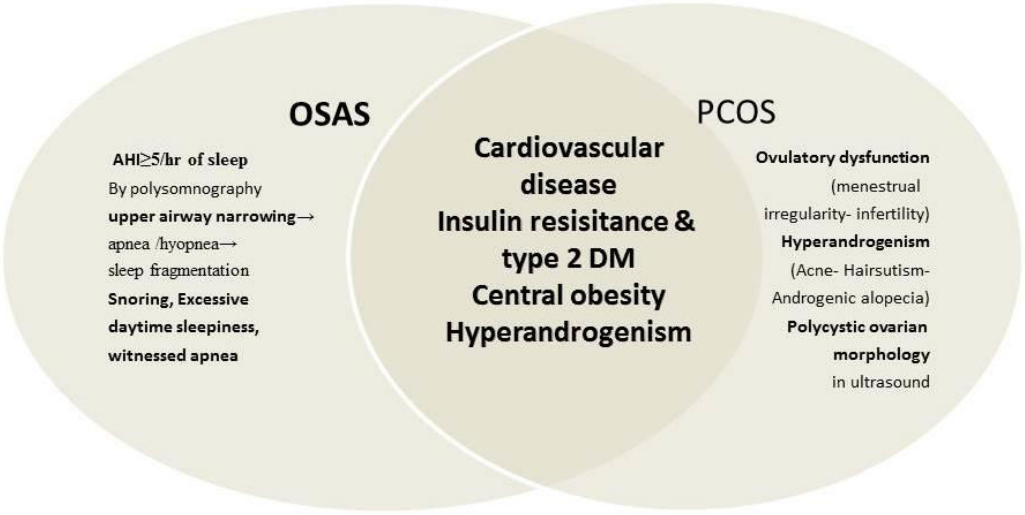

Fig.1. Summary of the mechanistic association of obstructive sleep apnea in polycystic ovary syndrome

References

- **Aldrich, Michael S, 1999.** Sleep medicine: Oxford University Press.
- **Almeida FR, Parker JA, Hodges JS, Lowe AA, Ferguson KA (2009).** Effect of a titration polysomnogram on treatment success with a mandibular repositioning appliance. Journal of Clinical Sleep Medicine, 5(3): 198-204.
- **Azziz R, Marin C, Hoq L, Badamgarav E, Song P. (2005).** Health care-related economic burden of the polycystic ovary syndrome during the reproductive life span. The Journal of Clinical Endocrinology & Metabolism, 90(8): 4650-4658.
- **Badawy A, Elnashar A. (2011).** Treatment options for polycystic ovary syndrome. International journal of women's health, 3, 25.
- **Chatterjee B, Suri J, Suri JC, Mittal P, Adhikari T. (2014).** Impact of sleep-disordered breathing on metabolic dysfunctions in patients with polycystic ovary syndrome. Sleep medicine, 15(12): 1547-1553.
- **Chung F, Yegneswaran B, Liao P, Chung Sharon A, Vairavanathan S, Islam S, et al. (2008).** STOP Questionnaire: A Tool to Screen Patients for Obstructive Sleep Apnea. Anesthesiology, 108(5):812-21.
- **Cistulli PA, Grunstein RR, Sullivan CE. (1994).** Effect of

testosterone administration on upper airway collapsibility during sleep. American journal of respiratory and critical care medicine, 149(2): 530-532.

- **Dunaif A, Hoffman AR, Scully RE, Flier JS, Longcope C, Levy LJ, et al. (1985).** Clinical, biochemical, and ovarian morphologic features in women with acanthosis nigricans and masculinization. Obstetrics and gynecology, 66(4): 545-552.
- **Dunaif A, Segal KR, Futterweit W, Dobrjansky A. (1989).** Profound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome. Diabetes, 38(9): 1165-1174.
- **Ehrmann DA. (2005).** Polycystic ovary syndrome. New England Journal of Medicine, 352(12): 1223-1236.
- **Ehrmann DA, Barnes RB, Rosenfield RL, Cavaghan MK, Imperial J. (1999).** Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome. Diabetes care, 22(1): 141-146.
- **Fauser, Chang, Azziz, Legro, Dewailly, Franks, et al. (2004).** Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Human reproduction, 19: 41-47.
- **Fogel RB, Malhotra A, Pillar G, Pittman SD, Dunaif A, White DP. (2001).** Increased prevalence of obstructive sleep apnea syndrome in obese women with polycystic ovary syndrome. The Journal of Clinical Endocrinology & Metabolism, 86(3): 1175-80.
- **Friedman M, Tanyeri H, La Rosa M, Landsberg R, Vaidyanathan K, Pieri S, et al. (1999).** Clinical predictors of obstructive sleep apnea. The Laryngoscope, 109(12): 1901-1907.
- **Gay P, Weaver T, Loube D, Iber C (2006).** Evaluation of positive airway pressure treatment for sleep related breathing disorders in adults. Sleep, 29(3): 381-40.
- **Haponik EF, Smith PL, Bohlman ME, Allen RP, Goldman SM, Bleecker ER. (1983).** Computerized tomography in obstructive sleep apnea: correlation of airway size with physiology during sleep and wakefulness. American Review of Respiratory Disease, 127(2): 221-226 .
- **Johns MW. (1991).** A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep, 14(6): 540-5.
- **Morgenthaler TI, Kapen S, Lee-Chiong T, Alessi C, Boehlecke B, Brown T, et al. (2006).** Practice parameters for the medical therapy of obstructive sleep apnea. Sleep, 29: 1031-1035 .
- **Nitsche K, Ehrmann DA. (2010).** Obstructive sleep apnea and metabolic dysfunction in polycystic ovary syndrome. Best Practice & Research Clinical Endocrinology & Metabolism, 24(5): 717-730.
- **Popovic, R. M., & White, D. P. (1995).** Influence of gender on waking genioglossal electromyogram and upper airway resistance. American journal of respiratory and critical care medicine, 152(2): 725-731 .
- **Punjabi N. M. (2008).** The epidemiology of adult obstructive sleep apnea. Proceedings of the American Thoracic Society, 5(2): 136-143.
- **Salehi M., Bravo-Vera R., Sheikh A., Gouller A., & Poretsky, L. (2004).** Pathogenesis of polycystic ovary syndrome: what is the role of

obesity? Metabolism, 53(3): 358-376.

- **Schneider B. K., Pickett C. K., Zwillich C. W., Weil J. V., McDermott M. T., Santen R. J., et al. (1986).** Influence of testosterone on breathing during sleep. Journal of applied physiology, 61(2): 618-623.
- **Schwartz S. M., Fry J. M., Eskin B. A. & Wallace T. (1989).** Hormonal status in premenopausal women with obstructive sleep apnea. Sleep Res, 18, 243-248.
- **Simpson L, Mukherjee S, Cooper MN, Ward KL, Lee JD, Fedson AC, et al. (2010).** Sex differences in the association of regional fat distribution with the severity of obstructive sleep apnea. Sleep, 33(4): 467-474.
- **Sullivan CE, Issa FG, Berthon-Jones M, Eves L. (1981).** Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. The Lancet, 317(8225) 862-865.
- **Tock L, Carneiro G, Togeiro SM, Hachul H, Pereira AZ, Tufik S, et al. (2014).** Obstructive sleep apnea predisposes to nonalcoholic Fatty liver disease in patients with polycystic ovary syndrome. Endocrine Practice, 20(3): 244-251.
- **Vgontzas AN, Legro RS, Bixler EO, Grayev A, Kales A, Chrousos GP. (2001).** Polycystic ovary syndrome is associated with obstructive sleep apnea and daytime sleepiness: role of insulin resistance. The Journal of Clinical Endocrinology & Metabolism, 86(2): 517-20.
- **Whittle AT, Marshall I, Mortimore IL, Wraith PK, Sellar RJ, Douglas NJ. (1999).** Neck soft tissue and fat distribution: comparison between normal men and women by magnetic resonance imaging. Thorax, 54(4): 323-328.
- **Wild R. A. & Bartholomew M. J. (1988).** The influence of body weight on lipoprotein lipids in patients with polycystic ovary syndrome. American journal of obstetrics and gynecology, 159(2): 423-427.
- **Yang HP, Kang JH, Su HY, Tzeng CR, Liu WM, Huang SY. (2009).** Apnea–hypopnea index in nonobese women with polycystic ovary syndrome. International Journal of Gynecology & Obstetrics, 105(3): 226-229.