

Obstructive Sleep Apnea During Pregnancy – Myth or Functional Condition with Potentially Serious Complications

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Abstract

Sleep disordered breathing (SDB) during pregnancy covers a diverse spectrum of pathological conditions provoked by physiological changes in maternal organism and growing fetus. Most of the symptoms (sleepiness, fatigue, vomiting, snoring, obstructed nasal breathing, etc.) are considered to be „normally“-related to the physiological changes during pregnancy. In fact, that subtle complains could be a harbinger of more complex disorders, which could remain

neglected and undiagnosed by the consulting obstetric and gynecology specialist or primary physician. In view of the potential serious complications related to the SDB during pregnancy it is essential to consider even the mild complains of the pregnant woman as prospective alarming symptoms. Interdisciplinary consultation with otorhinolaryngologist and subsequent detailed polysomnographic study are essential for proper diagnosis in order to avoid possible life threatening complications.

Introduction

There is a lot of “confusing” specialized terminology associated with sleep disordered breathing applicable in the daily routine clinical practice of the otorhinolaryngologists¹. According to the second international classification of sleep disorders (ICSD II), based on the strict clinical observations and precise diagnostic criteria, SDB is considered to be a descriptive term for wide range of clinical pathology – simple (habitual) snoring, upper respiratory resistance syndrome (URRS), obstructive sleep apnea (OSA), central sleep apnea (CSA) and obesity-related hypoventilation syndrome (OHS)². Apnea is described as a complete restriction or $\geq 90\%$ obstruction of the airflow for minimum period of 10 seconds, which is usually associated with reduction of blood oxygen concentration (desaturation) and sleep fragmentation with abrupt change of brain activity from deep sleep to wakefulness (arousals). Hypopnea is presumably less severe condition than apnea and is caused

by partial obstruction of the airway. Hypopnea is controversially defined as a different flow limitation during sleep ($\geq 30\%$ or $\geq 40\%$) which last at least 10 seconds and are associated with varying desaturation rate ($\geq 4\%$ or $\geq 3\%$ respectively). AHI is the average number of apnea and hypopnea episodes for a period of 1 hour during sleep. Respiratory effort-related arousals (RERA) – arousals observed when increased respiratory efforts are generated during sleep for more than 10 seconds as an outcome of elevated resistance of the upper respiratory tract (URT). Cessation of breathing last shorter, don't meet the criteria for hypopnea and apnea, results in transition from the deeper to more superficial sleep stage and disappear subsequently. Usually RERA are ironically called “wannabe hypopnea” and are measured by nasal cannula with pressure transducer, pneumotachograph or esophageal manometry during polysomnography (PSG)³. Reparatory distress index (RDI) stands for the sum up of all pathologically registered breathing disturbances – RERA, apnea and hypopnea



for one hour and represent more precise predictive criterion for the gravity of sleep-related disorders. Nevertheless the simple snoring is generally considered as an annoying disturbance, it could be early and alarming symptom of obstructive sleep apnea, requiring full medical attention. Habitual snoring is not pathophysiologically associated with

flow limitations, desaturations or arousals during sleep. The difference between typical clinical presentation of moderate to severe URRS and OSA in adult patients slightly differs and could be validated by ENT-specialist on the basis of clinical examination and PSG sleep characteristics as summarized in Table 1.

Table 1. Differences in clinical presentation and sleep characteristics between URRS and OSA.

Clinical presentation	URRS	OSA
age	younger	40 – 60 years old
female : male ratio	1:2	1:8
body weight	non-obese	obese
sleepiness	fatigue	excessive day-time sleepiness
blood pressure	hypotension (orthostatic)	hypertension
Seep characteristics	URRS	OSA
onset	insomnia (sleep-onset & sleep-maintenance) parasomnias (sleep walking, sleep terror)	short sleep onset
desaturation	not significant	significant
sleep fragmentation	AHI < 5	AHI ≥ 15
RERA	≥10	5-10

Obstructive sleep apnea is defined as a desaturation rate bigger than 4% from the baseline in awaken condition and minimum 50% decrease on airflow or complete stop of breathing for at least 10 seconds during sleep. The exact frequency of OSA among pregnant woman is not statistically proven by meta-analysis, but it is approximately estimated that about 6 % of reproductive female population could be affected⁴. The main reason for this inaccuracy is that the clinical assessment is based predominantly on the questionnaire survey and usually the results are not confirmed by PSG.

„Hormonal storm“ and pathophysiological changes

Normal pregnancy is usually related to the series of biochemical and hormonal changes during the first and second trimester of pregnancy, while the mechanical changes (progressive weight gain, upward displacement of the diaphragm) are associated with the growing fetus inside the maternal organism, could affect significantly the sleeping patterns during the third trimester. Estrogen and progesterone levels are noticeably elevated during pregnancy and could provoke physiological changes with pathological outcome. Estrogen induces hyperemia and edema of the nasopharyngeal mucosa⁵, which result in increased upper respiratory tract resistance. During pregnancy the nasal patency could be obstructed mainly by the physiological actions of different hormones – placental trophoblastic hormone (hypertrophy of the nasal mucosa)⁶, progesterone (local vasodilatation and increased blood flow) and estrogen (increased histamine receptors on the nasal epithelial cells and endothelial cells with subsequent stimulation of the neo-microvascularisation)⁷. Increased resistance of upper respiratory tract in a combination with physiological hypervolemia in pregnant women could amplify significantly the risk of SDB during pregnancy, which is more pronounced in the third trimester⁸. Estrogen disrupts significantly the sleep architecture by inhibiting REM sleep⁹. Progesterone is produced mainly by the placental tissue at the moment of implantation and overrides the effect of other hormones during the first trimester. It is considered that progesterone exerts strong sedative effect resulting in increased total sleep time and decreased sleep latency¹⁰. On the other hand, progesterone has a stimulating effect over the sensitivity of respiratory center towards CO₂ and thus stimulates respiration¹¹. Physiological levels of cortisol start progressively to increase from 25th to 28th gestational week and rapidly normalize after delivery. The pathophysiological effect of the cor-

ryngeal mucosa⁵, which result in increased upper respiratory tract resistance. During pregnancy the nasal patency could be obstructed mainly by the physiological actions of different hormones – placental trophoblastic hormone (hypertrophy of the nasal mucosa)⁶, progesterone (local vasodilatation and increased blood flow) and estrogen (increased histamine receptors on the nasal epithelial cells and endothelial cells with subsequent stimulation of the neo-microvascularisation)⁷. Increased resistance of upper respiratory tract in a combination with physiological hypervolemia in pregnant women could amplify significantly the risk of SDB during pregnancy, which is more pronounced in the third trimester⁸. Estrogen disrupts significantly the sleep architecture by inhibiting REM sleep⁹. Progesterone is produced mainly by the placental tissue at the moment of implantation and overrides the effect of other hormones during the first trimester. It is considered that progesterone exerts strong sedative effect resulting in increased total sleep time and decreased sleep latency¹⁰. On the other hand, progesterone has a stimulating effect over the sensitivity of respiratory center towards CO₂ and thus stimulates respiration¹¹. Physiological levels of cortisol start progressively to increase from 25th to 28th gestational week and rapidly normalize after delivery. The pathophysiological effect of the cor-

tisol is probably related to reduction of REM sleep duration throughout the pregnancy¹². Functional residual capacity (FRC) of the lungs is decreased by upward displacement of the diaphragm during the third trimester, which is supplementary to the physiological reduction of FRC during sleep¹³. The described pathophysiological changes are associated with diminished maternal oxygenation¹⁴ as well as increased collapsibility of the pharynx¹⁵.

Clinical considerations and complications

Pregnancy-related SDB could be demonstrated in the wide range of symptoms during sleep in the clinical spectrum from habitual snoring to obesity-related hypoventilation syndrome, which is arguably considered as the most severe form of the disease in pregnant women¹⁶. Snoring is very common clinical finding among pregnant women and the prevalence is estimated about 14%, which is significantly higher in comparison with the incidence in non-pregnant female population (approximately 4%)¹⁷. Furthermore snoring is a nonspecific clinical observation and usually starts at the end of the second trimester. In the same time snoring is the most frequent complaint of OSA during pregnancy, especially in obese women. Gestational rhinitis (GR) is a pathological condition which differs significantly from the more familiar and popular entity rhinitis during pregnancy (RPr). RPr encompass all types of rhinitis, which could possibly appear before, during and after pregnancy, regardless of the etiology (inflammatory, allergic, non-allergic, drug induced, vasomotor and etc.). GR typically emerges during pregnancy in the second or third trimester, lasts at least 6 weeks or longer and disappears about 2 weeks postpartum¹⁸. GR is not associated with allergic or inflammatory conditions and usually is attributed to the hormonal changes. On the basis of clinical signs and questionnaire survey the prevalence of GR is estimated about 9 % at the time of delivery¹⁹. Obstructed nasal breathing, rhinorrhea and impaired quality of life are not the only outcomes of GR. Worsening of the sleep quality, snoring and gravity of apnea of the childbearing woman with OSA could be attributed to the GR, especially in those clinical cases associated with overweight during pregnancy²⁰. Furthermore, oral breathing as a result form nasal obstruction leads to decrease in nitric oxide (NO) inhalation in the lungs with further negative effect on the maternal blood pressure, preeclampsia, retarded intrauterine fetus

growth, lower Apgar score of the newborn and etc.²¹ Recently an attempt has been made to establish the exact prevalence of obstructive sleep apnea among pregnant women overcoming the imperfections of the traditional screening tools and has been validated that the occurrence is about 4.9%²². OSA is characterized by repeated cessation of the respiratory airflow, accompanied by oxygen desaturation and arousals. Significant reduction of nocturnal saturation of the peripheral blood during the third trimester of pregnancy has been reported in comparison with the results of the postpartum PSG studies of the same subjects²³. Recurring episodes of respiratory obstruction during sleep could lead to maternal hypoxemia. Hypoxemia during sleep has been established both in normotensive and hypertensive pregnancies around the third trimester²⁴. It has been speculated that SDB-related intermittent hypoxia could in turn provoke oxidative stress and endothelial activation²⁵, which are major factors in development of pregnancy-induced hypertension²⁶. Maternal complications such as hypertension and preeclampsia are frequently reported to be related to OSA during pregnancy and generally have been characterized by the absence of nocturnal dipping in systolic blood pressure^{27, 28}. Mild sleep-induced inspiratory flow limitations were detected during the polysomnography in preeclamptic women and subsequently disappear after continuous positive airway pressure therapy. This process is accompanied by normalization of the blood pressure, demonstrating a possible causative connection between OSA and hypertension²⁹. The described minor inspiratory flow limitations couldn't be classified as apnea or hypopnea and typically are not associated with arousals. As a negative outcome in pregnant women with OSA has been also described gestational diabetes³⁰. Clinical course of maternal OSA is frequently related to hypertension and peripheral vasoconstriction, which could possibly play a role in reduction of placental flow and subsequent harmful for the fetus. It has been proven by clinical survey with questionnaires and subsequently validated through PSG that even the mild OSA cases could contribute for the fetus growth retardation and increased risk of stillbirth in the late pregnancy³¹. On the other hand, increased number of pathologic conditions in the postnatal period is attributed to the OSA during pregnancy – low birth weight, small for gestation age infant, preterm birth and low Apgar scores³².



Diagnostic approach

Questionnaires are very effective tool for screening purposes and early detection of the subtle precursors indicative for OSA during pregnancy such as: sleepiness, fatigue, snoring, witnessed apneic episodes and etc. Daytime sleepiness associated with pregnancy is considered to be normal clinical observation and taking into account the natural women hesitation to complain about snoring, gasping and other “uncomfortable” topics, frequently leads to significant delay of OSA diagnosis. Epworth Sleepiness Scale (ESS) has been routinely used for assessment of the degree of daytime sleepiness and probability to fall asleep in different situations. The maximal test score is 26 and the results ≥ 10 are with increased risk for OSA. It has to be mentioned that sleepiness is not very specific for OSA during pregnancy because of the regular daytime nap or subjective interpretation of the symptom rather as a fatigue, “unrefreshed” condition or tiredness than sleepiness. Additionally, sleepiness could not be typically observed in pregnant and preeclamptic women³³ which requires supplementary screening tools for objective and precise evaluation such as multiple sleep latency test (MSLT). MSLT was originally proposed as a diagnostic tool for narcolepsy which evaluates the degree of sleepiness and how fast the patient falls asleep. MSLT is a full day test, which consists of 5 scheduled naps throughout the day separated by 2 hours intervals. The combination of ESS and MSLT could be an effective tool for early detection of OSA during pregnancy. The quality of sleep and sleep disordered breathing are effectively evaluated by another symptom based screening questionnaire, called Berlin questionnaire (BQ)³⁴. BQ consists of 10 questions subdivided in 3 groups – snoring, sleepiness and body weight (plus chronic hypertension) and the effectiveness of clinical application of BQ for early OSA diagnosis in non-pregnant population has been estimated at up to 86% sensitivity and 95% specificity³⁵. Controversially the high-score results from BQ in pregnant women are not reliable predictors for OSA, especially in those risk groups related to obesity³⁶.

ENT consultation is major diagnostic approach for establishing the presence and gravity of increased upper respiratory tract resistance during pregnancy. Anterior rhinoscopy is valuable and informative method which determines the level of obstruction

(nasal septum deviation, hypertrophy of the inferior turbinate, etc). The most important anatomical sites, which could generate significant obstruction in the upper respiratory tract, lay at the level of the nasal valve and glottis area. Nasal segment of the URT is capable of creating almost 5-6 times higher resistance than the pharyngeal segment³⁷. Nasal endoscopy is effective method for discovering of co-morbid pathology (sinusitis, nasal polyposis) which could contribute to increase URT resistance. Müller’s maneuver (MM) is easy to perform yet informative tool for fast evaluation of collapsibility of the retropalatal and retroglottal areas in awoken condition. Regardless the inconsistencies of result interpretation and relatively low predictive value for development of OSA, MM is still applicable in daily routine practice of otorhinolaryngologists for determining the level of obstruction. Originally developed for assessment of anatomical difficulties created by the palatal tonsil and the tongue during endotracheal intubation, the Mallampati score is easy to calculate and to determine the degree of pharyngeal edema accompanying different periods of pregnancy (mainly 12 and 38 gestation week) as a prerequisite of increased URT resistance³⁸.

Polysomnography is the golden standard for diagnosis of obstructive sleep apnea during pregnancy. Generally PSG study of pregnant women could be conducted in the same manner as in non-pregnant women, without any concern about possible contraindications³⁹. It should be taken into consideration that generally pregnant women prefer to lay in bed in lateral position, which could affect the precise registration of AHI score. PSG study is recommended not only in cases with severe complications (gestational hypertension, gestational diabetes preeclampsia, intrauterine growth retardation of the fetus, etc.) and clinical cases with obesity-complicated pregnancies⁴⁰. The evaluation of specific diagnostic criteria such as: inspiratory flow limitations (IFL) and RDI required overnight full PSG study using nasal cannula with pressure transducer and thermistor, which is not possible in conventional polygraphy used predominantly for screening purposes⁴⁰. Determining IFL is essential step in precise diagnosis of abnormal respiratory events in preeclamptic women, which are generally not associated with apneic episodes and are detected during the abnormal rise of blood pressure⁴¹.

Treatment strategies

Symptomatic conservative treatment is defined by the application of different medication which doesn't have curative effect, but rather temporally relieve of the clinical complaints. The general prophylactic measures⁴² (elevated $> 30^\circ$ position of the head during sleep, sleeping on a lateral position, physical exercises, weight control, improving sleep hygiene, avoiding alcohol and sedatives, etc.)⁴³ and topical application of saline solutions (especially hypertonic) could be beneficial for the save and temporally relieve of GR symptoms¹⁸. Pregnant women with GR are frequently obsessed with the usage of topical decongestants for a prolonged period of time. The inadequate usage (longer than 5 days, application during the 1st trimester or close to delivery term as well as inappropriate higher dosage) of α -mimetics (phenylephrine, naphazoline, oxymetazoline and xylometazoline) leads to tachyphylaxis and negative effect on the nasal mucosa (drug-associated rhinitis), increased contractility of the uterus (preterm birth) plus possible congenital defects (pyloric stenosis, renal abnormalities)⁴⁴. Systemic decongestants (pseudoephedrine, phenylpropanolamine) taken especially during the 1st trimester of pregnancy are associated with life threatening conditions such as: gastroschisis, endocardial wall closure defects and external ear malformations⁴⁵. Considering the negligible clinical improvement of the natural course of GR and possible teratogenic effects of wide range of drugs (local and systemic corticosteroids, antihistamines, anti-leukotrienes inhibitors) it is not recommended to be used as a treatment strategy in co-morbid allergic rhinitis during pregnancy. In those cases it is more appropriate to use sodium cromoglycate or topical ipratropium bromide to cope with the severe rhinorrhea of moderate to severe allergic rhinitis during pregnancy¹⁸.

Oral appliances are effective in reduction of upper respiratory tract resistance by pulling forwards genioglossus muscle, expanding pharyngeal antero-posterior dimensions. Dental appliances usually find application for treatment of habitual snoring and mild to moderate OSA. As a major drawback of mandibular advancement devices could be pointed out a relatively long period of time necessary for fabrication and adjustment (titrating) according to individual needs of the patient⁴⁶.

Positive airway pressure (PAP) is a gold standard for conservative treatment of OSA during pregnancy. Continuous positive airway pressure

(CPAP) therapy is safe, generally well-tolerated and effective treatment with significant outcomes both for the mother (overcome apneic episodes, improves flow limitations, increase nocturnal oxygenation, reduce arterial pressure, etc.) and the fetus (improved fetal movements, change in movement patterns, reduced fetal hiccups) especially in preeclamptic patients⁴⁷. The application of CPAP therapy during pregnancy is recommended for mild to moderate (AHI, 5-30/hour) and severe (AHI, > 30 /hour) OSA cases associated with desaturation level $\leq 90\%$ ⁴⁸. CPAP therapy during pregnancy is consistent with very good compliance level³⁹, even in cases when OSA is combined with preeclampsia as co-morbidity⁴⁹. The usage of nasal CPAP during pregnancy is not associated with any adverse effects⁵⁰ and usually is terminated 2 weeks after delivery. The main target of CPAP therapy is to achieve favorable improvement of the saturation level ($> 90\%$) and to acquire RDI level < 5 per hour during sleep⁴⁸. Pregnant women diagnosed before or in the beginning of the pregnancy with SDB usually required recalibration of the CPAP equipment around the 6 month⁴⁹. In severe cases associated with obesity-related OSA pregnancies or multiple gestations (twin pregnancies) is more favorable to use bi-level positive airway pressure (BiPAP) instead of CPAP ventilation. In order to improve the effectiveness of PAP treatment it is recommended to combine the artificial ventilation with supplementary oxygen therapy (OXT). OXT is not recommended as a primary treatment of OSA during pregnancy because of the potential risk of prolonged episodes of apnea, raised level of carbon dioxide in the circulating peripheral blood (hypercapnia) and increased ventricular irritability⁵¹.

Surgery is limited only for the most severe cases of OSA uninfluenced by the conservative treatment, patients with low compliance rate toward CPAP therapy or those clinical cases posing high-grade risk of serious complications for the pregnant woman and her baby. In cases with severe OSA secondary to GR and refractory to conservative treatment could be recommended a volume reduction of the inferior turbinate¹⁸. Considering the increased surgical risk and inconsistent long-term results performing a conventional uvulopalatopharyngoplasty (UVPP)⁵² is not recommended for treatment of OSA during pregnancy⁵³. There is just one case in the literature reporting benefits from tracheostomy in a pregnant woman with obstructive sleep apnea⁵⁴.



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