Severity of Sleep-Disordered Breathing Improves Following Parturition

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Study Objective: Changes in sleep-disordered breathing associated with late pregnancy have not previously been systematically investigated; however, a number of case reports indicate exacerbation of obstructive sleep apnea in late pregnancy, often in association with maternal hypertension. We aimed to compare the severity of sleep-disordered breathing and associated maternal blood-pressure responses in late pregnancy with the nonpregnant state.

Design: Case-controlled, longitudinal study of sleep-disordered breathing during late pregnancy and postpartum.

Study Patients: Ten women referred for suspected sleep-disordered breathing during the third trimester of pregnancy.

Interventions: None.

Measurements and Results: Full overnight polysomnography and continuous systemic blood pressure were measured during the third trimester of pregnancy and 3 months following delivery. Parameters of sleep-disordered breathing, including apnea hypopnea index and minimum overnight arterial oxyhemoglobin saturation, were compared between antenatal and postnatal studies. An improvement in both apnea-hypopnea index and minimum arterial oxyhemoglobin saturation occurred consistently in all subjects postnatally. In non-rapid eye movement sleep, mean apnea-hypopnea index was reduced from 63 ± 15 per hour antenatally to 18 ± 4 per hour postnatally (P = .03), and in rapid eye movement sleep, from 64 ± 11 per hour to 22 ± 4 per hour (P = .002). Minimum arterial oxyhemoglobin saturation was increased from 86% ± 2% antenatally to 91% ± 1% postnatally (P = .01). Arterial blood-pressure responses to apnea peaked at 170 to 180 mm Hg antenatally, while they only peaked at 130 to 140 mm Hg postnatally.

Conclusion: This study indicates that late pregnancy may be associated with increased severity of sleep-disordered breathing and associated blood-pressure responses.

Key Words: Obstructive sleep apnea, pregnancy, blood pressure.

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INTRODUCTION

OBSTRUCTIVE SLEEP APNEA (OSA) IS A COMMON DISEASE CURRENTLY ESTIMATED TO AFFECT APPROXIMATELY 6.5% OF WOMEN OF CHILDBEARING AGE.1 It has been suggested that the augmented ventilatory drive associated with increased circulating progesterone concentrations during pregnancy is protective against the development of OSA;2 however, snoring is linked to a greater incidence of breathing disorders during sleep, and the incidence of snoring is markedly increased during pregnancy, occurring in an estimated 14%3 to 23%4 of pregnant women. Nonetheless, there have been no systematic longitudinal studies of the severity of sleep-disordered breathing (SDB) in pregnancy.

There are also limited data on the consequences of SDB during pregnancy, although most case reports suggest that it has important adverse impacts on both maternal and fetal health. Simple snoring has been linked to an increased incidence of both maternal hypertension and preeclampsia, as well as an increased incidence of low birth weight infants and significantly poorer Apgar scores at birth.4 Furthermore, case reports of OSA in pregnancy have been associated with maternal pulmonary hypertension,5 fetal death,6 and evidence of fetal compromise.7

OSA has now been established as an independent cause of systemic arterial hypertension in nonpregnant patients,8,9 and it is therefore important to determine what, if any, role OSA plays in maternal systemic arterial blood pressure control.

The aim of this study was to investigate the interaction between pregnancy and SDB, and its effects on systemic blood pressure, by comparing the severity of OSA, and its effects on nocturnal arterial blood pressure during late pregnancy with these parameters 3 to 6 months following delivery.

METHODS

Subjects

Ten women were referred to our clinic during their third trimester of pregnancy with suspected OSA. This cohort represents a consecutive series of patients who were referred to the clinic over a period of approximately 12 months. The majority of patients were referred to the clinic from their primary healthcare providers (general practitioner, n = 8), while the remaining 2 patients were referred to us via sleep physicians. The mean ± SD (range) age and gestation (respectively) were 32 ± 4 (27-40) years and 33 ± 2 (30-35) weeks. All women were within 15 kg of the highest recommended weight for their height and stage of pregnancy (mean weight and body mass index [BMI] were 83 ± 14 kg and 30 ± 3 kg/m², respectively). All but 1 of these subjects was nulliparous (the current pregnancy being the first to reach the third trimester), with the remaining subject having a 2-year-old child. Aside from salbutamol for asthma (2 of 10), no subject was taking any other medication. All reported feeling well and only reported occasional snoring prior to the current pregnancy. One subject had borderline hypertension (140/85 mm Hg) not requiring medica-
tion, which had developed during the current pregnancy. All of the subjects presented to their respective physicians with a history of loud snoring and excessive daytime sleepiness, and 7 of the 10 also had witnessed apneas. All subjects participated following provision of informed consent.

Antenatal Sleep Studies

We performed full overnight polysomnography on each subject using the Compumedics portable Sleepwatch system (Compumedics, Melbourne, Australia). Polysomnography included standard cardiorespiratory and neurologic measurements. Parameters monitored included electroencephalogram (C3/A2 and O2/A1), left and right electrooculogram, submental electromyogram, electrocardiogram, nasal flow measured via nasal oxygen cannulae attached to a high fidelity pressure transducer and sampled at 50 Hz; thoracic and abdominal effort, right and left leg movement, position, and arterial oxyhemoglobin saturation (SaO2). We also measured beat-to-beat blood pressure using the Portapres device (TNO-BMI, Amsterdam, The Netherlands). All studies were performed in the subjects’ homes. Preparation for the study was begun approximately an hour before the normal bedtime, and, following this, subjects adhered to their normal bedtime routine.

Treatment of OSA With Nasal Continuous Positive Airway Pressure

All patients diagnosed with SDB were treated with nasal continuous positive airway pressure (CPAP) during the remainder of their pregnancy, with withdrawal of nasal CPAP therapy in the early postnatal period (within the first 2 weeks following delivery). Thereby subjects were untreated for a mean of 3 months prior to the postnatal sleep study.

Postnatal Sleep Studies

Postnatal sleep studies were performed exactly as described for antenatal sleep studies. Studies were performed at a mean of 4 ± 2 months after delivery (range, 3 to 6 months). As a group, these women lost a mean of 10 ± 2 kg in body weight between the antenatal and postnatal sleep studies. The mean BMI for the group during the postnatal sleep study was 27 ± 3 (24-31) kg/m2. Of the 10 subjects included in the study, 7 were fully breastfeeding their infants at the time of the postnatal sleep study, while the infants of the other 3 subjects were exclusively bottle fed.

Analysis

Sleep-stage scoring was performed according to current criteria,11 respiratory events were scored according to the following criteria: obstructive apnea: cessation of nasal airflow with continued respiratory effort for ≥ 10 seconds accompanied by arousal and/or SaO2 decrease ≥ 4%; obstructive hypopnea: reduction of airflow of ≥ 50% of unobstructed breaths with continued respiratory effort for ≥ 10 seconds accompanied by arousal and/or SaO2 decrease ≥ 4%; and central apnea: cessation of nasal airflow for ≥ 10 seconds accompanied by arousal and/or SaO2 decrease ≥ 4% with absence respiratory effort. Central hypopneas were not scored in this study.

Arousals were scored according to current American Sleep Disorders Association criteria,12 which in non-rapid eye movement (NREM) sleep includes a shift in electroencephalogram frequency for a minimum of 3 seconds either with or without an increase in submental electromyogram tone; in rapid eye movement (REM) sleep, a shift in electroencephalogram frequency is associated with an increase in submental electromyogram tone.

To standardize the duration of obstructive respiratory events for comparison between antenatal and postnatal sleep studies, only those obstructive events meeting the criteria for apnea (not hypopnea) were included in the analysis of the duration of such events.

Statistical Analysis

Antenatal and postnatal sleep study variables were compared using paired student t-tests. A level of .05 was considered significant. Values reported are mean ± SD.

RESULTS

All studies were technically reliable enough to perform both sleep staging and respiratory-event and arousal scoring for the entirety of the night.

Changes in Sleep Architecture

Sleep was considerably altered in the postnatal sleep studies when compared with those conducted during the antenatal period (Table 1). REM sleep was significantly augmented during the postnatal sleep study, while both latency to sleep and latency to REM were markedly reduced.

Changes in Sleep Position

During the antenatal sleep study, subjects spent, on average, less than 10% (8%±6%) of the time asleep in the supine position (87%±8% of the time was spent in either the left or right lateral positions). Subjects spent 16%±9% of the sleep time in the supine position during the postnatal sleep study (P = .07 compared with the antenatal sleep study).

Changes in Respiratory Parameters During Sleep

There was a marked improvement in severity of SDB during the postnatal sleep studies when compared with the antenatal sleep studies, which occurred consistently in all subjects. This was reflected in both the apnea hypopnea index (AHI), and in the average minimum overnight SaO2 (Figures 1 and 2, respectively). While there was a wide variability in the AHI during the antenatal sleep studies, with a range of 22 to 136 events per hour, there

<table>
<thead>
<tr>
<th>TST, min</th>
<th>Sleep Latency, min</th>
<th>NREM, %</th>
<th>REM Latency, min</th>
<th>REM, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antenatal</td>
<td>369 ± 45</td>
<td>35 ± 23</td>
<td>87 ± 6</td>
<td>150 ± 26</td>
</tr>
<tr>
<td>Postnatal</td>
<td>387 ± 46</td>
<td>15 ± 9</td>
<td>79 ± 3</td>
<td>75 ± 18</td>
</tr>
</tbody>
</table>

P value .42 .04 .003 < .001 .003

TST refers to total sleep time; NREM, non-rapid eye movement; REM, rapid eye movement.

Table 1—Indexes of Sleep Architecture During Antenatal and Postnatal Polysomnography
was a clinically and statistically significant reduction in AHI during the postnatal sleep studies. Similarly, the average decrease in SaO$_2$ resulting from obstructive respiratory events also improved from the antenatal to the postnatal sleep studies, decreasing from 5.1% ± 0.4% to 2.3% ± 0.9%, $P = .03$ (Figure 3 shows an example of the overnight SaO$_2$ in 1 subject). While the maximum apnea duration was significantly reduced during the postnatal when compared with the antenatal studies, neither the mean nor the maximum apnea duration was statistically different between the postnatal and antenatal sleep studies (Table 2).

There appeared to be no relationship between the change in either weight or BMI from the antenatal to the postnatal sleep studies and the change in AHI ($R^2 < 0.001$, $P = .83$ and $R^2 = 0.02$, $P = .68$ comparing weight with AHI and BMI with AHI, respectively).

**Arousals**

The arousal index was markedly reduced during the postnatal sleep study (40 ± 7 per hour of sleep) when compared with the antenatal sleep study (84 ± 13 per hour of sleep, $P = .004$). The reduction in arousal indexes was most noticeable in REM sleep, decreasing from 89 ± 16 per hour of sleep during the antenatal study to 37 ± 10 per hour of sleep during the postnatal sleep study ($P = .001$).

**Blood Pressure Data**

Overnight blood pressure was moderately elevated during the antenatal sleep studies (average mean arterial pressure over the duration of the night 91 ± 4 mm Hg) when compared with the postnatal sleep studies (average mean arterial pressure over the duration of the night 78 ± 7 mm Hg, $P = .03$ compared with the antenatal sleep study). More clinically significant, however, were the marked fluctuations in nocturnal blood pressure during antenatal studies as a result of apneic cycles, with systolic blood pressure typically reaching maxima of 170 to 180 mm Hg. In contrast, the typical systolic maxima during the antenatal sleep studies was only 130 to 140 mm Hg. It was not possible to compare the pres-
Fetal Outcome

Infant birth weight was variable among the 10 participants in this study, ranging from 1850 g to 3300 g (mean 2880 ± 250 g), with gestations of 35 to 40 weeks (38 ± 2 weeks). The weight at birth corresponded to a wide range of percentiles for gestational age (from the third to the 80th percentile). Interestingly, the mother of the infant who was at the third percentile for growth of their pregnancy (6 ± 2 weeks), with withdrawal of nasal CPAP during the early postnatal period.

Discussion

This study has demonstrated that sleep apnea diagnosed during late pregnancy improves markedly following delivery. Most notably, subjects ubiquitously demonstrated a marked improvement in both AHI and minimum overnight SaO₂. There was also a consistent improvement in arousal indexes in all subjects.

Potential study participants were identified during pregnancy when they presented to a physician with symptoms of OSA (including loud frequent snoring, excessive daytime sleepiness, and witnessed apneas). For this reason, it was necessary to perform nonpregnant studies subsequent to the pregnancy as opposed to prior to the pregnancy; however, the hormonal changes that are specifically associated with pregnancy return to nonpregnant levels within 2 weeks of delivery, and all studies were performed well outside this timeframe. Thus, the postnatal results represent a true reflection of the nonpregnant state in these women.

While 7 of the subjects presented in this study were breastfeeding postnatally, there was no difference in severity of SDB postnatally between the breastfeeding and the nonbreastfeeding subjects, suggesting that the hormones associated with breastfeeding (most notably, prolactin) are unlikely to have contributed to the improvement. There was a difference in NREM sleep architecture between the breastfeeding and nonbreastfeeding subjects during the postnatal study, with a far greater proportion of NREM sleep time spent in slow-wave sleep. This is consistent with our previous study in which a link was identified between breastfeeding and increased maternal slow-wave sleep.³⁵ While an increase in the proportion of slow-wave sleep may have altered the overall AHI during sleep, the reduction in AHI occurred consistently throughout all sleep stages. Furthermore, there was no difference in the decrement in AHI between the breastfeeding and nonbreastfeeding subjects (with a decrease of 46 ± 34 per hour of sleep in the breastfeeding subjects and a decrease of 44 ± 21 per hour of sleep in the nonbreastfeeding subjects, P = .94).

Both antenatal and postnatal sleep studies were performed in the patients’ homes, in the absence of an adaptation night. However, it is unlikely that this compromised the validity of the study, as the second study in each instance was performed at least 3 months after the first study, and thus both studies would have been equally influenced by a “first-night effect.” The use of a portable polysomnographic system enabled us to study women in their homes, thus eliminating 1 of the predominant sources that may contribute to a first-night effect, that of sleeping in a laboratory. Furthermore, sleep architecture was not an important factor in this study, rather, the severity of SDB was the primary variable being assessed, rendering a first-night effect relatively inconsequential.

On the basis of ethical considerations and being aware of the likely impact of SDB on the growing fetus, once moderate to severe OSA had been diagnosed on full polysomnography, all subjects were offered the use of nasal CPAP therapy for the remainder of their pregnancy. However, subjects were withdrawn from nasal CPAP therapy within the early postnatal period, and, therefore, subjects were untreated for 3 months prior to the postnatal sleep study. The probability that use of nasal CPAP would have had an influence on apnea severity during the postnatal period is thus minimal.

Subjects included in this study spent a greater proportion of the time during sleep in the supine position during the postnatal sleep study (although this did not reach statistical significance). The supine position is clearly associated with an exacerbation of SDB.¹⁶⁻¹⁸ Therefore, sleeping position during the postpartum period is unlikely to have contributed to the improvement that occurred in severity of SDB.

The mean change in body weight of these subjects from the antenatal sleep study to the postnatal sleep study was -10 ± 2 kg. The mean weight of the placenta, maternal blood volume, increased breast and uterine tissue, maternal fluid volume, maternal muscle, and amniotic fluid at the end of the third trimester is approximately 6.8 kg.¹⁹ The mean fetal weight in this group of patients was 2.8 kg. Thus, nonfat maternal weight in these subjects would have been in the order of 9.6 kg; loss of fat mass following delivery (on average) was therefore minimal (< 0.5 kg), and an improvement in SDB of the magnitude demonstrated in this study is unlikely to have been predominantly attributable to loss of fat mass. Furthermore, analysis of the relationship between weight lost and improvement in AHI between the antenatal and postnatal studies revealed a lack of any relationship.

While changes in sleep position, maternal fat mass, and postnatal treatment are unlikely to have contributed significantly to the improvement in SDB, many physiologic factors associated with

Table 2—Comparison of the Mean And Maximum Apnea Duration During Antenatal and Postnatal Polysomnography

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<thead>
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<th>Antenatal</th>
<th>Postnatal</th>
<th>P value</th>
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<tbody>
<tr>
<td></td>
<td>Mean apnea duration, min</td>
<td>Maximum apnea duration, min</td>
<td></td>
</tr>
<tr>
<td>NREM</td>
<td>15 ± 3</td>
<td>26 ± 10</td>
<td>.38</td>
</tr>
<tr>
<td>REM</td>
<td>12 ± 5</td>
<td>20 ± 7</td>
<td>.30</td>
</tr>
<tr>
<td>P value</td>
<td>.06</td>
<td>.103</td>
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</table>

NREM refers to non-rapid eye movement; REM, rapid eye movement.

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pregnancy are highly conducive to upper-airway obstruction during sleep. Elevated serum progesterone concentrations have a 2-fold effect. Primarily, progesterone increases vascular permeability, resulting in tissue edema. Edema within the maternal upper airway can lead to a physical narrowing of the internal lumen, which has previously been demonstrated during the third trimester of pregnancy. Secondly, progesterone is a powerful respiratory stimulant, which increases diaphragmatic effort without increasing upper airway dilator muscle activity. A further contributor to exacerbation of SDB may be increased circulating estrogen concentrations, which cause vasodilatation, particularly in the nasal vasculature, leading to rhinitis. The interaction of these 2 factors during late pregnancy is almost certainly sufficient in this group of patients to exacerbate preexisting SDB.

While there was a marked reduction in arousal indexes from the antenatal to the postnatal sleep study, the arousal index during the postnatal period was still elevated above that expected for women in a similar age group; however, these women still clearly had a degree of SDB (with AHI in the range of 6 to 34 events per hour), and thus many of these arousals still occurred as a result of obstructive respiratory events.

This study has provided crucial clinical information as to the impact that pregnancy has on SDB. There are now a number of studies that suggest SDB to be associated with adverse maternal outcomes, including pregnancy-induced hypertension and pre-eclampsia. While we were able to demonstrate significantly reduced blood pressure during the postnatal sleep studies, it is difficult to draw physiologic conclusions, as the severity of SDB was not comparable between the 2 studies. Nonetheless, frequent marked blood pressure fluctuations associated with apneic cycles will almost certainly be associated with maternal vascular and placental compromise. While available data are scarce in regard to fetal effects of maternal OSA, of 9 case reports, 3 have reported intrauterine growth restriction, while another reported fetal heart-rate decelerations that were specifically associated with maternal apneic cycles. The findings in this study clearly have important implications for antenatal care. If SDB has been diagnosed prior to pregnancy, the condition needs to be reassessed, particularly toward the latter stages of the pregnancy, and treatment options need to be discussed with the patient. Furthermore, if OSA is not present prior to pregnancy, but risk factors for SDB exist, including obesity or facial structural abnormalities that are conducive to the development of apnea are present, it is essential that the patient be assessed during the pregnancy in order to detect a precipitator of SDB.

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