Sleep Disturbances and Their Relationship to Glucose Tolerance in Pregnancy

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OBJECTIVE—To explore relationships among sleep disturbances, glucose tolerance, and pregnancy outcomes.

RESEARCH DESIGN AND METHODS—Four validated sleep questionnaires were administered to 169 pregnant women at the time of 50-g oral glucose tolerance testing (OGTT) during the second trimester. Pregnancy outcomes were analyzed in 108 women with normal glucose tolerance (NGT).

RESULTS—Of the participants, 41% had excessive daytime sleepiness (Epworth Sleepiness Scale [ESS] >8); 64% had poor sleep quality; 25% snored frequently; 29% had increased risk of sleep-disordered breathing (SDB); 52% experienced short sleep (SS); 19% had both increased SDB risk and SS (SDB/SS); and 14% had daytime dysfunction. Reported sleep duration inversely correlated with glucose values from 50-g OGTT ($r = -0.21$, $P < 0.01$). Each hour of reduced sleep time was associated with a 4% increase in glucose levels. Increased likelihood of gestational diabetes mellitus (GDM) was found in subjects with increased SDB risk (odds ratio 3.0 [95% CI 1.2–7.4]), SS (2.4 [1.0–5.9]), SDB/SS (3.4 [1.3–8.7]), and frequent snoring (3.4 [1.3–8.8], after adjustment for BMI). Among NGT subjects, preterm delivery was more frequent in those with increased ESS ($P = 0.02$), poor sleep quality ($P = 0.02$), and SS ($P = 0.03$). Neonatal intensive care unit admissions were associated with increased ESS ($P = 0.03$), SDB/SS ($P = 0.03$), and daytime dysfunction ($P < 0.01$) in mothers.

CONCLUSIONS—Pregnant women experience significant sleep disturbances that are associated with increased risk of GDM and unfavorable pregnancy outcomes. Pregnant women with increased SDB risk, frequent snoring, and sleep duration of <7 h/night have increased risk of developing GDM.

Diabetes Care 34:2454–2457, 2011

Sleep-disordered breathing (SDB) is present in 24% of men and 9% of women in the U.S. population (1) and has been linked to insulin resistance and type 2 diabetes (2–5). Recent studies reveal that SDB is present in up to 86% of patients with type 2 diabetes (6,7). SDB severity has been associated with poorer glucose control (6).

Decreases in both duration and quality of sleep are common in pregnant women as a result of hormonal and physical factors (8,9). Collectively, these disorders have been termed pregnancy-associated sleep disorders by the International Classification of Sleep Disorders (10).

Prospective studies show that SDB symptoms increase during pregnancy (11). SDB in pregnancy has been associated with preeclampsia, intrauterine growth retardation, and preterm delivery (12,13). A few recent studies using questionnaires that variably assess snoring, SDB symptoms, and/or sleep duration report an association between short sleep (SS) and/or frequent snoring and glucose intolerance and gestational diabetes mellitus (GDM) (14–16).

We used four validated sleep questionnaires to obtain a comprehensive evaluation of sleep duration and quality and assess associations with glucose tolerance and pregnancy outcomes.

RESEARCH DESIGN AND METHODS

—Pregnant adult women scheduled to undergo a 50-g oral glucose tolerance test (OGTT) during the second trimester of gestation were invited to participate. Exclusion criteria were history of pre-GDM; sleep disorders; severe pulmonary, cardiac, or renal diseases; steroid use; substance abuse; current neurologic or psychiatric disorders; use of prescription or over-the-counter medications known to affect sleep or glucose metabolism; cigarette smoking; significant alcohol or caffeine consumption; recent travel across time zones; and shift work. Written informed consent was obtained. The study was approved by the institutional review board of the University of Chicago.

Age, ethnicity, prepregnancy BMI, current weight, height, and medical and family history were recorded. Subjects completed four standardized questionnaires: the Epworth Sleepiness Scale (ESS), which assesses daytime somnolence (normal score ≤8) (17); the Berlin Sleep Questionnaire, which assesses SDB risk (18); the Pittsburgh Sleep Quality Index (PSQI) to assess sleep during the past month (normal score ≤5) (19); and the Nocturia, Nocturnal Enuresis, and Sleep-Interruption Questionnaire (20).

Subjects with a 1-h glucose value <140 mg/dL post 50-g glucose were considered to have normal glucose tolerance (NGT). If the value was ≥140 mg/dL, they underwent a 100-g OGTT to formally confirm or exclude GDM (21). Subjects whose 1-h glucose value was ≥200 mg/dL post 50-g glucose challenge were diagnosed as having GDM without further testing.

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Received 25 April 2011 and accepted 11 August 2011.
DOI: 10.2337/dc11-0780

Pregnancy outcomes were extracted from delivery and postdelivery medical records, including birth weight, gestational age at delivery, gestational hypertension, primary cesarean section, and admissions of the newborns to a neonatal intensive care unit (NICU).

Statistical analysis

Questionnaire data were compared between groups using two-sided *t* tests and χ^2 tests. Correlations between sleep parameters and log-transformed glucose values were analyzed. Logistic regression was used to examine the relationship between sleep parameters and pregnancy outcomes and to further analyze factors associated with GDM. Values are presented as mean ± SD unless otherwise noted. STATA Version 11 was used (StataCorp., College Station, TX).

RESULTS

Questionnaires

A total of 169 women with a singleton pregnancy completed the four questionnaires (Table 1). The majority of women (92%) reported that their sleep was interrupted, most commonly as a result of an urge to void (55%) or feeling thirsty (52%).

Nearly two-thirds of the women (64%) had overall poor sleep quality as reflected by a PSQI >5 (mean of 7.4 ± 4.0), and 41% reported excessive daytime sleepiness (ESS >8). A total of 48 women (29%) had increased SDB risk, and 41 (25%) were frequent snorers (snore >3–4 days per week). More than half of the women (52%) experienced SS (<7 h/night), and 32 subjects (19%) had a combination of increased SDB risk and SS (SDB/SS). Daytime dysfunction was reported by 24 subjects (14%). Only 18% of the women had normal sleep-wake regulation with normal overall sleep quality (PSQI ≤5, ESS ≤8, and no SDB risk).

Glucose tolerance

Of the participants, 116 women (68%) had NGT based on the 50-g OGTT. Of those who failed the 50-g OGTT and underwent the 100-g OGTT, 26 (15%) met the criteria for GDM. A total of 27 women had an abnormal 50-g OGTT but a 100-g test that was not diagnostic of GDM.

There was an inverse correlation between sleep duration and 1-h glucose values post 50-g OGTT ($r = -0.21$, $P < 0.01$) such that each hour of shorter sleep was associated with a 4% glucose increase.

Compared with the NGT group, GDM subjects were older, had a higher prepregnancy BMI, and were more likely to have a family history of diabetes and a personal history of GDM (Table 1). The women were more likely to have GDM if they had an elevated SDB risk (odds ratio [OR] 3.0 [95% CI 1.2–7.4]; $P = 0.02$), if they reported frequent snoring (3.4 [1.3–8.8]; $P = 0.01$ after BMI adjustment), if they experienced SS (2.4 [1.0–5.9]; $P = 0.06$), and if they had the combination SDB/SS (3.4 [1.3–8.7]; $P = 0.01$).

Pregnancy outcomes

When compared with NGT women ($n = 108$), GDM women ($n = 26$) had a higher prevalence of gestational hypertension (23 vs. 5%, $P < 0.01$), a higher fetal birth weight (3,666 ± 597 vs. 3,232 ± 413 g, $P < 0.01$), and more frequently had newborns requiring NICU admission (46 vs. 18%, $P < 0.01$). There were no significant differences in frequency of primary cesarean sections (17 vs. 32%, $P = 0.16$) or preterm deliveries (12 vs. 12%, $P = 1.00$).

Because of the relatively small numbers of GDM subjects, we examined the association between pregnancy outcomes and sleep parameters in NGT subjects only. The risk of preterm delivery was increased in subjects with higher ESS (OR 1.2 [95% CI 1.0–1.3]; $P = 0.02$), higher PSQI (1.2 [1.0–1.3]; $P = 0.02$), and SS (4.3 [1.1–16.7]; $P = 0.03$). In addition, there was a higher risk of NICU admission for newborns from mothers with elevated ESS (1.1 [1.0–1.3]; $P = 0.03$), SDB/SS (3.5 [1.1–11.4]; $P = 0.03$), and from mothers who had reported daytime dysfunction (5.2 [1.7–15.6]; $P < 0.01$).

There were no significant associations between sleep parameters and the risk of primary cesarean section, gestational hypertension, and birth weight among term infants.

Table 1—*Baseline characteristics and questionnaire results*

	All subjects ($n = 169$)	NGT ($n = 116$)	GDM ($n = 26$)	*P* value (NGT vs. GDM)
Age (years)	28.5 ± 5.5	27.4 ± 5.3	30.1 ± 5.5	0.03
Gestational age (weeks)	26.2 ± 4.4	26.4 ± 3.5	25.8 ± 6.6	0.63
BMI (kg/m^2)	32.3 ± 8.3	31.4 ± 8.3	37.1 ± 8.4	<0.01
Prepregnancy BMI (kg/m^2)	29.0 ± 8.3	27.9 ± 8.0	34.8 ± 8.7	<0.01
Family history of diabetes, *n* (%)	50 (30)	24 (21)	15 (60)	<0.01
History of GDM, *n* (%)	19 (13)	4 (4)	12 (50)	<0.01
1-h glucose (mg/dL)	120.3 ± 41.4	97.8 ± 20.2	184.5 ± 39.6	<0.01
Interrupted sleep, *n* (%)	156 (92)	105 (91)	25 (96)	0.70
ESS	8.0 ± 4.6	8.1 ± 4.6	7.9 ± 4.0	0.85
ESS >8, *n* (%)	69 (41)	50 (44)	11 (42)	0.89
PSQI score	7.4 ± 4.0	7.4 ± 4.2	7.7 ± 3.8	0.75
PSQI >5, *n* (%)	107 (64)	74 (64)	18 (69)	0.64
Increased SDB risk, *n* (%)	48 (29)	31 (27)	12 (52)	0.02
Frequent snorer, *n* (%)	41 (25)	25 (22)	13 (54)	0.01*
SS, *n* (%)	88 (52)	56 (49)	18 (69)	0.06
SDB/SS, *n* (%)	32 (19)	20 (17)	10 (42)	0.01
Daytime dysfunction, *n* (%)	24 (14)	20 (17)	1 (4)	0.12†

Data are mean ± SD, unless otherwise indicated. *P* values are from *t* tests for continuous variables and χ^2 tests for categorical variables unless otherwise noted. *From logistic regression models with GDM status as the dependent variable; adjusted for BMI. †Fisher exact test.

CONCLUSIONS—Our assessment of sleep disturbances in pregnancy using a set of four validated sleep questionnaires revealed that a majority of pregnant women experience significant sleep disturbances. Women who reported shorter sleep duration had a higher glucose response to a 50-g OGTT. Each hour of reduced sleep time was associated with a 4% increase in glucose levels. In addition, specific sleep disturbances, including frequent snoring (after adjustment for BMI), increased SDB risk, SS, and a combination of increased SDB/SS, were associated with a significantly higher risk of developing GDM. These findings are consistent with well-documented associations between sleep disturbances and increased diabetes risk in nonpregnant populations. They confirm and greatly extend recent reports linking sleep disturbances during pregnancy and abnormal glucose tolerance (14–16,22).

SDB involves hypoxic stress, shallow and fragmented sleep, and reduced total sleep time. These abnormalities have been linked to insulin resistance and reduced glucose tolerance in nonpregnant populations (3,4,23). It is likely that similar mechanisms are involved in the pathogenesis of GDM in pregnant women with sleep disturbances and/or SDB.

We observed that sleep disturbances in pregnant women are associated with unfavorable outcomes, including preterm delivery and NICU admissions of the newborns. This result is in concordance with previous studies finding that self-reported symptoms or a diagnosis of SDB during pregnancy were associated with gestational hypertension, premature delivery, increased rate of unplanned cesarean sections, and possibly intrauterine growth retardation (13,14,22,24). Several underlying mechanisms have been proposed, including altered uteroplacental blood flow, increased levels of oxidative stress and proinflammatory cytokines (tumor necrosis factor-α and interleukin-6), increased sympathetic activation, peripheral vasoconstriction, and endothelial dysfunction (24,25).

Further studies are needed to characterize the impact of sleep disturbances on glucose tolerance and pregnancy outcomes and to explore the potential benefits of optimizing sleep duration and quality during pregnancy.

Acknowledgments—This study was supported by the ResMed Foundation and D.A.E. and E.V.C. have received research/grant support from the ResMed Foundation. The sponsor had no role in the study design, data collection, analysis, interpretation, or writing of the manuscript. This study was also supported by a grant from the Diabetes Research Training Center at the University of Chicago (P60 DK20595), a Specialized Center of Research (SCOR) on Women's Health Grant (5P50HD057796), the Blum-Kovler Family Foundation, and Grant UL1-RR-024999 from the National Center for Research Resources. The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the National Center for Research Resources or the National Institutes of Health.

E.V.C. has received grant support from Philips/Respironics and Amylin/Lilly; is a consultant for sanofi-aventis, Actelion, and the Hershey Company; is a member of the Strategic Plan Working Group for the Sleep Disorders Research Advisory Board of the National Institutes of Health; is associate editor for the journal *SLEEP* and for a volume titled *Sleep Loss and Obesity: Intersecting Epidemics* published by Springer Science & Business, LLC; and serves as an expert witness for Lamson, Dugan, and Murray, LLP (Omaha, NE). No other potential conflicts of interest relevant to this article were reported.

S.R. collected data, drafted the manuscript, contributed to discussion, and reviewed and edited the manuscript. N.Z. collected data, contributed to discussion, and reviewed and edited the manuscript. K.W. analyzed data, contributed to discussion, and reviewed and edited the manuscript. H.H.K and M.I. researched data, contributed to discussion, and reviewed and edited the manuscript. D.A.E. and E.V.C. obtained funding, contributed to data analysis and interpretation, contributed to discussion, and reviewed and edited the manuscript.

Parts of this study were presented in abstract form at the 70th Scientific Sessions of the American Diabetes Association, Orlando, Florida, 25–29 June 2010 and at the 93rd Annual Meeting & Expo of the Endocrine Society, Boston, Massachusetts, 4–7 June 2011.

The authors would like to thank Harry Whitmore, Section of Endocrinology, University of Chicago, and the staff of the General Clinical Research Center, University of Chicago, for their assistance in the study. The General Clinical Research Center is supported by a Clinical Translational Science Award (CTSA; U54 RR023560). The authors would like to especially thank all research subjects for their participation in this study.

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