Brief Communication

Objectively measured sleep duration and plasma glucose values following an oral glucose tolerance test amongst pregnant women with obesity in the UK

Kathy M. Redfern [a], [*], Rachel S. Hine [a], Heidi J. Hollands [b], C. Ross Welch [b], Jonathan H. Pinkney [c], Gail A. Rees [a]

[a] School of Biomedical Sciences, Faculty of Medicine and Dentistry, University of Plymouth, United Kingdom
[b] Maternity Department, University Hospitals Plymouth NHS Trust, United Kingdom
[c] Institute of Translational & Stratified Medicine, Faculty of Medicine and Dentistry, University of Plymouth, United Kingdom

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ABSTRACT

Background/objectives: Short sleep duration has been linked to maternal hyperglycaemia following a 1-h 50 g oral glucose tolerance test (OGTT) in observational studies conducted primarily in the USA. Our objective was to examine the relationship between objectively measured sleep duration and plasma glucose values following the 2-h 75 g OGTT routinely used in the UK amongst women with obesity.
Methods: Sleep and OGTT data were available for 49 pregnant women who wore wrist actigraphs for at least two nights, and took a 2-h 75 g OGTT at the end of their second trimester. Multivariable regression was used to evaluate associations between sleep duration and OGTT results.
Results: Higher 2-h plasma glucose values were significantly associated with shorter sleep duration and higher maternal age and BMI, with no association observed between wake after sleep onset (WASO) and 2-h plasma glucose values. No associations were observed between fasting plasma glucose values and any sleep parameters.
Conclusions: We found that shorter sleep duration, as measured using actigraphy, is associated with higher 2-h plasma glucose values following a 2-h 75 g OGTT in the UK. These findings are in keeping with those observed elsewhere in the world, employing alternative OGTT protocols. Future studies should investigate sleep extension as a potential candidate for inclusion in future RCTs aiming to improve glucose tolerance and prevent GDM amongst those at risk.

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1. Introduction

It is well documented that maternal obesity, excessive gestational weight gain and the development of gestational diabetes mellitus (GDM) are risk factors for multiple adverse maternal and infant outcomes during pregnancy [1—3]. Numerous maternal lifestyle interventions aiming to limit gestational weight gain, prevent gestational diabetes mellitus and improve other maternal and infant outcomes have been conducted to date, with the majority of studies focusing on diet and physical activity [4,5].

Sleep is another potentially modifiable maternal lifestyle factor, and short sleep duration has been associated with metabolic disturbances and increased risk of obesity and type 2 diabetes in non-pregnant populations [6]. A recent meta-analysis of individual patient data demonstrated that objectively measured short sleep duration during pregnancy (<6.5 h) was associated with higher 1-h glucose levels following a 50 g oral glucose tolerance test (OGTT) and increased risk of gestational diabetes melitus [7]. However, of the four studies included in analysis, three measured sleep duration using a single overnight polysomnography (PSG), which as the authors acknowledge, may not reflect habitual sleep duration as measured by actigraphy, which was reported for just one study.

The diagnostic criteria for gestational diabetes mellitus varies worldwide, as does the dose of glucose administered as part of an OGTT. In the UK, the National Institute for Health and Care Excellence (NICE) recommend the use of the 2-h 75 g OGTT to test for gestational diabetes mellitus in women with known risk factors [8].

* Corresponding author. School of Biomedical Sciences, Plymouth University, Drake Circus, Plymouth, PL4 8AA, United Kingdom.
E-mail address: kathy.redfern@plymouth.ac.uk (K.M. Redfern).

The studies included in Reutrakul and colleagues' meta-analysis [7] were conducted in the US or Canada with different diagnostic criteria for gestational diabetes mellitus. To our knowledge, no studies have examined the impact of objectively measured sleep duration on blood glucose values following a 75 g 2-h OGTT according to NICE guidelines in the UK. It is important to ascertain whether a relationship exists before sleep is considered for incorporation into RCTs or antenatal advice in the UK. The aim of the present study is to investigate the impact of sleep duration assessed using actigraphy on OGTT results amongst a cohort of women with obesity in Plymouth, UK.

2. Materials and methods

2.1. Study population and design

Participants in the present study were part of a larger observational study examining the impact of gestational weight gain (GWG), diet and physical activity on maternal and infant outcomes.

Inclusion criteria included: age $\geq$18 and $<$ 40 years, BMI $\geq$30 and $<$ 40 kg/m^2, gestation $\leq$12 weeks at first antenatal appointment and a singleton pregnancy. Women with multiple pregnancies, pre-existing type I or type II diabetes mellitus or women identifying as any ethnicity other than white Caucasian were not eligible to participate, as the study was not powered to detect differences between these groups. Eligible women were identified from their first antenatal appointment notes and approached at their 12 week dating scan at Derriford Hospital in Plymouth, UK. Ethical approval was obtained from the NHS Health Research Authority National Research Ethics Service and local approval was obtained from Plymouth Hospitals NHS Trust.

2.2. Data collection

Following recruitment, verbal and written informed consent was obtained, and a questionnaire was administered to participants between 12 and 14 weeks gestation.

In the present study, sleep data were collected at the end of the second trimester. Women wore an Actigraph wrist-worn accelerometer (Actigraph wGT3X-BT, Florida, USA) on their dominant wrist for four days following the study visit, after which the device was analysed on the corresponding computer software program (Actilife 6.0, Florida, USA).

Participants with <2 valid days of sleep data were excluded from analyses. Sleep was identified using the Cole-Kripke sleep scoring algorithm [9] which has been validated for use in an adult population and recently used to assess sleep duration and disruption in late pregnancy [10]. For each participant, mean sleep duration, mean wake after sleep onset (WASO), WASO as a percentage of total sleep and sleep fragmentation was reported. WASO is defined as the total minutes spent awake between the onset of sleep and the end of rest interval, while sleep fragmentation is an index of restlessness during the sleep period expressed as a percentage.

All women enrolled in the study received a routine 2-h 75 g OGTT at approximately 28 weeks, as per NICE guidance [8]. Fasting and 2-h plasma glucose values were reported in mmol and the incidence of gestational diabetes mellitus according to NICE diagnostic criteria was recorded for each participant.

2.3. Statistical analysis

All data were entered into and analysed using SPSS (Statistics Package for the Social Sciences) for Windows version 21 (IBM, Chicago USA). The level of significance was set to a probability (p) < 0.05 for all statistical tests performed. Multiple regression was used to evaluate the extent to which maternal sleep duration and WASO influence maternal fasting and 2-h plasma glucose values following an OGTT after adjustment for age and BMI at first antenatal appointment. Sleep fragmentation was not included in the model in order to avoid multi-collinearity, as it was correlated with WASO.

3. Results

Of 75 women enrolled in the study, 49 had at least two days of valid sleep data in trimester two and an OGTT result. Table 1 shows the descriptive characteristics of these women. Women slept for an average of 7.0 $\pm$ 0.3 h per night and the average time spent in WASO was 9.0 $\pm$ 4.3%. Ten of the 49 women were diagnosed with GDM according to UK NICE guidance.

No statistically significant associations were found between maternal age, BMI, sleep duration or WASO and fasting plasma glucose values. Higher 2-h plasma glucose values were significantly associated with shorter sleep duration, higher maternal age and higher maternal BMI, with no association observed between WASO and 2-h plasma glucose values (Table 2).

4. Discussion

Results from our study indicate that sleep duration is inversely associated with 2-h, but not fasting plasma glucose values, following a 2-h 75 g OGTT, even after adjustment for maternal age, BMI and WASO. To our knowledge, this is the first study to examine the impact of objectively measured sleep duration using actigraphy on plasma glucose values amongst women in the UK, who receive a 2-h 75 g OGTT according to NICE guidelines [8].

Findings from our study are similar to those of Herring et al., [11] who observed that objectively measured short sleep duration using actigraphy was associated with incidence of gestational diabetes mellitus and higher 1-h plasma glucose values following a 50 g-OGTT in their cohort of 63 low-income urban women in the US. Other studies using self-reported measures of sleep duration have also reported an inverse relationship [12], and in some cases a U-shaped relationship between sleep duration and incidence of gestational diabetes mellitus [13]. Findings from the present study therefore suggest that the relationship between sleep duration and glucose intolerance is similar for women in the UK undergoing a 75 g 2-h OGTT to those in the US, who have typically undergone a 50 g 2-h OGTT in the current literature [7].

Experimental data from non-pregnant populations has demonstrated adverse effects on glucose tolerance, insulin

Table 1
Maternal characteristics.

	n = 49
Age, years	30.0 $\pm$ 4.4
BMI, kg/m^2	33.2 $\pm$ 2.1
Nulliparous, n (%)	20 (40.8)
Median gestation at sleep data collection, weeks^{+days} (IQR)	28 $^{+ 4}$ (5.5)
Fasting glucose, mmol/l	4.6 $\pm$ 0.6
2-h glucose, mmol/l	6.3 $\pm$ 1.6
GDM diagnosis, n (%)	10 (20.4)
Sleep duration, hours	7.0 $\pm$ 0.3
WASO, minutes	35.2 $\pm$ 17.1
WASO, %	9.0 $\pm$ 4.3
Sleep fragmentation index, %	27.4 $\pm$ 14.9

Mean $\pm$ SD unless otherwise stated.
IQR: interquartile range.
GDM: gestational diabetes mellitus.

Table 2
Summary of multiple regression analyses for associations between blood glucose, maternal age, BMI, sleep duration and WASO.

	Fasting glucose			2-h glucose		
	β	95% CI	p	β	95% CI	p
Maternal age, years	0.11	−0.027–0.058	0.477	0.41	0.045–0.246	0.006
BMI, kg/m^2	0.21	−0.026–0.145	0.165	0.28	−0.011–0.414	0.036
Sleep duration, minutes	−0.05	−0.002–0.002	0.777	−0.35	−0.009––0.001	0.025
WASO, %	0.05	−0.043–0.057	0.774	−0.04	−0.131–0.103	0.809

response, insulin sensitivity and glucose disposal with short sleep, but not regular sleep [14,15]. To our knowledge, no such experimental data has been collected from women during pregnancy, but Twedt and colleagues are currently conducting a pilot RCT to determine whether sleep education during pregnancy improves glycemic control amongst women with gestational diabetes mellitus in Pittsburgh, US [16].

A strength of the present study is that sleep duration has been measured objectively using actigraphy. Actigraphy correlates well with PSG and enables the assessment of habitual sleep in research participants' homes rather than in the laboratory [17]. Actigraphy has also been shown to be preferable to self-report questionnaires for estimation of sleep duration during pregnancy [18]. The accelerometers were programmed to collect data from 00.00 to 00.00 over four days, as a primary aim of the study was to collect four days of physical activity data. This meant that two nights of potential sleep data collection were interrupted, so that only a maximum of three night's data were available for each participant.

The present study was conducted amongst a cohort of women with obesity, with a BMI ≥30 and <40 kg/m^2. Obesity is a well-documented risk factor for impaired glucose metabolism during pregnancy and GDM [2], and the majority of intervention studies aiming to prevent gestational diabetes mellitus have been conducted amongst this group of women [19]. The women in this cohort were all receiving antenatal care in Plymouth, UK, where the majority of women are White Caucasian. As such, only women from this group were eligible to participate, as the study was not powered to identify differences between other ethnic groups without recruiting a larger sample of women, which was not feasible. As the prevalence of gestational diabetes mellitus is well-known to vary between different ethnic groups [20], the findings from the present study cannot be generalised beyond the present population. Future work in a larger cohort should include women of different ethnicities and from different geographical areas of the UK. It was also not possible to include daytime sleeping in our analysis as the majority of women did not sleep during the day, and thus the study was not powered to examine whether this practice influenced plasma glucose values. This is something that should be examined in future work, in a larger cohort.

In summary, we found that shorter sleep duration, as measured using actigraphy, is associated with higher 2-h plasma glucose values following a 2-h 75 g OGTT in the UK, after adjustment for age, maternal BMI and WASO. These findings are in keeping with those observed elsewhere in the world, with different OGTT protocols, and thus suggest sleep extension as a potential candidate for inclusion in future RCTs aiming to improve glucose tolerance and prevent gestational diabetes mellitus amongst those at risk. However, since long sleep duration has also been associated with impaired glucose tolerance and risk of gestational diabetes mellitus, larger, more diverse studies using objective measures of sleep duration are first required in order to identify optimal sleep duration during pregnancy.

Conflict of interest

The authors declare no conflict of interest.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2019.01.017.

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