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The impact of exercise on sleep in adults with type 1 diabetes

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Abstract

The aim of this pilot study was to investigate the impact of exercise on sleep and nocturnal hypoglycemia in adults with type 1 diabetes (T1D). In a 3-week crossover trial, 10 adults with T1D were randomized to perform aerobic, resistance or no exercise. During each exercise week, participants completed two separate 45-minute exercise sessions at an academic medical center. Participants returned home and wore a continuous glucose monitor and a wrist based activity monitor to estimate sleep duration. Participants on average lost 70 (± 49) minutes of sleep ($p = 0.0015$) on nights following aerobic exercise and 27 (± 78) minutes ($p=0.3$) following resistance exercise relative to control nights. The odds ratio with confidence intervals of nocturnal hypoglycemia occurring on nights following aerobic and resistance exercise was 5.4 [1.3, 27.2] and 7.0 [1.7, 37.3], respectively.

Aerobic exercise can cause sleep loss in T1D possibly from increased hypoglycemia.

Introduction

Regular structured physical activity (PA) in adults with type 1 diabetes (T1D) provides physiological and psychological benefits including reduction in macrovascular complications, improvement in lipid profiles, increased lean body mass, and enhanced self-esteem (1). However, PA is associated with an increased risk of hypoglycemia that may occur during, shortly after or even many hours after PA, and the risk for nocturnal hypoglycemia can persist for several days (2–4). The risk of nocturnal hypoglycemia ranges from 14% to as high as 56% in children and adults (5). Nocturnal hypoglycemia increases anxiety levels and is associated with a negative impact on the quality of life due to its impact on sleep quality and quantity (5, 6). While prior groups have related PA to increased nocturnal hypoglycemia, no one has yet quantified the amount of sleep loss either due to nocturnal hypoglycemia or due to the increased risk of nocturnal hypoglycemia on nights following different types of exercise. While exercise has been shown to increase sleep duration in people without type 1 diabetes (7), the impact of exercise in people with T1D is unknown. The purpose of the current study was to examine the effect of late afternoon PA on nocturnal hypoglycemia and sleep duration. We hypothesized that there would be increased nocturnal hypoglycemia and related sleep loss after aerobic exercise and also after resistance exercise relative to nights following control days of no structured PA.

Methods

In this study, participants carried wearable glucose sensors, actigraphy sensors, their own an insulin pump, and a custom built food-tracking Android smart-phone app that measured their glucose, physical activity, insulin, food, and sleep continuously for four consecutive weeks. The first week of the study was a run-in week where participants became accustomed to the wearable sensors. After the run-in week, participants performed one week of in-clinic aerobic exercise twice that week, one week of in-clinic resistance exercise done twice that week, and one control week when no structured exercise was done by the participants. The order of the aerobic, resistance, and control weeks were randomized for each subject. The Institutional Review Board at the Oregon Health and Science University (OHSU) approved the study protocol and consent form. Eligibility criteria were age 21–45 years, a duration of type 1 diabetes >1 year, current insulin pump use, an absence of diabetes-related complications and participating in physical activity at least 30 minutes three or more times per week. Ten adults (6F) were recruited (mean $\pm$ SD: age 33 ± 6 years, BMI 24.4 ± 2.1 kg/m², duration of diabetes 18 ± 10 years, HbA_{1c} $7.4 \pm 1\%$ [57 ± 11 mmol/ml], VO_{2 peak} 46.8 ± 11.55 mL/kg/min). All participants completed a screening visit, training visit, and four structured exercise sessions.

After providing informed consent, enrolled participants were given a VO_{2max} test according to the standard Bruce Protocol on a Medtrack ST 55 treadmill. Participants returned on a separate day to be trained on how to use a Dexcom G4 or G4 Share (continuous glucose monitor) CGM system (Dexcom, San Diego, CA, USA) and how to use the activity monitor (ActiGraph wGT3X-BT; ActiGraph, Pensacola, FL, USA). Participants replaced the CGM each week (at least a day before the exercise visit) and calibrated the sensor at least twice daily using a Contour Next glucose meter (Ascensia Diabetes Care, NJ, USA). Although participants were blinded to CGM values, for safety, glucose alerts were set at 55 mg/dL [3.0 mmol/L] and 300 mg/dL [16.7 mmol/L]. Hypoglycemia was defined as CGM values less than 70 mg/dL [3.9 mmol/L]. A one-repetition maximum (1-RM) test for bench press, leg press and seated row was performed to set the exercise intensity (i.e., weight lifted) for resistance training sessions. Participants completed three validated sleep questionnaires, the Pittsburgh Sleep Quality Index (8) (PSQI), the Epworth Sleepiness Scale (9) (ESS) and the Berlin Questionnaire (10) (BQ). These were used to assess sleep quality, excessive daytime sleepiness, sleep apnea risk. Computer randomization was used to determine the sequence of the exercise and control weeks.

Participants wore ActiGraph wGT3X-BT—a small, lightweight (19g), triaxial accelerometer with a light sensor on their non-dominant wrist for the entire duration of the study. Sleep was measured using this activity monitor and data was analyzed using the ActiLife software (ActiGraph) with the Cole-Kripke algorithm (11).

Experimental Visits

Subjects participated in 2 sessions of aerobic training during the aerobic exercise week and 2 sessions of resistance training during the resistance week. Participants arrived at the laboratory at 4:00 pm for each of the exercise sessions. For both the aerobic and resistance exercise weeks, the same exercises were performed on two separate days with one day in

between (e.g. resistance training session on a Tuesday and Thursday). The days on which exercise sessions were conducted were identical for each participant across weeks. All exercise sessions were conducted on weekdays excluding Friday. Control nights were selected to be on the same nights as the exercise nights. Resistance exercise sessions included three sets of 8–12 repetitions (~60–80% of 1-RM) of five different exercises [leg press, bench press, leg extension, leg flexion and seated row] with a 90 second rest period between exercises and sets (duration ~45min). The Borg perceived exertion scale was used to estimate fatigue by the participant and with the goal to not exceed the moderate intensity rating of 12–14 for each exercise performed. Aerobic exercise consisted of 45 min of treadmill exercise (60% of $\text{VO}_{2\text{max}}$). The duration of the exercise intervention was kept consistent for the two types of exercise; but the energy expenditure for these two types of exercises was not controlled for in this study. Capillary glucose was checked before the start of the exercise period and immediately after exercise. If the subject was below 70 mg/dL or above 300 mg/dL, exercise was delayed until glucose returned to within range. Glucose tablets or juice was provided to treat hypoglycemia. Each exercise session was followed by 60 minutes of monitored resting recovery. Participants selected one of two meals to eat during the recovery period and the identical meal was consumed during subsequent study visits.

All statistical analyses were performed using R-Software (12). A paired means power analysis was used to carry out sample size power analysis. A total sample size of 10 achieved 90% power to detect a mean of paired differences of 30 minutes in sleep loss. This is with an estimated standard deviation of differences of 25 and with a significance level (alpha) of 0.05 using a two-sided paired t-test comparing sleep loss during the weeks of exercise interventions with the week without any explicit exercise. Two analyses were done: one to assess impact of exercise on sleep duration and the second to assess impact of exercise on occurrence of a single hypoglycemia event in a night. For the first analysis, duration of sleep after the exercise sessions (resistance and aerobic) was analyzed and compared with the duration of sleep on nights when no explicit exercise was done (control). Since each subject had two aerobic exercise sessions, two resistance sessions, and two corresponding control days, we averaged sleep duration, carbohydrate intake, insulin dosed, and time in severe hypoglycemia across both nights and compared the average between weeks of exercise interventions with the week without any explicit exercise. Paired sample t tests were used to perform pairwise post hoc comparisons for average of nights between resistance and aerobic interventions relative to the control. Since two interventions were compared against a single control, significance was adjusted to 0.025. For the second analysis, a randomized mixed effects logistic regression model with subject as random effect was used to estimate the odds ratio of a single hypoglycemic episode occurring on nights (9 PM – 9 AM) following aerobic and resistance exercise compared with control nights. For this analysis, each night was used as a binary variable indicating whether a single hypoglycemic event occurred during that night (9 PM – 9 AM). We further considered the order of the nights as a repeated measure and evaluated the significance of the order.

Results

All participants completed the full protocol. In this active participant cohort none of the participants reported sleep issues at baseline with no excessive daytime sleepiness (ESS score <7), with two subjects reporting habitual snoring but no other symptoms of sleep apnea based on the BQ. Participants had good overall sleep quality (PSQI score < 3). The mean ($\pm$ SD) sleep duration was 6.8 ($\pm$ 0.8) hours/night during the control week (weeknights only), 5.6 ($\pm$ 1.1) hours/night during nights following aerobic exercise, and 6.4 ($\pm$ 1.5) hours/night during the nights following resistance exercise. The 70 minutes of sleep loss on the nights following aerobic exercise compared with control nights was statistically significant ($p=0.0015$) but the sleep loss on the nights following resistance exercise compared with control nights was not ($p=0.3$). Figure 1(a) shows how all but one participant experienced less sleep on nights following aerobic exercise compared with the control week. The average sleep onset latency was 0.5 ($\pm$ 1.4) min/night and the average bedtime was 11:30 pm ($\pm$ 65 min) and there was no difference in either sleep latency or bed time between the different weeks. The percentage of nights where at least one hypoglycemia event occurred (CGM<70 mg/dL) was 30%, 65%, and 70% for nights following control, aerobic, and resistance days. Average insulin on board concentration at bed time was lower following both aerobic and resistance exercise days as compared with the control and the reported carbohydrate intake was higher following aerobic and resistance exercise days as compared with the control (See Table S1 in Supplementary Materials). Figure 1(b) shows the Kaplan-Meier plot for the percentage of subjects who remained hypoglycemia-free on nights following exercise and control nights. Severe hypoglycemia (CGM <54mg/dL [3.0mmol/L]) occurred on 8 nights following aerobic exercise as compared with 3 nights on nights following resistance and 3 nights for control nights. The average percent of time spent in severe hypoglycemia was 3.7($\pm$ 8.4) %, 1.8($\pm$ 7.3) %, 2.4($\pm$ 6.1) % during the nights following aerobic, resistance and control, respectively. A majority of the hypoglycemic events for the nights following the resistance exercise occurred earlier in the night. The odds of hypoglycemia occurring increased by 5.4 [1.3, 27.2] on nights after aerobic exercise compared with nights after non-exercise control days and by 7.0 [1.7, 37.3] on the nights following resistance exercise. We did not observe an order effect on hypoglycemia in between day 1 and day 2 of exercise for either intervention. While nocturnal hypoglycemia was related to PA (chi-square=7.4, $p=0.025$, $R^2 = 0.30$), nocturnal hypoglycemia was not found to relate with sleep duration in this small sample size. This may have been due to the substantial variability in the response of the participants to hypoglycemia. For example, some subjects slept through hypoglycemia while others treated their hypoglycemia at night and experienced sleep loss. Figure 2 shows the sensor glucose and the sleep data overlaid for a single subject across the different nights of the study. This subject experienced multiple hypoglycemic events during the nights following aerobic exercise and each hypoglycemic event caused sleep loss.

Conclusions

This study assessed the impact of structured exercise on sleep duration related to nocturnal hypoglycemia in physically active individuals with T1DM. Results here also confirm higher hypoglycemia after structured physical activity. These results indicate that aerobic activity can negatively impact sleep by reducing total sleep duration on the night following exercise

by an average of 70 minutes. While resistance exercise also led to sleep loss, the impact was less and not statistically significant in this small sample size. This study may have been strengthened if we had included a healthy cohort to observe whether stress from physical activity was a potential confounding factor that may have influenced sleep. However, prior research has shown that in people without T1DM, sleep duration is increased with physical activity, even in people who do not exercise regularly (7). All participants in the current study were required to be physically active and to do regular exercise (minimum of 30 minutes 3 times per week). Aerobic and resistance exercise are known to impact glycemic control in different ways, and prior findings indicate that aerobic exercise can lead to sharper drops in glucose levels in people with T1DM (13). It is currently not known whether this is because less energy is expended during resistance exercise compared with aerobic exercise or if there is some other mechanism. It has been reported that the increase in catecholamine levels during resistance activities could contribute to increased hepatic glucose production and inhibit insulin-mediated glucose uptake (13). While people with T1DM may be aware of the increased risk of hypoglycemia during PA, immediately after PA and overnight up to 7 to 11 hours later (14), they may not be aware of the impact on sleep loss. Given the interaction between sleep disturbance and T1DM is complex and the loss of sleep could result in decreased insulin sensitivity on the day after a poor night's sleep (15), increased vigilance and improved recommendations for post-exercise insulin delivery are needed to help overcome nocturnal hypoglycemia and the associated sleep loss.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

(a) Average sleep loss (min) for each of the intervention week as compared with the control week. The and the number next to it, indicate the mean value of the sleep loss. All but one participant experienced sleep loss on nights following aerobic exercise.

(b) Kaplan-Meier plot for hypoglycemia-free subjects and the incidences of hypoglycemic events. The solid line indicates--control nights, the dashed line indicates--aerobic nights and the dotted line indicates--resistance nights.

Figure (2).

Representative subject data: Here we show the CGM sensor and the actigraphy data overlaid. The CGM sensor data is shown as a solid black line and the actigraphy data is shown below the sensor data, as indicated by the gray squares for sleep and black squares for being awake. Capillary blood glucose (BG) checks performed by the subject are indicated with a black triangle. Column one shows the aerobic nights, column two shows the resistance nights and column three shows the control nights. The dashed line indicates hypoglycemia at 70mg/dL [3.9mmol/L] and the dotted line indicate severe hypoglycemia at 54mg/dL [3.0mmol/L]. Hypoglycemic events following the aerobic exercise and the associated sleep loss can be observed by the change in the actigraphy state. Hypoglycemic events for the resistance nights occur during the early part of the but are not associated with sleep loss and the control nights' following days with no exercise was spent in the hyperglycemia.