Original Research

Dim Light Exposure or Melatonin Ingestion Lowers a Type 2 Diabetic's Blood Glucose Removal Rate: A Single Case

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ABSTRACT

International Journal of Exercise Science 12(2): 1161-1168, 2019. The purpose of this case study is to compare a Type 2 diabetic's postprandial glucoregulatory ability under two different room lighting conditions. The subject was a 56-year-old physically active male with well controlled blood glucose levels (HbA1c ≤ 6% for 5 y) from a combination of diet, exercise, and medication. Two hours post evening meal (380 kcal, 18 g fat, 44 g carbohydrate, 12 g protein), a 45 g carbohydrate challenge was given, and blood glucose was measured every 30 minutes for 2.5 hours under three conditions: dim light (<50 lux) (DL), bright light (>40000 lux) (BL), and bright light plus 6 mg melatonin (BLM). Each condition was repeated 3 times over a period of 6 months with each trial a minimum of seven days apart. The area under the average glucose concentration *vs.* time plot was different between the three conditions (BL = 909 $\pm$ 76; DL = 1078 $\pm$ 106; and BLM = 1130 $\pm$ 45 mmol·min·l^{-1}). Visual inspection of the average blood glucose *vs.* time plot suggested that DL and BLM displayed very similar patterns and magnitude, with both DL and BLM having the blood glucose concentrations at each time point that are noticeably greater than BL. Additionally, the average (± standard deviation) blood glucose concentrations for DL (8.8 ± 0.9 mmol·l^{-1}) and BLM (9.1 ± 1.1 mmol·l^{-1}) were respectively 18% and 22% greater than BL (7.5 ± 0.5 mmol·l^{-1}). Melatonin and/or dim light can reduce a Type 2 diabetic's glucoregulatory ability.

KEY WORDS: metabolic disease, glucose regulation, melatonin supplementation, light intensity, case study

INTRODUCTION

Melatonin (N-acetyl-5-methoxytryptamine) is a hormone primarily produced by the pineal gland, and its production increases as ambient light intensity decreases. Since insulin levels show a circadian rhythm in humans that changes in an opposite manner to melatonin (i.e., insulin is at a maximum when melatonin is at a minimum and vice versa) (1), some research has tried to tie exposure to differing light intensities to blood glucose levels. For example, blood glucose concentration immediately after supramaximal exercise was significantly lower after bright light exposure compared to dim light (17), nightshift workers showed higher blood glucose after a nighttime meal than after a daytime meal (11), and healthy humans endogenous glucose production and gluconeogenesis were lower during the night than that of human's with

type 2 diabetes (14). Moreover, the relationship between melatonin and blood glucose levels have been studied and conflicting data have been published concerning this relationship. For instance, exogenous melatonin increases blood glucose in pigeons (5), but in rats it can either have no influence on plasma glucose levels (6,8) or it can cause increases blood glucose (10,16). In two exercise-to-exhaustion studies, muscle and liver glycogen content were significantly higher in melatonin treated exercised animals compared to untreated exercised animals (10,16). Similar to rat studies, resting human studies have been equivocal, showing melatonin to either decrease glucose usage (2), or have no correlation with glucose removal and utilization (14).

Many individuals during the winter months try to economize by reducing home lighting. Since a few research studies relate dim light conditions, such as watching television in a dark room, to higher blood glucose, it is possible that postprandial sitting in dim light during the evening hours could negatively influence the glucoregulatory ability of people with Type 2 diabetes. To test this, blood glucose levels of an individual with Type 2 diabetes were carefully tracked under differing light conditions nine times during a winter season.

METHODS

Participants
The participant was a 56-year-old male (height = 185 cm, body mass = 89 kg, BMI = 26.0 kg/m^2), who had been diagnosed with Type 2 diabetes 6 years and 3 months prior to study inception. Blood glucose was under control through a program combining diet, exercise, and medication. Two months prior to study inception, HbA1c = 5.9%, and one month post study HbA1c = 6.1%. The participant was physically active and exercised at least 5 days a week doing 30 minutes of treadmill walking up at 6% grade at 96.6 m·min^{-1} (3.6 mph). A total of seven prescription medications were taken at least once a day at either ~0500 h (22.5 mg pioglitazone hydrochloride, 2.5/250 mg glyburide/metformin, and 5 g 1% testosterone gel), or at ~2130 h (22.5 mg pioglitazone hydrochloride, 2.5/250 mg glyburide/metformin, 10 mg benazepril hydrochloride, 10 mg rosuvastatin calcium, 145 mg fenofibrate, and 2 drops 0.03% bimatoprost ophthalmic solution).

Protocol
During each testing session (Figure 1), the participant's blood glucose was monitored for 2.5 hours under one of the following conditions: dim light (< 50 lux) (DL), bright light (> 40000 lux) (BL), or bright light plus 6 mg melatonin (BLM). The participant was tested three times under each condition, resulting in nine testing sessions conducted on nine separate evenings. Each session was conducted on the same day of the week across nine weeks over a six month period, with daytime physical activities and dietary intake maintained at similar levels across experimental days. The conditions were randomly assigned to the nine testing sessions in the following order: DL, BL, BL, DL, BLM, BL, BLM, DL, and BLM. For the duration of each test session, the participant sat on a reclining chair in a 4.9 m (16 ft) x 4.3 m (14 ft) x 2.5 m (8 ft) climate-controlled room. The only light source in the room for the DL sessions came from a 25 cm (diagonal measure) television positioned 12ft away from the subject. For the BL and BLM sessions the room was lit by not only the television but also by 10 lamps, each with an unshaded

60 W incandescent bulb. On each study day at 1700 h the participant consumed a can of soup (380 kcal, 18 g fat, 44 g carbohydrate, and 12 g protein by label) for his evening meal. At 1900 h the study commenced in the appropriate light condition with an initial blood glucose reading taken from a finger prick drop of blood using a portable glucometer (Accu-Chek Compact, Roche Diagnostics; Indianapolis, IN). The Accu-Chek portable glucose meter was calibrated according to company guidelines and has been shown accurate in previous research (18). After the initial blood glucose measurement, the participant drank a 355 ml (12 fl oz) can of fruit juice containing 45 g of carbohydrate (by label). For the BLM sessions, the participant also consumed two 3g tablets of melatonin with the juice (Pharmavite LLC; Mission Hills, CA). Thereafter, the participant sat quietly, and blood glucose was measured at 1930 h, 2000 h, 2030 h, and 2130 h. The blood glucose reading for each time point was an average between drops obtained from the opposing fingers on both hands. If the two readings were not within 0.22 mmol·l^{-1} (4 mg·dl^{-1}), two new readings (one from each hand) were taken until both readings fell within the desired range. The experiment was IRB approved and the subject gave informed consent.

Statistical Analysis
For each condition (BL, DL, BLM) blood glucose concentration (mmol·l^{-1}) was plotted across the five time points for each testing session (block), and the area under each of the nine curves was calculated (mmol·min·l^{-1}) as the dependent variable (blood glucose concentration). A single-case randomized block analysis (19), which is analogous to a one-way repeated measures ANOVA but is appropriate for use in single-case designs, was used to determine if the areas under the curves (blood glucose concentration) were different between the three conditions. The level of significance for this analysis was set *a priori* at $p \leq 0.10$. Additionally, blood glucose concentration (mmol·l^{-1}) averaged within the three blocks for each condition (BL, DL, BLM) was plotted across the five time points (min). This average blood glucose *vs.* time plot was used to visually inspect for specific differences in glucose concentration between the conditions in the event that the single-case randomized block analysis returned a significant overall difference between the conditions (7).
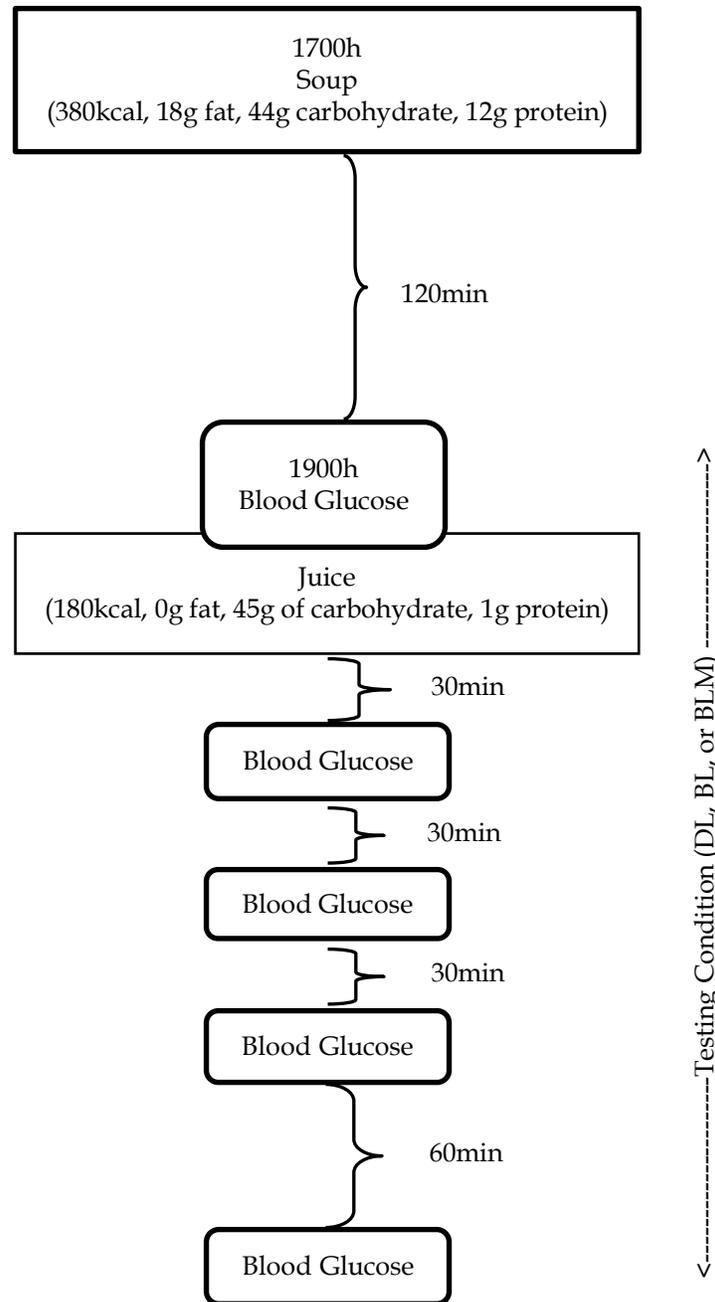
Figure 1. Protocol Design: The subject's blood glucose was monitored for 2.5 hours with the first measure being taken immediately before drinking 45g of carbohydrate. The testing conditions began at 1900h and were either dim light (DL), bright light (BL), or bright light plus 6mg melatonin (BLM).

RESULTS

The analysis of the prediction that the areas under the curve (blood glucose concentration) (Table 1) would differ between the three conditions yielded that the percentage of random data arrangement yielding differences at least as large as the differences obtained in the present study to be at 0.0785 (i.e., $p = 0.0785$). This infers that the overall differences between the conditions were significant ($p < 0.10$). The *post-hoc* visual inspection of the average blood glucose *vs.* time

plot (Figure 2) to assess specific differences between the conditions suggests that DL and BLM display very similar patterns and magnitude, with both DL and BLM having the blood glucose concentrations at each time point that are noticeably greater than BL. Additionally, over the total daily test period, the average (± standard deviation) blood glucose concentrations for DL (8.8 ± 0.9 mmol·l⁻¹) and BLM (9.1 ± 1.1 mmol·l⁻¹) were respectively 18% and 22% greater than BL (7.5 ± 0.5 mmol·l⁻¹). Likewise, the total area under the average glucose concentration *vs.* time plot was lower for BL than for either DL or BLM (Table 1).

Table 1. Blood glucose concentration with light exposure.

Condition	Session (Block)	Blood Glucose (mmol·min·l⁻¹)
DL*	1	1147
	2	1131
	3	956
	Mean ± SD	1078 ± 106
BL*	1	988
	2	837
	3	902
	Mean ± SD	909 ± 76
BLM*	1	1078
	2	1152
	3	1161
	Mean ± SD	1130 ± 45

Values reflect total areas under the blood glucose concentration (mmol·l⁻¹) *vs.* time curves for each session. DL = dim light exposure; BL = bright light exposure; BLM = bright light exposure + melatonin. *conditions were significantly different ($p < 0.10$).
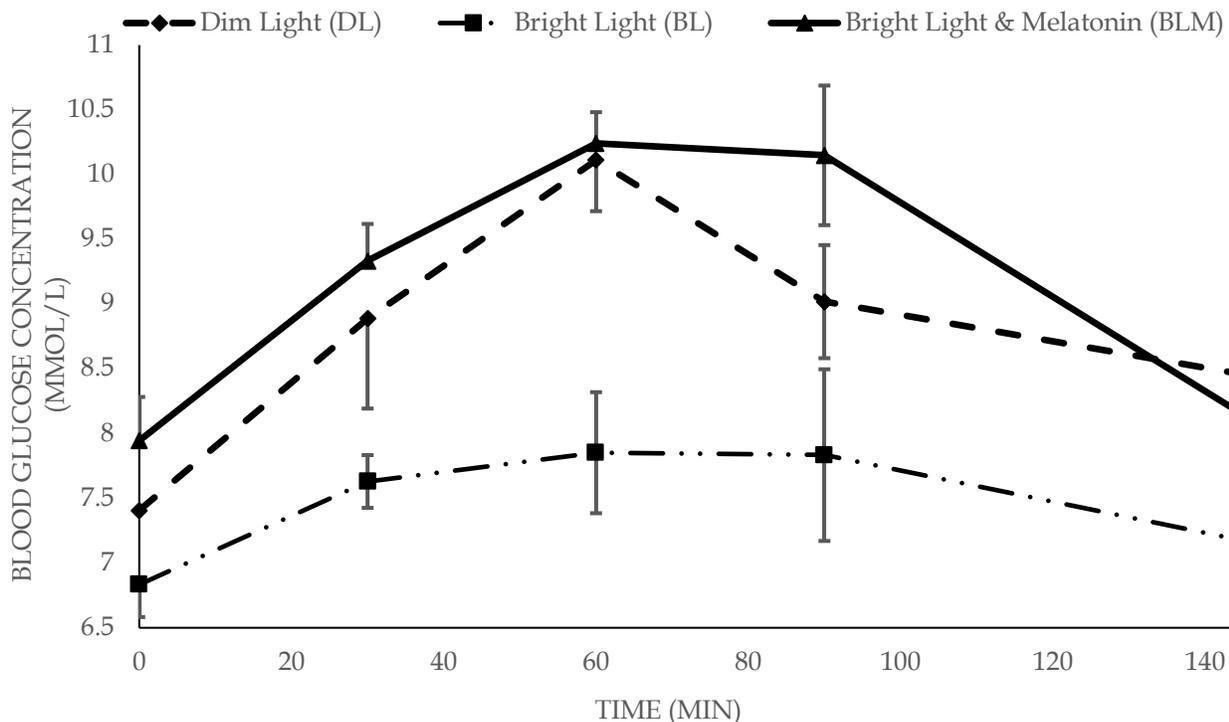

Figure 2. Blood glucose concentrations after ingesting a carbohydrate load under three lighting conditions. Error bars represent standard error for the three trials under each treatment condition (DL, BL, and BLM).

DISCUSSION

As mentioned above, some research has tried to tie exposure to differing light intensities to blood glucose levels. In a 2002 review, Morgan et al. (11) showed that nightshift workers had higher blood glucose after a nighttime meal than after a daytime meal. Moreover, Radziuk and Pye (14) showed that the effect of light exposure on blood glucose levels was more pronounced in individuals with type 2 diabetes. Additionally, the work of Cagnacci et al. (2) suggested that the elevated blood glucose could be due to the higher levels of melatonin. The results of this investigation are in line with the implications of the aforementioned research. For the individual tested, quiet sitting under dim light conditions after consuming a glucose load resulted in a longer period of elevated blood glucose. In addition, the pattern of elevated glucose closely followed that of sitting still in bright light conditions following ingestion of both a glucose load and 6 mg of melatonin.

It could be argued that our results may not be representative of the general population of type II diabetics as our study included a subject whose diabetes could be considered 'well controlled,' and we utilized a single case study design. Nevertheless, finding an impact of dark and light on blood glucose with a more controlled individual does make one wonder if a less controlled person would have a more deleterious response. Furthermore, with respect to our use of only a single subject, the decision was impacted by the desire to have a tightly controlled investigation that limited the influence of the confounding factors of varied daily activity, differing medications, fluctuating daily dietary intakes, diverging daily light exposures, etc. It was difficult to recruit subjects willing to commit an evening on the same day of the week for nine consecutive weeks for data collection. Since this was a single case, it required non-traditional data analysis. In single-case designs it is common for visual inspection to be the sole analysis used to determine the relationship between interventions and dependent variables (12,19) While this form of analysis was used here, it was employed as a supplement to a statistical analysis in an attempt to lend strength to inferences. Additionally, given the exploratory nature of the study, its single-case design, and relatively low Type I error cost, an *a priori* $\alpha = 0.10$ was chosen for the analysis. Support for the use of less rigorous levels of significance is such preliminary investigations have been supported elsewhere (4,15).

The glucose load and meal timing in this study were novel compared to standard literature examining glucose removal. For example, an oral glucose tolerance test typically uses a 75g glucose load versus the 45g load used here. Additionally, this research includes a meal 2 hours prior to glucose loading, versus the more standard practice of an overnight fast prior to testing. The rationale for the above methodology was adherence to the subject's dietician recommendations, a 45g CHO snack, and an interest in mimicking a normal evening routine, having a snack a couple hours after a meal and watching television in the evening. Melatonin supplementation in this study was more standard, as our dosage of 6mg is comparable to the 5-6mg used in much of the research examining the ergogenic effects of melatonin (3).

Given that this is a single-case investigation, it is suggested that the findings presented here are best utilized as a 'springboard' for further investigations into the influences of light intensity

and/or melatonin upon blood glucose levels, especially as it pertains to individuals with metabolic disorders. Interestingly, Peschke (13) and Korkmaz et al. (9) have suggested that melatonin ingestion might be a beneficial treatment for individuals who have pre-diabetes or metabolic syndrome. The findings of this investigation, however, would appear to contraindicate the use of melatonin for those conditions. Obviously, the need for more research on the relationship of light intensity and/or melatonin upon blood glucose is warranted by this single-case investigation. Additionally, since the data for each condition were similar for the repeated measures over the nine weeks, it is probably not as necessary to collect data on subjects multiple times over extended weeks. This would allow for similar experiments with larger sample sizes. Also, this would allow such manipulations as discontinuing diabetic medications for 24-48 hours, thus eliminating the effects of medications without incurring threatening conditions for the participants.

For the individual tested, quiet sitting under dim light conditions after consuming a glucose load resulted in a longer period of elevated blood glucose. Moreover, the pattern of elevated glucose closely followed that of sitting still in bright light conditions following ingestion of both a glucose load and 6 mg of melatonin. Future research should further explore findings of this single-case study, which suggests that people with Type 2 diabetes should pay attention to lighting conditions following food ingestion. It also suggests that nighttime may be an ideal time to partake diabetes medications. Finally, it calls into question the recommendations of melatonin supplementation as a treatment modality for metabolic syndrome and pre-diabetes and supports the need for further investigation on the relationship between melatonin and blood glucose levels.

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