Research Letter Title: Exploring the Relationship between Regular Physical Activity and the 24-hour Glucose Cycle in Gestational Glucose Intolerance or Gestational Diabetes Mellitus

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Conflict of Interest Disclosure: Dexcom, Inc. donated the CGM equipment for this study. The authors have no other relevant conflicts of interest to disclose.

Word Count: 490

Figure: 1

Keyword: gestational diabetes, gestational glucose intolerance, continuous glucose monitoring, physical activity
**Objective:** Physical activity (PA) is recommended for gestational diabetes mellitus (GDM) for its metabolic benefits, but PA’s impact on the 24-hour glucose cycle has yet to be explored.

**Methods:** Our pilot feasibility trial (ClinicalTrials.gov NCT04209348) compared a behavioral PA intervention to a general wellness intervention for gestational glucose intolerance (GGI, glucose ≥130 mg/dL on the 50g, 1-hr screening at 24-28 weeks) or gestational diabetes (GDM, by the Carpenter and Coustan criteria). Patients from the University of Tennessee Medical Center were enrolled (N= 20, IRB # 4547) and completed study visits at 30-31 weeks and 36-37 weeks. Due to COVID-19 protections, participants ‘opted in’ to the continuous glucose monitor (CGM) assessment. Thus, a subset wore Dexcom G6 CGMs, linked to a masked receiver, on the posterior of the upper arm for 7-days: 14 participants at baseline and 11 at follow-up (10 at both). Participants also completed surveys, which included the Stanford Leisure-Time Activity Categorical Item (L-Cat), a single item that has strong psychometrics. The L-Cat categorized PA behavior in the past month according to national PA recommendations (i.e., sufficient versus insufficient PA).

Typical 24-hour glucose functions were estimated with B-splines (i.e., 3rd degree polynomials with 17 knots) via Functional Data Analysis in JMP software (version 16) from SAS. Standard least squares regression of the Functional Data Analysis-generated 24-hour mean glucose, controlling for GDM, were also run in JMP. Visual assessment of the functions revealed that glucose in the early morning period might be lower for those with sufficient PA as compared to insufficient PA. Proc Mixed in SAS compared mean midnight-6am glucose by sufficient versus insufficient PA, controlling for GDM.
Results: Figure 1 displays the 24-hr glucose functions for sufficient PA (red) versus insufficient PA (blue), and their 95% CIs (shaded areas), at baseline (panel A) and follow-up (panel B). At baseline (n= 14), 4 participants (29%) had GDM, and 3 (21%) reported sufficient PA; 2 of the 3 reporting sufficient PA at baseline also had GDM. Adjusted mean 24-hr glucose at baseline was 90.9 mg/dl (SE 6.7) for sufficient PA and 96.6 mg/dl (SE 4.2) for insufficient (P = .51). Adjusted mean midnight-6am glucose at baseline was 88.4 mg/dl (SE 7.2) for sufficient PA and 93.3 mg/dl (SE 4.5) for insufficient (P = .59). At follow-up (n= 11), 3 participants (27%) had GDM and 5 (45%) reported sufficient PA; 2 of the 5 reporting sufficient PA at follow-up also had GDM. At follow-up, adjusted mean 24-hr glucose was 95.8 mg/dl (SE 4.3) for sufficient PA and 102.1 mg/dl (SE 4.5) for insufficient (P = .33). Adjusted mean midnight-6am glucose at follow-up was 94.8 mg/dl (SE 4.9) for sufficient PA and 98.1 mg/dl (SE 5.1) for insufficient (P = .64).

Conclusion: Findings in this small sample of GGI or GDM with variable diets are clinically interesting and support further investigation using CGM to explore the association of targeted PA with glucose and perinatal outcomes6 in pregnancies complicated by glucose intolerance.

Acknowledgements

Dr. Ehrlich is supported by grant K01DK105106 from NIH-NIDDK and is the guarantor of this work. Dexcom, Inc. donated the CGM equipment for the Project Wellness pilot feasibility randomized controlled trial. The authors have no other relevant conflicts of interest to disclose.


**Figure 1.** Typical 24-hour Glucose Functions and their 95% Confidence Intervals estimated by Functional Data Analysis (FDA) for Sufficient Physical Activity (Red) versus Insufficient Physical Activity (Blue) at the Baseline and Follow-up Study Visits, Project Wellness, the University of Tennessee Medical Center, 2020-2021.

A. Typical 24-hour Glucose Functions at BASELINE

B. Typical 24-hour Glucose Functions at FOLLOW-UP