The Impact of Prenatal Exercise Type and Intensity on Glucose Control in Women with Gestational Diabetes Mellitus

Date: September 19, 2024

STUDY PROTOCOL

Participants. Twenty-three pregnant women in the 2nd/3rd trimester will be recruited through IRB approved paper advertisements posted in physician offices and local community buildings (**NOTE**: participants will not be *actively* recruited at physician offices or by physicians). When participants express interest, they will be pre-screened through a phone call to determine eligibility, and, if eligible, they will be asked to get physician clearance. When clearance is obtained, the first visit will be scheduled. Inclusion criteria consist of biological female, one fetus, 24-30-wks gestation, 18-35 yrs old, sedentary, and conception without fertility treatments. Exclusion criteria will consist of metabolic disorders, medication that affects metabolism, drugs/tobacco, or alcohol during pregnancy, and contraindications to exercise.

Study design. This study will be a crossover design with four conditions: low intensity RT (RT-LOW), moderate intensity RT (RT-MOD), low intensity AT (AT-LOW), moderate intensity AT (AT-MOD). Participants will come for five visits. Visit 1 will consist of the informed consent, baseline data collection, and scheduling the exercise visits. During Visit 1, we will record the participant's height, weight, body mass index (obesity level), resting heart rate, and blood pressure. We will also record the participant's age, race, ethnicity, and gestational week.

Visits 2 to 5 will be the exercise visits, completed in random order separated by ≥3d to avoid a training effect (i.e., how one exercise bout can affect the next). Participants will come to the lab in the early morning, fasted, and under the same diet and physical activity conditions. Diet will be confirmed using a 24-hr food log, and physical activity will be reported using a 3-d exercise log. The length of each exercise session will be the same (~45 minutes). ***Intensity*** will be controlled using the rate of perceived exertion (RPE), a subjective rating of exertion. This scale runs from 1 to 10, with 1 being very light activity, and 10 being maximal effort. During sessions, exercise intensity will be adjusted (weight during RT, speed during AT) so that the participant maintains a 5-6 for low and a 7-8 for moderate intensity.

Continuous glucose monitoring (CGM) to measure glucose control. In the beginning of Visit 2, a CGM (FreeStyle Libre 3, a wearable device with a small sensor that is inserted under the skin and tracks glucose levels), will be placed on the back of the participants' arm (**NOTE**: placement does *not* require a medical professional; the PI will do it). CGMs last 2 weeks, therefore, each participant will have up to 2 CGMs placed. CGMs will capture information (e.g., post-meal glucose, high/low glucose times[18]) for 24 hours after each exercise bout.

Insulin sensitivity quantification. Before and immediately after exercise bouts, a blood sample will be collected from the antecubital vein into EDTA-coated plasma vacutainers and centrifuged for 15 min at 1370 × g at 4◦C. Samples will be stored at −80◦C for later analysis of insulin (cat. no. RE53171, IBL International). Blood will also be collected in serum vacutainers and immediately analyzed for glucose (RediOn Blood Glucose Monitoring System). Insulin sensitivity will be calculated using the quantitative insulin sensitivity check index (QUICKI = $1/(\log(I_0) + \log(G_0))$, in which I_0 is the fasting insulin, and G_0 is the fasting glucose value). The change in insulin sensitivity from pre- to post-exercise bout will be calculated. Blood will also be analyzed for C-reactive protein (CRP, inflammatory marker) and tumor necrosis factor alpha (TNF alpha, anti-inflammatory marker).

Exercise training. Participants will first complete a low intensity aerobic warm-up for five minutes. During both RT sessions, participants will perform eight exercises that will target the whole body. Exercises will be performed using dumbbells at 4 sets of 10 repetitions, with 1-min rest between sets. The first set will be done with very light weight (warm-up). The next three sets will be the "working sets," done with a weight that will elicit the proper intensity. If the participant reports a low RPE, the weight will be increased by ~5% for upper body, and ~10% for lower body until the desired intensity is achieved. During AT, participants will use either a treadmill or an elliptical. Throughout the 45-minute session, every 5 minutes, the participant will report their RPE, and if they report low, their speed will be increased by 0.1-0.5 mph until the proper intensity is achieved. Participants will end with full body stretching cool-down, and will be given a meal bar.

Statistical analysis. A power analysis was performed using a standard online calculator[19] with 2-hour postprandial blood glucose (mmol/L) as the primary outcome variable. The analysis revealed a need for 18 participants with a power of 0.80, an α level of 0.05, and a standard deviation of 6.48 mmol/L (from the AT control group)[20]. To account for a 25% attrition rate common to exercise studies[21], we will recruit 23 total participants. A repeated-measures ANOVA will be used to compare the differences in all outcome variables between conditions. If a significant finding is noted, a Tukey's honestly significant difference test (HSD) post hoc analysis will be used to locate where the difference exists.

Timeline. Recruitment will occur during Fall, 2024 and Spring, 2025. Data collection will occur from Spring to Summer, 2025. Data analysis will occur in Summer, 2025.

Short- and Long-Term End-Products. In the short term, this study will contribute to the body of knowledge that supports exercise as a form of medicine. It will inform professionals about the appropriate dose of exercise type and intensity to help regulate blood sugar levels in populations with dysregulated blood sugar levels. The short-term (2-yr) goal will be to complete this study, write/submit/publish a manuscript for this study, and present research findings locally and nationally. In the long-term (up to 10 years), this study and others like it will help create the most optimal exercise prescription for women with GDM so that they are not longer prescribed exercise for general health, but rather, they are prescribed exercise to treat their main physiological issue. In this time, the PI will apply to larger external and internal grant mechanisms (see section F) to fully optimize the best exercise prescription for women with GDM, and then implement this prescription and assess its effect on the health of both the mother and the baby (e.g., baby metabolism and growth rate).