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The Role of Inter-Set Rest Periods in High-Intensity Interval Training on Acute Glucose and Insulin Sensitivity in Type I Diabetic Children: A Randomized Crossover Study

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Authors' contributions

This work was carried out in collaboration among all authors. Author JRVS performed all steps of this manuscript, performed the administrative, supervised the study, did data visualization and participated in drafted the manuscript, did data curation and treatment analysis, wrote all versions and revisions and worked as a laboratory supervisor. Both Authors prepared the final version. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Aims: To investigate the impact of different inter-set rest periods on blood glucose levels and insulin sensitivity (IS) in children with type 1 diabetes.
Study Design: An experimental randomized crossover trial.
Place and Duration: Recruitment took place in the public health network of Rio Branco, Acre, Brazil.
Methodology: Twenty subjects participated in three different HIIT protocols with varying rest intervals. The first protocol consisted of 20 seconds of exercise followed by 10 seconds of rest (HIIT20-10), the second with 20 seconds of rest (HIIT20-20), and the third with 60 seconds of rest (HIIT20-60). The exercise used in all protocols was the burpee, performed at maximum effort for a total of 12 minutes, comprising 24 sets. Blood glucose levels were measured through finger-prick tests before exercise, immediately after, and at 15, 30,60,and120 minutes post-exercise. For insulin sensitivity, 4 ml of venous blood was drawn before, immediately after, and at 30, 60, and 120minutes post-exercise, and the TyG Index was used to calculate IS.
Results: No significant differences were observed between the HIIT20-20 and HIIT20-60 groups ($p>0.05$) regarding glucose levels. However, the HIIT20-10 protocol showed significantly lower glucose levels from 15 minutes to 120 minutes post-exercise ($p<0.05$) and improved IS at 60 minutes ($p<0.05$) and 120 minutes ($p<0.01$) after the exercise session.
Conclusion: The inter-set rest period influences glucose metabolism during HIIT in children with type 1 diabetes.

Keywords: Metabolic health; glucose metabolism; type I diabetes; high-intensity interval training; insulin sensitivity.

1. INTRODUCTION

Type 1 diabetes (T1D) is a chronic autoimmune disease that destroys the insulin-producing β-cells of the pancreas, leading to insulin deficiency. This condition is a significant public health concern worldwide due to its silent progression and associated complications[1]. T1D is often accompanied by metabolic disorders, including insulin resistance and central fat accumulation, which are predictive factors for cardiovascular disease [2].

Consistent evidence shows that a sedentary lifestyle is linked to metabolic impairments, while physical exercise can prevent or reverse these effects [3]. Exercise has been shown to improve the body's systemic responses to various nutrients, including glucose [4]. Specifically, physical activity is recognized for its positive effects on metabolic diseases such as diabetes [5–7]. In contrast, a sedentary lifestyle is associated with the development and worsening of conditions like diabetes [1].

Our research group has demonstrated that high-intensity interval training (HIIT) is an effective tool for combating metabolic diseases in both young and older adults with diabetes or metabolic syndrome [8]. HIIT-based programs offer non-pharmacological benefits in treating insulin resistance (IR) and diabetes [9], particularly through the use of HIIT [10].

In 2017, the American Diabetes Association recommended 30-60 minutes of moderate-intensity exercise for children and adolescents with T1D [11]. However, the optimal exercise guidelines for improving both acute and long-term glycemic control in youth with T1D are still unclear. Previous studies have shown that fasted HIIT is safe [12] and can consistently increase blood glucose levels during exercise. Intense interval exercise is often linked to higher blood glucose profiles and a lower risk of hypoglycemia during exercise compared to continuous exercise [13]. These findings are largely due to increased counter-regulatory hormone secretion, which enhances hepatic glucose production and reduces peripheral glucose disposal [14,15].

In healthy adolescents, a single bout of time-efficient HIIT improves glucose tolerance and insulin sensitivity, suggesting HIIT as a viable strategy for managing glycemic control in youth with T1D [12,14]. However, the relationship between exercise stimulus, rest periods, total exercise volume, and intensity-key variables in exercise prescription has not been thoroughly investigated [8], This results in inconsistent evidence supporting the optimal HIIT dosage for improving glycemic control in children with T1D.

This study's findings are particularly significant for the scientific community as they provide insights into how different HIIT protocols may manage glucose levels in children with type 1 diabetes. Given the increasing prevalence of diabetes in children, understanding the effects of various exercise regimens on metabolic health is crucial. We hypothesize that exercise induces positive acute adaptations in glucose metabolism and insulin resistance. Thus, we aimed to investigate the impact of different interest rest on blood glucose levels, and insulin sensitivity (IS).

2. METHODS

2.1 Study Type, Participants and Ethic

This study employed a randomized crossover design with blinding during the selection process to minimize bias. Children with type 1 diabetes were selected based on specific inclusion criteria, such as a medical history free of cardiovascular complications and no limitations on physical exercise.

Participants: During the initial week of the experiment, 20 children (age: 12.8±2.1 years, weight: 60.4±16.8 kg, height: 145±22.35 cm, BMI: 28.7±14.8 kg/m²) were randomly assigned to different intervention groups using a 1:1:1:1 ratio. Over the course of the study, each group was reassigned to different interventions weekly, following a randomized sequence. A 6-day washout period between interventions was implemented to mitigate the influence of prior exercise sessions. Fig. 1 illustrates the crossover method utilized in this study.

Interventions: Three HIIT protocols with varying rest intervals were tested:

- **HIIT20-10:** 20 seconds of exercise followed by 10 seconds of rest.
- **HIIT20-20:** 20 seconds of exercise followed by 20 seconds of rest.
- **HIIT20-60:** 20 seconds of exercise followed by 60 seconds of rest.

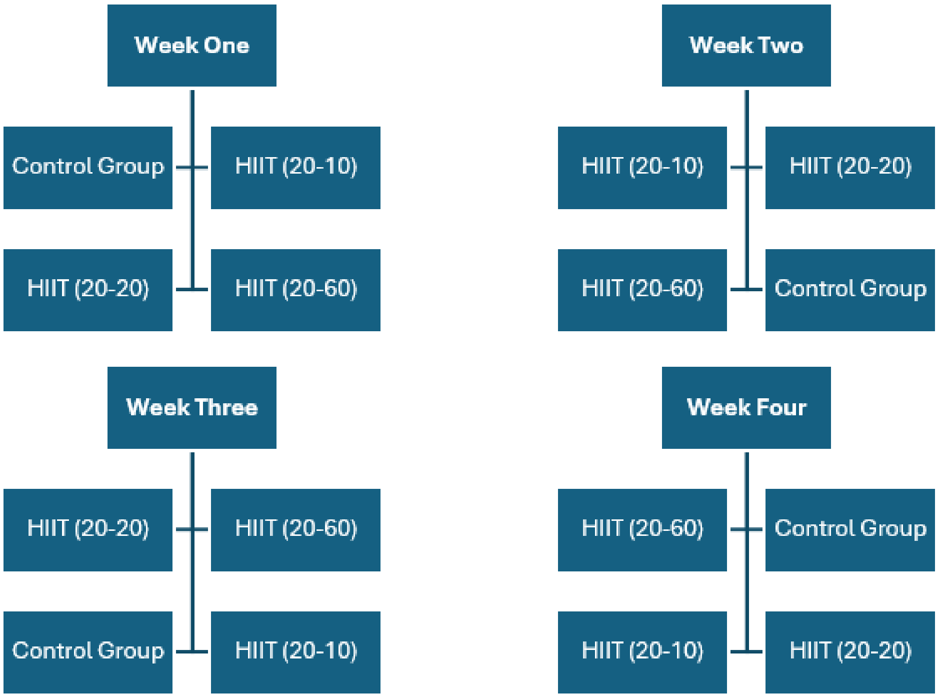

Fig. 1. The crossover method used to insert the groups into different intervention each week

All protocols involved performing burpees at 90% or higher of maximum heart rate, monitored using a G-Tech (Model ONE) finger oximeter. Each session lasted 12 minutes, consisting of 24 sets of exercises. Participants followed a standardized warm-up routine, including stretching and light gymnastics for 5 minutes, followed by the main workout, and ended with a 5-minute cool-down.

2.2 Basic Proceedings

Blood samples were collected at eight time points: baseline (before the intervention), immediately after the session, and at 5, 15, 30,60,90, and 120 minutes post-exercise. Each blood sample was processed twice independently, yielding four measurements per participant. Discrepant results were excluded, and the average of consistent measurements was calculated.

2.3 Exercise Protocols

Three models of high-intensity interval training (HIIT) programs were evaluated to address our problem. All protocols maintained an intensity level at 90% of maximum heart rate, monitored using a G-Tech (Model ONE) finger oximeter. The first protocol, HIIT20-10, consisted of 20 seconds of exercise followed by 10 seconds of rest. The second protocol, HIIT20-20, involved 20 seconds of exercise followed by 20 seconds of rest. The third protocol, HIIT20-60, comprised 20 seconds of exercise followed by 60 seconds of rest. The exercise performed was the burpee, completed over a total duration of 12 minutes, resulting in 24 sets of stimuli. All exercises were performed without equipment, relying solely on body weight.

To perform a burpee, start by standing with your feet shoulder-width apart and your arms at your sides. Lower your body into a squat position, placing your hands on the floor in front of you, just inside your feet. With your weight on your hands, kick your feet back to land in a plank position, keeping your body in a straight line from head to heels. You can add an optional push-up at this stage by lowering your chest to the ground and then pushing back up to the plank position. Jump your feet forward to return to the squat position, with your hands still on the ground. Finally, explode up from the squat position into a jump, reaching your arms overhead. Land softly and immediately lower back into the squat position to begin the next repetition.

Do a standardized 5-minute gentle warm-up including stretching and gymnastics for 5 minutes each day. This is followed by the main workout, and finally, a 5-minute cool down was performed to promote cool down.

2.4 Blood Sampling Acquisition and Glucose Measurement

A finger blood samples were collected at eight time points: baseline (before the intervention), immediately after the session, and at 5, 15, 30-, 60-, 90-, and 120-minutes post-exercise. Each blood sample was processed twice independently, yielding four measurements per participant. Discrepant results were excluded, and the average of consistent measurements was calculated.

For glucose curve assessment, blood glucose levels were measured using a glucometer (ROCHE, Accutrend Plus) at each time point. Additionally, 4 ml of venous blood was drawn at baseline, 60 minutes, and 120 minutes after the intervention to determine serum triglyceride concentrations.

2.5 Insulin Resistance Assessment

The TyG index, calculated as the product of serum triglyceride concentration and fasting blood glucose, was used to assess insulin resistance. The TyG index is a cost-effective and clinically applicable method, with a cut-off point of 4.5, as suggested by Guerrero-Romero et al. [16].

$$3 - \mathrm{TyG} = \frac{\{\mathrm{Try\ x\ Glu}\}}{2}$$

Equation 1: TyG Index. 3= Tyg Index, Try= Tryglicerides, Glu= Glucose.

2.6 Statistical Procedures

Descriptive data were expressed as mean, percentage, and standard error. The Shapiro-Wilk test was used to assess data normality. A two-way ANOVA with Sidak's post hoc test was employed to determine differences between groups, using the "GraphPad Prism 9.5.1" software. A significance level of $p < 0.05$ was set for all analyses.

3. RESULTS

The anthropometric characteristics of the participants, including BMI and body fat

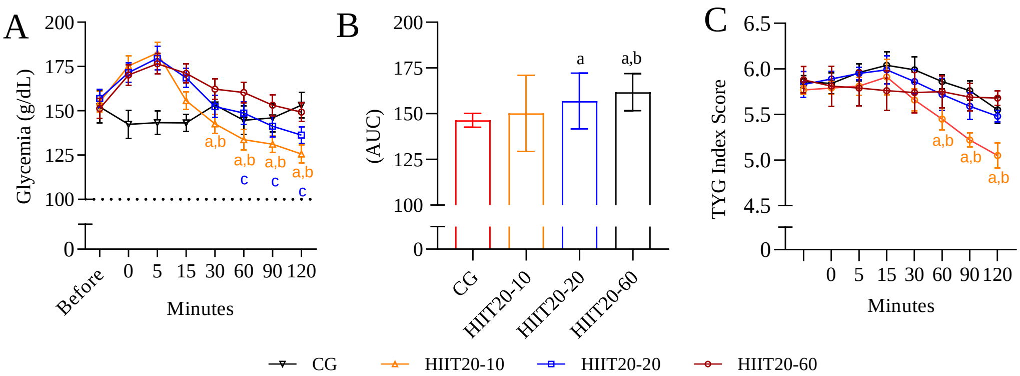

Fig. 2. Blood glucose levels and insulin sensitivity

The Figure A represent the blood glucose concentration along the time of investigation; Figure B the Area Under the Curve of the Glucose, and C is the Insulin Sensitivity. The ANOVA TWO WAY with Sídâk Pos-Hoc Test set up at 5% was used to determine the differences between groups. ***Legend:*** *(a,b= difference to baseline, 5 minutes, and 15 minutes, and c= difference to HIIT20-60 and control).*

percentage, were comparable across all groups ($p > 0.05$ for all). Analyzing the intragroup data, no significant differences were observed in glucose control and insulin sensitivity (IS) between the HIIT20-60 and the other protocols ($p > 0.05$ for both). However, the HIIT20-20 protocol showed significant differences at 30, 60, 90, and 120 minutes compared to 15 minutes post-exercise ($p < 0.05$, 0.05, 0.01, and 0.01, respectively). Notably, the HIIT20-10 protocol resulted in lower glucose levels at 30, 60, 90, and 120 minutes and improved IS when comparing baseline, time 0, 5, and 15 minutes with 120 minutes post-exercise ($p < 0.05$, 0.05, 0.01, and 0.0001, respectively), as well as 15 with 60 minutes post-exercise.

4. DISCUSSION

This study aimed to investigate the effects of three different rest intervals in high-intensity interval training (HIIT) on acute blood glucose levels and insulin sensitivity. We found that shorter rest intervals significantly impacted the body's acute adaptations to exercise, leading to greater metabolic perturbations and a more pronounced glucose response. Specifically, shorter rest periods led to a peak in glucose levels at 15 minutes, often coinciding with a high concentration of insulin in response to the glucose surge. Subsequently, blood glucose levels decreased at 30, 60, 90, and 120 minutes, demonstrating the expected metabolic curve. Additionally, the reduction in glucose concentration during HIIT contributed to improved insulin sensitivity.

Although the area under the glucose curve did not differ significantly between the HIIT20-10 and control groups, the HIIT20-10 protocol exhibited a more substantial decrease in glucose levels, which likely accounts for the observed improvement in insulin sensitivity. These findings align with previous studies showing that HIIT can significantly impact blood glucose levels and insulin resistance. For example, De Teles et al. [17], investigated two HIIT protocols and reported reductions in blood glucose levels, which are consistent with our results [18].

In terms of comparison De teles [19] investigated two HIIT protocols: a long HIIT (2 minutes at 100% VO2peak followed by 2 minutes of passive rest) and a short HIIT (30 seconds at 100% VO2peak followed by 30 seconds of passive rest). They reported reductions in blood glucose levels of 32.14 mg/dL and 31.40 mg/dL for the long and short HIIT protocols, respectively. These findings are consistent with our results, which showed reductions of 12.35, 21.35, 23.79, and 29.4 mg/dL at 30, 60, 90, and 120 minutes after the exercise session, respectively.

Despite the clinical relevance of these findings, there is no consensus on the optimal combination of parameters for designing exercise programs for individuals with metabolic disorders. However, our study highlighted the importance of carefully planning rest intervals between each stimulus [20,21]. Our study highlights the importance of carefully planning rest intervals within HIIT protocols, as they significantly influence the metabolic and physiological outcomes. Longer rest periods may allow for higher exercise overload, while shorter rest periods may induce greater metabolic stress, impacting glucose metabolism and insulin sensitivity.This is important because when performing exercises with increased overload, the rest period needs to be adjusted to maintain the exercise, focusing the stimulus more on the muscular system. Conversely, shorter rest periods suggest less overload but impact the metabolism, as many myokines are overexpressed in this exercise approach [22,23].

Interleukin-6 (IL-6), a cytokine often elevated during high-intensity exercise, may play a role in the metabolic adaptations observed in this study. IL-6 is known to regulate the expression of glucagon-like peptide 1 (GLP-1), which has been shown to improve glucose control in diabetic models [24,25]. Ellingsgaard et al., (2011), demonstrated that high-intensity exercise induces the overexpression of IL-6, which upregulates GLP-1 in L cells and alpha cells, leading to improved glucose control in diabetic mice. Therefore, we suggest that the overexpression of IL-6 during HIIT may contribute to the improved glucose and insulin sensitivity observed in our participants.

4.1 What does this Article Add and Practical Implications?

This study highlights the potential of high-intensity interval training (HIIT) to acutely improve glycemic control, making it a valuable exercise option for individuals looking to manage their blood glucose levels more effectively. The findings suggest that shorter rest intervals in HIIT protocols may enhance insulin sensitivity and reduce blood glucose concentrations more significantly. These insights can assist fitness professionals and healthcare providers in designing more effective exercise programs for individuals with or at risk of metabolic diseases such as diabetes. Incorporating HIIT into regular exercise routines could provide a time-efficient and effective strategy for improving overall metabolic health. Future research should explore the role of IL-6 and other biomarkers in optimizing HIIT protocols further.

5. CONCLUSION

The manipulation of the inter-set rest period is crucial in promoting different metabolic responses. Shorter recovery durations appear to affect metabolism more profoundly than longer recovery periods, leading to a more significant acute impact on blood glucose levels and insulin sensitivity in children with T1D. However, these findings should be interpreted with caution. The combination of HIIT protocols, medication, and insulin therapy requires close monitoring due to the potential risk of inducing a hypoglycemic state, which could be dangerous.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

The authors hereby declare that generative AI technology, CHAT GPT 4.0, was used for editing the English language of the manuscript. The request was solely to correct spelling, punctuation, and grammar, without altering, adding, omitting information or data, or changing the meaning of the text.

CONSENT AND ETHICAL APPROVAL

The study adhered to all mandatory ethical requirements as per the Brazilian National Health Council Ethics Law 466/2012 and received approval from the Ethics Committee of the Federal University of Rondônia (approval report number 2066823). All participants and their parents signed informed consent forms after being informed of the study's risks, benefits, and procedures. Participation was voluntary, and subjects could withdraw at any time without any penalties.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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