

Effects of prior exercise on glycemic responses following carbohydrate ingestion in individuals with type 2 diabetes

Gisela Arsa, Laila Cândida de Jesus Lima, Daisy Motta-Santos, Lucieli Teresa Cambri, Carmen
Silvia Grubert Campbell, John Eugene Lewis, Herbert Gustavo Simões

Corresponding author:

Gisela Arsa, Universidade Federal de Mato Grosso, Boa Esperança, Cuiabá, MT, Brazil

Handling editor:

Michal Heger

*Department of Experimental Surgery, Academic Medical Center, University of Amsterdam, Amsterdam,
The Netherlands*

Review timeline:

Received: 2 June, 2015

Editorial decision: 21 June, 2015

Revision received: 3 July, 2015

Editorial decision: 4 July, 2015

Published online ahead of print: 17 July, 2015

1st editorial decision:

Date: 21-Jun-2015

Ref.: Ms. No. JCTRes-D-15-00001

EFFECTS OF PRIOR EXERCISE ON GLYCEMIC RESPONSES FOLLOWING
CARBOHYDRATE INGESTION IN INDIVIDUALS WITH TYPE 2 DIABETES

Journal of Clinical and Translational Research

Dear Dr. Arsa,

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was **FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.**

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at <http://www.jctres.com/en/author-guidelines/> under "Manuscript preparation." I have also attached an exemplary Word document that you may modify. Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Jul 05, 2015.

To submit a revision, go to <http://jctres.edmgr.com/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

*****Reviewer comments*****

Reviewer #2: Although it may not have been a goal of the study, it is not clear if any analyses were done to determine if there were any gender differences (7 men vs 2 women). Some studies indicate gender differences in regards to certain types of medical conditions such as cardiovascular disease.

Reviewer #3:

General Comments:

The study in question is an original article, which aimed to investigate the effect of a 20min of aerobic exercise on blood glucose and insulin responses before and after the ingestion of a substance with high carbohydrate content, in individuals with type-2 Diabetes Mellitus. Such kind of study is very relevant because it may have high ecological validity. Moreover, the results of present study may help to choose the best strategy for glycemic control as well as energy replacement during the post-exercise recovery for individuals with type-2 Diabetes Mellitus engaged in physical exercise practices. The addressed subject is within the scope of the journal. So this reviewer only suggests to authors to perform an English language review and to review the units of measurement used throughout the text (specifically p. 7, lines 35 and 43) in order to standardize their form of presentation. This reviewer also presents a concern regarding the “no description” related to body composition, such as the percentage of body fat, free fat mass of the volunteers, once these variables, that were not reported, may influence the insulin, and blood glucose responses, safeguarding the gender peculiarities as investigated in both groups.

Pontual comments:

Title: The title is suitable and describes the topic being discussed by the authors, thus attracting the attention of researchers related to the topic in question.

Abstract: This session is written in a very clear and concise form, being able to express the study in an objective way.

Introduction: The introduction contextualizes the "state of the art" and presents the scientific gap to be addressed in this study. Thus for this reviewer there are no suggestions for this session.

Methods: The procedures are well defined and converge to the focus of the study. However, it is suggested to add more details regarding the type of sample studied. In addition, it is suggested the inclusion of variables related to body composition, such as the percentage of fat and lean mass, favoring for the reproducibility of present work. As for Statistical Analysis adopted, there is a concern regarding the utilization of analysis of variance instead a repeated measures ANOVA,

once the variables were analyzed at different moments in the same session. The t test used should also be informed.

Results: The results are represented accordingly, followed proper description, which facilitates their interpretation.

Discussion: The authors presented a wide discussion on the topic. Both actual and classic studies on literature are mixed in harmony. However, the limitations of this study were not described, so it is suggested that they should be added.

Conclusions: It is written in an objective and clear manner, addressing the scientific gap that the authors proposed to answer.

References: This reviewer asks to carry out a standardization following the guidelines.

Authors' rebuttal:

Reviewer #2:

Although it may not have been a goal of the study, it is not clear if any analyses were done to determine if there were any gender differences (7 men vs 2 women). Some studies indicate gender differences in regards to certain types of medical conditions such as cardiovascular disease.

Answer: The reviewer is right regarding his concern. Gender differences have been shown for certain types of medical conditions. However, we believe that this possible gender influence, if any, was not important in our study as the same participants (7 men and 2 women) were evaluated in the different studied conditions/interventions. So we did not investigate any possible gender effect. Maybe the reviewer had this interpretation because of the Statistical Analysis section, which, as indicated by reviewer #3 (below), was not clear. So this section was rewritten for clarification, as you can observe below as well as in page 8 of the manuscript:

Page 8 of the manuscript: "The data were expressed as means and standard error of the means. The Shapiro-Wilk test was used to confirm data normality. A repeated measures ANOVA with Bonferroni as a post-hoc was used to compare specific and correspondent moments within and between sessions for glycemia and insulinemia. Paired student t-test was used to compare the TAUC for glycemia and insulinemia between the control and the 20-min exercise sessions. Student t-test was also applied to analyze the effect of 10-min of exercise, performed after hiperglycaemia induction, on blood glucose control. The level of significance was set at $p \leq 0.05$."

Reviewer #3:

General Comments: The study in question is an original article, which aimed to investigate the effect of a 20min of aerobic exercise on blood glucose and insulin responses before and after the ingestion of a substance with high carbohydrate content, in individuals with type-2 Diabetes Mellitus. Such kind of study is very relevant because it may have high ecological validity. Moreover, the results of present study may help to choose the best strategy for glycemic control as well as energy replacement during the post-exercise recovery for individuals with type-2 Diabetes Mellitus engaged in physical exercise practices. The addressed subject is within the scope of the journal. So this reviewer only suggests to authors to perform an English language

review and to review the units of measurement used throughout the text (specifically p. 7, lines 35 and 43) in order to standardize their form of presentation. This reviewer also presents a concern regarding the “no description” related to body composition, such as the percentage of bod fat, free fat mass of the volunteers, once these variables, that were not reported, may influence the insulin, and blood glucose responses, safeguarding the gender peculiarities as investigated in both groups.

Answers:

Review on the English: We are grateful for your comments regarding our manuscript. It is so nice when another researcher identifies value in our study. In spite of our manuscript was translated by a specialized company in Brazil, and revised by a native speaker before submission, we did an additional review, including units standardization, following your comments. Thank for your suggestions.

Description of body composition: Every participant was sedentary, so we consider that BMI would be adequate to verify a possible overweight condition (BMI: $30.7 \pm 1.8 \text{ kg.m}^{-2}$). Unfortunately, the percentage of body fat (i.e. skinfolds measurement) was not determined. However, as a result of the comments pointed by reviewers #2 and #3, we added more information in the Results section (please see table 1). In general, the participants were considered either overweight or obese, and thus with excessive body fat, which is a common characteristic of individuals with type 2 diabetes. The excessive body weight (and, in this case, body fat) were also confirmed though the elevated abdominal circumference besides BMI. While the BMI is a good indicator of excessive body fat, the waist circumference is correlated with visceral fat, a main type of fat deposition related to insulin resistance.

Differences inter-genders: For the present study the same participants (7 men and 2 women) were compared for the experimental interventions. However, we did not realize analysis to compare genders. Maybe the reviewer had this interpretation because the Statistical Analysis section was not clear. So the statistics section was rewritten for clarification, as can be observed below as well as in page 8 of the manuscript:

Page 8 in the manuscript: “The data were expressed as means and standard error of the means. The Shapiro-Wilk test was used to confirm data normality. A repetead measures ANOVA with Bonferroni as a post-hoc was used to compare specific and correspondent moments within and between sessions for glycemia and insulinemia. Paired student t-test was used to compare the TAUC for glycemia and insulinemia between the control and the 20-min exercise sessions. Student t-test was also applied to analyze the effect of 10-min of exercise, performed after hiperglycaemia induction, on blood glucose control. The level of significance was set at $p \leq 0.05$.”

Pontual comments:

Title: The title is suitable and describes the topic being discussed by the authors, thus attracting the attention of researchers related to the topic in question.

Answer: The title was kept. Thank for your consideration.

Abstract: This session is written in a very clear and concise form, being able to express the study in a objective way.

Answer: Thank you for the comments.

Introduction: The introduction contextualizes the "state of the art" and presents the scientific gap to be addressed in this study. Thus for this reviewer there are no suggestions for this session.

Answer: Thank you for the comments.

Methods: The procedures are well defined and converge to the focus of the study. However, it is suggested to add more details regarding the type of sample studied. In addition, it is suggested the inclusion of variables related to body composition, such as the percentage of fat and lean mass, favoring for the reproducibility of present work. As for Statistical Analysis adopted, there is a concern regarding the utilization of analysis of variance instead a repeated measures ANOVA, once the variables were analyzed at different moments in the same session. The t test used should also be informed.

Answer:

Body Composition: Every participant was sedentary, so we consider that BMI would be adequate to verify a possible overweight condition ($BMI: 30.7 \pm 1.8 \text{ kg.m}^{-2}$). Unfortunately, the percentage of body fat (i.e. skinfolds measurement) was not determined. However, as a result of the comments pointed by reviewers #2 and #3, we added more information in the Results section (please see table 1). In general, the participants were considered either overweight or obese, and thus with excessive body fat, which is a common characteristic of individuals with type 2 diabetes. The excessive body weight (and body fat) were confirmed though the elevated abdominal circumference. Moreover, while the BMI is a good indicator of excessive body fat, the waist circumference has been correlated with visceral fat, a main type of fat deposition related to insulin resistance.

As a result of the referee's comments, the following was added to the text, in page 9:

Page 9 "Results": "The characteristics of the sample are presented in table 1. The T2D individuals were obese and exhibited elevated abdominal circumference, both of them related with metabolic complications observed in T2D individuals"

Statistical Analysis adopted:

Page 8: "The data were expressed as means and standard error of the means. The Shapiro-Wilk test was used to confirm data normality. A repeated measures ANOVA with Bonferroni as a post-hoc was used to compare specific and correspondent moments within and between sessions for glycemia and insulinemia. Paired student t-test was used to compare the TAUC for glycemia and insulinemia between the control and the 20-min exercise sessions. Student t-test was also applied to analyze the effect of 10-min of exercise, performed after hiperglycaemia induction, on blood glucose control. The level of significance was set at $p \leq 0.05$."

Results: The results are represented accordingly, followed proper description, which facilitates their interpretation.

Answer: Thank you for your considerations.

Discussion: The authors presented a wide discussion on the topic. Both actual and classic studies on literature are mixed in harmony. However, the limitations of this study were not described, so it is suggested that they should be added.

Answer: Added in page 15: “Our study has some limitations. The absence of exercise and control sessions without carbohydrate consumption is one of them. In addition, we did not measure insulin concentrations in all moments as it was done for glycemia. However, our measurements did not impair for the analysis of present study.”

Conclusions: It is written in an objective and clear manner, addressing the scientific gap that the authors proposed to answer.

Answer: Thank you for the comment.

References: This reviewer asks to carry out a standardization following the guidelines.

Answer: We have reviewed and standardized the references as suggested. References, page 16.

Requests of Editor in Chief:

Adjustments in format of the Abstract:

Answer: The sections “Aim” and “Relevance for patients” were added. These alterations can be seen in the manuscript and below:

Background: Exercise is effective in reducing glycemia, especially when it is performed in the post-prandial period. However, no consensus exists in the literature about the effect of exercise on post-prandial glucose control after it is performed before carbohydrate consumption.

Aim: The main purpose of the present study was to determine whether exercise performed prior to carbohydrate consumption reduces the posterior glycemic and insulinemic responses. Secondly, the effectiveness of short-term exercise bouts (10 and 20 min) in reducing post-prandial glycemia was analyzed.

Methods: Nine individuals with type 2 diabetes (54.9 ± 1.7 years; 30.7 ± 1.8 kg.m²-1; and glycemia of 167.0 ± 10.6 mg.dL-1) participated in the study and underwent the following: incremental test to determine the lactate threshold; exercise session for 20 minutes at moderate intensity (90% of the lactate threshold); and control session. The last two sessions were randomized, and the participants were monitored for 135 minutes of post-exercise recovery. A standard meal was consumed two hours before the experimental session started; a dextrose solution was administered at 45 minutes of post-exercise recovery, while monitoring glucose and insulin concentrations. After this at 135 min of post-exercise recovery, eight of the participants performed an additional 10-min exercise bout in a condition of induced hyperglycemia.

Results: Exercise reduced glycemia (-46.6 ± 7.9 mg.dL⁻¹) and the insulin/glucose ratio (from 1.73 ± 0.59 to 0.93 ± 0.22 μ U.mL⁻¹/mmol.L⁻¹) during the first 45 minutes of post-exercise recovery. Glycemia was significantly increased after carbohydrate consumption, reaching its highest values at 105 minutes of post-exercise recovery (261.8 ± 15.8 mg.dL⁻¹) or control (281.3 ± 13.4 mg.dL⁻¹), without any effect of the previous exercise in attenuating glycemia or reducing the area under the curve for glucose and insulin after carbohydrate consumption. However, the effectiveness of exercise in reducing glycemia was shown again when it was performed at the end of the experimental session, even with a duration of only 10 min (reduction of -44.53 ± 4.88 mg.dL⁻¹).

Conclusions: Although the previous 20 min of moderate exercise did not induce changes in the kinetics or in the area under the curve for glycemia and insulinemia after subsequent carbohydrate consumption, moderate exercise, even if performed for only 10-20 minutes, was shown to be effective in reducing post-prandial glycemia in individuals with type 2 diabetes.

Relevance for patients: The moderate-intensity exercise, even of short duration, may benefit individuals with type-2 diabetes on blood glucose control. A fast reduction of the postprandial glycemia can be obtained with only ten minutes of exercise what, in turn, may be of relevance to avoid complications associated to the disease.

Key words: brief exercise; glycemia; insulinemia; carbohydrate

2nd editorial decision:

Date: 4-Jul-2015

Ref.: Ms. No. JCTRes-D-15-00001R1
EFFECTS OF PRIOR EXERCISE ON GLYCEMIC RESPONSES FOLLOWING
CARBOHYDRATE INGESTION IN INDIVIDUALS WITH TYPE 2 DIABETES
Journal of Clinical and Translational Research

Dear Dr. Arsa,

I am pleased to inform you that your work has been accepted for publication in Journal of Clinical and Translational Research.

Comments from the editor can be found below.

Thank you for submitting your work to JCTR.

With kind regards

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Comments from the Editors and Reviewers:

I will proofread the document myself before sending it to production, as there were some linguistic errors in the revised version. You will receive the pdf page proofs very soon. I kindly ask you to go over these thoroughly at your earliest convenience and check for any residual errors. Many thanks, Michal.