Author's response to reviews

Title: Exercise in pregnant women and birth weight: a randomized controlled trial

Authors:

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Author's response to reviews: see over
Dear Editor-in-Chief, Dr Eyal Sheiner

Thank you for the thorough and constructive review of our manuscript “Exercise in pregnant women and birth weight: a randomized controlled trial”. We appreciate the invitation to re-submit the manuscript with revisions. Below are our answers to the comments and questions from two reviewers. Any changes in the new manuscript are highlighted using red colour text.

Reviewer 1 (Michelle Mottola)

Major Compulsory Revisions

1. As suggested, we have included the research hypothesis of the present study (page 4).
2. We thank you for the comment and have changed the wording on page 5 (line 3) to: “The complete study (including this secondary analysis) was conducted in agreement with the most recent CONSORT statement (http://www.consort-statement.org).”
3. We have changed the wording in order to better explain what we mean by the postpartum examination, and have as suggested now written postpartum visit instead of postpartum test.

Explanation to what do we mean by lost to the test:
Our aim was to examine all the participants three times during the study period. The baseline visit (I), the visit after the intervention (II) and the visit after delivery (III). Unfortunately, a limitation of the study is that ten women in the exercise group (19.2%) and 11 women in the control group (20.8%) were lost to follow-up visit immediately following the exercise intervention. However, some of these women who were lost to the second visit, re-entered the study at the postpartum visit. We have acknowledged your
confusion concerning this matter in the previous manuscript and have tried to rewrite the text (page 6, line 4-8).

4. We have tried to explain some of this above, and the results of the secondary analysis (presented in this article) have actually less loss of data than the previously published study with the primary analysis (weight gain). However, a limitation of the present RCT is that withdrawals and drop-outs make an ideal ITT analysis impossible, and missing data may have reduced the power of the study and the ability to draw clear conclusions, as imputation techniques can never compensate for, or exactly reproduce, missing data. However, as recommended by several researchers and to complement the pragmatic approach provided by ITT, we also performed “per protocol” analyses (≥ 80% of the recommended exercise sessions) and analyses of “women attending 24 exercise sessions”. This type of analysis may provide an answer to the efficacy of the treatment, but on the other hand may also overestimate the effect size due to selection bias.

We corrected the misspelling of asthma in figure 1.

5. We have added more detailed information about what happened to women randomized to the control group in the method section, page 8, line 1-5: “It was not considered unethical to use a control group not receiving treatment in the present study. However, control participants were neither encouraged to, nor discouraged from, exercising, as we considered asking the CG not to exercise to be against current guidelines. In order to treat the two groups identically apart from for the experimental intervention, the CG underwent all tests and completed the same interview as the EG.”

6. As recommended we have deleted the sentence on page 7, line 13: “We did not use conventional heart rate target ranges for aerobic exercise as it is less dependable and precise during pregnancy compared with the non-pregnant state. “

7. We have changed “ethnicity” to descent” and “Ethnicity of” to “Countries of origin for the other women were...” (page 9, line 1-2)

8. This means that 85.7% of the participants met at the postpartum visit and gave information about birth records. As mentioned previously, unfortunately some women were lost (9 in the EG and 6 in the CG). These are reflected both in the text (page 10, paragraph 2, line 4-5) and in Figure 1.

We do not understand what you mean by please see number 4 above????

9. We have added “birth weight” to the present statement, page 11, paragraph 2, line 1-2: “We did not find statistically significant differences between the two groups in mean birth weight, length, head circumference, and length of gestation, according to ITT-analysis.”

10. We thank you for the comment and have changed the wording related to the two sentences on page 11, paragraph 3, line 1-3 to: “No major adverse effects or health problems resulting from
the exercise program were reported. Two preterm deliveries occurred in the EG (gestational age: 36.1 and 36.5) and one preterm delivery in the CG (gestational age: 35.0).

11. We have rewritten this paragraph and hopefully this better reflects the synopsis of our key findings (page 12, paragraph 1): “This is one of very few RCTs investigating the effect of a supervised structured exercise program on birth weight. No negative effects of 12 week aerobic dance in 2nd and 3rd trimester of pregnancy in previously sedentary women were found and there was no statistically significant difference between groups in mean birth weight, low birth weight (<2500 g) or macrosomia (≥4000 g). Regular exercise during pregnancy did not affect gestational age or prematurity.”

As suggested, the statement that fewer women in the EG give birth to a child >4000 g is deleted.

12. We are not convinced about the significance of an Apgar score < 7 and have therefore chosen to delete the sentence (page 12, paragraph 1): “No newborn in the EG had a Apgar score<7, compared with two newborns in the CG.” We hope this is ok with the reviewers and the editorial board. If not we will of course make changes.

13. As recommended, we have deleted the statement (page 12, paragraph 2, line 7): “However, this was a RCT and possible changes in eating patterns should be equally distributed in the groups.” In the next statement, we have deleted “In addition” and replaced it with “However”.

14. Mean birth weight in the exercise and control group (3426 g vs. 3569 g) for the study of Hopkins et al [40] is now reported on page 13, paragraph 1, line 8. We agree that this would fit nicely with what we stated for the Clapp study [25].

15. In the manuscript, we have defined low birth weight (LBW) in the method section (outcome measure), page 8, paragraph 2, line 7: “In addition, newborns birth weight was grouped according to low birth weight (LBW) (<2,500 g).........”

16. We thank you for the comment, understand your argument and have now tried to rewrite the sentences (page 13, paragraph 2, line 7-11): “This is consistent with findings of Barakat et al [23], showing higher prevalence of macrosomic babies in the control group than in the training group (1.4% vs.10%). In Finland, Kinnunen et al [42], found a 15% incidence of newborns above 4000 g in the control group, whereas there was no newborns exceeding 4000 g in the intervention group.”

17. We agree with your recommendations regarding page 14, paragraph 2 and have deleted the text.

18. We approve and have given expanded information in the text (page 1, paragraph 2): “Another interesting finding in the present study was that mean Apgar score of the newborns was higher in the EG compared to the CG at 1-minute. However, by 5-minutes there was no difference. Clinically, the 5-minute score may be more relevant, as this score assesses how well the newborn is adapting to the new environment, comparing to how well the baby has tolerated the birthing process (1-minute score). Nevertheless, the results of the present study confirm previous data, not showing negative effect of moderate intensity aerobic exercise.....”
19. We have changed the last sentence at page 15, par 1: “In addition, time management is vital if an exercise program is to be successful”.

Minor Essentials Revisions
1. We have changed the sentence in the abstract (line 2) according to your suggestions.
2. We have added “s” to “trimester” in the abstract, line 4.
3. “Newborn” is deleted from line 6 and last line in the abstract, as well as page 4, line 5.
4. “Has” is deleted from page 3, line 9.
5. Page 3, line 12, “has” is changed to “have”.
6. Page 3, line 14, “s” is deleted from “restrictions”.
7. We do not understand to add “s” to “muscles” at page 7, line 5?
8. Page 10, last line, “to have” is changed “to exercising”.
9. We have added “s” to “strength”, page 12, paragraph 2, line 1.
10. Page 12, paragraph 2, line 6, “is” is changed to “was”.
11. Page 13, paragraph 2, line 11, “kvasi” is changed to “quasi”.
12. Page 13, line 1, “macosome” is changed to “macrosomic”.

Reviewer 2 (Anca Gaston)
Minor Essential Revisions
1. We thank you for the comment and have changed the sentence on page 3, paragraph 1, line 3-6. The US and Canadian exercise guidelines are now referred to individually: “According to the present guidelines, all pregnant women are encouraged to be physically active for at least 30 minutes on most days of the week, in the absence of medical or obstetrical contraindications [1,3,4]”. Wolfe and Davies [3] recommended that previous sedentary women should start moderate exercise for a minimum of 15 minutes, 3-5 times a week and increase to 30 minutes.
2. In total, the participants were examined three times during the study period. The first visit was between 12 and 24 weeks of gestation (baseline visit), the second at week 36-38 (after the intervention) and the last 6-12 weeks after delivery (postpartum visit). Except for the second visit, data collected are used in analyses and results presented in the in the present paper.
3. We agree. The sentence was unclear and we have added “sessions” to the following sentence (page 10, paragraph 3, line 1): “Adherence to the EG was in mean 17.0 (SD 12.5) sessions and 21 (40.4%) attended ≥ 80% of the exercise sessions”.
4. In order to treat the two groups identically apart from for the experimental intervention, the control group (CG) underwent all tests and completed the same interview as the exercise group (EG). However, awareness of being randomized to the CG, may have influenced the “usual-care” intervention. We know that some participants may have been disappointed by not being randomized to the EG and therefore initiated exercise regimens comparable to the RCT intervention (exercised ≥ 2 times per week for 60 minutes of moderate intensity similarly to the minimum recommended exercise dosage for the EG).
This type of bias has been referred to as the “Avis effect”. Hence, to obtain information about the PA habits in the CG, the CG underwent the same follow-up questions about PA and exercise after the intervention period as the EG. This was also done to ensure that the primary investigator was “blind” to the treatment received. The CG did not complete a training diary. In contrast to the EG, none of the exercises performed by the CG were supervised. Following the CONSORT statement for reporting RCTs, all analyses were based on assigned treatment (EG or CG) at the time of the randomization, regardless of adherence status.

We hope that our answers and changes according to the reviewer’s comments are satisfactory and that the new version of our manuscript is acceptable for publication in the BMC Pregnancy and Childbirth. We look forward to your response.

Yours sincerely

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