Reviewer's report

Title: Blood pressure and endothelial function in healthy, pregnant women after acute and daily consumption of flavanol-rich chocolate: a pilot, randomized controlled trial

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Reviewer: Audrey F Saftlas

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This report is one of the first trials to examine the effects of flavanol-rich chocolate consumption during pregnancy.

- Major Compulsory Revisions

1. The statements in the abstract and in the text, which assert that no trials have examined the effects of chocolate in pregnant women are no longer accurate. Findings from a chocolate trial among pregnant women in Italy were recently published and should be incorporated into the manuscript (see: Di Renzo GC, Brillo E, Romanelli M, Porcaro G, Capanna F, Kanninen TT, Gerli S, Clerici GJ. Potential effects of chocolate on human pregnancy: a randomized controlled trial. Matern Fetal Neonatal Med. 2012 Oct;25(10):1860-7. Epub 2012 Jun 5).

2. A major design flaw of the trial was the decision to measure plasma flavanols in blood samples collected following a 12-hour fast, which accounts for non-detectable levels of epicatechins in samples collected following 6- and 12-weeks of daily high-flavanol chocolate intake. As noted in the discussion, it is well known that epicatechin clearance from the plasma is rapid and most would be eliminated over the 12 hours following ingestion. Therefore, the study provides no direct evidence of high-flavanol exposure to test for an association of chronic high-flavanol chocolate intake (versus low-flavanol intake) with the study outcomes of blood pressure and flow mediated dilation. a) This point needs to be made clear in the abstract, results, and discussion sections. Currently, the conclusion of the abstract states that the study results “demonstrate higher plasma concentration of epichatechin and theobromine in the intervention group”. This statement should be revised and clarified to indicate that increased levels of epicatechins could only be demonstrated with acute ingestion of flavanol-rich chocolate.

3. The experimental chocolate differed from the “placebo” chocolate only on the flavanol content while all other key components of chocolate (ie, theobromine, caffeine) were identical. These similarities should be emphasized in the Methods section and a rationale for this choice of a placebo should be provided.

4. Methods. Dose: What is the authors’ rationale for prescribing a total daily intake of 20-g of chocolate?
5. Methods. Timing of intake: Why were women followed in the first 24 weeks of pregnancy rather than later in pregnancy when blood pressures tend to rise from the nadir at 22-24 weeks? The choice of the gestational age at intervention and its potential impact on study findings should also be addressed in the Discussion.

6. Results (1st paragraph and Consort diagram): The number of women who declined to participate (n=45) should also include women who had transportation problems (n=4) and those who cited personal reasons (n=33). The 5 women who had a miscarriage should be categorized with the other women who failed to meet inclusion criteria (n=27); and the breakdown of reasons for exclusion should be given. The study’s participation rate and response rate should also be provided. The authors should comment on how the low participation rate may have impacted their study.

7. Results (p. 13, 2nd paragraph): “... significant increase in plasma theobromine concentrations was observed in both groups at 180 minutes and was slightly but significantly more marked in the experimental group. Therefore, theobromine concentrations served as a marker of chocolate compliance.”

a. Theobromine is a well-established marker of chocolate intake, but it’s not clear why there would be a greater increase in theobromine levels in the experimental group when the theobromine content was identical in the high-flavanol and low-flavanol chocolate bars.

b. Table 5: Is the standard deviation for high-flavanol chocolate at 180 minutes correct (i.e, 6.51 + 0.08) correct? It is much lower than the standard deviations shown for the other measures of theobromine.

8. Tables 4-5. The measurements taken at 60 minutes and 120 minutes after a single dose acute intake should be included in the tables.

- Minor Essential Revisions
1. Tables 4-10. Note in the table headings that the data reflect means with standard deviations.

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests'.