Author's response to reviews

Title: Acupuncture to improve live birth rates for women undergoing in vitro fertilisation a protocol for a randomised controlled trial

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Author's response to reviews: see over
Tuesday, 28 February 2012

Dear Dr Altman

Re: MS 1587138264623042 Acupuncture to improve live births for women undergoing in vitro fertilisation: a protocol for a randomised controlled trial.

Thank you for the reviewers’ comments. Please find attached a revised manuscript in responses to the reviewers’ comments. I have also outlined below point by point our response to the comments.

1. The background outlines the main sources of heterogeneity between trials, and how we planned to address this heterogeneity. I draw your attention to the development of our treatment protocol to reduce the clinical heterogeneity. We have included two control groups, including a placebo control. This device we have used successfully in other areas of research, and been able to demonstrate statistical differences between groups. We have included the most significant clinical outcomes relating to reproductive medicine.

2. The rationale for our inclusion criteria is based on a possibility that where the baseline pregnancy rates are high for some IVF settings, the added value of acupuncture maybe reduced. We have identified a group of women were the pregnancy rates are lower, and for whom adding acupuncture may improve their clinical outcomes. The characteristics of the inclusion criteria for this study relating to age and undergoing a fresh IVF cycle, reflect characteristics of the majority of women undergoing IVF in Australia and New Zealand. In other overseas settings there maybe a lower age restriction.

3. We agree the group of women in the non randomised cohort may have different outcomes, and we recognise that incorporating a usual care group to provide baseline pregnancy rate is problematic. The analysis of the usual care only group will be treated as an observational study with known confounding factors adjusted for in the analysis.

4. Thank you for seeking clarification on the discrepancy with the numbers. I have consulted with the statistician and revised this section to:

We expect a larger treatment effect (10%) when comparing acupuncture and standard care. To detect a 10% increase in the proportion of women that report a live birth between the treatment and standard care, with 80% power at the 5% significance level will require 193 women in the non randomised group. Allowing for a 30% loss, due to cancelled cycles, or no ET, 251 women in the non randomised group are required.
5. A statement describing that the Park needle and supporting device has been shown to be effective with maintaining blinding has been inserted, and a reference added.

6. Practitioner intent has been clarified as treatment aspirations.

7. De qi has been clarified as a needling sensation following needle insertion.

8. The analysis section has been revised to: *Analyses of the endpoints will undertake an ‘intention to treat’ approach and compare differences in the primary and secondary endpoints between groups. The primary analysis will compare the proportions of patients with live births. Logistic regression will be used to identify baseline variables which are associated with outcomes. Linear models will be used to test for between group differences in the continuous outcome measures (e.g. health status).*

9. A CONSORT diagram has been included.

We trust these revisions are acceptable to the journal and I look forward to hearing from you.

Yours sincerely

Caroline Smith