Reviewer’s report

**Title:** Arabin Cervical Pessary for Prevention of Preterm Birth in Cases of Twin-to-twin Transfusion Syndrome Treated by Fetoscopic LASER Coagulation: The PECEP LASER Randomised Controlled Trial

**Version:** 1  **Date:** 12 Sep 2016

**Reviewer:** Amanda Henry

**Reviewer’s report:**

I was not a reviewer on the first draft of this protocol, from the response back to the original reviewers there has obviously been an effort to improve the English standard of the manuscript. I just have a few more specific comments regarding the English expression to improve the readability of the manuscript. Also there are a few times where references have not been inserted and I have noted these also to be fixed prior to publication.

1) Abstract: methods section of abstract, final sentence currently begins "352 women will be included in order to decrease the rate of preterm delivery from 40% to 26%" - should read "352 women will be included in order to decrease the rate of preterm delivery before 32 weeks' gestation from 40% to 26%".

2) Background section of manuscript, lines 38 to 40, sentence beginning "It is obvious that the majority of cases...". I suggest changing this sentence to "Although many cases are delivered prematurely for medical indications (mainly selective intrauterine growth restriction), a large proportion also develop spontaneous preterm labour". You also need to give references for this sentence. I would then make your next sentence "Spontaneous preterm labour in TTTS may be partly due to overdistension of the uterus caused by polyhydramnios, or even uterine manipulation inherent to FLC procedures, neither of which can be avoided." Remove the sentence "These stressors can obviously not be avoided ab initio"

3) Methods/design section, aims subsection, second paragraph. Better English expression would be "This is a multicenter study to be conducted in the Hospital Universitari Vall d'Hebron in Barcelona (Catalunya, Spain), the Universitaire Ziekenhuizen in Leuven (Belgium), and the University Medical Centre Hamburg-Eppendorf (UKE) in Hamburg (Germany). All centers have approval from the respective Medical Ethics Committees to conduct the trial." As I presume you have prospectively registered this clinical trial in a clinical trial registry, this should also be stated in this paragraph, and the website details and the clinical trial number/unique trial identifier should be given.

4) Methods section, intervention subsection, first sentence (lines 14-15) - The term "exploration room" is not familiar to me. Do you mean the minor procedures/assessment room on your regular antenatal ward, Delivery Suite or outpatients Department? (the sort of room where you could insert a cervical catheter, have an examination bed to do proper speculum examination etc?). If yes then "in the assessment room of antenatal ward/Delivery Suite/outpatients" (use
whichever term is the correct one) I think will be more easily understood by most readers. For the following sentence I would also suggest "the operating theatres" rather than "a surgery room".

5) Methods section, intervention subsection, line 19 - "with clinical controls every two weeks" - again, I am not quite sure what this means here. I think you most like mean clinical review and ultrasound every two weeks, so I would say that instead.

6) Methods section, outcome subsection, first sentence - rather than "main outcome" "primary outcome". For the next sentence, where the secondary outcomes are listed, I would also suggest that rather than "neonatal morbidity (with a composite of intraventricular haemorrhage......)" to use "and composite neonatal morbidity (any of intraventricular haemorrhage,......)".

7) Methods section, Statistics subsection, expected sample size paragraph - The first sentence here is confusing. Suggest to replace with "From a pilot study (reference 18), we based our sample size calculations on the assumption that the pessary will reduce the primary outcome (preterm birth <32 weeks) from 40% in the control group to 26% in the pessary group." Then you can continue with the sentence about study power, although instead of "drop out retain" use "drop out rate", instead of "requested sample size" "required sample size", and "has been estimated to 352 patients" "has been estimated to be 352 patients".

8) Methods section, Data analysis, last paragraph (lines 25-26): suggest add a few words to clarify here "We also intend to perform a subgroup analysis according to the cervical length before laser surgery: over 25mm, 15 to 25mm, and less than 15mm".

9) Methods section, interim analysis paragraph: The O'Brien and Fleming rule needs to be referenced.

10) Discussion, second paragraph (lines 50-51) - I would leave "no matter the reason" out of this sentence. You also need to give the references regarding the high rate of delivery by 32 weeks in these babies (not just say that many authors have published before). For the next sentence "given the fact that most of these twins are electively delivered at 34 weeks", please also give a reference or references to support this statement.

11) Discussion, 3rd paragraph, line 60 - need reference for statement that rate of spontaneous preterm delivery is very high even if cervical length normal at the time of surgery.

12) Discussion, 4th paragraph, lines 1-3. Again, references regarding bed rest and progesterone not being useful in twins, and use of cerclage being questioned (I agree these are all correct statements about current knowledge, but they still need to be referenced!).

**Are the methods appropriate and well described?**

If not, please specify what is required in your comments to the authors.

Yes
Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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