Author's response to reviews

Title: Immunization interventions to interrupt hepatitis B virus mother-to-child transmission: a meta-analysis of randomized controlled trials

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Author's response to reviews: see over
Dear editor:

Thank you and two reviewers for reading our article carefully and giving reasonable suggestions. Now we reply below:

Reviewer #1: Reviewer's report:
Minor Essential Revisions: The introduction part should be shortened. It is a well written manuscript.
Answer: yes, we have tried to shorten the introduction part. The article has been revised by an English editor.

Reviewer #2: Reviewer's report:
Major concerns:
1. Novelty? Although the authors pointed out the deficiencies of previous reports, their own findings did not provide better results.
Answer: yes, similar reports have been published and biases are hard to avoid. Although the final results were similar as previous studies, we tried to update previous meta-analysis and adjust some factors, such as adjustment of inclusion criteria, inclusion of more studies, analysis based on intend-to-treat principle, considerations about multiple immunization strategies, etc. For example, the studies published after 2010 were included in order to find the newly outcome. Compare with previous meta-analysis, the quality of the studies was evaluated using the Cochrane handbook 5.1.0 recommended standard. Subgroup analysis about non-high risk of bias facilitated improved appraisal of evidence and lead to better healthcare. More importantly, some common deficiencies in included studies were pointed out, such as willingness group, imbalance between two groups. Hope to help these researchers to change their idea and behavior.

2. Why did the authors use "ectopic" as a key word for search?
Answer: because we want to search more references about hepatitis B virus mother to infant transmission, including normal pregnancy and ectopic pregnancy. However, all of the final included studies were normal pregnancy.

3. Although the authors analyzed the quality of enrolled studies, the quality of individual studies should be described. They did not exclude studies with low quality. Data extracted from low quality studies might not be convincing.
Answer: yes, the quality of individual studies should be described. Please see figure S1. Due to space limitations, we removed the figure S1.

We used subgroup analysis to understand the difference between studies with higher quality and ones with lower quality. Please see table 3 and 4.
4. The diagnosis of newborn HBV infection is based on peripheral or umbilical blood, and the latter could be contaminated by maternal body fluids.
   Answer: yes, the fact that the latter could be contaminated by maternal body fluids, could bias the results. We have added it into the discussion.

5. The schedules of HBIG in pregnant women, as well as HBIG and HBVac application in the newborns should be described. It has been reported that 3-dose of HBIG is more effective than 1-dose or 2-dose HBIG in pregnancy. Also an additional dose at labor onset might improve the outcome.
   Answer: Please see table 1 and 2. The schedules of HBIG in pregnant women were mainly 3-dose or more than 3-dose without an additional dose at labor onset.

6. The mode of delivery and gestational age at time of delivery are not described.
   Answer: yes, we did not describe the mode of delivery and gestational age at time of delivery because of not any information about them. We have added it into the discussion.

7. For results at 7–12 months of age, and after 12 months of age, breastfeeding and maternal HBV change of conditions should be considered.
   Answer: yes, we did not consider these factors because of no information about them, although some included studies kept the balance of breastfeeding between two groups at first. We have added it into the discussion.

8. English needs to be improved by native speakers
   Answer: yes, the article has been revised by an English editor.
Minor concern:
Page 6, line 2, what does "event" mean?
Answer: the event mean the occurrence of HBsAg-positive infections when HBsAg positive was detected for newborn at any time > 1 month of age.

Best Wishes,
Pei Liu