Treatment of Schistosomiasis in Pregnancy: A Systematic Review of Fetal and Infant Outcomes

Hira Raheel1, Rachel Lau2, Shveta Bhasker3, Chelsea Watson1, Geilia Alemayheu1, Robert B. Chris1, Swana Kopalakrishnan1, Leila Makhani1, Sharmistha Mishra3, Andrea K. Boggild1,2

1Tropical Disease Unit, Toronto General Hospital, Toronto, ON, Canada, 2Global Health Ontario Laboratories, Toronto, ON, Canada, 3Jal Shih Knowledge Institute, St. Michael’s Hospital, Toronto, ON, Canada, 4Tropical Disease Unit, Toronto General Hospital, University of Toronto, Toronto, ON, Canada

BACKGROUND:

• Treatment of parasitic infections in pregnancy necessitates consideration of numerous factors including the potential safety and developmental outcomes for fetus and newborns exposed to these drugs
• Schistosomiasis remains one of the most prevalent parasitic infections and has significant economic and public health consequences with an estimated 261 million infected worldwide1
• For these considerations, a substantial knowledge gap exists in the treatment of schistosomiasis infections during pregnancy, with few published and authoritative resources to guide clinical decision-making.
• We assessed the current literature for the impact that schistosomiasis can have on maternal and fetal outcomes during pregnancy, and evaluated the efficacy, tolerability and safety of praziquantel used for schistosomiasis during pregnancy

METHODS:

• A literature search was conducted on Medline, Embase, Cochrane Central, Cochrane DSB and CINAHL databases with the search terms “intestinal parasites”, generic and organism specific, and “pregnant/pregnancy” from database inception to June 2019, without language restrictions
• Duplicate articles were removed and title, abstract and full-text articles were systematically double screened and arbitrated by a third reviewer
• Systematic reviews, randomized controlled trials, cohort studies, smaller observational studies, case-control studies, case series, and case reports assessing or reporting the efficacy, safety, or tolerability of praziquantel treatment during pregnancy were screened
• Inclusion criteria: Pregnant women + Treated with praziquantel during pregnancy +Schistosomiasis + Fetal and/or Infants Outcome(s) reported
• Two independent reviewers extracted the data and assessed quality using the GRADE approach. Risk of bias for each study was determined
• Data were summarized using qualitative and quantitative measures for safety of praziquantel on the fetus and infant

RESULTS:

Figure 1. PRISMA Flow Diagram

Table 1. Data Synthesis Table

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Period</th>
<th>Study Setting</th>
<th>Exclusion Criteria</th>
<th>Study Population</th>
<th>Study Design</th>
<th>Trimester of Treatment</th>
<th>Drug Treatment and Sample Size</th>
<th>Fetal/Infant Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ndibazza 20121, RCT</td>
<td>2003 to 2005</td>
<td>Entebbe Hospital, Uganda</td>
<td>Hemoglobin level &lt;8 g/dL, liver disease, dianhea with bloody stool, abnormal pregnancy, previous adverse reaction to anthelminthics, or enrollment during a previous pregnancy</td>
<td>Infants of 2507 pregnant women ~458 with S. mansoni</td>
<td>RCT, double-blind, albendazole vs matching placebo and praziquantel vs matching placebo, 2x2 factorial design</td>
<td>2nd and 3rd</td>
<td>N=104 women with S. mansoni infection in Praziquantel/placebo arm</td>
<td>Praziquantel had no effect on the mean birth weight, perinatal mortality or congenital abnormalities of babies born to mothers with S. mansoni infection</td>
</tr>
<tr>
<td>Mpaiwwe 20122, RCT</td>
<td>2003 to 2005</td>
<td>Entebbe Hospital, Uganda</td>
<td>Same as Ndibazza 2012</td>
<td>2345 newborns of 2507 pregnant women assessed at birth</td>
<td>Same as Ndibazza 2012</td>
<td>2nd and 3rd</td>
<td>Same as Ndibazza 2012</td>
<td>Maternal praziquantel treatment for S. mansoni, associated with increased risk of infant eczema vs. placebo</td>
</tr>
<tr>
<td>Webb 20124, RCT</td>
<td>2003 to 2005</td>
<td>Entebbe Hospital, Uganda</td>
<td>Same as Ndibazza 2012</td>
<td>Delivery for 2356 women, 2345 live births, 2115 infants for 1 year follow-up</td>
<td>Same as Ndibazza 2012</td>
<td>2nd and 3rd</td>
<td>Same as Ndibazza 2012</td>
<td>No effect on infant response to BCG, tetanus or measles immunization, including cytokine and antibody production or antigen-specific response, or adverse reactions</td>
</tr>
<tr>
<td>Tweyongye 20135, RCT</td>
<td>2003 to 2005</td>
<td>Entebbe Hospital, Uganda</td>
<td>Same as Ndibazza 2012</td>
<td>1343 children born to mothers in the Entebbe Mother and Baby study at age 5</td>
<td>Same as Ndibazza 2012</td>
<td>2nd and 3rd</td>
<td>Same as Ndibazza 2013</td>
<td>Maternal treatment of S. mansoni by praziquantel during pregnancy caused higher IL 10 response in children exposed to a schistosomum worm BUT had no other effects on immune responses (cytokine and antibodies)</td>
</tr>
</tbody>
</table>

CONCLUSION:

• Praziquantel administration during pregnancy for the treatment of Schistosoma mansoni does not appear to have any adverse birth outcomes for the fetus/infant or lead to any major adverse outcomes for the child later in life
• We performed data synthesis and analysis on 4 studies from the same randomized control trial, a more comprehensive analysis on the remaining studies that meet our inclusion criteria will be performed to validate its safety accurately

REFERENCES:

3) Mpaiwwe, H et al. (2012) “Anthelminthic treatment during pregnancy is associated with increased risk of infantile eczema: randomised-controlled trial results.” Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology 23, 305-312 DOI: 10.1111/j.1399-3038.2010.01222.x

CONTACT: Dr. Andrea Boggild - andrea.boggild@utoronto.ca @BoggildLab Website: www.boggildlab.ca