Efficacy and safety of ascending dosages of tribendimidine against hookworm and concomitant soil-transmitted helminth infections in children: a randomised controlled trial

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The current standard drugs against soil-transmitted helminths, albendazole and mebendazole, have shown excellent efficacy against *A. lumbricoides*, but against hookworm, albendazole has shown only moderate efficacy.

Tribendimidine was developed and approved in China in 2004 after having undergone detailed pre-clinical and clinical studies.

Tribendimidine has an activity spectrum similar to albendazole, which might serve as a backup drug in case drug resistance against albendazole and mebendazole would emerge.

Dose-finding studies in China in adults revealed a 400 mg dose to be the most suitable to treat hookworm infections, while a 200 mg dose for children was empirically selected.

Up to date, the optimal dose of tribendimidine in children has not yet been identified.
**Trimendimidine dose-finding trial**

<table>
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<th>Trial synopsis</th>
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<td><strong>Indication</strong></td>
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Trial flowchart

1875
Children assessed for eligibility

1757 excluded
Hookworm negative

118
Randomly assigned

27
Placebo
25 light infections
2 moderate infections
1 absent at follow-up
26

29
100 mg
28 light infections
1 moderate infections
1 absent at follow-up
28

32
200 mg
31 light infections
1 moderate/heavy infections
3 absent at follow-up
29

30
400 mg
30 light infections
0 moderate infections
1 absent at follow-up
29
Diagnostics for hookworm infection

**Stool sample**
2 stool samples before and 2 samples after treatment

**Kato-Katz**
Preparation of 2 Kato-Katz thick smears from each stool sample

**Kato-Katz thick smears**
Up to 400 slides per day
10% re-read for quality control
Baseline characteristics

- Overall prevalence of 7.8% in school-aged children

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Placebo</th>
<th>100 mg</th>
<th>200 mg</th>
<th>400 mg</th>
<th>Total</th>
</tr>
</thead>
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<tr>
<td></td>
<td>26</td>
<td>28</td>
<td>29</td>
<td>29</td>
<td>112</td>
</tr>
<tr>
<td>Female N (%)</td>
<td>10 (38.5)</td>
<td>12 (42.9)</td>
<td>10 (34.5)</td>
<td>7 (24.1)</td>
<td>39 (34.8)</td>
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<tr>
<td>Age, years; median</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Weight, kg; median</td>
<td>27</td>
<td>26</td>
<td>23</td>
<td>22</td>
<td>25</td>
</tr>
<tr>
<td>Height, cm; median</td>
<td>131</td>
<td>130</td>
<td>129</td>
<td>123</td>
<td>128</td>
</tr>
<tr>
<td>Co-infections N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><em>A. lumbricoides</em></td>
<td>1 (3.8)</td>
<td>1 (3.6)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>2 (1.8)</td>
</tr>
<tr>
<td><em>T. trichiura</em></td>
<td>2 (7.7)</td>
<td>0 (0.0)</td>
<td>2 (6.9)</td>
<td>2 (6.9)</td>
<td>6 (5.4)</td>
</tr>
<tr>
<td><em>S. mansoni</em></td>
<td>5 (19.2)</td>
<td>2 (7.1)</td>
<td>3 (10.3)</td>
<td>4 (13.8)</td>
<td>14 (12.5)</td>
</tr>
<tr>
<td><em>P. falciparum</em></td>
<td>13 (50.0)</td>
<td>13 (46.4)</td>
<td>18 (62.1)</td>
<td>19 (65.5)</td>
<td>63 (56.2)</td>
</tr>
</tbody>
</table>
For the first time a dose-response relationship trial with tribendimidine against hookworm in children was conducted.

A clear dose-response was observed.
No difference in mild adverse events seen among treatment arms

Most commonly observed: thrill, headache, itching, stomach ache, diarrhea

1 episode of moderate adverse event, no heavy adverse event
Conclusion

• Acceptable efficacy of tribendimidine against hookworm was observed

• A dose-response relationship was apparent

• Tribendimidine was safe in children, up to the highest dose (400 mg) assessed

• The ongoing Emax model will inform on the dose need for a egg reduction rate of 99%

• Pharmacokinetic part of the study will deepen our understanding of observed cure and egg reduction rates
Project partners

Financial source

**European Research Council**

Research Institutions

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Institut Tropical et de Santé Publique Suisse

**CSRS**
Centre Suisse de Recherches Scientifiques en Côte d’Ivoire

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Thank you!!!