Efficacy of Ivermectin and Albendazole Alone and in Combination for Treatment of Soil-Transmitted Helminths in Pregnancy and Adverse Events: A Randomized Open Label Controlled Intervention Trial in Masindi District, Western Uganda

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Abstract. A randomized open-label trial, including 834 pregnant women, examined efficacy and recorded adverse events of ivermectin (ivc) and albendazole (alb) alone and combined (comb) on soil-transmitted helminth infections (STHs) in the second trimester of pregnancy. One abortion occurred in the alb group and 10 stillbirths (1, 5, 3, and 1) in the ivc, alb, comb, and the reference group (ref) with no STHs, respectively. Two babies were born with congenital abnormalities (1[ivc] and 1[ref]). The prevalence of anemia at first antenatal care (ANC) visit was 20.6% (23.7% [ivc], 21.1% [alb], 22.2% [comb], and 16.1% [ref]). Anemia was reduced to 8.5% at 36 weeks of gestation with 10.9% (ivc), 11.5% (alb), 7.7% (comb), and 6.9% (ref). Hookworm cure rates were 29.4% (ivc), 95.5% (alb), and 92.6% (comb). No severe adverse events were reported by the women after the administration of ivc, alb, or comb during the second trimester of pregnancy, but long-term pharmacovigilance is needed to assess safety of ivc, alb, or comb in pregnancy.
ment. Women with severe anemia were treated with a single dose of sulfadoxine-pyrimethamine (SP), and ferrous sulphate 200 mg was given three times a day for at least three weeks. Gestational age was assessed by palpation of fundus height combined with information on last menstrual period. Hemoglobin (Hb) was measured using a portable HemoCue photometer. One stool sample was collected and duplicate 50-mg Kato-Katz cellophane thick smears were prepared for the detection of STHs. The stool smears were examined immediately after preparation for hookworm eggs and at a later stage for other intestinal helminths. Egg counts were given as eggs/gram feces (epg). Women infected with any intestinal helminth were randomly assigned to receive albendazole administered as a single dose of 400 mg or ivermectin or a combination of both. Ivermectin was administered according to height, as it is the current practice in ivermectin distribution programs (African Program for Onchocerciasis Control).10

Sample size estimation was based on the differences in cure rate for ivermectin and albendazole against hookworm. The estimated cure rate of the combination of ivermectin and albendazole was 75%, and the estimated cure rate of albendazole was 60%. Using a power of 90% and a significance level of 5% and a loss to follow-up of 30%, 216 women were needed in each group (total 864 pregnant women). The drugs were taken under direct supervision and women in addition received the routine ANC package (anti-tetanus toxoid, iron supplements, and intermittent preventive treatment with sulfadoxine-pyrimethamine [SP]). The study was an open label randomized controlled trial with four arms. Group A received ivermectin and Group B received albendazole. Group C received a combination of ivermectin and albendazole, whereas Group D was a reference group without STHs. The mothers were asked to return to the health unit whenever they had any problem or illness at any time and were examined for any possible adverse events. The mothers were followed up on day 21 after treatment and any maternal ill health was recorded. A stool sample was collected and examined as mentioned previously. Efficacy (cure rate of STHs) was defined as the proportion of pregnant women who were excreting eggs in their stool before treatment, but who had a negative test result at 21 days follow-up. Abortions and premature deliveries were recorded in time relation to the administration of the drug through weekly community surveillance. The Hb measurement was repeated at 36 weeks of gestation for women in all the four groups. At birth, the weight of the babies was measured to the nearest 10 gm and stillbirths were recorded. The babies were examined for any malformations. The babies was measured using heel prick blood. The babies were examined for any malformations or illness at any time and were examined for any problem or illness at any time and were examined for any possible adverse events. The mothers were asked to return to the health unit whenever they had any problem or illness at any time and were examined for any possible adverse events. The mothers were followed up on day 21 after treatment and any maternal ill health was recorded. A stool sample was collected and examined as mentioned previously. Efficacy (cure rate of STHs) was defined as the proportion of pregnant women who were excreting eggs in their stool before treatment, but who had a negative test result at 21 days follow-up. Abortions and premature deliveries were recorded in time relation to the administration of the drug through weekly community surveillance. The Hb measurement was repeated at 36 weeks of gestation for women in all the four groups. At birth, the weight of the babies was measured to the nearest 10 gm and stillbirths were recorded. The babies were examined for any malformations and for clinical jaundice and anemia. The Hb of newborns was measured using heel prick blood. The babies were followed up at one month and examined by a midwife for clinical jaundice, any other illness, and malformations.

Data analysis. Data were entered and analyzed using EPI-INFO version 6 (CDC, Atlanta, GA) supplemented by SPSS version 10.0 (Chicago, IL). Egg counts were normally distributed after log transformation and geometric mean parasite density was calculated. Student’s t-test was used for comparison of two means and analysis of variance (ANOVA) for comparison of three or more means. Proportions were compared using $\chi^2$ and P values < 0.05 were considered significant in all tests.

Ethical considerations. The objectives of the study and its implications were explained to the pregnant women. Approval of the study was obtained from the National Council for Science and Technology in Uganda (ref.: MV 726). The Danish National Committee for Biomedical Research Ethics also reviewed the study and recommended it (ref.: 624-03-0004). Participation was voluntary after informed consent and a participant could withdraw from the study at any time without consequences for ongoing treatment or ANC services.

RESULTS

Although 864 women were needed to be recruited for the study according to sample size calculations, it was found as the study progressed that the assumption of a loss to follow-up of 30% was too high. Actual loss to follow-up was about 15%. Therefore, recruitment was stopped before the originally planned 864 study participants were reached. As shown in Table 1, the baseline characteristics of the pregnant women were comparable except for Hb level, which was significantly higher in the reference group (difference in mean Hb between intervention and reference groups: A versus D, $P = 0.027$; B versus D, $P = 0.09$; and C versus D, $P = 0.0006$). Of the 832 pregnant women who were included, 5 women delivered twins (1 in Groups A, C, and D, and 2 in Group B) and were excluded from further birth weight analysis (Figure 1). There were 1 abortion and 10 stillbirths whose birth weights were not measured. Another 63 women had migrated to deliver at their mothers’ homes or had migrated to the Democratic Republic of Congo (DRC) because of tribal clashes between the Alurs from DRC and the indigenous Banyoro people. These were 8, 10, 13, and 32 in Groups A, B, C, and D, respectively. Data at delivery was thus included for 170, 160, 171, and 207 women in Groups A, B, C, and D, respectively.

A total of 834 pregnant women were examined for STHs at their first ANC clinic visit between January 2003 and May 2005 (Figure 1). Stool examination results were missing for two women (1 in Group A and 1 in Group B), and these were excluded from further analysis. Of the 832 pregnant women who had the stool examination results recorded, 591 (71%) were infected with one or more STHs (hookworm, *A. lumbricoides*

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**TABLE 1**

Baseline characteristics of enrolled pregnant women at first antenatal care (ANC) visit by intervention group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>A (ivermectin)</th>
<th>B (albendazole)</th>
<th>C (ivermectin-albendazole)</th>
<th>D (reference)</th>
<th>$P$ value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, mean ± SD</td>
<td>23.1 ± 5.2 (198)†</td>
<td>24.0 ± 6.3 (193)</td>
<td>23.7 ± 6.0 (199)</td>
<td>23.7 ± 6.7 (241)</td>
<td>0.55</td>
</tr>
<tr>
<td>Weight in kg, mean ± SD</td>
<td>56.1 ± 7.4 (198)</td>
<td>56.7 ± 8.1 (193)</td>
<td>56.7 ± 7.2 (198)</td>
<td>57.3 ± 8.6 (241)</td>
<td>0.47</td>
</tr>
<tr>
<td>Height in cm, mean ± SD</td>
<td>156.0 ± 9.4 (195)</td>
<td>156.3 ± 10.5 (193)</td>
<td>156.7 ± 7.0 (197)</td>
<td>155.0 ± 15.8 (241)</td>
<td>0.45</td>
</tr>
<tr>
<td>Hemoglobin in g/L, mean ± SD</td>
<td>110.6 ± 14.5 (198)</td>
<td>111.2 ± 15.3 (194)</td>
<td>108.8 ± 14.2 (198)</td>
<td>113.7 ± 16.5 (241)</td>
<td>0.001</td>
</tr>
<tr>
<td>Gestational age in weeks, mean ± SD</td>
<td>23.0 ± 3.4 (198)</td>
<td>23.2 ± 3.4 (194)</td>
<td>22.9 ± 3.8 (199)</td>
<td>22.8 ± 3.4 (241)</td>
<td>0.60</td>
</tr>
</tbody>
</table>

* Analysis of variance (ANOVA) test for significance of difference among the group.
† Number in parenthesis indicates number of women.
or *T. trichiura*. A total of 198 (23.8%) were allocated to Group A (ivermectin), 194 (23.3%) to Group B (albendazole), and 199 (23.9%) to Group C (ivermectin plus albendazole). A total of 241 (29%) had no STH infections and were allocated to Group D (no intervention, reference group). The prevalence of hookworm infection was 66.6% (554), with 93.9% (186), 91.8% (178), and 95.5% (190) in Groups A, B, and C, respectively (Table 2). Only 4 persons were infected
with *A. lumbricoides* (2 in each of the Groups A and B). The prevalence of *T. trichiura* was 4.6% (38) with 4.5% (9) in Group A, 6.2% (12) in Group B, and 8.5% (17) in Group C, respectively. The prevalence of *Schistosoma mansoni* was very low (3.7% [31]), and those infected were treated with praziquantel 40 mg/kg as a single dose because the drug is now recommended for use in pregnancy.8,11 A total of 802 women had a blood smear prepared and 282 (35.2%) were parasitaemia rate between any of the interventions (Table 2). The prevalence of hookworm infection from 93.9% to 70.6%, and 95.5% to 7.4%, respectively (Table 2). A comparison was made between each of the intervention groups and reference group on the frequency of LBW (birth weight < 2.5 kg) among the groups (P = 0.47). A comparison was also made between each of the intervention groups and reference group on the frequency of LBW. There was no significant difference between Groups A and D (P = 0.52) and between Groups A and D (P = 0.41), Groups B and D (P = 0.83), and Groups C and D (P = 0.29). Similarly, there was no significant difference in the frequency of LBW (birth weight < 2.5 kg) among the groups (P = 0.47). A comparison was made between each of the intervention groups and reference group on the frequency of LBW. There was no significant difference between Groups A and D (P = 0.56), Groups B and D (P = 0.25), and Groups C and D (P = 0.14).

**Efficacy of ivermectin, albendazole, and the combination on STH infections.** Of the pregnant women seen at first ANC visit having STH infections, 180 (91.4%) in Group A, 178 (92.2%) in Group B, and 188 (94.5%) in Group C were available for follow-up at 21 days post treatment. Forty-five were lost to follow-up because of migration, and they were 18, 16, and 11 in Groups A, B, and C, respectively (Figure 1). Ivermectin, albendazole, and ivermectin/albendazole had reduced the prevalence of hookworm infection from 93.9% to 70.6%, 91.8% to 4.5%, and 95.5% to 7.4%, respectively (Table 2). A total of 53, 170, and 174 were negative for hookworm infection at 21 days follow-up in Groups A, B, and C, respectively (Table 2). The prevalence of *T. trichiura* at 21 days follow-up was 2.2%, 4.5%, and 2.7% in Groups A, B, and C, respectively (Table 2). Because of the low prevalence of other intestinal helminth infections, the intensity of infection was calculated only for hookworm (Table 4).

**Adverse reactions to ivermectin, albendazole, and the combination among pregnant women.** Overall, 47 pregnant women reported having experienced mild and short lived adverse reactions; 23 (48.9%) in Group A, 16 (34%) in Group B, and 8 (17%) in Group C, and the difference among the groups was significant (P = 0.005). Significant difference was noted in reported mild adverse reactions between Groups A and C (P = 0.001) but not between Groups A and B (P = 0.14) and Groups B and C (P = 0.061). The most common reactions were: abdominal pain (7 [30.4%], 8 [50%], and 4 [50%] in Groups A, B, and C, respectively [P = 0.39]). There was no significant difference in reported abdominal pain between Groups A and B (P = 0.22), Groups A and C (P = 0.57), and Groups B and C (P = 0.67). Another reported reaction was fever (4 [17.4%], 2 [12.5%], and 4 [50%] in Groups A, B, and C, respectively [P = 0.087]), and there was no significant difference between Groups A and B (P = 0.97), between Groups A and C (P = 0.18), and between Groups B and C (P = 0.13). Body rash/itchiness was the least reported mild adverse reaction with (4 [17.4%], 2 [12.5%], and 2 [25%] in Groups A, B, and C, respectively [P = 0.74]), and there was no significant deference between Groups A and B (P = 0.97), Groups A and C (P = 0.96), and Groups B and C (P = 0.13). Six women reported headache (4 [17.4%] in Group A and 2 [12.5%] in Group B). Three women reported anorexia/vomiting (2 [8.7%] in Group A and 1 [6.3%] in Group B). No women reported any severe adverse event.

**Effect of the interventions on mean birth weight and low birth weight (LBW).** As shown in Table 5, there was no significant difference in mean birth weight among the groups (P = 0.52) and between Groups A and D (P = 0.41), Groups B and D (P = 0.83), and Groups C and D (P = 0.29). Similarly, there was no significant difference in the frequency of LBW (birth weight < 2.5 kg) among the groups (P = 0.47). A comparison was also made between each of the intervention groups and reference group on the frequency of LBW. There was no significant difference between Groups A and D (P = 0.56), Groups B and D (P = 0.25), and Groups C and D (P = 0.14).

**Effect of interventions on abortions, premature deliveries, stillbirths, and congenital abnormalities.** Only one abortion was recorded (Group B). According to the midwife’s assessment, there were 13 premature deliveries with 3 (1.8%), 2 (1.3%), 3 (1.8%), and 5 (2.4%) in Groups A, B, C, and D, respectively (P = 0.87). A comparison was made between each of the intervention groups and reference group on premature deliveries, and there was no significant difference between any of the intervention groups and the reference group (A versus D, P = 0.94; B versus C, P = 0.67; C versus D, P = 0.94). Babies were also categorized as premature and full

### Table 2

<table>
<thead>
<tr>
<th>Intervention group</th>
<th>% Infected (no. examined at first ANC visit)</th>
<th>% Infected (no. examined at 21 days post treatment)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hookworm</td>
<td>A (ivermectin)</td>
<td>93.9 (198)</td>
</tr>
<tr>
<td></td>
<td>Hookworm</td>
<td>4.5 (198)</td>
</tr>
<tr>
<td></td>
<td>B (albendazole)</td>
<td>91.8 (194)</td>
</tr>
<tr>
<td></td>
<td>Hookworm</td>
<td>6.2 (194)</td>
</tr>
<tr>
<td></td>
<td>C (ivermectin + albendazole)</td>
<td>95.5 (199)</td>
</tr>
<tr>
<td></td>
<td>Hookworm</td>
<td>8.5 (199)</td>
</tr>
</tbody>
</table>

### Table 3

<table>
<thead>
<tr>
<th>Intervention group</th>
<th>No. of women with STH infection at ANC visit (%)</th>
<th>No. of women negative for STH 21 days post treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hookworm</td>
<td>A (ivermectin)</td>
</tr>
<tr>
<td></td>
<td>Hookworm</td>
<td>186 (93.9)</td>
</tr>
<tr>
<td></td>
<td>Hookworm</td>
<td>2 (1.0)</td>
</tr>
<tr>
<td></td>
<td>Hookworm</td>
<td>9 (4.5)</td>
</tr>
<tr>
<td></td>
<td>Hookworm</td>
<td>53 (29.4)</td>
</tr>
<tr>
<td></td>
<td>Hookworm</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td></td>
<td>Hookworm</td>
<td>174 (92.6)</td>
</tr>
<tr>
<td></td>
<td>Hookworm</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

**ANC** = antenatal care.
term using Ballard score where a score < 46 (gestational age 36.7 weeks) was considered as premature. According to Ballard score, 36 babies were premature of which 9 (5.3%) were in Group A, 9 (5.6%) in Group B, 8 (4.7%) in Group C, and 10 (4.8%) in Group D (P = 0.98), and there was no significant difference between any of the intervention groups and the reference group (A versus D, P = 0.65; B versus D, P = 0.74; C versus D, P = 0.95). There were 10 stillbirths with 1 (0.6%), 5 (3.1%), 3 (1.8%), and 1 (0.5%) in Groups A, B, C, and D, respectively (P = 0.13). A comparison was made between each of the intervention groups and reference group on stillbirths, and there was no significant difference between any of the intervention groups and the reference group (A versus D, P = 0.99; B versus D, P = 0.12; C versus D, P = 0.49). Only 2 babies (one in Group A and one in Group D) were born with congenital abnormalities. The one in Group A had talipes equinovarus of the right foot, whereas the one in Group D had talipes equinovarus of the left foot, cleft palate, and multiple fingers, and the baby died shortly after birth.

**Effect of the interventions on maternal and neonatal Hb concentration**. The mean maternal and infant Hb levels and anemia status are summarized in Table 6. A total of 832 pregnant women had their Hb measured at first ANC visit and the mean Hb was 110.6 g/L, 111.2 g/L, 108.8 g/L, and 113.7 g/L in Groups A, B, C, and D, respectively (P = 0.001). Significant differences were noted in mean Hb levels at first ANC visit between Groups A and D (P = 0.027) and between Groups C and D (P = 0.0006) but not between Groups B and D (P = 0.09). Overall, 171 (20.6%) pregnant women were anemic at first ANC visit with 23.7%, 21.1%, 22.2%, and 16.1% in Groups A, B, C, and D, respectively (P = 0.22). The difference in the prevalence of anemia at first ANC visit was significant between Groups A and D (P = 0.047) but not between Groups B and D (P = 0.19) and Groups C and D (P = 0.11). At 36 weeks of gestation, 579 women had their Hb measured, and the mean Hb level was 113.8 g/L, 117.9 g/L, 115.6 g/L, and 117.8 g/L in Groups A, B, C, and D, respectively (P = 0.062). The difference in mean Hb levels at 36 weeks of gestation was significant between Groups A and D (P = 0.015), but not between Groups B and D (P = 0.96) and between Groups C and D (P = 0.13). The difference in mean Hb levels between first ANC visit and at 36 weeks of gestation was significant in all the groups except in Group A (Table 6). At 36 weeks of gestation, 8.5% pregnant women were anemic (Group A 10.9%, Group B 11.5%, Group C 7.7%, and Group D 6.9% [P = 0.40]). The difference in maternal anemia at 36 weeks of gestation was insignificant between any of the intervention groups and the reference group (Groups A and D [P = 0.21], Groups B and D [P = 0.16], and Groups C and D [P = 0.85]). A total of 693 infants had their Hb measured at birth (Group A 170, Group B 157, Group C 170, and Group D 196). Overall, 4.5% (31) infants were anemic at birth (infant anemia defined as Hb concentration < 140 g/L)\(^1\). Of those who were anemic at birth, 10 (5.8%), 6 (3.8%), 6 (3.5%), and 9 (4.6%) were in Groups A, B, C, and D, respectively (P = 0.73). There was no significant difference in infant anemia between Groups A and D (P = 0.58), Groups B and D (P = 0.72) and between Groups C and D (P = 0.61). As shown in Table 6, the mean infant Hb at birth was not significantly different among the groups (P = 0.12), but significant difference was noted between Groups C and D (P = 0.044) but not between Groups A and D (P = 0.71) and Groups B and D (P = 0.074).

**Effect of the interventions on maternal and neonatal mortality**. Of the 708 women who delivered live singleton babies, 636 (89.8%) were seen at one month post delivery with 148, 140, 146, and 202 in Groups A, B, C, and D, respectively (Figure 1). After delivery, 70 mothers had migrated to DRC because of tribal clashes or to their homes (22, 19, 24, and 5 in Groups A, B, C, and D, respectively). Fourteen babies had died at one-month post partum (6 [4.1%], 1 [0.7%], 2 [1.4%], and 5 [2.5%] in Groups A, B, C, and D, respectively [P = 0.23]). A comparison was made between each of the intervention groups and reference group on neonatal mortality, and there was no significant difference between any of the intervention groups and the reference group (A versus D, P = 0.60; B versus D, P = 0.42; C versus D, P = 0.74). The cause of death was respiratory tract infection (57.1%), prematurity related death (21.4%), and gastroenteritis/vomiting (14.3%). Of those mothers who had live babies at one-month post delivery, 204 reported that their children had problems, most of which were flu/cough (32.4%), skin rashes (16.7%), eye infection (5.9%), fever (4.9%), and anemia (4.4%). There were no differences among the groups (data not shown). Two women died of which 1 was in Group C who died shortly after an injection of procaine penicillin, and the cause of death was thought to be anaphylactic shock. Another woman (in Group B) died shortly after a caesarean section.

**DISCUSSION**

Anthelmintics are not widely used during pregnancy because of a lack of adequate information regarding their safety in pregnancy. However, in a review of 49 cases of inadvertent treatment with albendazole in the first trimester, no abnormal birth outcomes were recorded.\(^12\) In another report on the safety of albendazole use in pregnancy, there were no cases of malformation after inadvertent exposure of 15 patients with albendazole, but the sample size was small in all these stud-

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**Table 4**

Mean parasite density among hookworm positives by intervention group at enrollment and at 21 days post treatment in Masindi district, western Uganda.

<table>
<thead>
<tr>
<th>Intervention group</th>
<th>Mean parasite density (eggs/g) ±SD at first ANC visit</th>
<th>Mean parasite density (eggs/g) ±SD at 21 days post treatment</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (ivermectin)</td>
<td>503.5 ± 4.7 (186)†</td>
<td>493.2 ± 4.3 (127)†</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>B (albendazole)</td>
<td>653.5 ± 4.4 (178)†</td>
<td>237.1 ± 33.3 (8)‡</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>C (ivermectin + albendazole)</td>
<td>629.5 ± 4.3 (190)‡</td>
<td>227.5 ± 2.8 (14)‡</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>P value‡</td>
<td>0.24</td>
<td>0.074</td>
<td></td>
</tr>
</tbody>
</table>

* Student’s t test for significance of difference in the groups between first antenatal care (ANC) visit and at 21 days post treatment.
† Number in parenthesis indicates number of pregnant hookworm positives women.
‡ Analysis of variance (ANOVA) test for significance of difference among the groups at first ANC visit and 21 days post treatment.
Infant anemia status (Hb < 140 g/L) at birth is stillbirths. We still found that the abortion rate in our study is lower than what has been recorded in earlier reports. This might be because of exclusion of women with a history of severe anemia at birth in Masindi district, western Uganda. A (ivermectin group) B (albendazole group) C (ivermectin + albendazole) D (reference group) 2.98 ± 0.43 (170) 2.97 ± 0.46 (171) 3.02 ± 0.46 (207) 3.03 ± 0.46 (160)

Mean (SD) maternal Hb concentration in g/L [No. of pregnant women] at first visit:
A (ivermectin) 110.6 (14.5) [198] B (albendazole) 111.2 (15.3) [194] C (ivermectin + albendazole) 108.8 (14.2) [198] D (reference) 113.7 (16.5) [241]

P value* 0.52

At first visit:

Table 5

<table>
<thead>
<tr>
<th>Intervention group</th>
<th>Mean birth weight in kg ± SD (no. of pregnant women)</th>
<th>No. of babies with LBW (%) [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (ivermectin)</td>
<td>2.98 ± 0.43 (170)</td>
<td>16 (9.4%) [5.6–15.1]</td>
</tr>
<tr>
<td>B (albendazole)</td>
<td>3.03 ± 0.46 (160)</td>
<td>18 (11.3%) [6.8–17.2]</td>
</tr>
<tr>
<td>C (ivermectin + albendazole)</td>
<td>2.97 ± 0.46 (171)</td>
<td>21 (12.3%) [7.8–18.2]</td>
</tr>
<tr>
<td>D (reference)</td>
<td>3.02 ± 0.46 (207)</td>
<td>16 (7.7%) [4.5–12.0]</td>
</tr>
</tbody>
</table>

P value* 0.52

* Student’s t test for significance of difference in mean birth weight and Hb among the groups.

P value**: 0.001

A (ivermectin) B (albendazole) C (ivermectin + albendazole) D (reference) 3.2 6.7 6.8 4.1

P value** 0.063 < 0.001 < 0.001 0.007

Maternal anemia status (Hb < 100 g/L), number (%)
At first visit:
A (ivermectin) 47 (23.7) B (albendazole) 41 (21.1) C (ivermectin + albendazole) 44 (22.2) D (reference) 39 (16.1)
P value* 0.005

At 36 weeks of gestation:
A (ivermectin) 15 (10.9) B (albendazole) 12 (11.5) C (ivermectin + albendazole) 11 (7.7) D (reference) 12 (6.9) P value* 0.003 0.023 0.0003 0.004

Mean (SD) maternal Hb concentration in g/L [No. of subjects] at first visit and 36 weeks of gestation:
A (ivermectin) 113.8 (15.7) [138] B (albendazole) 117.9 (18.0) [131] C (ivermectin + albendazole) 115.6 (11.9) [135] D (reference) 117.8 (13.2) [175]
P value** 0.062

Maternal mean hemoglobin (Hb) levels and anemia status at first antenatal care (ANC) visit and at 36 weeks of gestation and infant mean Hb and anemia status at birth in Masindi district, western Uganda:

Table 6

Mean (SD) infant Hb at birth (g/L) at birth:
A (ivermectin) 180.8 (24.5) [170] B (albendazole) 184.6 (24.6) [157] C (ivermectin + albendazole) 184.9 (22.5) [170] D (reference) 179.8 (25.3) [196]
P value* 0.12

Mean (SD) infant Hb at birth (g/L) at birth, number (%)
A (ivermectin) 10 (5.8) B (albendazole) 6 (3.8) C (ivermectin + albendazole) 6 (3.5) D (reference) 9 (4.6)
P value* 0.73

* Significance of difference among the groups.
† Student’s t test for significance of difference in mean Hb in the groups at first visit and 36 weeks of gestation.
‡ χ² test for significance of difference in the prevalence of anemia in the groups at first visit and 36 weeks of gestation in each group.
mia status among the groups at 36 weeks of gestation. Mass ivermectin treatment and the co-administration of ivermectin and albendazole for the control of onchocerciasis and LF, respectively, will in the long term improve the quality of life by controlling STH infections. The commonly reported adverse events after administration of ivermectin or albendazole and a combination of both drugs were abdominal pain, fever, and body rashes, and they were all mild. No severe adverse events were reported. In this study, administration of ivermectin or albendazole or the drugs combined during the second trimester of pregnancy showed no severe adverse effects. To interrupt transmission of LF where it is co-endemic with onchocerciasis, co-administration of ivermectin and albendazole to pregnant women should be encouraged. However, there is a need to establish a pharmacovigilance system to monitor MDA programs for LF and STH infection to report side effects and safety of ivermectin and albendazole treatment in women who inadvertently have taken the drugs in the first trimester of pregnancy. Safety studies of the co-administration of ivermectin and albendazole in the first trimester of pregnancy are needed because it might be difficult to identify only pregnant women in the second or third trimester based on the last normal menstruation period, especially during large-scale MDA programs. Safety studies on administration of ivermectin or co-administration of ivermectin and albendazole in children < 5 years of age are also desirable, because some of these children are LF microfilaria carriers and remain a source of re-infection to the treated population.23 For treatment of STH infections during pregnancy, albendazole alone is recommended, as ivermectin has no added advantage in the treatment of STHs, particularly hookworm infection, the commonest intestinal parasite in pregnancy.24,25

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