Impact of ivermectin drug combinations on *Pediculus humanus capitis* infestation in primary schoolchildren of south Indian rural villages

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Abstract

Background Antifilarial drug combinations including ivermectin provide antifilarial activity with ancillary benefits on intestinal helminths and ectoparasites, such as chiggers and lice. The impact of single oral dose of antifilarial drugs, viz (1) diethylcarbamazine (DEC) alone, (ii) DEC + albendazole (ALB), (iii) ivermectin (IVA) + DEC and (iv) IVA + ALB, was determined, on the head louse (*Pediculus humanus capitis*) in primary school children in a rural community in south India.

Methods Primary school children (*n* = 534) of age 6–10 years from four villages of South India were examined for the presence of head lice before and after single dose of DEC + ivermectin drug combination. The effectiveness and the duration of cure sustained by these drugs were quantified. The head louse was examined by “combing method” during post-treatment periods at 15, 45, 60 and 75 days interval.

Results The antifilarial drug consumption rate was similar (96–98%) in all treatment arms. In pre-treatment survey the prevalence of head lice in children administered with DEC, DEC + ALB, IVA + DEC and IVA + ALB arm was 86%, 80%, 87% and 80%, respectively, with the latter two arms demonstrating significant reduction in louse infestation (*P* < 0.05) for 60 days.

Conclusion Single dose with IVA combination demonstrates a greater impact in reducing head louse infestation in the endemic rural communities for nearly 60 days. Therefore, in regions such as Africa where ivermectin is part of the antifilaria campaign, this drug will have an additional benefit in reducing head lice infestation.

Introduction

Each year, millions of children are reported to be infested with the head louse (*Pediculus humanus capitis*), a condition known as pediculosis. The condition is most prevalent in school-age children, and is responsible for tens of millions of lost school days. Pediculosis is a serious public health problem in various parts of the world, inflicting various forms of physical and psychologic infirmity. *Pediculus humanus capitis* is transmitted through physical contact. Symptoms associated with infestation are constant itching and scalp irritation. When the ectoparasites are associated with poor social conditions (with heavy lice infestation, where blood intake is more than three times daily) and inadequate iron in the diet, the infestation may even lead to anaemia. It has been suggested that transmission of *P. b. capitis* is caused by shared combs, hairbrushes, mats, hats, bed linen, and clothes. A filariasis control program aimed at interrupting the transmission of *Wuchereria bancrofti*, the causative agent of human lymphatic filariasis, has relied solely on community-level mass drug administration (MDA) on a yearly basis. Several anthelmintic drugs, especially when given in combination, have been shown to have a significant antifilarial effect, thus providing a number of efficient tools to control filariasis. A combination of diethylcarbamazine (DEC) or ivermectin (IVR) with albendazole (ALB) has been shown to be highly effective in the management of microfilariae because of lymphatic-dwelling filarial worms. The drug ALB provides additional ancillary benefits on intestinal helminth infections. IVR, which is a drug of choice in the antifilariasis campaign under the Global Programme to Eliminate Lymphatic Filariasis (GPELF), provides ancillary benefits on ectoparasites, such as those causing scabies and lice-borne infections. When administered orally, IVR has been documented to have a significant effect in the control of body lice.
the fact that IVR is recommended for use in combination with ALB for lymphatic filariasis elimination only in African countries reporting Onchocerciasis, it is hereby considered opportune to bring on record results of our studies on the effectiveness of IVR, when used in combination with DEC, for the control of head louse infestation in a rural community.

As a part of the World Health Organization/Training in Tropical Diseases (WHO/TDR) filariasis control trial studies in south India, six villages were mass administered with an annual single combination dose of DEC (6 mg/kg) + IVR (200 µg/kg) for 2 years in 1995 and 1996.\(^{15}\) During the routine post-treatment entomological evaluation to determine the impact of MDA on filariasis transmission parameters, the villagers, especially the women, reported reduced/zero head lice infestation after drug consumption and requested further drugs. This prompted us to evaluate the role of antifilarial drugs in curing P. h. capitis infestation by carrying out a detailed study in schoolchildren during various MDA programmes employing DEC alone, DEC + ALB, IVR + DEC, or IVR + ALB in lymphatic filariasis at the village level.

### Materials and Methods

The study was conducted in four villages of Tirukollur taluk (latitude 11°57'00"; longitude 79°12'00"), Tamil Nadu, south India, where bancroftian filariasis was endemic. Most of the villagers live in thatched houses and are landless laborers, dependent on agriculture for their livelihood; paddy, sugar cane, groundnuts, and millets are the main crops grown. Each village has a primary school attended by children between 6 and 10 years of age. For higher classes, the students must travel to a nearby town. Primary school children aged 6–10 years were surveyed for head lice infestation before and after the MDA programme (carried out as part of the antifilarial campaign) with the four treatment strategies. The treatment strategies administered to all age groups, including children in the four villages, were as follows: (1) DEC (6 mg/kg); (2) DEC with ALB (400 mg/person); (3) DEC with IVR (200 µg/kg); and (4) IVR with ALB. MDA was carried out by door-to-door visit, and more than 95% of the eligible residents were treated (children under 2 years, and pregnant and lactating women were excluded from MDA). Informed oral consent was obtained from villagers at the time of drug administration. A total of 164, 127, 128, and 115 primary schoolchildren in the four villages were surveyed during the pre-treatment period. All the children who were present during the survey were screened for P. h. capitis. Examination for head lice was carried out by the “combing method” using an appropriate comb. Each child was examined by combing several times and, after combing, the comb was stroked onto a white sheet of cloth. Different life stages of lice were collected (nits, nymphs, and adults). The white sheet was carefully examined using a hand lens. Children were considered to be positive for head lice infestation if the sheet revealed any one of the life stages of the head louse (i.e. nymphs or adults). After examining each child, the comb was cleaned thoroughly using a brush and the white sheet was changed. The collected lice were discarded in a pan containing hypochlorite solution. All of these children were treated during the MDA programme. The post-treatment evaluation of lice infestation in these four villages was carried out at different time periods, namely after 15, 45, 60 and 75 days (i.e. until the prevalence reached the pretreatment level). During post-treatment surveys, we checked that each child examined for P. h. capitis had consumed the drug provided during the MDA campaign. The study was approved by the institutional ethical committee.

The data were analyzed using SPSS software package version 11.0 (SPSS Inc., Chicago, IL, USA). The prevalence was expressed as the percentage of schoolchildren found to be positive for lice infestation, and the differences in the prevalence rates pre- and post-treatment were expressed as a reduction in prevalence. The statistically significant differences in the prevalence observed between the treatment strategies at different time points were tested by chi-squared analysis.

### Results

The drug consumption rates in all the study villages were comparable (97, 96, 98, and 97\%) (Table 1). The prevalence of P. capitis during baseline survey in all children (four villages) was similar for the groups receiving DEC alone, DEC + ALB, IVR + DEC, and IVR + ALB (85.98, 80.31, 86.72, and 80.00\%, respectively). There was no significant difference in prevalence between the four arms (\(P > 0.05\)) (Table 2). During the post-treatment survey after 15 days, the

### Table 1 Drug coverage in the four treatment arms during mass drug administration campaign

<table>
<thead>
<tr>
<th>Treatment arm</th>
<th>Eligible population in all age groups</th>
<th>Population treated</th>
<th>Percentage treated</th>
<th>Eligible population in 6–10-year age group</th>
<th>Population treated</th>
<th>Percentage treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEC alone</td>
<td>2067</td>
<td>2005</td>
<td>97</td>
<td>440</td>
<td>380</td>
<td>88.36*</td>
</tr>
<tr>
<td>DEC + ALB</td>
<td>1775</td>
<td>1699</td>
<td>95.72</td>
<td>273</td>
<td>247</td>
<td>90.46*</td>
</tr>
<tr>
<td>IVR + DEC</td>
<td>2172</td>
<td>2123</td>
<td>97.74</td>
<td>386</td>
<td>339</td>
<td>87.37*</td>
</tr>
<tr>
<td>IVR + ALB</td>
<td>627</td>
<td>607</td>
<td>96.81</td>
<td>137</td>
<td>120</td>
<td>87.59*</td>
</tr>
</tbody>
</table>

ALB, albendazole; DEC, diethylcarbamazine; IVR, ivermectin.

*No significant difference among percentage treated (based on \(X^2\) test).
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ALB, albendazole; DEC, diethylcarbamazine; IVR, ivermectin.

Data sharing the same superscript letter do not differ significantly (based on \( \chi^2 \) test).

<table>
<thead>
<tr>
<th>Pretreatment</th>
<th>Post-treatment period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number examined</td>
<td>Percentage positive</td>
</tr>
<tr>
<td><strong>Treatment arm</strong></td>
<td></td>
</tr>
<tr>
<td>DEC alone</td>
<td>164</td>
</tr>
<tr>
<td>DEC + ALB</td>
<td>127</td>
</tr>
<tr>
<td>IVR + DEC</td>
<td>128</td>
</tr>
<tr>
<td>IVR + ALB</td>
<td>115</td>
</tr>
</tbody>
</table>

**Figure 1** Percentage reductions in *Pediculus humanus capitis* infestation in schoolchildren of two treatment arms. IVR, ivermectin

The prevalence rates of *P. b. capitis* in the non-IVR arm (DEC and DEC + ALB) were 85 and 78%, but 3 and 4% for IVR + DEC and IVR + ALB, respectively. During this period, the first two arms did not show any statistically significant difference (\( \chi^2 = 1.77, P = 0.1835 \)). Similarly, the last two arms (IVR + DEC and IVR + ALB) did not differ significantly (\( \chi^2 = 0.03, P = 0.85 \)). The survey was repeated; the prevalence rates after 45, 60, and 75 days in the IVR + DEC arm were 13, 49, and 81%, respectively; in the IVR + ALB arm, the rates were 14, 48, and 72%, respectively (Table 2).

The prevalence rates during the post-treatment periods, i.e. after 15, 45, and 60 days, showed a significant difference (\( P < 0.05 \)) in the IVR combination drug arms, but not in the other two groups. At 75 days post-treatment, the prevalence of *P. b. capitis* was comparable with the baseline figures in all treatment arms, with no significant difference (\( P > 0.05 \)). During different post-treatment observations, no significant differences were observed between the two arms with the IVR combination (i.e. IVR + DEC and IVR + ALB). Similarly, no difference was found between the arms with the drug combinations without IVR (i.e. DEC alone and DEC + ALB).

Hence, during analysis, the two arms of the IVR combination were pooled as one group and the two arms without IVR as the second group. The percentage reductions were not significant in the non-IVR arm, but, in the IVR arm, the reductions were

96, 84, 42, and 8% during 15, 45, 60, and 75 days, respectively (Fig. 1). The prevalence changes (with 95% confidence intervals) in *P. b. capitis* infestation in the IVR arm can be seen clearly in the error bar chart (Fig. 2).

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Alb, Albendazole; DEC, diethylcarbamazine; IVR, ivermectin.
Discussion

Pediculus humanus capitis is a prevalent and highly communicable condition infesting millions of elementary school students annually. The prevalence is generally 1–3% in industrialized countries; however, it may, on occasion, exceed 25% in elementary schools. In public rural schools in Uberlandia, state of Minas Gerais, central Brazil, a prevalence rate of 3.5% was observed for P. b. capitis in 884 children. In our study, the prevalence of P. b. capitis was as high as 84%, reflecting the low socioeconomic conditions prevalent in this part of India. Among schoolchildren in Argentina, an infestation rate of 8.5% was observed. In primary schoolchildren of north-western Venezuela, the overall prevalence of P. capitis was 28.8%. A prevalence of 84.9% for body lice was observed in a cohort of homeless men from a shelter in Marseilles, France. The infestation was reduced to 18.5% with three doses of oral IVR (12 mg each), administered at 7-day intervals, and the reduction was sustained for 45 days.

In our study, single-dose IVR combinations were found to be effective for 60 days against head lice. Head lice may be more susceptible than body lice to IVR. Levamisole has been suggested to be effective against pediculosis if administered for 10 days, and no adverse reactions have been observed. ALB has also been reported to be effective against adult lice when used as a repeated dose over 3 days and re-treated 1 week later. Such an effect by ALB was not demonstrated in our study, as a single oral dose was administered here. The administration of 1% permethrin with oral trimethoprim/sulfamethoxazole (TMP/SMX) may provide a synergistic effect, especially in instances of drug resistance associated with P. b. capitis. In our study, a single dose of oral IVR + DEC or IVR + ALB was found to be highly effective against P. b. capitis, in addition to its antifilarial activity and reduced intestinal helminth infection, without necessitating a second dose with an 8-day interval, as recommended by Burkhart and Burkhart. Oral treatment with IVR could substitute for topically applied compounds, particularly in resource-poor communities where polyparasitism is common.

IVR resistance has not been reported in W. bancrofti, but the level of resistance in helminths of animals is high. Resistance has been documented in insects and mites of plants. For human use, resistance was seen in scabies. Side-effects are rare, but severe hepatitis has been reported, and deaths have been associated with the treatment of scabies. As the abusive use of IVR can cause secondary side-effects, it is advocated that appropriate care should be taken when administering this drug.

A better understanding of local epidemiology is required to develop control measures. This knowledge must be applied in combination with environmental sanitation, health education, and culturally acceptable interventions that are affordable by the underprivileged. Health departments generally rate pediculosis as a low-priority health issue; however, parents believe that lice pose a health risk, not only a simple undesirability. In order to reduce the proportion of children infested with head lice, active involvement of health and educational authorities, as well as parents, is important. Health authorities should regularly screen children and advocate the use of antilouse products. Academic institutions should support health staff during screening programs and also in creating awareness about pediculosis among parents. Parents need to be encouraged to inspect their children and to try to avoid creating stigma and emotional problems for them. Even in economically developed countries, such as Australia, the proportion of children missing school as a result of pediculosis is 24–50%, and parents were found to be unaware of pediculosis management. In developing and underdeveloped countries, the prevalence rate is expected to be more than 80% in primary schoolchildren (as observed in our study). In African countries with low socioeconomic conditions, the prevalence rate will certainly be high. Therefore, IVR, recommended for the antifilariasis campaign in areas in which onchocerciasis is coendemic (as in African countries), could provide an additional perceived benefit in reducing head lice infestation. In our study, it is clear that a single-dose IVR combination (IVR + ALB and IVR + DEC) is effective in reducing lice infestation for about 60 days post-treatment in endemic communities (i.e. in areas with high Pediculus infestation), which is an ancillary benefit derived in the lymphatic filariasis elimination programme. This additional benefit perceived by the community will certainly enhance drug compliance during the MDA programme targeted at the elimination of lymphatic filariasis.

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