Targeting malaria control to schoolchildren

See Articles page e1277

The burden of malaria in school-aged children has been underappreciated.[1] Typically, by the time African children are old enough to attend school, they have acquired antimalarial immunity through repeated exposure and can tolerate malaria infections without developing severe symptoms.[2] School-aged children, however, can still suffer the negative consequences of malaria infection on health and cognition, and, as transmission reduces due to intensified control, the risk of clinical malaria in school-aged children might increase.[3] Older children are often asymptomatic carriers of malaria parasites and are major contributors to the infectious reservoir for onwards malaria transmission.[4,5]

As progress on malaria control accelerates, school-aged children will become an increasingly important target population. Intermittent preventive treatment for malaria in school-aged children (IPTsc) benefits individual children,[6] and might reduce community-level transmission.[7] In 2022, WHO issued a conditional recommendation for IPTsc in areas of moderate-to-high perennial or seasonal malaria transmission.[8]

In *The Lancet Global Health*, Geofrey Makenga and colleagues report the results of an individually randomised controlled trial of the efficacy and safety of IPTsc in Tanzanian schoolchildren.[9] Children aged 5–15 years from seven schools were enrolled and randomised to one of three groups: dihydroartemisinin–piperaquine, artesunate–amodiaquine, or standard of care (control). IPTsc regimens were administered by teachers supervised by study nurses, according to weight-based guidelines. Three rounds of IPTsc were administered during the first year, at baseline, month 4, and month 8. Given the association between parasitic infections and anaemia, all participants were treated with the anthelmintic albendazole at baseline and again after 1 year, and children diagnosed with schistosomiasis were treated with praziquantel. The primary outcomes were change from baseline in mean haemoglobin, clinical malaria incidence, and malaria parasitaemia prevalence at months 12 and 20 of follow-up.

Children were enrolled in March–April, 2019, and were followed up until December, 2020. Clinical assessments were conducted every 4 months, with the first year of follow-up designed to assess the efficacy of IPTsc, and the remaining 8 months (non-intervention) to assess for possible rebound effects. Unfortunately, the 12-month evaluation fell in March, 2020, when schools were closed due to the COVID-19 pandemic, which limited follow-up at this key timepoint to children attending only two of the seven schools (384 [24·5%] of the 1566 children originally enrolled); however, the authors reassure us that the study retained 80% power to detect the target effect size.

In the intention-to-treat analysis, mean change from baseline in haemoglobin concentration was increased significantly in both intervention groups compared with the control: 0·5 g/dL (95% CI 0·2–0·8, p<0·0001) in the dihydroartemisinin–piperaquine group and 0·5 g/dL (0·2–0·7; p=0·0020) in the artesunate–amodiaquine group. However, on closer inspection, the findings are less straightforward. Overall, mean haemoglobin concentration at 12 months was essentially unchanged compared with the respective baseline concentrations in the two intervention groups; the reported increase was only relative to the control group, in which mean haemoglobin decreased by 0·5 g/dL in the same period. Notably, children who were assessed at 12 months had a higher mean haemoglobin concentration at baseline (12·3 g/dL [SD 1·3]) than children who were not sampled due to COVID-19-related school closures (11·4 g/dL [1·3]). Thus, the mean haemoglobin concentration results should be interpreted with caution as they might not be generalisable to the full study population. Mean haemoglobin concentration also fluctuated over the 12 months of follow-up in both intervention groups. The reasons for these fluctuations are not clear, but probably reflect the differences in study populations assessed at the various timepoints and the complex aetiology of anaemia. Although malaria is a major cause of anaemia in endemic areas, other factors can contribute, including nutritional status, helminth and other infections, and health system factors.

Encouragingly, the findings for other key endpoints were clearer. The incidence of clinical malaria was significantly lower in both IPTsc groups than in the control group at 12 months. Additionally, the prevalence of malaria parasitaemia decreased at month 12 in both intervention groups as compared with the control group: from 28·0% at baseline to 12·0% in the

dihydroartemisinin–piperaquine group (difference –21·6 percentage points [95% CI –31·9 to –11·3] *vs* control group), and from 24·7% to 16·0% in the artesunate–amodiaquine group (–17·6 percentage points [–28·4 to –6·9] *vs* control). IPTsc did not appear to have an effect on cognitive or psychomotor function, although this might be due to limitations in sample size and duration of follow-up. Results from the non-intervention period did not suggest that rebound had occurred, although clinical indicators had returned to baseline levels by 20 months.

Despite its limitations, the results of this trial are compelling and provide further evidence of the potential benefits and feasibility of IPTsc. The 2023 WHO guidelines on IPTsc suggest that further research to support policy decisions is called for, including investigation of monthly versus termly dosing, the effect of IPTsc on cognition and school performance, and the effect on community-level transmission.[8] Although these and other important questions about sustainability remain, the rationale for chemoprevention of malaria in schoolchildren is strong. As Cohee and colleagues said, the time for malaria control in school-aged children has come.[10]

We declare no competing interests.

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