can be inconclusive and may lead to misidentification. Molecular methods, such as WGS, might be needed for accurate identification.

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Tolerance of Atovacuona/proguanil in off-label indication in children

Tolerancia de Atovacuona/proguanil en niños con indicación fuera de ficha técnica

Dear Editor,

Malaria is a severe disease caused by a parasite of *Plasmodium* genus, transmitted by the bite of an Anopheles mosquito vector.[1] Malaria is endemic in many tropical countries; in 2022, 93.6% of cases and 95.4% of deaths (more than 78% of these in children under 5 years old) occurred in Africa.[2] It is the leading cause of fever in tropical travellers and it can cause severe illness.[1] Globally, in 2022, there were 249 million cases and 608,000 deaths.[2] Therefore, the World Health Organization (WHO) and the Centers of Disease Control and Prevention (CDC) recommend antimalarial chemoprophylaxis for all travellers visiting endemic areas.[2,3] With the major roll-out of malaria prevention and treatment measures, more than 11 million deaths were averted globally since 2000.[1] Malaria deaths in Africa reduced by 36% between 2000 and 2021.[1] Although malaria prevention in children is a significant challenge, Atovacuona/proguanil (A/P) is only authorised for those whose weight is ≥11 kg according to its technical datasheet.[4]

We conducted a retrospective study to determinate tolerance and side effects (SE) during and after travel in children under 11 kg taking paediatric A/P (25 mg/62.5 mg) as an off-label prophylactic measure.

Children weighing under 11 kg, who attended an International Vaccination Centre at a reference hospital in Madrid between 2018 and 2022 and were recommended chemoprophylaxis with paediatric A/P according to their weight, were included. Children weighing 5 kg to <8 kg received ½ pediatric tablet daily; those weighing 8 kg to <10 kg received ¾ pediatric tablet daily and those weighing 10 kg to <20 kg received 1 pediatric tablet daily. The medication was administered one to two days prior to exposure, during exposure, and for one week following exposure. If needed, tablets could be broken or crushed and mixed with a drink. We recommended taking it in the morning with food beginning and with a milk drink.

Parents were informed that we rely on recommendations from the Spanish Ministry of Health, CDC and WHO, which indicate chemoprophylaxis in children weighing 5–11 kg when travelling to high-risk countries.[2,3,5] A contact telephone number was provided in case of any SE, and a follow-up telephone call was made to all families after their travel.

A total of 32 children received a chemoprophylaxis recommendation, but 4 (12.5%) did not take the drug due to parental decision. In 9 cases (28.1%), none of the parents answered the follow-up telephone call and, although none reported SE, they were considered lost to follow-up. The remaining 19 children were analysed. As they were infants, all parents followed the recommendations closely and did not miss any doses.

Ten (52.6%) were girls, the median age was 9 months (interquartile range [IQR] 6–13), and the median weight 9 kg (IQR 8–10). The majority, 16/19 (84.2%), were healthy; two were late preterm and one was a carrier of sickle-cell anaemia. All were well vaccinated and without allergies. They were all born in Spain and in 17 cases (89.4%) it was their first trip to a high-risk area, making it crucial to prescribe malaria prophylaxis and split the tablets if necessary. Two infants (10.5%) had previously travelled to the same country and also received chemoprophylaxis on that occasion. The most common reason for travel was visiting friends and relatives (16 cases, 84.2%). All travelled to highly endemic areas, with Africa being the most frequent destination (18 cases, 94.7%). The median duration of the travel was 30 days (IQR 15–90). The most frequent travel periods were summer (7 cases, 36.8%) and autumn (7 cases, 36.8%), corresponding with the months of June to November, when the rainy season occurs in African countries, leading to a higher risk of malaria infection due to mosquito bites. This excludes one case who

travelled to Brazil in June, outside of the rainy season. The median dose of the drug (tablets per day) was 0.75 (IQR 0.5–1), adjusted by weight.

When contacted, none reported severe SE and only two children (10.5%) experienced self-limited diarrhea during the trip (1–2 bowel movements per day for two days, without vomiting), which is considered a very frequent SE (≥1/10) in the technical datasheet.[4] There were no malaria cases among the children.

Our study supports the use of A/P in children under 11 kg, as already endorsed by health authorities (WHO, CDC, Spanish Ministry of Health) for children weighing less than 11 kg travelling to high-risk destinations as a preventive treatment, given the severity and high mortality of malaria at this age and the few SE reported. However, further research is needed to determine the best posology, efficacy and pharmacokinetics of antimalarial drugs used for chemoprophylaxis in children.

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Conflict of interest

The authors declare no conflict of interest.

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