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[Intervention Review]

Atovaquone-proguanil for treating uncomplicated malaria

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ABSTRACT

Background

Many conventional treatments for uncomplicated malaria are failing because malaria parasites develop resistance to them. One way to combat this resistance is to treat people with a combination of drugs, such as atovaquone-proguanil.

Objectives

To compare atovaquone-proguanil with other antimalarial drugs (alone or in combination) for treating children and adults with uncomplicated *Plasmodium falciparum* malaria.

Search methods

We searched the Cochrane Infectious Diseases Group Specialized Register (June 2005), CENTRAL (*The Cochrane Library* Issue 2, 2005), MEDLINE (1966 to June 2005), EMBASE (1980 to June 2005), LILACS (1982 to June 2005), reference lists, and conference abstracts. We also contacted relevant pharmaceutical manufacturers and researchers.

Selection criteria

Randomized controlled trials comparing atovaquone-proguanil with other antimalarial drugs for treating children and adults confirmed to have uncomplicated *P. falciparum* malaria.

Data collection and analysis

Three authors independently assessed trial eligibility and the risk of bias in the trials, and extracted data for an intention-to-treat analysis (where possible). We used risk ratio (RR) and 95% confidence intervals (CI) for dichotomous data. We contacted trial authors for additional information where needed.

Main results

Ten trials, with a total of 2345 participants, met the inclusion criteria. The trials were conducted in four geographical regions and were often small, but they included comparisons across eight drugs. Nine trials were funded by a pharmaceutical company, only three carried out an intention-to-treat analysis, and allocation concealment was unclear in seven. Atovaquone-proguanil had fewer treatment failures by day 28 than chloroquine (RR 0.04, 95% CI 0.00 to 0.57; 27 participants, 1 trial), amodiaquine (RR 0.22, 95% CI 0.13 to 0.36; 342 participants, 2 trials), and mefloquine (RR 0.04, 95% CI 0.00 to 0.73; 158 participants, 1 trial). There were insufficient data to draw a conclusion for this outcome from comparisons with sulfadoxine-pyrimethamine (172 participants, 2 trials), halofantrine (205 participants, 1 trial), artesunate plus mefloquine (1063 participants, 1 trial), quinine plus tetracycline (154 participants, 1 trial), and dihydroartemisinin-piperaquine-trimethoprim-primaquine (161 participants, 1 trial). Adverse events were mainly common symptoms of malaria and did not differ in frequency between groups.

Authors' conclusions

Data are limited but appear to suggest that atovaquone-proguanil is more effective than chloroquine, amodiaquine, and mefloquine. There are insufficient data for comparisons against sulfadoxine-pyrimethamine, halofantrine, artesunate plus mefloquine, quinine plus tetracycline, and dihydroartemisinin-piperaquine-trimethoprim-primaquine in treating malaria. There are not enough data to assess safety, but a number of adverse events were identified with all drugs. Large trials comparing atovaquone-proguanil with other new combination therapies are needed.

22 March 2019

Update pending

Authors currently updating

The update is due to be published in 2019.

PLAIN LANGUAGE SUMMARY

Atovaquone-proguanil appears to be more effective than individual drugs for treating uncomplicated malaria, but there are few data comparing atovaquone-proguanil to other combination therapies

Many conventional treatments for uncomplicated malaria are failing because malaria parasites develop resistance to them. This can be reduced by treating people with combination drugs such as atovaquone-proguanil. The review found 10 trials, most of low methodological quality and most funded by a single pharmaceutical company. In addition, trials were small and had few participants thus evidence suggesting atovaquone-proguanil as more effective than a number of single drug treatments at eliminating the *Plasmodium falciparum* malaria parasite from the blood was limited. There were few good quality data comparing atovaquone-proguanil with other new combination therapies. There were not enough data to assess adverse events, but all trials recorded some adverse events.