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Evidence Assessment: Summary of a Systematic Review

Who is this summary for?
For doctors and other health personel; administrators and managers of health facilities, Community Health Workers and the partners involved in the management of uncomplicated malaria

Dihydroartemisinin-piperaquine for treating uncomplicated *Plasmodium falciparum* malaria

Key findings

- Dihydroartemisinin-piperaquine cures slightly more patients than Artemether-Lumefantrine, and it also prevents further malaria infections for longer after treatment.
- Dihydroartemisinin-piperaquine is as effective as Artesunate plus Mefloquine in treating malaria.
- Artesunate plus Mefloquine probably causes more nausea, vomiting, dizziness, sleeplessness, and palpitations than dihydroartemisinin-piperaquine.

Background

Uncomplicated malaria is the mild form of malaria which usually causes a fever, with or without headache, tiredness, muscle pains, abdominal pains, nausea, and vomiting. If left untreated, uncomplicated malaria can develop into severe malaria with kidney failure, breathing difficulties, fits, unconsciousness, and eventually death. Dihydroartemisinin-piperaquine is one of five Artemisinin-based combination therapies the World Health Organization currently recommends to treat malaria. These combinations contain an Artemisinin component (such as Dihydroartemisinin) which works very quickly to clear the malaria parasite from the person's blood, and a longer acting drug (such as Piperaquine) which clears the remaining parasites from the blood and may prevent new infections with malaria for several weeks.

Question

What is the effectiveness and safety of dihydroartemisinin-piperaquine compared to other Artemisinin-based Combination Therapy for the treatment of uncomplicated *P. falciparum* malaria in adults and children?

Dihydroartemisinin-piperaquine for treating uncomplicated malaria in Cameroon: Malaria is responsible for 40% of hospitalizations and 18% of all deaths in Cameroon according to Demographic and Health Survey, 2011. Dihydroartemisinin-piperaquine is already used in the treatment uncomplicated malaria in Cameroon.

Table 1: Summary of the systematic review

	What the review authors searched for	What the review authors found
Studies	Randomized controlled trials (RCT)	Twenty seven randomized controlled trials were included
Participants	Adults and children (including pregnant women and infants) with symptomatic, microscopically confirmed, uncomplicated *P. falciparum* malaria.	The African trials focused on children, while Asian trials included older populations and excluded children below one year of age. All trials excluded pregnant and lactating women.
Interventions	A three-day course of dihydroartemisinin-piperaquine	All the included trials had at least one arm with a three-day course of dihydroartemisinin-piperaquine.
Controls	A three-day course of an alternative World Health Organization recommended multiple Artemisinin-based Combinations Therapies.	Eleven trials compared dihydroartemisinin-piperaquine with Artesunate plus Mefloquine, 16 trials compared dihydroartemisinin-piperaquine with Artemether-Lumefantrine, four trials compared Dihydroartemisinin-piperaquine with Artesunate plus Amodiaquine, and one trial compared dihydroartemisinin-piperaquine with Artesunate plus Sulfadoxine-pyrimethamine. Some trials had more than two arms and compared multiple Artemisinin-based Combination Therapies.
Outcomes	**Primary outcomes** Total failure at days 28, 42, and 63; polymerase chain reaction-adjusted and polymerase chain reaction-unadjusted. **Secondary outcomes** • Gametocyte carriage at day 7 or 14 (preference for day 14 in data analysis). • Gametocyte development (negative at baseline and positive at follow-up). • Change in haemoglobin from baseline (minimum 28 day follow-up). **Adverse events** • Deaths occurring during follow-up; • Serious adverse events (life threatening, causing admission to hospital, or discontinuation of treatment); • Haematological and biochemical adverse effects (for • example, neutropenia, liver toxicity); • Early vomiting; • Other adverse events.	The outcomes reported were: • Total failure • Gametocytes • Anaemia • Adverse events
Date of the most recent search: 29 July 2013		
Limitations: This is a high quality systematic review, AMSTAR =10/11		
Citation: Zani B, Gathu M, Donegan S, Olliaro PL, Sinclair D. Dihydroartemisinin-piperaquine for treating uncomplicated *Plasmodium falciparum* malaria. Cochrane Database of Systematic Reviews 2014, Issue 1. Art. No.: CD010927. DOI:10.1002/14651858.CD010927.		

Table 2: Summary of findings

Outcomes		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
Treatment failure Day 28	Polymerase chain reaction-unadjusted	0.34 [0.30-0.39]	6200 (9)	**High**
Treatment failure Day 63	Polymerase chain reaction-unadjusted	0.71 [0.65-0.78]	3200 (2)	**High**

Applicability

Twelve trials were conducted in Africa; Uganda (three trials), Kenya (three trials), Sudan (one trial), Rwanda (one trial), Burkina Faso (one trial), and three multi-centre trials with sites in Kenya, Uganda, Rwanda, Mozambique, Zambia, Gabon, Burkina Faso, Nigeria, Senegal, Côte d'Ivoire, and Cameroon. Fourteen trials were conducted in Asia and Oceania; Thailand (five trials), Myanmar (two trials), Laos (one trial), Vietnam (one trial), Cambodia (one trial), Indonesia (two trials), Papua New Guinea (one trial); and one multi-centre trial had sites in Thailand, Laos, and India. These findings may be applied in low resources settings.

Conclusions

In Africa, dihydroartemisinin-piperaquine reduces overall treatment failure compared to Artemether-Lumefantrine, although both drugs have failure rates of less than 5%. In Asia, dihydroartemisinin-piperaquine is as effective as Artesunate plus Mefloquine, and is better tolerated.

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