

Evidence Update

Summary of a Cochrane Review

Malaria Series

Is artesunate better than quinine for treating severe malaria?

Yes. The research shows that fewer patients will die.

Cochrane Collaboration researchers conducted a review of the effects of using artesunate instead of quinine for treating severe malaria. After searching for relevant studies, they identified eight randomized controlled trials including 1664 adults and 5765 children. This Evidence Update summarizes the findings.

What is severe malaria and how might artesunate work?

Severe malaria occurs when infection with the malaria parasite is complicated by serious failure of the body's major organs, and results in over a million deaths every year. Sometimes severe malaria is associated with coma, which is known as cerebral malaria. Following cerebral malaria a small proportion of children suffer with long-term neurological problems.

Artesunate is one of a number of antimalarials derived from artemisinin, the active ingredient in a Chinese herbal remedy for fever. It may be given by intramuscular or intravenous injection, and has been shown to reliably reach peak concentrations within one hour of administration.

The artemisinin derivatives have been shown to clear malaria parasites from the blood faster than quinine. This review looks at whether this results in fewer deaths.

What does the research say?

The effects of using artesunate instead of quinine:

- Fewer adults and children with severe malaria will die.
- There is probably a small increase in the number of children with neurological problems at the time of discharge from hospital.
- There is probably no difference in the number of children with long-term neurological problems.

Is the research reliable?

Yes. The trials were generally well conducted with a low risk of bias. When the trials which were less well conducted were excluded, the significance of the results did not change.

Can the results of the research be applied to my setting?

The trials were conducted in both adults and children from a variety of African and Asian countries. The benefits with artesunate appear to be consistent throughout Africa and Asia.

The trials used the standard doses of artesunate and quinine recommended by the World Health Organization Malaria Treatment Guidelines.

Pregnant women were excluded from the trials and the safety of artesunate for pregnant women is being carefully evaluated.



The effects of using artesunate instead of quinine

This table provides more detail about what happens to people who take artesunate instead of quinine. These numbers are based on the results of the research, when available. The quality of evidence is either ranked as high, moderate, low or very low. The higher the quality, the more certain we are about what will happen.

Outcome	Quinine	Artesunate	What happens	Quality of evidence
How many people die?	Adults		Fewer adults and children with severe malaria will die	High
	241 per 1,000	147 per 1,000		
	Children			High
	109 per 1,000	83 per 1,000		
How many people still have neurological problems at the time of hospital discharge?	Adults		There is probably a small increase in the number of children with neurological problems at the time of discharge from hospital	Moderate
	3 per 1,000	9 per 1,000		
	Children			Moderate
	28 per 1,000	38 per 1,000		
How many people still have neurological problems one month later?	Adults		There is probably no difference in the number of children with long-term neurological problems	Moderate
	Not reported	Not reported		
	Children			Moderate
	11 per 1,000	14 per 1,000		

More information

WHO Malaria Treatment Guidelines:

World Health Organization. Roll Back Malaria Dept. 'Guidelines for the treatment of malaria'. <http://www.who.int/malaria/publications/atoz/9789241547925/en/index.html>; Second edition. Geneva: World Health Organization, 2010.

This summary is based on the following systematic review:

Sinclair D, Donegan S, Lalloo DG. Artesunate versus quinine for treating severe malaria. Cochrane Database of Systematic Reviews 2011, Issue 3. Art. No.: CD005967. <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005967.pub3/abstract>

What is a systematic review?

A systematic review seeks to answer a well formulated and specific question by identifying, critically appraising, and summarising the results of all relevant trials, published and unpublished, according to pre-stated and transparent methods.

What is The Cochrane Collaboration?

The Cochrane Collaboration is an international network of more than 28,000 people from over 100 countries. The collaboration is one of the biggest producers of systematic reviews on the effects of healthcare interventions, and Cochrane Systematic Reviews are recognized internationally as the benchmark for high quality information. The *Cochrane Database of Systematic Reviews* is available from www.thecochranelibrary.com and free for eligible countries.

How has the quality of evidence been assessed?

The quality of evidence has been assessed using methods developed by the GRADE working group (www.gradeworkinggroup.org). The GRADE system considers 'quality' to be a judgment of the extent to which we can be confident that the estimates of effect are correct. The level of 'quality' is judged on a 4-point scale. Evidence from randomized controlled studies is initially graded as HIGH and downgraded by one, two or three levels after full consideration of: the risk of bias of the studies, the directness (or applicability) of the evidence, and the consistency and precision of the results.

- High:** Further research is very unlikely to change our confidence in the estimate of effect.
- Moderate:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- Low:** Further research is very likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- Very low:** We are very uncertain about the estimate.

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