Evidence Update

Summary of a Cochrane systematic review published on 13 April 2015

Question: Tafenoquine is used for preventing relapse in people diagnosed with Plasmodium vivax malaria - is it effective & safe?

Conclusion: Tafenoquine 300mg or more, in single or divided doses, given in addition to a standard dose of chloroquine reduces relapses of P. vivax malaria up to 6 months.

Vivax malaria relapse - what are the issues?

- Vivax malaria is caused by the parasite Plasmodium vivax. The disease includes a stage of liver infection in the form of hypnozoites, and this can cause relapse unless adequately treated.

- P. vivax seldom causes death. However, it causes substantive illness-related burden in endemic areas, becoming particularly important in countries aiming for malaria elimination.

- The only drug available for elimination of vivax hypnozoites until recently was primaquine, but this requires a 14-day course of treatment.

- One of the alternatives that have been tried is tafenoquine, which has a longer half-life, and does not need a long course of treatment.

- Both primaquine and tafenoquine can cause haemolysis in people with glucose-6-phosphate dehydrogenase (G6PD) enzyme deficiency, which is a common genetic defect.

Key findings of this review

Which Population?
Adults with proven vivax malaria (normal G6PD status)

What Intervention?
Tafenoquine 300 mg & above, given in a single or divided doses, in addition to standard chloroquine

Compared to what?
Chloroquine alone (without tafenoquine)

What was the effect on key outcomes?

- Reduction in relapses over 6 months follow-up.
- No additional risk of any adverse event

Tafenoquine given as a single dose of 600 mg resulted in similar benefits of fewer relapses and no additional adverse events, when compared to a standard 14-day treatment with primaquine.

What is the quality of this evidence?
Moderate to Low quality evidence

Can this evidence be applied in my setting?
The findings of this review would be applicable to vivax endemic areas.
**Tafenoquine to prevent relapses of vivax malaria**

This data is based on the Summary of Findings table from this Cochrane systematic review.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Chloroquine alone</th>
<th>Tafenoquine (TQ) + Chloroquine (CQ) (95% Confidence Interval)</th>
<th>No. of participants</th>
<th>Inference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recurrent P. vivax parasitaemia</strong></td>
<td>57 per 100</td>
<td>11 per 100 (95% CI, 5 to 23) developed relapse with CQ alone</td>
<td>110 (1 trial)</td>
<td>(Tafenoquine 300 mg + CQ) resulted in 46 fewer relapses per 100 persons treated. 95% CI shows that this estimate could at best be 52 fewer relapses, or at least 34 fewer relapses per 100 treated, when compared to “CQ only”.</td>
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<tr>
<td><strong>No. of participants</strong></td>
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<tr>
<td><strong>Serious adverse events</strong></td>
<td>6 per 100</td>
<td>6 per 100 (95% CI, 2 to 16) developed relapse with CQ+ 300mg TQ</td>
<td>358 (3 trials)</td>
<td>(Tafenoquine 300 mg + CQ) resulted in the same number of adverse events as the (CQ only) treatment– 6 per 100 persons treated. 95% CI shows that this estimate could at best be 4 fewer serious adverse events, or at worst be 10 more serious adverse events with (TQ+CQ).</td>
</tr>
</tbody>
</table>

*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 estimate of effect, and may change the estimate.

*Very low:* We are very uncertain about the estimate.

**More information**

This Evidence Update is only a summary of the key findings of the following Cochrane systematic review. For details, please read the full text: Rajapakse S, Rodrigo C, Fernando SD. Tafenoquine for preventing relapse in people with Plasmodium vivax malaria. Cochrane Database of Systematic Reviews 2015, Issue 4. Art. No.: CD010458. DOI: 10.1002/14651858.CD010458.pub2

**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 Cochrane?**

Cochrane is an international network of more than 28,000 people from over 100 countries. Cochrane Systematic Reviews are recognized internationally as the benchmark for high quality information on health evidence. www.thecochranelibrary.com

**How has the quality of evidence been assessed?**

The GRADE system (http://www.gradeworkinggroup.org/intro.htm) considers ‘quality’ to be a judgment of the extent to which we can be confident that the estimates of effect of intervention are correct. The quality of evidence is graded after full consideration of the risk of bias of the studies, the directness (or applicability) of the evidence, the consistency and the precision of the results.

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This Evidence Update has been prepared by Cochrane South Asia, March 2016

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