

Evidence Update

Malaria Series

August 2003

Should all people with cerebral malaria be given anticonvulsant drugs?

Routine phenobarbitone in cerebral malaria is associated with fewer convulsions but possibly more deaths.

Inclusion criteria

Types of studies:

Randomized and quasi-randomized controlled trials.

Types of participants:

People with cerebral malaria, defined as coma with no localizing response to pain; plus presence of asexual *Plasmodium falciparum* in peripheral blood; in the presence of normal cerebrospinal fluid.

Types of intervention:

Intervention: Anticonvulsant drugs started immediately after diagnosis and randomization.

Control: No prophylactic anticonvulsant drugs.

Types of outcome measures:

Primary: death within 6 months post-randomization; proportion of people experiencing convulsions within 4 weeks of randomization.

Secondary: people still in a coma by day 7 post-randomization; people with deficits in cognitive function; people with long term epilepsy; number with a physical handicap at 12 months.

Results

- Three trials with a total of 573 participants met the inclusion criteria; all these trials compared phenobarbitone with placebo or no treatment. Two were adequately concealed.
- In the two trials with adequate allocation concealment, death was more common in the anticonvulsant group (Relative Risk 2.0; 95% confidence interval 1.20 to 3.33; fixed effect model).
- In all three trials, phenobarbitone compared with placebo or no treatment was associated with fewer convulsions (Relative Risk 0.30; 95% confidence interval 0.19 to 0.45; fixed effect model).

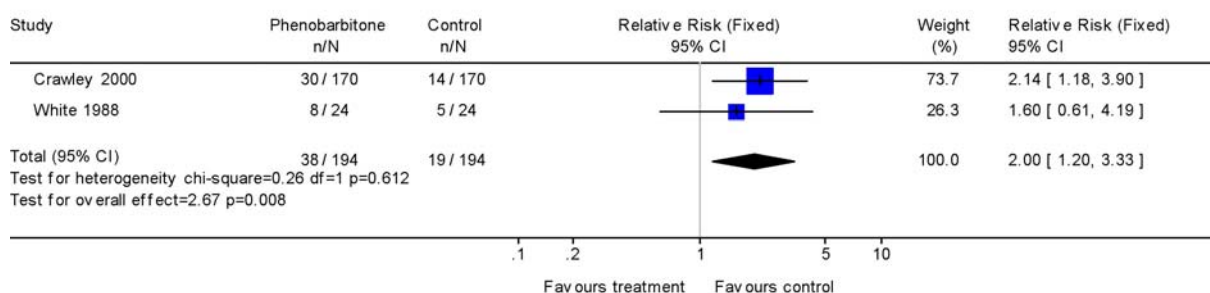


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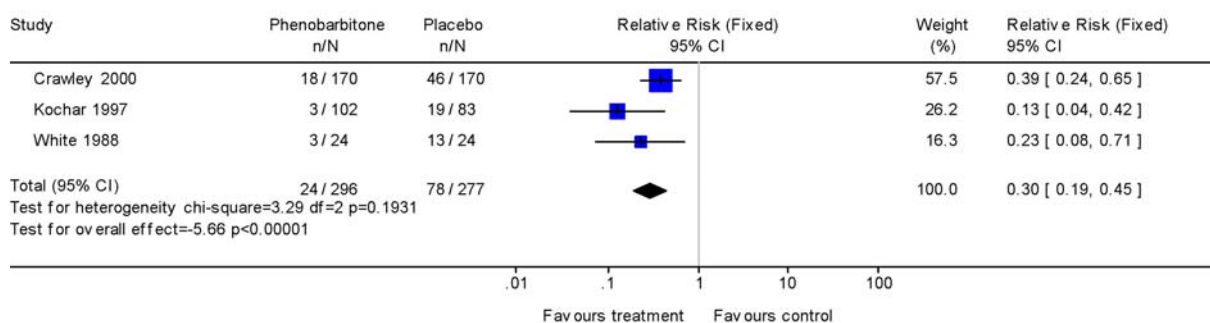
Adapted from Meremikwu M, Marson AG. Routine anticonvulsants for treating cerebral malaria (Cochrane Review). In: *The Cochrane Library*, Issue 3, 2003. Oxford: Update Software.

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Review: Routine anticonvulsants for treating cerebral malaria
 Comparison: 01 Phenobarbitone compared to placebo or nothing
 Outcome: 02 Death within 6 months in adequately concealed trials only



Review: Routine anticonvulsants for treating cerebral malaria
 Comparison: 01 Phenobarbitone compared to placebo or nothing
 Outcome: 03 Convulsions within 4 weeks



Reviewer's conclusions

Implications for practice:

Giving phenobarbitone routinely to people with cerebral malaria reduces the number of convulsions, but may increase the risk of death.

Implications for research:

Anticonvulsant drugs have potential for benefit. Larger clinical trials using lower doses of phenobarbitone or other anticonvulsant drugs, such as phenytoin, are needed.