A meta-analytic review of the preventive treatment of recurrences of febrile seizures

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Authors' objectives
To assess the efficacy of various medications in the prevention of recurrent febrile seizures.

Searching
MEDLINE was searched for randomised controlled studies on the prevention of febrile seizures, published in the English language. The authors also checked reference lists and articles known to them.

Study selection
Study designs of evaluations included in the review
Only randomised placebo-controlled trials were included.

Specific interventions included in the review
Phenobarbital, pyridoxine, phenytoin, valproate, diazepam, and placebo.

Participants included in the review
The authors do not provide specific details of the participants.

Outcomes assessed in the review
At least one recurrence, which was defined as treatment failure, was measured.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
The authors extracted the data independently using a predesigned data collection sheet.

Methods of synthesis
How were the studies combined?
The data were grouped by drug. Pooled estimates of the risks for each drug versus placebo were derived using the random-effects (unconditional) model, by calculating the weighted average of the risks; the inverse of the variance of the risk in each study was used as its weight. The 95% confidence intervals (CIs) on the estimates of the odds ratios (ORs) were calculated. The statistical significance of the OR was assessed using the Mantel-Haenszel chi-squared test. The number-needed-to-treat was also calculated, along with 95% CIs if the efficacy of the treatment was statistically significant.

How were differences between studies investigated?
The studies were tested for heterogeneity before inclusion in the meta-analysis; this test showed non significant results.

Results of the review
Nine randomised controlled trials were included; there were 4 placebo-controlled studies on phenobarbital, 3 on
diazepam, one on pyridoxine, and one on phenytoin. In one of the phenobarbital studies, valproate was also compared with placebo. There were 707 and 716 children in the active treatment and placebo groups, respectively.

The risk of recurrences was significantly lower in children receiving continuous phenobarbital therapy than placebo (OR 0.54, 95% CI: 0.33, 0.90, p=0.017).

The OR for recurrences in the valproate versus placebo group was 0.09 (95% CI 0.01, 0.78, p=0.011).

No difference in risk was found for recurrences between children receiving intermittent diazepam and placebo (OR 0.81, 95% CI: 0.54, 1.22, p=0.31).

The risk for pyridoxine or phenytoin did not differ from the risk among children receiving placebo.

Four children would have to be treated with valproate (95% CI: 2, 11) or eight children would have to be treated with phenobarbital (95% CI: 5, 27) continuously, to prevent one febrile seizure.

The test for heterogeneity performed before including the studies in the meta-analysis showed insignificant results, justifying the combination of the data.

**Authors’ conclusions**
Prophylaxis of febrile seizures cannot be recommended because both valproate and phenobarbital (found to be effective in prevention of recurrent seizures) have known adverse effects.

**CRD commentary**
This review searched for articles using MEDLINE and examined the reference lists of those articles. The search was restricted to English language studies in MEDLINE and so relevant studies could have been missed. No attempt was made to identify unpublished articles.

Some inclusion criteria were stated, and the methods for extracting the data were given. However, this process was not discussed further, and there was a lack of quality assessment of the included trials. The data were synthesised for each individual drug versus placebo comparison. The authors’ recommendations, that the effective treatments should not be used because of known adverse effects, do not follow since adverse effects were not investigated in this review.

**Implications of the review for practice and research**
The authors state that the efficacy of different drugs should be tested in randomised placebo-controlled trials.

**Bibliographic details**

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Subject indexing assigned by NLM

**MeSH**
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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.