Anticonvulsant drugs in cocaine dependence: a systematic review and meta-analysis
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CRD summary
The review evaluated efficacy of anticonvulsant medications compared with placebos in patients with cocaine dependence and found no evidence of any advantageous effect on retention in treatment or cocaine use. The authors' cautious conclusions appeared justified on the basis of the evidence provided and may be reliable, but limited reporting of quality assessment results should be borne in mind.

Authors' objectives
To evaluate the efficacy of anticonvulsant medications compared to placebos in patients with cocaine dependence.

Searching
EMBASE, the Cochrane Library and PubMed were searched from inception to 2008 for English- and Spanish-language studies; search terms were reported. References of selected articles, reviews and meta-analyses were searched for additional studies. The authors contacted experts and searched conference abstracts and two clinical trials registries to identify unpublished studies.

Study selection
Randomised controlled trials (RCTs) of anticonvulsant medication compared to placebo in patients identified as cocaine users by the presence of the cocaine metabolite benzoylecgonine in urine were eligible for inclusion. Studies with a Jadad quality score of less than 2 points were excluded.

All trials included patients with cocaine dependency defined by Diagnostic and Statistical Manual of Mental Disorders or Psychiatric Diagnostic Interview classification systems. Most patients were male and African-American. Median age of patients was 36 years. Patients were included with additional chemical dependencies and psychiatric disorders. Psychosocial treatment was also given in all trials except one. Anticonvulsant medications were carbamazepine (200 to 800mg/day) phenytoin (300mg/day), valproic acid (1,500mg/day), tiagabine (12 to 20mg/day), gabapentin (1,800 to 2,400mg/day), lamotrigine (150mg/day) and topiramate (200mg/day). The outcomes evaluated related to retention of patients for treatment and cocaine use at the end of the study as measured by benzoylecgonine in urine. All the trials were conducted in USA.

The reviewers did not state how many reviewers performed the study selection.

Assessment of study quality
Two reviewers independently assessed each study using the Jadad scale. Studies were assessed according to randomisation, blinding and dropouts or withdrawals (maximum 5 points). Any differences between the reviewers were resolved by discussion.

Data extraction
Data were extracted to calculate relative risks (RRs) and corresponding 95% confidence intervals (CI) for the outcomes of retention in treatment and presence of benzoylecgonine.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Pooled relative risks and 95% confidence intervals for each outcome were calculated using a random-effects model. \( \chi^2 \) and I\(^2\) tests were used to evaluate statistical heterogeneity across the trials. Subgroup analyses were performed on the basis of anticonvulsant type.

Results of the review
Fifteen RCTs (n=1,236) were included in the review. Sample sizes ranged between 30 and 183. Nine studies scored 4 on the Jadad scale and six studies scored 3. Approximately 50% of the included patients were lost to follow-up. Treatment duration in the trials ranged from eight to 13 weeks.

There were no differences in retention of patients in treatment programmes with use of anticonvulsant medication compared to placebo (RR 0.97, 95% CI 0.86 to 1.09; n=899). No statistical heterogeneity was reported (I²=0%). No particular anticonvulsant was found to be efficacious in terms of enhancing patient retention in treatment; gabapentin was found to have a detrimental effect on retention (RR 3.48, 95% CI 1.04 to 11.73; n=80).

There were no significant differences in cocaine use after treatment with anticonvulsant medication compared with placebo. In one small study that evaluated use of topiramate, the intervention was found to have benefits on cocaine use at the end of treatment (RR 0.61, 95% CI 0.40 to 0.93; n=40).

**Authors’ conclusions**

Anticonvulsant medications had not been effective in treating cocaine dependency by reducing cocaine use or increasing patient retention in treatment programmes.

**CRD commentary**

The review addressed a clear question and criteria for inclusion were stipulated. Appropriate electronic databases were searched and attempts were made to identify unpublished literature. The restriction to studies published in certain languages meant that there was a risk of language bias. Steps to minimise errors and bias were reported for the assessment of methodological quality, but were not reported explicitly for study selection and data extraction. The authors did not report the results of the quality assessment in terms of methods for blinding and randomisation; therefore, it was difficult to make a judgement about the overall strength of the evidence. Approximately half of the included patients were lost to follow-up. Low statistical heterogeneity was identified across the trials for the outcomes evaluated and the authors’ decision to pool the studies appeared to be justified. The authors acknowledged certain limitations of the review, which included differences in patients in terms of cocaine use and comorbidities and variation in the dosages of anticonvulsants.

The authors' cautious conclusions appeared justified on the basis of the evidence provided and may be reliable, but the limited reporting of the quality assessment results should be borne in mind.

**Implications of the review for practice and research**

**Practice:** The authors stated that available clinical trials showed insufficient evidence to justify use of anticonvulsant drugs in treating cocaine dependence.

**Research:** The authors stated that large clinical trials that evaluated specific anticonvulsants such as carbamazepine, topiramate and/or tiagabine in cocaine users may help ascertain the efficacy of these medications.

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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.