A meta-analysis of the efficacy of pregabalin in the treatment of generalized anxiety disorder

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CRD summary
The review concluded that pregabalin was an effective treatment for generalised anxiety disorder compared to placebo. Given limitations in the review process as well as uncertain quality of the included trials the authors conclusion may not be reliable.

Authors' objectives
To determine the efficacy of pregabalin for treatment of generalised anxiety disorder.

Searching
PubMed was searched up to December 2010 for relevant published peer-reviewed trials. Search terms were reported. References lists were searched.

Study selection
Randomised controlled trials (RCTs) that compared pregabalin with placebo for treatment of primary generalised anxiety disorder were eligible for inclusion in the review. Trials were required to use the Hamilton Anxiety Rating Scale (HARS) as the primary outcome measure and provide sufficient data to enable calculation of effect size.

Pregabalin dose regimens varied across trials from 150mg to 600mg daily to 150mg to 200mg three times a day. Most trials included a fixed dose. Two trials used a variable dose. Treatment duration ranged from four to eight weeks. All included trials were of adults.

The author did not state how many reviewers selected trials for inclusion in the review.

Assessment of study quality
The author did not state that the quality of the included studies was assessed formally but stated that all trials were double-blinded and there was an assessment of baseline similarity (in terms of HARS).

Data extraction
Baseline and change scores were extracted to calculate effect size (Hedges' g and Cohen's d). Where standard errors were reported these were converted into standard deviations. An estimate was used for the correlation between pre-treatment and post-treatment scores on the HARS as these were not available in the published results. Where individual trials used a range of doses the highest pregabalin dose was used in the analysis.

The author did not state how many reviewers extracted data from the included trials.

Methods of synthesis
Pooled effect sizes and their 95% confidence intervals (CIs) were calculated using a fixed-effect model. Statistical heterogeneity was assessed using the Q statistic. Bivariate correlation between change scores was calculated. Publication bias was assessed through observation of funnel plots and an analysis of the fail-safe n. Duval and Tweedie's trim-and-fit calculation was performed.

Results of the review
Seven RCTs were included in the review (2,413 patients).

There was a small but statistically significant effect size (hedges' g) of pregabalin on HARS total score (0.364, 95% CI 0.256 to 0.471; seven RCTs, 1,352 patients). The value of the Q statistic indicated that the sample was homogeneous. Duval and Tweedie's trim-and-fit calculation suggested a small reduction in the overall mean effect size (0.325, 95% CI 0.226 to 0.424).
Effect sizes for HARS subscales were 0.349 (95 CI 0.256 to 0.471; four RCTs) for psychic anxiety symptoms and 0.239 (95% CI 0.107 to 0.370; four RCTs) for somatic anxiety symptoms.

The fail-safe n calculation using the effect size for HARS total scores found that 77 new or unpublished studies with negative findings would be needed to reverse the present results.

**Authors’ conclusions**
Pregabalin was an effective treatment for generalised anxiety disorder compared to placebo although effect sizes to date were small to moderate.

**CRD commentary**
The review was based on a clearly defined question. The literature search was limited in its extent. Some evidence of publication bias was found. It did not appear that appropriate methods to minimise errors and bias, such as use of independent duplicate processes, were used to select or extract data from the included trials or that the quality of the trials was systematically assessed, which limited interpretation of the results. The synthesis appeared appropriate and heterogeneity was assessed.

The author acknowledged limitations that included dosing (large doses and various dosing regimens were included) and lack of treatment duration beyond eight weeks. Many of the trials reviewed shared the same authors and in each trial the authors had affiliations or positions with Pfizer.

Given the limitations in the review process as well as uncertain quality of the included trials the authors conclusion may not be reliable.

**Implications of the review for practice and research**
The author did not state any implications for practice.

**Research**
The author stated a need for further research to establish any additional treatment effect beyond eight weeks, provide information about predictors of treatment response (such as type of generalised anxiety disorder symptom) and optimal doses of pregabalin for treatment of generalised anxiety disorder.

**Funding**
None.

**Bibliographic details**

**PubMedID**
21959031

**Original Paper URL**
http://publications.cpa-apc.org/browse/documents/549

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adult; Anxiety Disorders /drug therapy; GABA Agents /therapeutic use; Humans; Multicenter Studies as Topic; Pregabalin; Randomized Controlled Trials as Topic; Treatment Outcome; gamma-Aminobutyric Acid /analogs & derivatives /therapeutic use

**AccessionNumber**
12011007249
Date bibliographic record published
27/03/2012

Date abstract record published
13/10/2012

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.