A meta-analysis of the efficacy of psycho- and pharmacotherapy in panic disorder with and without agoraphobia

Mitte K

CRD summary
This review assessed (cognitive) behavioural therapy ((C)BT) and pharmacological treatment for panic disorder and/or agoraphobia. The author's conclusions appeared to be that (C)BT reduced anxiety and depression and improved quality of life, while pharmacological treatments improved all symptoms. Poor reporting of the review methods, study details and study quality make it difficult to comment on the reliability of the author's conclusions.

Authors' objectives
To assess the efficacy of (cognitive) behavioural therapy ((C)BT) and pharmacological treatment in patients with panic disorder and/or agoraphobia.

Searching
MEDLINE and PsycINFO were searched from inception to May 2002 for studies published in English or German; the search terms were reported. Major journals and reviews were handsearched. Unpublished studies were sought by searching the Internet and by contacting researchers and pharmaceutical companies.

Study selection
Study designs of evaluations included in the review
Controlled studies with four or more patients were eligible for inclusion if sufficient data for the calculation of effect sizes (ESs) were reported; details of the required data were reported.

Specific interventions included in the review
Studies that compared (C)BT or pharmacological treatment with waiting-list, pill placebo, therapy placebo (excluding BT, CBT and relaxation) or each other were eligible for inclusion. Studies of pharmacological treatment had to last at least 14 days and had to provide the non-proprietary name for the drug. The most commonly used (C)BT was exposure with or without cognitive components; other CBT studies used self-help programmes. Pharmacological studies used twenty-five different pharmacological drugs, the most common of which were benzodiazepines (BZDs), tricyclic antidepressants (TCAs) and selective serotonin re-uptake inhibitors (SSRIs).

Participants included in the review
Studies of adults who had been diagnosed with panic disorder and/or agoraphobia using a standardised diagnostic classification system, or with precise description of the condition, were eligible for inclusion. The studies had to report the duration of symptoms. Studies of patients who had not responded to other treatments were not included. The mean age of the participants in the included studies was about 35 to 36 years, and patients had generally had the disorder for an average of 8 or 9 years. The majority of the participants were female.

Outcomes assessed in the review
Studies were eligible if they used self-report, observer-rated measures or behavioural tests to assess anxiety, depression, quality of life or clinical significance of anxiety, including meaningful response (defined as a change of 50% in an assessment scale), status at end-point or status compared with the normal population. The review also assessed drop-outs and effects on attrition and three types of anxiety (avoidance, cognition and arousal). The review did not assess physiological measures. Many studies used more than one measure to assess symptoms.

How were decisions on the relevance of primary studies made?
The author did not state how the studies were selected for the review, or how many reviewers performed the selection.
Assessment of study quality
The author did not state that they assessed validity.

Data extraction
At least two reviewers extracted the data using a coding form; the number of reviewers was not explicitly stated but the author reported inter-rater reliability, hence the assumption that more than one reviewer was involved. Authors of studies with insufficient data for calculation of an ES were contacted for further data.

Means, standard deviations (SDs) or results of relevant statistical tests were extracted, where reported, and used to calculate an ES (standardised mean difference, calculated as Hedges’ g statistic); methods used to calculate ESs using other types of data were reported. For studies reporting more than one measure for a symptom, the mean ES was calculated for each symptom. For studies assessing more than one psychological treatment or more than one drug, the ESs were calculated separately for each treatment. Where possible, the data were extracted on an intention-to-treat basis, otherwise complete data were extracted.

Methods of synthesis
How were the studies combined?
The studies were grouped by type of treatment and comparator and combined using meta-analyses. Pooled ESs and 95% confidence intervals (CIs) were calculated using a random-effects model. The studies were weighted using the inverse of the variance. Differences between active treatments (CBT versus BT and CBT versus pharmacotherapy) were calculated using studies directly comparing these treatments and for studies comparing each treatment separately with a comparable control. Publication bias was assessed using Begg's rank correlation test, and a trim-and-fill sensitivity analysis was used to take account of publication bias where present.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the Q statistic. The meta-analyses were repeated using a fixed-effect model and after excluding outlying ESs (ESs more than 3 SDs smaller or higher than the unweighted average) and excluding all studies not reporting means and SDs. A random-effects multiple regression analysis was used to assess the influence on ESs of study characteristics (e.g. sample size and duration of therapy after inserting average values for missing values, and drop-out rate after excluding studies not reporting drop-out rates). Separate meta-analyses were conducted for BZDs, TCAs and SSRIs.

Results of the review
One hundred and twenty-four studies were included: 53 studies of pharmacotherapy (n=1,811), 47 studies of psychosocial treatments (n=7,725) and 24 studies that used both treatments (n=1,747).

(C)BT versus no treatment control: (C)BT was more effective than no treatment in reducing anxiety (ES 0.87, 95% CI: 0.71, 1.03) and depression (ES 0.72, 95% CI: 0.54, 0.90) and in increasing quality of life (ES 0.85, 95% CI: 0.48, 1.21). No significant heterogeneity was found for any of these meta-analyses.

CBT versus BT: treatment had similar effects on anxiety, but CBT improved depression (ES 0.18, 95% CI: 0.01, 0.35) compared with BT in studies directly comparing these interventions. No significant heterogeneity was found for either of these meta-analyses.

Pharmacotherapy versus placebo: pharmacotherapy was more effective than placebo in reducing anxiety (ES 0.38, 95% CI: 0.31, 0.45) and depression (ES 0.34, 95% CI: 0.21, 0.47) and in improving quality of life (ES 0.35, 95% CI: 0.22, 0.48), but significant heterogeneity was detected for all of these meta-analyses. Further analysis showed no difference in efficacy between BZDs, TCAs and SSRIs. Smaller studies had larger ESs. There was evidence of publication bias.

(C)BT versus pharmacotherapy: (C)BT was as effective as pharmacotherapy for anxiety and depression in the 11 studies directly comparing these interventions, but significant heterogeneity was found for these meta-analyses.

(C)BT alone versus (C)BT plus pharmacotherapy: there was little difference between treatments for the main meta-
analyses, but the results varied with the study characteristics included in the sensitivity analyses.

Attrition: the drop-out rate was 15.1% with (C)BT, 18.3% with BT, 12.7% with CBT and 20.4% with pharmacotherapy. There were significantly more drop-outs with pharmacotherapy in comparison with psychotherapy (P<0.05).

**Authors' conclusions**
The author's conclusions appeared to be that (C)BT effectively reduced anxiety and depression and improved quality of life, that BT and CBT were equally effective, and that pharmacological treatments improved all symptoms of panic disorder.

**CRD commentary**
The review addressed a clear question that was defined in terms of the participants, intervention and outcomes; the inclusion criteria for study design were broad and eligible psychological interventions were not clearly defined. Several relevant sources were searched and attempts were made to locate unpublished studies. The review was restricted to studies in English or German, which means that relevant studies could have been missed. Methods were used to minimise errors and bias in the extraction of data, but it was unclear whether similar steps were taken at the study selection stage. Validity was not assessed and the design of the included studies was not reported, hence the quality of the studies and the strength of the evidence cannot be judged.

Details of the included studies were reported to be available from the author, but none were presented in the paper. The comparability of the patient populations and other study characteristics could not, therefore, be assessed and the appropriateness of pooling studies using a meta-analysis cannot be judged. Statistical heterogeneity was assessed for all meta-analyses and the influence of various factors was explored. Where heterogeneity was significant, the author correctly advised caution in interpreting the results. The lack of reporting of review methods, details of the included studies and study quality make it difficult to comment on the reliability of the author's conclusions.

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

Research: The author stated that further research to examine the impact of patient and treatment characteristics on self-help treatment and on comparisons of (C)BT with BT, and to investigate the long-term negative effects of combinations of (C)BT plus pharmacotherapy, is required. The author also stated that future studies should assess all aspects of panic disorder (cognitive, behavioural and arousal), and that studies of pharmacological treatments should take account of the effectiveness of double-blinding.

**Funding**
State of Thuringia (Germany).

**Bibliographic details**

**PubMedID**
16005982

**DOI**
10.1016/j.jad.2005.05.003

**Indexing Status**
Subject indexing assigned by NLM

MeSH
Adult; Agoraphobia /diagnosis /psychology /therapy; Cognitive Therapy; Comorbidity; Controlled Clinical Trials as Topic; Depressive Disorder /diagnosis /psychology /therapy; Humans; Panic Disorder /diagnosis /psychology /therapy; Psychotropic Drugs /therapeutic use; Treatment Outcome

AccessionNumber
12005001156

Date bibliographic record published
31/07/2006

Date abstract record published
31/07/2006

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.