Evaluation of the efficacy of pharmacotherapy and psychotherapy in treatment of combat-related post-traumatic stress disorder: a meta-analytic review of outcome studies

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CRD summary
The authors concluded that pharmacotherapy resulted in greater reductions in post-traumatic stress disorder symptoms than psychotherapy in combat veterans within a comparable time frame, but further research was needed. Potential for review bias, uncertain quality of the included studies and indirect comparison between treatments mean that the authors’ conclusions should be treated with caution.

Authors' objectives
To assess the effectiveness of pharmacotherapy and psychotherapy in the treatment of combat-related post-traumatic stress disorder (PTSD).

Searching
PsycINFO was searched for relevant articles published in English. Some search terms were reported. Bibliographies of retrieved articles were searched manually.

Study selection
Studies that assessed the effectiveness of pharmacotherapy and psychotherapy in the treatment of combat-related PTSD (previously diagnosed using Diagnostic and Statistical Manual of Mental Disorders) in exclusively military populations were eligible for inclusion if they reported sufficient pre- and post-treatment data for analysis. Case studies were excluded, as were studies that provided pharmacotherapy and psychotherapy simultaneously.

Included pharmacotherapy studies of PTSD used tricyclic antidepressants, monoamine oxidase inhibitors (MAOIs) and selective serotonin reuptake inhibitors (SSRIs). Treatment duration ranged between four and 12 weeks. Previously published measures were used to measure baseline symptoms and end-of-treatment outcome measures. Standardised mean baseline PTSD severity scores ranged between 30.60 and 101.60. Psychotherapy studies of PTSD included the treatments: time-limited, group-based, transcending, trauma-focused, person-centered, understanding PTSD, stress management, anger management and cognitive processing. Treatment lengths ranged from six to 52 weeks. Standardised mean baseline PTSD scores ranged between 41.61 and 125.30. Patients in pharmacotherapy studies were required to have a wash out period. Patients in psychotherapy studies were allowed to remain on psychotropic medications before commencement of the study.

The authors did not state how many reviewers screened studies for inclusion.

Assessment of study quality
The authors did not state that they performed a validity assessment.

Data extraction
Baseline and post-treatment measures were extracted to calculate standardised means and standard deviations (SDs) separately for PTSD and depression for pharmacotherapy and psychotherapy interventions. Where necessary, subscales for arousal and intrusion on the Impact to Event Scale were combined to obtain a total Impact to Event Scale score.

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

Methods of synthesis
Independent sample t-tests were used to compare mean differences in PTSD symptoms and depression between pharmacotherapy and psychotherapy studies. An analysis of covariance (ANCOVA), which assumed fixed-effects, was undertaken to account for variance in length of treatment duration between studies. A random coefficient model was
used to address whether trends in the standardised PTSD measures over time varied significantly between pharmacotherapy and psychotherapy studies; this took into account fixed effects of the time on the standardised outcome measures, random study effects and the correlation of repeated standardised measures within a given study and identifying other potential explanations of variance between studies. Assumptions of normality of the distribution of the data and homogeneity of variance among study groups were assessed.

**Results of the review**

Eleven pharmacotherapy studies (13 study arms) and nine psychotherapy studies (12 study arms) were identified; total number of participants was unclear. One pharmacotherapy study was not included in the statistical analysis due to high mean PTSD symptoms at baseline compared to other studies.

At baseline, standardised mean severity of PTSD was significantly greater in the pharmacotherapy (12 studies) compared to psychotherapy (12 studies) group (t(22)=2.032, \( p=0.054, d=0.27 \)). Follow-up in the studies of PTSD was limited to six months. Patients who received pharmacotherapy showed statistically significantly greater reductions in PTSD symptoms from baseline compared with psychotherapy (t(22)=-2.74, \( p=0.01, d=0.05 \)).

ANCOVA indicated a significant interaction between study types when controlling for length of study (p=0.02), which suggested greater reductions in pharmacotherapy compared to psychotherapy studies in the rate of change in the standardised PTSD outcome measures as a function of time. The random coefficient model confirmed the significant difference between study types over time.

Similar findings were reported for depression. There were greater reductions in depression reported in the pharmacotherapy compared to psychotherapy group (t(15.77)= -2.26, \( p=0.04, d=0.16 \)). The number of studies included in the analysis was unclear.

The authors reported marginal significant difference between type of study when controlling for length of study (p<0.10); this was also indicated by the random coefficient model.

Assessments confirmed assumptions of normality and homogeneity of variance for PTSD and depression.

**Authors' conclusions**

The authors appeared to conclude that pharmacotherapy studies indicated a greater reduction in PTSD symptoms compared to psychotherapy in the treatment of combat veterans within a comparable time frame (less than six months). The also concluded that there were limitations with the included studies and further research was needed.

**CRD commentary**

The review question was clearly defined and supported by appropriate inclusion criteria, although these were broad for study design and outcomes. The literature search was somewhat limited and was restricted to publications in English, so potentially relevant studies may have been missed. The authors did not state the designs of the included studies and did not state that validity was assessed, which meant that the quality of the included studies was unclear. The authors did not state whether each stage of the review process was undertaken in duplicate and so reviewer error and bias could not be ruled out. Assumptions of normality and homogeneity of variance were confirmed, but the authors acknowledged that there was variability between study populations and methods and these may have limited the applicability and generalisability of the results. The authors acknowledged the inclusion of a number of patients in the psychotherapy studies who received concurrent pharmacotherapy. They authors acknowledged that most studies were of populations who had not seen combat for as many as 25 to 30 years, and follow-up was only short term. It was unclear how many studies were included in the analysis of depressive symptoms and how many participants were involved. No direct comparisons between pharmacotherapy and psychotherapy were undertaken.

Potential for bias in the review, uncertain quality of the included studies and indirect comparison of pharmacotherapy and psychotherapy interventions, suggest the authors' conclusions should be treated with caution. The recommendation for further research seemed appropriate.

**Implications of the review for practice and research**
Practice: The authors stated that pharmacological treatment should be considered as the initial intervention for combat veterans, particularly in those whose symptoms affect their ability to participate effectively in psychotherapy treatment.

Research: The authors stated that there was a need for further research into multimodal PTSD treatments, such as individual therapy, group therapy and pharmacotherapy concurrently or consecutively throughout the course of the disorder. Generalisability of the findings to veterans from Iraq and Afghanistan would need further investigation.

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