Treatment of major depressive disorder and dysthymic disorder with antidepressants in patients with comorbid opiate use disorders enrolled in methadone maintenance therapy: a meta-analysis

Pedrelli P, Iovieno N, Vitali M, Tedeschini E, Bentley KH, Papakostas GI

CRD summary
This narrow review concluded that there was no difference in clinical response when patients with depression enrolled in methadone maintenance treatment programmes were treated with antidepressant medication or placebo. Only four small trials were identified which were reported to contain multiple potentially confounding variables; this suggests that the evidence base is insufficient to draw firm conclusions on effectiveness.

Authors' objectives
To examine the efficacy of antidepressants in patients with unipolar depression/dysthymic disorder and comorbid opiate-use disorders currently in methadone maintenance treatment.

Searching
PubMed was searched from January 1980 up to June 2010. References were checked. Search terms were partially reported.

Study selection
Randomised double blind placebo controlled trials of antidepressants used as monotherapy to treat patients diagnosed with uni-polar major depressive disorder or dysthymic disorder were eligible provided that the patients were also opiate-users currently in methadone maintenance treatment. Forty antidepressant pharmacological agents were listed as eligible. Trials were required to be of at least four weeks in duration and had to report outcomes from the Hamilton Depression Rating Scale (HDRS), Montgomery-Asberg Depression Rating Scale (MADRS), or the Clinical Global Impression-Improvement scale (CGI-I).

The included trials studied imipramine, fluoxetine or sertraline in patients aged from 29 years to 48 years. All trials included concomitant counselling (standard, weekly group or individual sessions). In half of the trials, patients had been receiving methadone maintenance treatment for a minimum of 30 days; in the other half of trials this was set at 90 days. Over half of participants were men in all trials.

Although it was unclear who performed the study selection, final inclusion decisions were based on consensus between the authors.

Assessment of study quality
No quality assessment was reported.

Data extraction
Trial characteristics and clinical response were extracted by an unknown number of researchers. Clinical response was defined as a reduction of 50% from baseline to end point on the Hamilton Depression Rating Scale (HDRS) or Montgomery-Asberg Depression Rating Scale (MADRS); or where only Clinical Global Impression-Improvement scale (CGI-I) was reported the final score had to be less than three.

Where multiple scales were reported, HDRS outcomes were preferred. Where only CGI-I results were reported, authors were contacted for HDRS results or these were imputed. Where continuous outcomes only were reported, multiple regression was used to convert these into dichotomous results (full details reported).

Methods of synthesis
Random-effects meta-analysis was used to estimate the pooled risk ratio and 95% confidence interval of participants responding to antidepressants versus placebo. Analyses were also carried out on the risk of prematurely discontinuing treatment. Statistical heterogeneity was assessed using the Q statistic.
Results of the review
Four trials were included in the review with 317 patients, 164 receiving antidepressants and 153 receiving placebo. Trial duration ranged from eight to 12 weeks.

There were no statistically significant difference in clinical response between antidepressant versus placebo therapy in patients with depression and comorbid opiate addiction in methadone maintenance treatment (no significant heterogeneity noted). There were no significant differences in drop-out rates for any reason between antidepressant and placebo treatment.

Authors’ conclusions
There was no difference in the depressive outcomes of patients with comorbid opiate-use disorders enrolled in methadone maintenance therapy when treated with antidepressant medication or placebo.

CRD commentary
The review addressed a tightly defined research question with appropriate inclusion criteria. The search was limited to a single database plus reference checking, so potentially eligible trials may have been missed. The review processes were only partially described, which made it difficult to rule out reviewer error/bias.

No quality assessment was reported, so the reliability of each primary trial was unclear. Although only limited trial details were presented, additional information presented in the discussion suggested that the trials were clinically very varied (questions were raised over the method of administration for one trial). The synthesis appeared appropriate to the data available.

While the authors’ conclusion reflects the results of the meta-analysis, the variation between the trials and their various potential flaws suggest that the evidence base is insufficient to support claims of efficacy or ineffectiveness.

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

Research: The authors stated that further research exploring the effectiveness of antidepressants while controlling for variables such as psychosocial treatment and accounting for different classes of antidepressants was needed.

Funding
Not reported.

Bibliographic details

PubMedID
21869696

DOI
10.1097/JCP.0b013e31822ce0adf

Indexing Status
Subject indexing assigned by NLM

MeSH
Antidepressive Agents /therapeutic use; Depressive Disorder, Major /complications /drug therapy; Diagnosis, Dual (Psychiatry); Dysthymic Disorder /complications /drug therapy; Humans; Methadone /therapeutic use; Opiate Substitution Treatment /methods; Opioid-Related Disorders /complications /rehabilitation; Randomized Controlled Trials as Topic; Treatment Outcome
Accession Number
12011005980

Date bibliographic record published
15/02/2012

Date abstract record published
10/12/2013

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.