CRD summary
This review assessed the efficacy and safety of trazodone for the treatment of erectile dysfunction. The authors' tentatively concluded that trazodone may be a helpful treatment for erectile dysfunction, particularly at higher doses and in men with psychogenic erectile dysfunction. The authors discussed some of the limitations of the review and rightly advised caution when interpreting the findings.

Authors' objectives
To determine the efficacy and safety of trazodone for the treatment of erectile dysfunction (ED).

Searching
MEDLINE was searched from 1966 to the end of May 2002; the search terms were listed. The reference lists in identified reports and reviews were checked and abstracts from national AUA meetings were handsearched (January 1995 to May 2002). In addition, the Cochrane Library and the specialised register of the Cochrane Prostatic Diseases and Urological Cancers Group were screened for further studies. Studies in any language were eligible.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) that lasted at least 7 days were eligible for inclusion. Both parallel-group and crossover RCTs were included.

Specific interventions included in the review
Studies that compared trazodone with placebo or an active control treatment were eligible for inclusion. The included studies compared trazodone (50 to 200 mg, most commonly 150 mg) with either placebo, hypnotic suggestion, ketanserin or mianserin. Trazodone was administered as monotherapy in all studies but one, where it was used in combination with yohimbine. The duration of treatment in the included studies ranged from 4 to 13 weeks.

Participants included in the review
Studies that included men with ED were eligible for inclusion. The mean age of the participants in the included studies ranged from 38 to 65 years (mean 48 years). The cause of ED was definite or probable psychogenic ED in about 80% of men, vascular in about 9%, diabetes-related in 5%, and of mixed or unknown cause in about 6%.

Outcomes assessed in the review
Studies that assessed clinical outcomes relating to ED were eligible for inclusion. The included studies used a variety of outcome measures such as successful sexual intercourse (which was the primary review outcome), a study-specific sexual function questionnaire, or an overall definition of treatment response (patients happy and no problem with sexual activity, erections improved, or degree to which medication worked). Adverse effects and withdrawals were also assessed.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the studies for inclusion and resolved any disagreements through discussion.

Assessment of study quality
Validity was assessed based on concealment of randomisation (scored from 1 for poor quality to 3 for best quality), blinding of the participants and investigators, use of intention-to-treat analysis, and the percentage of participants who withdrew or were lost to follow-up. Two reviewers independently assessed validity.
Data extraction
Two reviewers independently extracted the data in a standardised manner and resolved any disagreements through discussion. The percentage of men achieving a positive treatment response, reporting side-effects and withdrawing from the trial, were extracted for each study where possible. For one partial crossover RCT, only data collected before the crossover were used.

Methods of synthesis
How were the studies combined?
The characteristics of the included studies were summarised in the text of the review, while the results of individual trials were tabulated. For studies comparing trazodone monotherapy with placebo, the pooled weighted relative benefit increase (RBI) and 95% confidence intervals (CIs) were calculated using a random-effects model for the outcome 'positive treatment response'. The weighted relative risk increases and their 95% CIs were also estimated using a random-effects model.

How were differences between studies investigated?
The authors stated that statistical heterogeneity was assessed (using a significance level of P<0.1), but no details were reported in the paper. Studies that assessed successful sexual intercourse attempts were discussed separately. The results were analysed separately for studies of men with psychogenic ED, physiological ED and ED of mixed aetiology, and for different doses of trazodone.

Results of the review
Six RCTs (n=396) were included.

One RCT reported an adequate method of randomisation and allocation concealment. Five RCTs were stated to double-blinded.

Efficacy.

The two RCTs assessing successful sexual intercourse attempts found that trazodone with and without yohimbine significantly improved the likelihood of successful intercourse in men with psychogenic ED. The RBI was 5.0 (95% CI: 1.7, 15.2) for the RCT comparing trazodone with placebo, and 4.5 (95% CI: 1.5, 13.9) for the RCT comparing trazodone plus yohimbine with placebo.

Trazodone monotherapy versus placebo (4 RCTs, 209 men): trazodone increased the likelihood of a positive treatment response compared with placebo, but the increase was not statistically significant. The pooled RBI was 1.6 (95% CI: 0.8, 3.3).

The results for treatment response according to type of ED and trazodone dose were also reported in the paper.

Adverse events.

Not all studies reported withdrawals and adverse effects. There was no significant difference between trazodone and placebo in the proportion of withdrawals for any reason, or for withdrawals due to adverse effects, but the CIs were wide and the authors stated that an increased risk of adverse effects could not be excluded. The RBI was 1.0 (95% CI: 0.4, 2.5) for all withdrawals (4 RCTs) and 2.6 (95% CI: 0.8, 8.6) for withdrawals due to adverse effects (3 RCTs). Data on specific adverse effects were not uniformly reported. There were no statistically significant differences between trazodone and placebo for specific adverse effects. The most common adverse effects in men treated with trazodone were dry mouth (19% versus 11% with placebo), sedation (16% versus 6% with placebo), dizziness (16% versus 0% with placebo) and fatigue (15% versus 8% with placebo).

Authors' conclusions
Trazodone may be a helpful treatment for erectile dysfunction, particularly at higher doses and in men with psychogenic ED.
CRD commentary
The review question was clear in terms of the study design, participants, intervention and outcomes. Several relevant sources were searched, the search terms were stated, attempts were made to locate unpublished studies, and no language restrictions were applied. Two reviewers independently selected the studies, assessed validity and extracted the data, which reduces the potential for bias and errors. Validity was assessed using established criteria.

Some relevant information on the included studies was tabulated, while additional information was described in the text of the review. The data were combined in a meta-analysis and the authors stated that statistical heterogeneity was assessed. However, the results of the assessment were not reported. The subgroup analyses do not appear to have been pre-specified. The authors discussed some of the limitations of the review: the heterogeneous populations, small sample sizes, brief duration of the treatment, and methodological limitations of the included studies. In their discussion, the authors correctly advised caution when interpreting the findings of the review, in particular the results from the subgroup analyses on the influence of the type of ED and trazodone dose on the response rates. This was reflected in the appropriately tentative conclusions.

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

Research: The authors stated that high-quality RCTs are required to compare trazodone with placebo and other therapies, especially in men with depression and psychogenic ED. They also stated that the outcomes assessed in future studies should include the proportion of successful sexual intercourse attempts, a validated depression scale and adverse events.

Funding
Veterans Health Administration, Office of Research and Development, Health Services Research and Development Service, Management Decisions and Research Center, Technology Assessment Programme; Veterans Affairs Medical Center (Minneapolis), Center for Chronic Disease Outcomes Research and Cochrane Review Group in Prostate Diseases and Urologic Malignancies.

Bibliographic details

PubMedID
12930437

Original Paper URL

Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Aged; Anti-Anxiety Agents /adverse effects /therapeutic use; Antidepressive Agents, Second-Generation /adverse effects /therapeutic use; Erectile Dysfunction /drug therapy /psychology; Humans; Male; Randomized Controlled Trials as Topic; Trazodone /adverse effects /therapeutic use; Treatment Outcome

AccessionNumber
12003001958

Date bibliographic record published
31/12/2004

**Date abstract record published**
31/12/2004

**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.