Sildenafil: a review of its use in erectile dysfunction

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Authors' objectives
This review evaluates data from published and some unpublished sources to present as accurate as possible a picture of the clinical efficacy and pharmacology of sildenafil at the time of publication.

Searching
Medical literature published in any language since 1966 on sildenafil, identified using AdisBase (a proprietary database of Adis International, Auckland, New Zealand), MEDLINE and EMBASE. Searches were last updated 3 May 1999. Additional references were identified from the reference lists of published articles. Bibliographic information, including contributory unpublished data, was also requested from the company developing the drug.

Study selection
Study designs of evaluations included in the review
All studies were randomised, placebo-controlled, double blind trials, most involved parallel groups, some had a cross-over design.

Specific interventions included in the review
Both fixed-dose and dose-titration studies were performed, testing doses from 5 to 100mg.

Participants included in the review
Men with erectile dysfunction. Results are presented separately for patients with broad-spectrum (organic, psychological or mixed origin) erectile dysfunction, patients with erectile dysfunction of unknown cause, patients with diabetes, spinal cord injury and other patient groups.

Outcomes assessed in the review
Three major end-points of clinical trials were assessed by a Global Efficacy Question (GEQ): 'Did the treatment improve your erections?' (yes/no), and by questions 3 and 4 of the International Index of Erectile Function (IIEF), Q3: 'When you attempted sexual intercourse, how often were you able to penetrate (enter) your partner?' and Q4: 'During sexual intercourse, how often were you able to maintain your erection after you have penetrated (entered) your partner?'; Scores on the questions ranged from 0 (did not attempt intercourse) to 5 (almost always/always), with scores of 4 (most times/much more than half the time) or greater being considered indicative of successful achievement or maintenance of an erection.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
Studies of men with erectile dysfunction who received sildenafil were selected. Inclusion of studies was based mainly on the methods sections of the trials. When available, large, well controlled trials with appropriate statistical methodology were preferred. Relevant pharmacodynamic and pharmacokinetic data were also included. It was not reported how many reviewers were involved in the data extraction. The authors do not state how the papers were assessed for validity, or how many of the reviewers performed the validity assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.
Methods of synthesis
How were the studies combined?
Studies were described in a narrative manner according to patient group.

How were differences between studies investigated?
The authors do not state how differences between the studies were investigated.

Results of the review
Fourteen trials, including 4039 patients were included.

Sildenafil was associated with dose-related improvements in the frequency, hardness and duration of erections and in patients' ability to achieve and maintain erections adequate for successful sexual intercourse. Sildenafil was significantly more effective than placebo in erectile dysfunction of all tested causes.

The efficacy of sildenafil was not affected by patient age or by antihypertensive or antidepressant medications. The drug was effective in patients with severe erectile dysfunction. Efficacy was maintained in long term (1-year) studies. Sildenafil also appears to improve the quality of life of both patients and their sexual partners.

Common adverse events associated with sildenafil were transient and mild or moderate and included headache, flushing, dyspepsia, nasal congestion, and abnormal vision. Tolerability was maintained in long term (<= 1 year) studies. No serious sildenafil related adverse events occurred in clinical trials; cardiovascular events seen in postmarketing surveillance generally occurred in patients with other known risk factors.

Authors' conclusions
Sildenafil is an effective oral treatment in men with erectile dysfunction. It was significantly superior to placebo in improving erections and allowing successful penetrative sexual intercourse.

CRD commentary
The review question was clear and the inclusion criteria seem well chosen. The databases searched and the search strategy used seem complete and appropriate. Authors did not report how decisions on inclusion or exclusion of studies were taken and how data extraction was done. There is no information on the quality of studies included.

The authors did not attempt to generate a summary estimate of effect across studies. Instead they described the results of primary studies in a narrative way, which seems appropriate given the heterogeneity of interventions.

The conclusions of the review's author seem to follow from the evidence presented although, due to the limitations mentioned above, they should be treated with caution.

Implications of the review for practice and research
The authors state that, although its place in disease management is still emerging and there are contraindications to its use, if preliminary positive reports are confirmed, sildenafil will be the pre-eminent first-line therapy for erectile dysfunction.

Bibliographic details
Langtry H D, Markham A. Sildenafil: a review of its use in erectile dysfunction. Drugs 1999; 57(6): 967-989

PubMedID
10400408
Indexing Status
Subject indexing assigned by NLM

MeSH
Clinical Trials as Topic; Drug Interactions; Erectile Dysfunction /drug therapy; Humans; Male; Phosphodiesterase Inhibitors /adverse effects /pharmacology /therapeutic use; Piperazines /therapeutic use; Purines; Sildenafil Citrate; Sulfones

AccessionNumber
11999001320

Date bibliographic record published
31/10/2000

Date abstract record published
31/10/2000

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.