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REVIEW ARTICLE

Systematic review and meta-analysis of phosphodiesterase type 5 inhibitors for the treatment of female sexual dysfunction

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ABSTRACT

Background: Clinical studies evaluating the effectiveness and safety of phosphodiesterase type 5 inhibitors (PDE5is) for female sexual dysfunction have reported conflicting results. *Objectives:* To systematically review evidence from studies comparing PDE5is with placebo in the treatment of female sexual dysfunction. *Search strategy:* Searches of PubMed, the Cochrane Library, and Embase databases were performed using the MeSH terms "females/female/women", "sexual", and "sildenafil/tadalafil/vardenafil/PDE5/PDE5i". *Selection criteria:* All randomized controlled trials, available in English, published no later than January 28, 2015 comparing the effectiveness of PDE5is, or PDE5is in combination with other agents, with placebo in improving female sexual function were included. *Data collection and analysis:* The inclusion criteria were met by 14 studies, which were analyzed by two reviewers. *Main results:* The randomized controlled trials included in the present study adopted different questionnaires for measuring sexual function; consequently, most of the data had to be considered separately rather than pooled. Generally, the use of PDE5is resulted in significant improvements in sexual function compared with placebo, with some studies demonstrating negative results. Pooled data regarding adverse events demonstrated significantly higher rates of headache, flushing, and changes in vision in PDE5i-treated patients. *Conclusions:* PDE5is could be an effective treatment modality for female sexual dysfunction. Although there were significant increases in adverse events in comparison with placebo, PDE5is were still relatively safe.

1. Introduction

Female sexual dysfunction (FSD) is an important public health concern with a reported prevalence of 43% [1,2]. To date, the definition of FSD is incomplete; it has undergone multiple changes resulting in it becoming longer and increasingly complex [3]. According to the female sexual response cycle, there are four subtypes of FSD that can occur individually or in combination: disorders of sexual interest and desire, disorders of sexual arousal, sexual orgasmic disorder, and sexual pain disorder [4]. However, the complete etiology of FSD is unknown. Similarly to male sexual dysfunction, FSD can be subdivided into organic, psychogenic, and mixed etiologies [4].

Standard management for patients with FSD should include collaborative and comprehensive education for both the patient and their partner, including modification of behavior and, in select patients, individualized pharmacotherapy [5]. Several methods have been employed in attempts to treat FSD but controversies have arisen. Among these methods, phosphodiesterase type 5 inhibitors (PDE5is), primarily sildenafil, have been used in the treatment of all subtypes of FSD across dozens of studies. However, study results have been inconstant, making the use of PDE5is for the treatment of FSD controversial. That aim of the present study is to evaluate the safety and efficiency of PDE5i use in the treatment of FSD through performing a meta-analysis of randomized controlled trials and a systematic review of the literature.

2. Materials and methods

2.1. Search strategy

A systematic search of three databases, PubMed, Embase, and the Cochrane Library, was performed independently by two reviewers (L.G. and L.Y.), who retrieved all articles available in English published on or before January 28, 2015. No other restrictions were imposed on the articles to be retrieved and the search was performed using the MeSH terms "females/female/women", "sexual", and "sildenafil/tadalafil/vardenafil/PDE5/PDE5i" individually and in combination. The reference lists from the identified documents were also searched. When multiple reports described the same population, the most recent report was used. For multicenter trials, reports were carefully inspected to avoid any duplication with single-center studies.

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2.2. Inclusion and exclusion criteria

All available randomized controlled trials comparing PDE5is with placebo for improving female sexual function were included in the analysis. Additionally, to achieve the most complete analysis possible, studies that compared combinations of PDE5is with other medicines against placebo were included. Conference abstracts, studies that were not extractable, or studies where data were not available for analysis were excluded.

2.3. Data extraction

Data were extracted and compiled by two reviewers (S.Q. and T.L.). Any disagreement regarding data extraction was resolved following discussion with a third reviewer (J.Y.). When trials included more than three treatment arms, only data relating to comparisons between a PDE5i (or a combination of a PDE5i with another agent) and placebo were included.

2.4. Outcomes of interest

The primary outcomes examined by the present review were sexual desire, sexual arousal, sexual orgasm, and sexual satisfaction. The secondary outcomes investigated were the adverse events headache, nausea, flushing, and changes in vision.

2.5. Quality assessment and statistical analysis

Meta-analyses of pooled data were performed with Review Manager 5.2 (Cochrane Collaboration, Oxford, UK). The weighted mean difference (WMD) and risk ratio (RR) were used to describe results for continuous and dichotomous variables, respectively. All results were reported with 95% confidence intervals (CIs).

Meta-analyses were performed using the random-effects method; if significant heterogeneity was not observed in the analyzed studies, the fixed-effects method was employed. Statistical heterogeneity between trials was evaluated using I^2 and χ^2 tests, with $P < 0.10$ considered

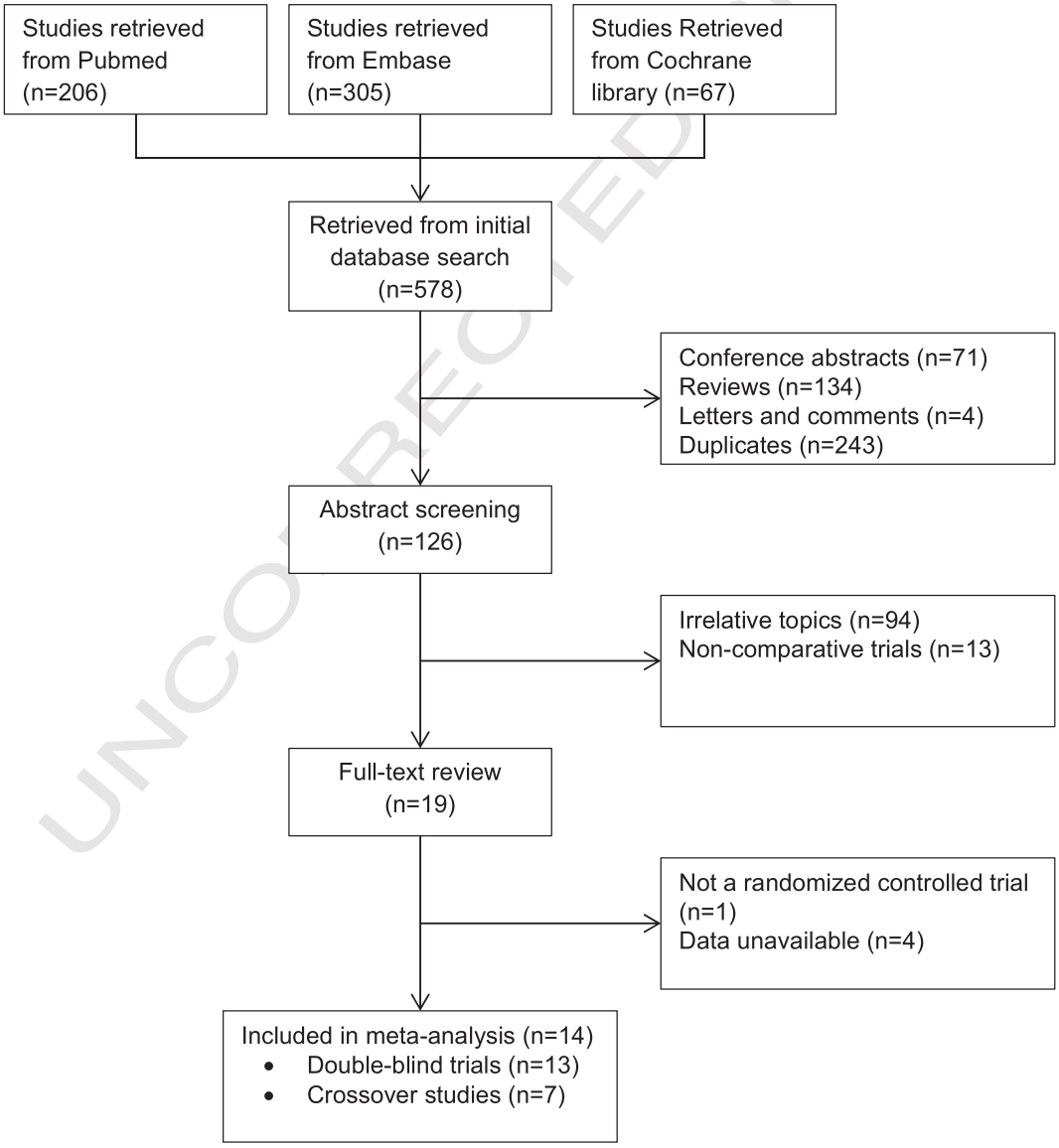

Fig. 1. Flow chart of study selection.

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