The effects of postmenopausal hormone therapies on female sexual functioning: a review of double-blind, randomized controlled trials

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CRD summary
This review assessed the effects of hormone therapies on female sexual function in postmenopausal women. The authors concluded that some oestrogen therapies and some testosterone therapies (combined with oestrogen) improved measures of sexual function, but the individual response was uncertain. It is difficult to assess the reliability of the authors' conclusions given the limited search and the lack of reporting of review methods.

Authors' objectives
To assess the effects of postmenopausal hormone therapies on female sexual function in women with natural and surgical menopause.

Searching
PubMed was searched, but the search terms and dates searched were not reported. The reference lists from identified studies were checked.

Study selection
Study designs of evaluations included in the review
Double-blind randomised controlled trials (RCTs) were eligible for inclusion. Single-blind studies were excluded. Some of the included studies were crossover studies.

Specific interventions included in the review
Studies of postmenopausal hormone therapies were eligible for inclusion. The studies had to compare the treatment with a placebo or another drug. The included studies used transdermal oestradiol conjugated equine oestrogens with and without cyclical medroxyprogesterone, oral ethinyl oestradiol with and without levonorgestrel, levonorgestrel alone, oestradiol with and without testosterone, previous oestrogen therapy plus testosterone, testosterone alone and placebo. Most of the studies used oestrogen and testosterone in steady doses; some studies used cyclic treatment. The studies treated patients for between 8 weeks and one year.

Participants included in the review
Studies of women with natural or surgical menopause were eligible and were included. The included studies were conducted in women with normal sexual function and women with sexual dysfunction.

Outcomes assessed in the review
Studies that assessed female sexual function using specific and comprehensive measures were eligible for inclusion. Studies that only measured vaginal dryness, or only compared treatment outcomes with baseline measures, were excluded. The review also assessed blood hormone levels. The included studies used validated and non-validated methods to measure sexual function (details were reported).

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

Assessment of study quality
The studies were assessed for sample size, study power and validity of sexual function measures. Only double-blind RCTs were included in the review. For each study, the reviewers calculated the sample size necessary for adequate power to detect an association between hormone treatment and the measure of sexual function. The authors did not
state who performed the validity assessment.

**Data extraction**
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. A medium effect size was assumed for total or composite scores on the sexual function scales. Small effect sizes were assumed for individual parameters of the sexual function scales.

**Methods of synthesis**

*How were the studies combined?*
The studies were grouped according to the type of menopause (natural, surgical, or a mix of the two) and combined in a narrative.

*How were differences between studies investigated?*
The results were discussed with reference to validity, effect on individuals as opposed to effects on sample, hormone treatment regimen, and interaction between various factors and sexual function.

**Results of the review**

Ten RCTs (n=17,587) were included.

Most of the studies did not report whether the sample size had adequate power to detect a treatment difference. According to the reviewers' calculations, 9 of the 10 studies used sample sizes smaller than that required to detect a small effect. The studies did not generally examine the effect of treatment on individual patients using cut-off scores.

**Women with natural menopause (4 RCTs, 17,118 women).**

One RCT provided 97% of the participants. Two studies found that, compared with placebo, transdermal oestrogen significantly improved measures of sexual function including McCoy Female Sexuality Scale (total score, satisfaction with sexual activity, sexual fantasies, sexual enjoyment, vaginal lubrication and frequency of sexual activity) and improved feelings of sexual attractiveness and improved sex life (assessed using the Women's Health Questionnaire and Nottingham Health Profile). One study found that conjugated equine oestrogen significantly improved sexual desire and arousal compared with the non-hormone phase of cyclical therapy. The largest study (n=16,608) found no significant improvement in satisfaction with sexual function, but used a single-item non-validated question.

**Women with surgical menopause (4 RCTs, 211 women).**

One study found that high-dose oral ethinyl oestradiol increased enjoyment and vaginal lubrication in comparison with placebo, and increased desire in comparison with placebo or levonorgestrel. One study found that, compared with no testosterone, higher dose testosterone (300 microg) plus oestrogen significantly increased scores for sexual activity, pleasure, and composite score on the Brief Index of Sexual Functioning in women with sexual dysfunction.

One study found that oral oestradiol plus testosterone significantly increased scores on the McCoy Female Sexuality Scale, and for sexual interest and satisfaction with frequency of sexual activity, compared with oestradiol alone. One study found no significant difference in sexual function between oestradiol 10 mg per month and placebo. It found that testosterone, either alone or in combination with oestrogen, increased sexual desire, thoughts and fantasies, and sexual arousal compared with oestradiol alone or placebo.

**Studies with a mix of natural and surgical menopause (2 RCTs, n 258 women).**

One study found that oral oestrogen plus testosterone increased pleasure from masturbation compared with oestrogen (with or without medroxyprogesterone) and placebo. The other study found that adding testosterone to oestrogen increased sexual interest or desire, and responsiveness (assessed using the Sexual Interest Questionnaire), in comparison with oestrogen alone in women with diminished sexual desire or interest.
Authors' conclusions
Certain types of oestrogen therapy were associated with increased frequency of sexual activity, enjoyment, desire, arousal, fantasies, satisfaction, vaginal lubrication and feeling physically attractive, and reduced dyspareunia, vaginal dryness and sexual problems. The addition of certain types of testosterone therapy to oestrogen-replete women further improved frequency and satisfaction with frequency of sexual activity, interest, enjoyment, desire, thoughts and fantasies, arousal, responsiveness and pleasure. However, the proportion of individuals responding to therapies, the optimal type of treatment and optimal regimen were uncertain.

CRD commentary
The review question was clear in terms of the study design, intervention, participants and outcomes. Only one database was searched and this might have resulted in the omission of other relevant studies. The search strategy was not reported. It was unclear whether any language restrictions had been applied and no attempts were made to minimise publication bias. The methods used to select the studies, assess validity and extract the data were not described, so it is not known whether any efforts were made to reduce errors and bias. Only double-blind RCTs were included. Some aspects of validity were assessed using specified criteria.

Given the small number of heterogeneous studies, a narrative synthesis was appropriate. The authors discussed some of the limitations of the studies, and summarised what was known and what was unknown. However, drop-outs, the adequacy of the washout period in crossover RCTs, and the effect of assessing multiple outcomes were not assessed. The limited search and lack of reporting of review methods limit the strength of the evidence underpinning the authors' conclusions.

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

Research: The authors stated that more research is required to examine the relationship between mood and sexual function, and to determine whether steady or cyclical therapy is best.

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Bibliographic details

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Other publications of related interest
This additional published commentary may also be of interest. McKay A. The effects of postmenopausal hormone therapies on female sexual functioning: a review of double-blind, randomized controlled trials. Can J Human Sex 2004;13:126.

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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.