Medical treatment for rectovaginal endometriosis: what is the evidence?

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CRD summary
The authors concluded that medical treatments of women with rectovaginal endometriosis were effective for pain relief. Given that the studies were limited by size, quality and were heterogeneous with regard to drug and dosage, this conclusion should be treated with caution.

Authors' objectives
To evaluate the efficacy of medical treatments for pain associated with rectovaginal endometriosis.

Searching
PubMed and EMBASE were searched for English-Language articles from January 1989 to March 2009. Search terms were reported. Bibliographies of retrieved articles and review articles, books and monographs published on endometriosis were handsearched for additional material. No attempt was made to search for unpublished material.

Study selection
Observational and randomised controlled trials (RCTs) on the effect of of medical treatments (without surgery) on pain associated with rectovaginal endometriosis (primary or recurrent lesions) were eligible for inclusion in the review. Eligible studies had a diagnosis of rectovaginal endometriosis by vaginal and rectal examination, transvaginal and/or transrectal ultrasonography and biopsy with histological confirmation. Eligible studies had pain measurements by means of visual analogue (VAS) or verbal rating scales (VRS). Studies were included if medication was provided after surgical interventions were stopped.

Included outcomes were pain (at baseline and during treatment), quality of life during treatment, satisfaction with treatment and mean lesion size (pre- and post-treatment).

Most of the included studies were prospective non-comparative patient preference studies; an RCT was included. The number of participants in a study ranged from nine to 90. Duration of treatment ranged from six to 12 months. Included interventions were: leuprolide acetate; levonorgestrel; anastrozole; ethinylestradiol plus cyproterone acetate; danazol; letrozole plus norethisterone acetate; and ethinylestradiol plus etonogestrel. Comparators varied. Interventions were delivered by intrauterine device, vaginally or orally.

Two reviewers independently selected studies for inclusion in the review.

Assessment of study quality
Two reviewers performed study quality assessment with correction or resolution of discrepancies by a third reviewer.

Data extraction
Two reviewers independently extracted data into standardised forms. Discrepancies were resolved by discussion or consultation of a third reviewer.

Methods of synthesis
Studies were synthesised narratively. Differences between studies were discussed in the text and presented in tables.

Results of the review
Seven studies (n=217) were included in the review. There were five prospective non-comparative studies (limited quality), one RCT (adequate quality) and one patient-preference cohort study (moderate quality).

Aromatase inhibitors: Administration of vaginal anastrozole 0.25mg/day for six months (n=9, non-comparative) significantly decreased pain during treatment. Administration of oral letrozole plus progestin (n=12) significantly decreased pain during treatment and improved quality of life. Neither drug influenced endometrial foci size.
Gonadotrophin-releasing hormone agonists: Administration of leuprolide acetate 3.75mg/28 days (n=15, non-comparative) for six months significantly reduced pain during treatment.

Progestins: Administration of a levonorgestrel-releasing intrauterine device for 12 months (n=11, non-comparative) significantly reduced pain during treatment and had a slight but significant reduction in lesion size.

Danazol: Administration of vaginal danazol 200mg/day for 12 months (n=21, non-comparative) significantly reduced pain during treatment and significantly reduced lesion size.

Oestrogen-progestin combinations: Studies of use of a vaginal ring ethinylestradiol 0.015 mg plus etonogestrel 0.12 mg/day (n=38, patient preference) or transdermal patch ethinyl oestradiol 0.02 mg plus norelgestromin 0.15 mg/day (n=21, patient preference) found that pain was reduced by both methods, but was more effective for the ring. More patients were satisfied with the ring (79%) treatment than the patch (57%).

Administration of oral treatments (n=90, RCT) reduced pain and reduced lesion size. Five patients withdrew due to side effects.

Authors’ conclusions
Medical treatment in women with rectovaginal endometriosis was effective in terms of pain relief.

CRD commentary
This review addressed a clear research question supported by clear inclusion criteria. Three databases were searched. Only English-language publications were included, which introduced a risk of language bias. There was no apparent search for unpublished material, so relevant trials may have been missed and publication bias could not be ruled out. Validity was assessed, but the method was not described and so it was difficult to comment on the quality of the studies. Adequate steps were taken throughout the review process to minimise errors and bias. Study details were presented. The chosen method of synthesis was appropriate given the levels of heterogeneity among the trials.

The authors’ conclusions reflected the data presented. Given the limited number of small studies, possibility of bias and variety of drugs and doses, the authors' conclusions should be treated with caution.

Implications of the review for practice and research
Practice: The authors stated that all different therapeutic options for rectovaginal endometriosis should be described and offered to patients in an unbiased manner.

Research: The authors stated that randomised trials on hormonal therapy versus excision were required to understand which offered the best therapy for individual patients.

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