Review 2012: Hormones (steroids)
Progesterone for premenstrual syndrome

Link: https://pubmed.ncbi.nlm.nih.gov/22419287/

Year: 2012

Pubmed classification: Review.

Objective: The objectives were to determine if progesterone has been found to be an effective treatment for all or some premenstrual symptoms, and if adverse events associated with this treatment have been reported.

Number of studies and types of papers: From 17 studies, only 2 met our inclusion criteria. Together they had 280 participants aged between 18 and 45 years. 115 yielded analysable results.

Databases searched: We searched the Cochrane Menstrual Disorders and Subfertility Group's Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE and PsycINFO to February 2011. We contacted pharmaceutical companies for information about unpublished trials, for the first version of this review, and we wrote to trial investigators for missing data.

Inclusion criteria: We included randomised double-blind, placebo-controlled trials of progesterone on women with PMS diagnosed by at least two prospective cycles, without current psychiatric disorder.

Methods for assessing research quality: Two reviewers extracted data independently and decided which trials to include.

Research quality: Both studies measured symptom severity using subjective scales. Both trials had defects. They intended to exclude women whose symptoms continued after their periods.

Statistical analysis methods: Differing in design, participants, dose of progesterone and how it was delivered, the studies could not be combined in meta-analysis.

Efficacy outcomes: When data from ineligible women were excluded from analysis in one trial, the other women were found to have benefited more from progesterone than placebo. The smaller study found no statistically significant difference between oral progesterone, vaginally absorbed progesterone and placebo, but reported outcomes incompletely.

Side-effects assessment: Adverse events which may or may not have been side effects of the treatment were described as mild.

Conclusion: The trials did not show that progesterone is an effective treatment for PMS nor that it is not. Neither trial distinguished a subgroup of women who benefited, nor examined claimed success with high doses.

Review 2004: Hormones (GnRH Analogues)

The effectiveness of GnRHa with and without 'add-back' therapy in treating premenstrual syndrome: a meta analysis

Link: https://pubmed.ncbi.nlm.nih.gov/15198787/

Year: 2004

Pubmed classification: Review.

Further review information : Meta-analysis.

Objective: To determine the effectiveness of gonadotrophin-releasing hormone analogues (GnRHa) with and without hormonal add-back therapy in the management of premenstrual syndrome.

Databases searched: Randomised Controlled Trials were identified by searching multiple databases.

Inclusion criteria: Published randomised placebo-controlled trials assessing the use of GnRHa in the management of premenstrual syndrome on women with pre-diagnosed premenstrual syndrome and/or premenstrual dysphoric disorder.

Statistical analysis methods: The standardised mean difference for each individual study, and subsequently an overall standardised mean difference, were calculated after demonstrating the consistency or homogeneity of the study results. Overall improvement in premenstrual symptomatology, and effectiveness of GnRHa with additional hormonal add-back therapy, were the main outcome measures assessed in this analysis. A secondary analysis was performed to assess the effectiveness of GnRHa in treating physical and emotional symptoms.

Efficacy outcomes: Overall standardised mean difference for all trials that assessed the efficacy of GnRHa was -1.19 (95% confidence interval [CI] -1.88 to -0.51). The equivalent odds ratio was 8.66 (95% CI 2.52 to 30.26) in favour of GnRHa. GnRHa were more efficacious for physical than behavioural symptoms, although the difference was not statistically significant. The addition of hormonal add-back therapy to GnRHa did not appear to reduce the efficacy of GnRHa alone, standardised mean difference 0.12 (95% CI -0.35 to 0.58).

Conclusion: GnRHa appear to be an effective treatment in the management of premenstrual syndrome. The addition of hormonal add-back therapy to reduce side effects does not reduce efficacy.

Review 2003: Hormones (GnRH Analogues)
Gonadotrophin -releasing hormone analogues for endometriosis: bone mineral density

Link: https://pubmed.ncbi.nlm.nih.gov/14583930/

Year: 2003

Pubmed classification: Review

Objective: To determine the effect of treatment with gonadotrophin-releasing hormone analogues (GnRHas) on the bone mineral density of women with endometriosis; compared to placebo, no treatment, or other treatments for endometriosis, including GnRHas with add-back therapy.

Number of studies and types of papers: 30 studies involving 2,391 women were included, however only 15, involving 910 women, could be included in the meta-analysis.

Databases searched: We searched the Cochrane Menstrual Disorders and Subfertility Group's specialised register of controlled trials (23rd October 2002) and the Cochrane Central Register of Controlled Trials (Cochrane Library, issue 4, 2002). We also carried out electronic searches of MEDLINE (1966 - March Week 2 2003) and EMBASE (1980 - March Week 2 2003). We also searched the reference lists of articles and contacted researchers in the field. Study authors were contacted for additional information.

Inclusion criteria: Prospective, randomised controlled studies of the use of GnRHas for the treatment of women with endometriosis were considered, where bone density measurements were an end point. The control arm of the studies was either placebo, no treatment, another medical therapy for endometriosis, or GnRHas with add-back therapy.

Methods for assessing research quality: Two reviewers (JF and MS) independently assessed trial quality and extracted data.

Research quality: Only one study comparing GnRH analogues with placebo was identified, but the study gave no data. No studies comparing GnRH with the oral contraceptive pill (OCP) or progestogens were identified.

Side-effects assessment: The meta-analysis showed that danazol and progesterone + oestrogen add-back are protective of BMD at the lumbar spine, both during treatment and for up to six and twelve months after treatment, respectively. Between the groups receiving GnRHa and the groups receiving Danazol/gestrinone, there was a significant difference in percentage change of BMD after six months of treatment, the GnRH analogue producing a reduction in BMD from baseline, and danazol producing an increase in BMD (SMD -3.43, 95 % CI -3.91 to -2.95).

Progesterone only add-back is not protective; after six months of treatment absolute value BMD measurements of the lumbar spine did not differ significantly from the group receiving GnRH analogues (SMD 0.15, 95 % CI -0.21 to 0.52). In the comparison of GnRHa versus GnRHa + HRT add-back, that is oestrogen + progesterone or oestrogen only, there was a significantly bigger BMD loss in the GnRHa only group (SMD -0.49, 95 % CI -0.77 to -0.21).

These numbers reflect the absolute value measurements at the lumbar spine after six months of treatment. Due to the small number of studies in the comparison we are unable to conclude whether calcium-regulating agents are protective. No difference was found between low and high dose add-back regimes but again only one study was identified for this comparison.

Conclusion: Both Danazol and progesterone + oestrogen add-back have been shown to be protective of BMD, while on treatment, and up to six and 12 months later, respectively. However, by 24 months of follow-up there was no difference in BMD in those women who had HRT add-back. Studies of Danazol versus GnRHa did not report long-term follow-up. The significant side effects associated with Danazol limit its use.

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Gonadotrophin -releasing hormone analogues for endometriosis: bone mineral density

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Review 2001: Hormones (steroids)

Efficacy of progesterone and progestogens in management of premenstrual syndrome: systematic review

LinK: https://pubmed.ncbi.nlm.nih.gov/11588078/

Year: 2001

Pubmed classification: Meta-analysis.

Further review information: Systematic review.

Objective: To evaluate the efficacy of progesterone and progestogens in the management of premenstrual syndrome.

Number of studies and types of papers: 10 trials of progesterone therapy (531 women) and 4 trials of progestogen therapy (378 women).

Inclusion criteria: Systematic review of published randomised, placebo-controlled trials.

Statistical analysis methods: Main outcome measures: Proportion of women whose symptoms showed improvement with progesterone preparations (suppositories and oral micronised). Proportion of women whose symptoms showed improvement with progestogens.
Secondary analysis: Efficacy of progesterone and progestogens in managing physical and behavioural symptoms.

Efficacy outcomes: Overall standardised mean difference for all trials that assessed efficacy of progesterone (by both routes of administration) was -0.028 (95% confidence interval -0.017 to -0.040). The odds ratio was 1.05 (1.03 to 1.08) in favour of progesterone, indicating no clinically important difference between progesterone and placebo.

For progestogens the overall standardised mean was -0.036 (-0.014 to -0.060), which corresponds to an odds ratio of 1.07 (1.03 to 1.11) showing a statistically, but not clinically, significant improvement for women taking progestogens.

Conclusion: The evidence from these meta-analyses does not support the use of progesterone or progestogens in the management of premenstrual syndrome.