

## **Trial 2011: Contraceptives (Oral)**

**Ethinyl estradiol 20µg/drospirenone 3mg 24/4 oral contraceptive for the treatment of functional impairment in women with premenstrual dysphoric disorder**

**Link:** <https://pubmed.ncbi.nlm.nih.gov/21338987/>

**Year published:** 2011

**Pubmed classification:** Randomised Controlled Trial.

**Further trial information:** Secondary analysis of a double-blind, randomized parallel-design trial.

**Objective:** To determine the effects of ethinyl estradiol (EE)/drospirenone in a 24/4 regimen (24 days of active and 4 days of inactive pills) on functional impairment (affecting work, partnership, and social activities) in women with premenstrual dysphoric disorder (PMDD).

**Blind/double blind?** Double-blind.

**Randomised?** Yes.

**Placebo?** Placebo group.

**Participant information:** 450 women with PMDD.

**Treatment length:** 3 cycles.

**Drug and dosage:** EE 20µg/drospirenone 3mg (232); or placebo (218).

**Measuring scales:** Participants completed the Daily Record of Severity of Problems (DRSP) scale daily.

**Efficacy outcomes:** The decrease in mean scores for all 3 DRSP functional impairment items (work, partnership, and social activities) from baseline to cycle 3 mirrored changes in the total DRSP symptom score; the greatest decreases were observed in cycle 1 with further small reductions through to cycle 3.

The proportional mean decreases from baseline to cycle 1 for the 3 functional items ranged from 47% to 48%. For all 3 functional items, the mean reductions from baseline to cycle 1 (but not from cycle 1 to cycles 2 and 3) were significantly greater with EE/Drospirenone than with placebo ( $P < 0.05$ ).

**Conclusion:** Ethinyl Estradiol 20µg/Drospirenone 3mg in a 24/4 regimen significantly improved functional impairment in women with PMDD. Symptoms improved in parallel.

**Trial 2010: Contraceptives (Lifestyle Factors)**  
**The United Kingdom Southampton Women's Survey:**  
**Lifestyle factors, hormonal contraception, and premenstrual symptoms.**

Link: <https://pubmed.ncbi.nlm.nih.gov/20156129/>

Year published: 2010

**Trial information:** Cross-sectional survey.

**Objective:** To estimate the prevalence of premenstrual symptoms in women from the general population in Southampton, U.K., and examine their association with lifestyle factors and contraceptive use.

**Participant information:** 974 women aged 20-34 years, in the city of Southampton.

**Trial length:** 6 weeks assessment.

**Measuring scales:** The survey consisted of interviews, questionnaires, and completion of a prospective 6-week menstrual symptom diary, recording on a daily basis the presence and severity of 11 common premenstrual symptoms. Premenstrual symptoms were identified from the diaries by two clinicians who reviewed them independently using a predefined algorithm to assess the onset and decline of symptoms in relation to the start of menstruation.

**Outcomes:** Of the women surveyed, 24% were considered to have premenstrual symptoms (95% confidence interval [CI] 21-27). Women were less likely to have symptoms if they had higher levels of educational attainment and suffered less from stress. No associations were found between premenstrual symptoms and diet, alcohol, or strenuous exercise nor, after adjustment for other factors, with age, smoking, or body mass index (BMI). Use of any form of hormonal contraceptives was associated with a lower prevalence of premenstrual symptoms (prevalence ratio 0.66, 95% CI 0.52-0.84).

**Conclusion:** Premenstrual symptoms were common in this cohort. Use of hormonal contraceptive methods was associated with a lower prevalence of these symptoms.

## **Trial 2007: Contraceptives (Oral)**

### **Long-term assessment of symptomatology and satisfaction of an extended oral contraceptive regimen**

**Link:** <https://pubmed.ncbi.nlm.nih.gov/17519150/>

**Year published:** 2007

**Pubmed classification:** Randomised Controlled Trial.

**Objective:** The study was conducted to assess hormone withdrawal symptoms, patient acceptance and occurrence and management of bleeding with an extended oral contraceptive (OC) regimen.

**Blind/double blind?** Unknown.

**Randomised?** Yes.

**Placebo?** No.

**Participant information:** 111 women began an extended OC regimen; 80 completed 1 year of use.

**Treatment length:** 52 weeks (+2 cycles 21/7 regime; + phone call follow-up 6 months later).

**Drug and dosage:** 3 mg drospirone (DRSP) and 30 microg ethinyl estradiol (EE), in the standard 21/7 fashion for two cycles; before conversion to an extended pattern of OC for women who had menstrually related symptoms such as headaches, cramping and mood swings.

**Measuring scales:** Daily assessments of bleeding, headache, pelvic pain, mood and number of pain pills were recorded. Results are reported as means with S.E., and values were compared using analysis of variance with Dunnett's post hoc test for comparison with 21/7 cycle; Duncan's post hoc test for comparison of changes during the course of the extended regimen; and Pearson's chi-square for comparison of proportions.

**Efficacy outcomes:** Mood scores, headache scores and pelvic pain were all improved in the extended OC intervals, compared to the 21/7 cycle ( $p < .001$  for all comparisons). Improvement in symptoms persisted throughout the 1 year extended regimen. At the 6-month follow-up, most subjects had continued the extended regimen on their own with a high level of satisfaction.

**Side-effects assessment:** The findings indicated that 53.7% of subjects had no breakthrough bleeding or breakthrough spotting (BTB/BTS) during any given 28-day interval of the extended regimen. BTB/BTS decreased in the second half compared to the first half of the extended regimen. To manage BTB/BTS, instituting a 3-day hormone-free interval (HFI) was significantly more effective than continuing OCs ( $p < .001$ ).

**Conclusion:** An extended OC regimen containing DRSP/EE significantly improved mood, headaches and pelvic pain scores throughout the 1 year of use, compared to a 21/7 cycle. Sustained BTB/BTS episodes occurred in 45 subjects (56%), decreasing in the second half of the study and effectively managed with a 3-day HFI.

**Trial 2005: Contraceptives (Drospirenone)**  
**Treatment of premenstrual Dysphoric Disorder with a new Drospirenone-containing oral contraceptive formulation**

**Link:** <https://pubmed.ncbi.nlm.nih.gov/16307962/>

**Year published:** 2005

**Pubmed classification:** Randomised Controlled Trial.

**Objective:** To evaluate the efficacy of a new oral contraceptive (OC) formulation in treating symptoms of premenstrual dysphoric disorder (PMDD).

**Blind/double blind?** Double-blind.

**Randomised?** Yes.

**Placebo?** Placebo controlled - crossover study.

**Participant information:** 64.

**Treatment length:** 3 cycles (active drug or placebo); 1 treatment-free cycle; 3 cycles (active drug or placebo).

**Drug and dosage:** Drospirenone 3 mg and Ethinyl Estradiol (EE) 20 mug; or placebo. 24 days in a 28-day cycle (24/4).

**Measuring scales:** Daily Record of Severity of Problems (DRSP) scores and Clinical Global Impressions-Improvement scale.

**Efficacy outcomes:** The mean decrease from baseline for total Daily Record of Severity of Problems (DRSP) scores while using Drospirenone/EE was significantly greater than for placebo (-12.47, 95% CI=-18.28, -6.66;  $p<.001$ ).

A positive response (i.e., a score of 1 or 2 in the Clinical Global Impressions-Improvement scale) occurred in 61.7% and 31.8% of subjects while taking drospirenone/EE and placebo, respectively ( $p=.009$ ).

**Conclusion:** Drospirenone/EE, given in a 24/4 regimen, was superior to placebo for improving symptoms associated with PMDD.

## **Trial 2005: Contraceptives (Drospirenone)**

### **Efficacy of a new low-dose oral contraceptive with Drospirenone in premenstrual dysphoric disorder**

**Link:** <https://pubmed.ncbi.nlm.nih.gov/16135578/>

**Year published:** 2005

**Pubmed classification:** Clinical trial.

**Objective:** To compare the efficacy of a new low-dose oral contraceptive pill (OCP) formulation with placebo in reducing symptoms of premenstrual dysphoric disorder.

**Blind/double blind?** Double-blind.

**Randomised?** Yes.

**Placebo?** Placebo group.

**Participant information:** 450 women with PMDD symptoms.

**Treatment length:** 3 treatment cycles (+2 run-in cycles).

**Drug and dosage:** OCP formulation containing drospirenone 3 mg and ethinyl estradiol 20 microg; or placebo. Hormones were administered for 24 days, followed by 4 days of inactive pills (24/4).

**Measuring scales:** Daily symptom charting using the Daily Record of Severity of Problems.

**Efficacy outcomes:** Scores on the total Daily Record of Severity of Problems decreased by -37.49 in the drospirenone/ethinyl estradiol group and by -29.99 in the placebo group (adjusted mean difference -7.5, 95% confidence interval [CI] -11.2 to -3.8;  $P < .001$  by rank analysis of covariance).

Mood symptom scores were reduced by -19.2 and -15.3 in active-treatment and placebo groups, respectively (adjusted mean difference -3.9, 95% CI -5.84 to -2.01;  $P = .003$ ); physical symptom scores were reduced by -10.7 and -8.6 in active-treatment and placebo groups, respectively (adjusted mean difference -2.1, 95% CI -3.3 to -0.95;  $P < .001$ ); and behavioural symptom scores were reduced by -7.7 and -6.2 in active-treatment and placebo groups, respectively (adjusted mean difference -1.5, 95% CI -2.251 to -0.727;  $P < .001$ ).

Response defined as a 50% decrease in daily symptom scores, occurred in 48% of the active-treatment group and 36% of the placebo group (relative risk 1.7, 95% CI 1.1 to 2.6;  $P = .015$ ) and corresponds to a number-needed-to-treat of 8 patients.

**Conclusion:** A 24/4 regimen of Drospirenone 3 mg and Ethinyl Estradiol 20 mug improves symptoms associated with premenstrual dysphoric disorder.

## **Trial 2001: Contraceptives (Oral)**

### **Evaluation of a unique oral contraceptive in the treatment of premenstrual dysphoric disorder**

**Link:** <https://pubmed.ncbi.nlm.nih.gov/11559453/>

**Year published:** 2001

**Pubmed classification:** Clinical trial.

**Objective:** Trial of a unique oral contraceptive for treatment of PMDD.

**Blind/double blind?** Double-blind.

**Randomised?** Yes.

**Placebo?** Placebo group.

**Participant information:** 82 women with PMDD (Diagnostic and Statistical Manual of Mental Disorders, 4th ed. [DSM IV]).

**Treatment length:** 3 cycles.

**Drug and dosage:** Oral contraceptive containing a combination of drospirenone (DRSP, 3 mg) and ethinyl estradiol (EE, 30 microg); or placebo.

**Measuring scales:** The primary end point was change from baseline in luteal phase symptom scores as assessed on the Calendar of Premenstrual Experiences (COPE) scale. The secondary end points were the Beck Depression Inventory (BDI) and Profile of Mood States (PMS).

**Efficacy outcomes:** Patients treated with DRSP/EE showed a numerically greater change from baseline compared with those treated with placebo on each of the 22 COPE items and each of the 4 symptom factors. Between-group differences in symptom improvement reached statistical significance in factor 3 only (appetite, acne, and food cravings,  $p = 0.027$ ).

The secondary end points, Beck Depression Inventory (BDI) and Profile of Mood States (PMS), were consistent with the primary end point in that patients treated with the oral contraceptive showed a numerically greater improvement from baseline compared with those treated with placebo.

**Conclusion:** The results of this study show a consistent trend in the reduction of symptoms that suggested a beneficial effect of DRSP/EE for the treatment of PMDD, despite limitations of the study design.

## **Trial 1992: Contraceptives (Oral)**

### **A prospective treatment study of premenstrual symptoms using a triphasic oral contraceptive**

**Link:** <https://pubmed.ncbi.nlm.nih.gov/1564678/>

**Year published:** 1992

**Pubmed classification:** Clinical trial.

**Objective:** Trial of a triphasic oral contraceptive in moderate to severe premenstrual syndromes.

**Blind/double blind?** Double-blind.

**Randomised?** Yes.

**Placebo?** Placebo group.

**Participant information:** 82 women with reported moderate to severe premenstrual symptoms were recruited. 23 women dropped out of the study (18 o.c., 5 placebo); 13 failed to show prospective confirmation of moderate to severe premenstrual symptoms; and 1 placebo subject had an anovulatory cycle. 45 women with prospectively-confirmed premenstrual changes completed the study.

**Treatment length:** 3 months treatment (+1min baseline cycle).

**Drug and dosage:** Triphasic oral contraceptive (20); placebo (25).

**Efficacy outcomes:** Premenstrual breast pain and bloating were significantly reduced with active treatment compared to placebo but there were no beneficial effects of the OC over placebo for any of the mood symptoms.

**Side-effects assessment:** Women who received OCs reported decreased sexual interest after starting treatment and this effect was independent of any adverse influence on mood.

## **Trial 1980s: Contraceptives (Oral)**

### **A prospective treatment study of premenstrual symptoms using a triphasic oral contraceptive - PIP**

**Link:** <https://pubmed.ncbi.nlm.nih.gov/1564678/>

**Year published:** Unknown

**Pubmed classification:** Clinical trial.

**Objective:** Study of a triphasic oral contraceptive for prospectively confirmed premenstrual syndrome (PMS).

**Blind/double blind?** Double-blind.

**Randomised?** Unknown.

**Placebo?** Placebo group.

**Participant information:** 212 subjects were recruited between April 1987 - June 1988, and 82 subjects who were prospectively confirmed to have premenstrual syndrome began the study. 59 subjects completed the study, and were later confirmed to have moderate to severe premenstrual symptoms. Completers had higher status occupations and lower symptom severity scores than dropouts.

**Treatment length:** 3 cycles (+ 1 baseline cycle).

**Drug and dosage:** Synphasic (Syntex, Mississauga, Canada) containing 35 mcg ethinyl estradiol and 0.5 mg, 1.0 mg, and 0.5 mg norethindrone (23); or placebo (36).

**Measuring scales:** Subject completed a menstrual history form and a 95-item retrospective questionnaire on premenstrual symptoms.

**Efficacy outcomes:** Both pill and placebo groups showed significant clinical improvement on every symptom except headache. Symptom scores decreased significantly between baseline and 3rd treatment cycle, and between menstrual phase scores and the variables "mood swings," "more sleep," "unhappy," and "tense" in the 2nd treatment cycle compared with the 1st treatment cycle in both groups.

In the pill group ratings of premenstrual breast pain were significantly lower in the 3rd treatment cycle compared with baseline ( $p < 0.05$ ), and to the 1st treatment cycle ( $p < 0.01$ ). No significant changes in breast pain were found in the placebo group. Some pill cycles showed significant reduction in edema. Those in the pill group who were initially rated as "depressed" showed greater improvement in work impairment, sleep requirements, and energy level premenstrually.

**Side-effects assessment:** The pill group reported significantly lower sexual interest during treatment.

**Conclusion:** This is the 1st reported double-blind, placebo-controlled, prospectively confirmed study of oral contraceptives for PMS.