



## P16. TRANSDERMAL ESTRADIOL TREATMENT OF PREMENSTRUAL DYSPHORIC DISORDER PREVENTS CATAMENIAL GENITAL HERPES: A PROOF-OF-CONCEPT STUDY

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**Context:** Transdermal estradiol has proven efficacy in treatment of mood symptoms of premenstrual dysphoric disorder (PMDD) and associated catamenially-triggered problems such as menstrual migraine and premenstrual supraventricular tachycardia. Many perimenopausal women with genital herpes suffer recurrences immediately premenstrually, first described as “Bouton de Règles” (Unna 1883), which can nowadays be suppressed by taking acyclovir in the luteal phase only.

**Objective:** To observe changes in frequency of herpes recurrences in women commencing estradiol treatment for perimenopausal PMDD.

**Methods:** Case note review of women who had mood symptoms meeting the criteria for PMDD subsequently defined in DSM-5 and also suffered catamenial genital herpes (CGH) recurrences. Subjects self-reported mood with a modified daily symptom chart and herpetic symptoms over 9 months follow-up, during which no aciclovir was taken pre-emptively. Intention-to-treat (ITT) analysis included 10 cycles where estradiol treatment was omitted in error and both conditions recurred.

**Patients:** 12 perimenopausal women median age 41 years (range 36–45) presented to two sexual health clinics between 2005–15. Each had had at least 4 consecutive monthly episodes of CGH (culture or PCR-proven HSV2) before commencing luteal-phase acyclovir suppression.

**Intervention:** Simultaneous cessation of acyclovir suppressive regimes and commencement of

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transdermal 17-beta estradiol gel 0.5mg (Sandrena®) daily for 14 days in the luteal phase or continuously for those using LNG-IUS (Mirena®).

Main Outcome Measures: Number of episodes of PMDD and genital herpes recurrence.

Results: All women experienced substantial or complete relief of PMDD in all but three treated cycles. Two required estradiol dose doubling to achieve mood control. Only 13 symptomatic CGH episodes occurred while on treatment in 108 woman-months' observation.

PMDD episodes in 9 months: Exp 108, Obs 13 (ITT) Ratio Exp/Obs 0.12

Herpes episodes in 9 months: Exp 108, Obs 23 (ITT) Ratio Exp/Obs 0.21

$p < 0.0001$  (Student's t-Test) for reduction in episodes from 9 per patient for both outcomes

Conclusions: This is the first scientific proof-of-concept study demonstrating that transdermal estradiol treatment is a successful, biologically plausible method of preventing catamenial genital herpes. The proposed mechanism is stabilization of the hormonal milieu which diminishes the extreme luteal phase immune suppression occurring in PMDD.