Table

Clinical trials of topical progesterone cream

Study	Subjects	Preparation Dose/Duration	Outcomes	Results
Pharmacokinetics studies				
Lewis[5]	Randomized, double-blind, placebo-controlled, 3-arm trial n = 24 postmenopausal women not on HRT (22 completed)	Compounded progesterone cream 1-2 g (20 mg or 40 mg progesterone/g) vs. placebo applied bid for two three-week periods with a one-week break in between	Progesterone levels in plasma, red blood cells, and saliva, and pregnanediol-3-glucuronide (P3G) excretion	Plasma progesterone increased significantly but slightly in both treated groups, compared to the placebo group (range 0.32-1.77 nmol/L in the 20 mg group, 0.59-3.53 nmol/L in the 40 mg group). P3G rose in the 40 mg group at weeks 1 and 3. Salivary progesterone levels were high and variable (range 0.25-82.11 nmol/L), and did not correlate with serum levels.
Carey[7]	Randomized, open-label, two-arm study, n = 24 postmenopausal women (19 completed)	Progesterone cream 40 mg/d or 20 mg bid × 42 days	Serum FSH, estradiol, testosterone, and urinary P3G	Serum progesterone increased to 2.5-3.0 nmol/L (with wide variation); P3G also increased; there was no change in FSH, estradiol, or testosterone.
O'Leary[6]	n = 12 women (6 postmenopausal, 6 premenopausal, during luteal phase)	Single 2 g application of Pro-femme cream (containing 64 mg progesterone)	Salivary and serum progesterone, urinary P3G	No change from baseline in serum progesterone 3 hours after treatment in either group. No change from baseline in urinary P3G. Salivary progesterone rose significantly in both groups within an hour, falling to baseline within 24 hours.
Burry[8]	n = 6 postmenopausal women	Pro-Gest, containing 30 mg/g qd (30 mg/d) × 2 weeks, then bid × for 2 weeks (60 mg/d) Transdermal estradiol patch 0.05 mg worn	Serum 17β-estradiol and progesterone levels	Mean serum progesterone levels rose to 1.0-3.3 ng/mL. Strong correlation between absorption of estradiol and progesterone was seen.
Cooper[9]	Crossover study, n = 20 surgically menopausal women	One teaspoon of Progest cream (2-4 times recommended daily dose) or placebo bid × 10 days; four day washout period between creams. Each subject then took oral natural progesterone (100 mg Uterogestan qam and 200 mg qpm) × 5 days	Plasma progesterone and 17-hydroxyprogesterone (17-OHP) and P3G	Compared to placebo, Progest median plasma progesterone levels after 10 days were 2.9 nmol/L, compared to 9.5 nmol/L with oral progesterone. 17-OHP values were similar between groups; urine P3G levels were 4.2 mcmol with Progest and 291 mcmol with Uterogestan.
Endometrium				
Wren[10]	Randomized crossover study, n = 27 postmenopausal women (23 completed, 21 endometrial biopsies obtained)	Pro-femme (16 mg, 32 mg, or 64 mg progesterone) for latter 2 weeks of each 4-week treatment cycle. 17β-estradiol patch worn throughout	Serum progesterone levels, endometrial biopsy	Serum progesterone levels rose to 0.6-3.2 ng/mL. None of the endometrial biopsies indicated a secretory endometrium.
Bone and hot flashes				
Leonetti[1]	Randomized, placebo-controlled study, n = 102 postmenopausal women (90 completed)	Compounded cream containing 20 mg progesterone/d (all subjects received 1,200 mg calcium and a multivitamin) × 1 year	Bone mineral density, vasomotor symptoms	No significant difference between groups in change in bone mineral density. Vasomotor symptoms decreased in 25/30 symptomatic treated subjects, compared with 5/26 controls, a significant difference. Eight progesterone-treated subjects experienced vaginal spotting.