
This randomized, controlled study involving 58 postmenopausal women demonstrated that topically applied progesterone cream (Pro-Gest) had an antiproliferative effect in postmenopausal women who had been given oral estrogens x 14 days prior to progesterone treatment. Treatment with topical progesterone did not differ in effects from vaginally applied progesterone (Crinone), and both progesterone applications demonstrated a significant effect over placebo. Patients preferred the topical application of progesterone cream.


Twenty estrogen-deprived women were given oral estrogen for 12 days followed by oral estrogen-vaginal progesterone gel for 12 days. Endometrial evaluation occurred before treatment, after the estrogen-only phase and after estrogen-progesterone gel treatment. Atrophy was present before treatment in all patients. Typical proliferative changes occurred after estrogen-only treatment, and secretory transformation occurred after estrogen-progesterone treatment, indicating that sustained release progesterone gel can effectively counteract the proliferative effects of estrogen treatment in postmenopausal women.


In this study of 35 postmenopausal women, twice-weekly administration of a progesterone vaginal gel (45mg P4/day) sufficiently protected the endometrium in women receiving transdermal estradiol (0.05mg/day) as revealed by endometrial thickness and histology. The authors present vaginally applied progesterone as a viable option for hormone replacement therapy at menopause.


This in vitro study demonstrated that progesterone acts through progesterone receptor B to inhibit endometrial cancer cell invasiveness via the down-regulation of adhesion molecules.

Three different doses of transvaginal progesterone gel were administered to 40 estrogen-deprived women aged 25-41 years. Estradiol was administered orally for 28 days, with progesterone added vaginally on alternate days from days 15-27. Plasma gonadotropins, E1, E2 and progesterone were measured, and an endometrial biopsy was obtained to assess endometrial status and estrogen and progesterone receptor determinations. Transvaginal progesterone induced normal secretory transformation despite low serum progesterone levels, suggesting a direct transit of progesterone into the uterus, or “first uterine pass effect.”


Although estrogen is known to stimulate the growth of uterine fibroids, the effect of progesterone is unclear. The role of progesterone in the development of uterine fibroids (leiomyoma) is examined in this study in an in vivo/in vitro mouse model. Progestins and antiprogestins were utilized to investigate progesterone receptor (PR) signaling in a leiomyoma cell line. Both progestins and antiprogestins inhibited estrogen-mediated growth. PR ligands were also shown to suppress estrogen receptor signaling and leiomyoma cell growth.


20 women completed a 1 year randomized, controlled, cross-over study comparing conjugated equine estrogen (Premarin, 0.625mg) paired with progesterone cream (Pro-Gest, 20mg) vs. conjugated equine estrogen paired with medroxyprogesterone acetate (Prempro). Endometrial biopsies were performed at the end of each 6 month arm of the study. No hyperplasia was found in either group. Incidence of spotting was similar in both groups. Participants preferred the progesterone cream composition (76% vs 5%, p<0.001).


This study evaluated the use of a progesterone-releasing IUD as a feasible treatment for early stage endometrial cancer (IA, grade 1). Twelve subjects were followed for 36 months. Results suggested IUD progesterone appeared to resolve some cases of early endometrial cancer.


It is often presumed that progesterone levels must be high enough to induce endometrial bleeding by withdrawal in order to convey protection during estrogen replacement therapy. In this expanded observational study, the authors sought to determine the influence of withdrawal bleedings, secretory transformation, and reduction of mitosis on the prevention of endometrial hyperplasia during long-term estrogen-replacement therapy. Hysteroscopy and endometrial biopsies were utilized to establish maturation patterns, glandular epithelial mitosis rates, and macroscopic endometrial appearance. The results showed an increase in withdrawal bleeding with higher levels of progesterone, with those levels producing distinct secretory responses. However, incidence of endometrial hyperplasia after 5 years of E2/P therapy was independent of secretory changes and withdrawal bleeding, and was more related to the control of mitosis, which was seen even with low doses of progesterone. The authors conclude that a relatively low dose of P may be offered to women seeking hormone replacement therapy with similar levels of endometrial safety.