197

A BIOADHESIVE PROGESTERONE VAGINAL GEL AS AN ALTERNATIVE TO SYNTHETIC PROGESTINS IN ESTROGEN REPLACEMENT REGIMENS. S. Shantha*, M.P. Warren*, T.L. Toth* and B.M.K. Biller*. (SPON: R. Neuwirth). Depts of Ob/Gyn and Medicine, St. Luke's-Roosevelt Hospital and Columbia College of Physicians & Surgeons, New York, NY and Neuroendocrine Unit and Division of Gynecology, Massachusetts General Hospital and Harvard Medical School, Boston, MA.

A bioadhesive gel containing progesterone (45mg or 90mg) in a polycarbophil base (Crinone-TVG™) is administered vaginally every other day. The bioadhesive base attaches to the vaginal epithelium and releases progesterone at a slow constant rate over 48-72 hours. This provides a vehicle for administering pure progesterone in close proximity to the uterus, which has been shown to provide a uterine first-pass effect. This drug was studied as an alternative to oral progestins, which may attenuate the beneficial effects of estrogen and can be associated with significant side effects with respect to mood.

The gel was studied in subjects with secondary hypothalamic amenorrhea and premature ovarian failure. Eighty-eight subjects were recruited. To date, 34 subjects have completed the study. Estrogen in the form of Premarin 0.625mg was used for replacement. After six weeks, the progesterone gel was administered beginning cycle Day 15 and every other day for a total of 6 doses. Endometrial biopsies were taken between Day 22 to 24 of the second treatment cycle. Hormone levels were measured at baseline, 6 weeks after beginning estrogen treatment, prior to beginning progesterone, and on Day 24 of the second treatment cycle.

Hormone	Baseline	6 weeks on Premarin	Day 24, 2nd treat. cycle
Estradiol (pg/ml)	27.5 ± 18.5	105.9 ± 38.4	100.9 ± 52.4
Progesterone (ng/ml)	0.36 ± 0.15	0.42 ± 0.15	3.81 ± 3.03

Results to date show 80% of women had bleeding after administration of the progesterone gel. Endometrial biopsy results will be presented. There was no significant change in the psychometric profiles of the subjects after the progesterone gel. Side effects were minimal and the subjects tolerated the vaginal gel well.

The bioadhesive vaginal progesterone gel is an effective mode of progesterone administration. The low peripheral levels which are achieved are associated with minimal side effects and good tolerance.

198

NOVEL REGULATION OF OVIDUCTAL GLYCOPROTEIN BY HUMAN CHORIONIC GONADOTROPIN IN MUCOSAL CELL CULTURES. T. Sun*, Z.M. Lei* and Ch.V. Rao. Dept. of Ob/Gyn, University of Louisville, Louisville, KY 40292.

Bovine uterus, like human uterus, contains luteinizing hormone (LH) / human chorionic gonadotropin (hCG) receptors. These findings led us to hypothesize that bovine oviduct, like human oviduct, also contains LH/hCG receptors and that LH may regulate the synthesis of oviductal glycoprotein (OGP). The present study investigated this hypothesis. Western blotting with a polyclonal receptor antibody raised against a synthetic N-terminus amino acid sequence of 15-38, detected 80 and 50 kDa LH/hCG receptor proteins in cultured mucosal cells. Ligand blotting demonstrated that these two proteins are also capable of binding ^{125}I-hCG and that this binding was inhibited by excess unlabeled hCG. To determine whether LH can regulate OGP, we cultured mucosal cells isolated from follicular phase ampullary segments of oviduct, in the presence or absence of highly purified hCG (CR-127, 14,900 IU/mg), used as a surrogate hormone for LH. Northern blotting with bovine OGP cDNA demonstrated that culturing with 10 ng/ml hCG resulted in a progressive increase in 2.3 kb OGP mRNA transcript levels with a peak at 3 days. Western blotting with a monoclonal anti bovine OGP antibody demonstrated that treatment with 10 ng/ml hCG resulted in a parallel increase in cellular levels of 95 kDa OGP. The increase at 3 days of culture was about 100% for both mRNA and protein of OGP. Both OGP mRNA and protein levels decreased after the 3rd day of culture and that this decrease was more rapid for protein than for mRNA. Mucosal cells from fimbriae also contain OGP mRNA transcripts and as in mucosal cells from ampulla, the transcript levels increased after treatment for 3 days with 10 ng/ml hCG as compared with control. In summary, we demonstrate for the first time that OGP, which is considered an estrogen regulated protein thus far, is also regulated in vitro by LH. Since this protein plays a pivotal role in fertilization of gametes and embryo development and that relatively high LH levels are also present when these events occur, we suggest that LH may directly regulate these events in oviduct.