109. EFFECT OF LONG-TERM PROGESTIN TREATMENT ON ENDOMETRIAL VASCULATURE IN NORMAL CYCLING MICE

B. Heryanto[1], Jane E. Girling[1], N. Patel[2] and P.A.W. Rogers[1]
[1]Centre for Women's Health Research, Monash University, VIC 3168; [2]Sugen Inc., East Grand Ave, San Francisco, CA 94080-4811, USA.

Although studies have shown that progestin-only contraception causes structural changes in endometrial vasculature, the precise mechanism leading to breakthrough bleeding has not been elucidated. The aim of this study was to develop a mouse model to investigate the effects of long-term progestin-only exposure on endometrial vascular structure. A silastic implant containing either medroxy progesterone acetate (MPA) or norgestrel (LNG) was inserted subcutaneously into normal cycling mice. Mice were dissected after 1, 2, 3 or 6 w. Endometrial vascular profiles were identified using a monoclonal antibody against mouse CD31. Endometrial vascular density was significantly increased after 1 w of MPA (482 ± 40.2 vessels/mm^2) or LNG (440 ± 26.5 vessels/mm^2) treatment in comparison to normal cycling mice (293 ± 10.5 vessels/mm^2); the increased density was sustained over 2, 3 and 6 w of treatment. Both MPA and LNG increased stromal cell density after 1 w of treatment (MPA: 13813 ± 1450 cells/mm^2, LNG: 11727 ± 851 cells/mm^2) in comparison to normal cycling mice (8256 ± 928 cells/mm^2); however, only MPA maintained this increased density over 2, 3 and 6 w of treatment. There was no significant change in the ratio of vascular density to stromal cell density between treated and normal cycling mice. Vascular endothelial growth factor (VEGF) immunostaining in luminal epithelium was significantly increased after 1, 2, 3 and 6 w of MPA or LNG treatment in comparison to normal cycling mice. VEGF immunostaining in stroma was only significantly increased from normal cycling mice after 6 of progestin treatment. There was no significant difference in VEGF immunostaining in glandular epithelium. These results demonstrate that one week of progestin-only treatment is sufficient to cause significant changes in the endometrium of normal cycling mice, including changes in endometrial vasculature. This mouse model may facilitate further investigations into breakthrough bleeding due to long-term progestin use.

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