THE EFFECTS OF PROGESTERONE ON ENDOMETRIAL ANGIOGENESIS IN PREGNANT AND OVARIECTOMISED MICE

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In mice, early pregnancy is associated with an increase in endometrial angiogenesis in preparation for the implanting embryo. The aims of this study were to quantify endometrial angiogenesis in pregnant mice and to investigate the role of progesterone in promoting endothelial cell (EC) proliferation in ovariectomised mice; we hypothesised that EC proliferation would increase with increasing plasma progesterone concentrations in pregnant mice and that progesterone would stimulate EC proliferation in ovariectomised mice, but only following oestrogen priming. Uterine tissue from CBA x C57 mice was collected on Days 1–4 of pregnancy (n = 4–5/day) when circulating progesterone concentrations are increasing but before implantation occurs. Prior to dissection, mice were injected with BrdU enabling proliferating EC to be quantified and localised within blood vessels by CD31/BrdU double staining immunohistochemistry. There was a significant increase in proliferating EC (Kruskal-Wallis statistic (KW) = 17.1, P = 0.002) on Day 3 of pregnancy (Days 1 and 2, no proliferation; Day 3,126.6 ± 45.6 proliferating EC/mm^2 (mean ± s.e.)), when plasma progesterone also began to increase (as measured by radioimmunoassay). To determine if the EC proliferation was due to progesterone, a second experiment was performed on ovariectomised mice. One group of mice (n = 6) were treated with a single injection of 100 ng of estradiol on day eight after ovariectomy, followed by a day with no treatment and three consecutive daily injections of 1 mg progesterone. Other groups were treated with either the vehicle (n = 5), estradiol (n = 4) or progesterone (n = 5) injections only. All groups were dissected following BrdU injection on Day 13 following ovariectomy. Unexpectedly, mice treated with progesterone only had the highest amount of EC proliferation (114.7 ± 30.9 proliferating EC/mm^2); oestrogen priming was not required and actually significantly reduced progesterone induced EC proliferation (44.8 ± 15.5 proliferating EC/mm^2; KW = 13.8, P = 0.008). We are currently investigating the interaction between progesterone and VEGF using immunohistochemistry and inhibition studies.

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