Effect of luteinising hormone surge on regulation of vascular endothelial growth factor and extracellular matrix-degrading proteinases and their inhibitors in bovine follicles.

The aim of the present study was to evaluate the pattern of regulation of vascular endothelial growth factor (VEGF)-A (isoforms 121, 165, 189), VEGF receptor tyrosine kinases (VEGF-R1 and VEGF-R2), matrix metalloproteinase (MMP)-1, MMP-2, MMP-14, MMP-19, tissue-specific inhibitor of metalloproteinases (TIMP)-1, TIMP-2, tissue plasminogen activator (tPA), urokinase plasminogen activator (uPA), urokinase plasminogen activator receptor (uPAR) and plasminogen activator inhibitor-1 (PAI-1) in time-defined follicle classes before (0 h) and after the application of gonadotrophin-releasing hormone (GnRH). Bovine ovaries containing periovulatory follicles or new corpora lutea (CL; Days 1–2) were collected 0, 4, 10, 20 and 25 h (follicles) or 60 h (CL) after the injection of GnRH. Transcripts of VEGF isoforms (VEGF121,VEGF165,VEGF189) were upregulated 4 h after GnRH injection (during the luteinising hormone (LH) surge) and decreased thereafter to lowest levels around ovulation. AllVEGF isoforms and their receptors were upregulated again after ovulation. The VEGF peptide concentration in follicular fluid decreased 20 h after GnRH injection, followed by an increase in follicles 25 h after GnRH. Expression of MMP-1 mRNA increased rapidly 4 h after GnRH injection and remained high.
during the entire experimental period. In contrast, MMP-19 mRNA increased significantly only after ovulation. Expression of TIMP-1 mRNA increased 4 h after GnRH and again after ovulation. Expression of tPA mRNA increased 4 h after GnRH and remained high during the entire experimental period, whereas expression of uPA transcripts increased significantly only after ovulation. Both uPAR and PAI-1 mRNA levels increased in follicles 4 h after GnRH and again after ovulation. The amount of MMP-1 protein (immunolocalisation) increased in follicles 10 h after GnRH: additional staining was observed in the granulosa cell layer. In conclusion, the temporal and spatial pattern of regulation of VEGF and extracellular matrix-degrading proteinases during periovulation suggests they are important mediators of the LH-dependent rupture of bovine follicles and for early CL formation (angiogenesis).

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