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Domestic Animal Endocrinology 28 (2005) 162–171
DOMESTIC ANIMAL ENDOCRINOLOGY
www.journals.elsevierhealth.com/periodicals/dae

Changes in bovine luteal progesterone metabolism in response to exogenous prostaglandin $F_{2\alpha}$

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Received 16 March 2004; accepted 27 July 2004

Abstract

An experiment was conducted to determine the effect of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) on luteal synthesis of progesterone (P_4) and related progestins. Sixteen beef heifers were assigned in equal numbers to four groups in a 2 × 2 factorial arrangement of treatments. The experiment consisted of two levels of $PGF_{2\alpha}$ analog (0 and 500 μg) and two levels of time (4 and 24 h after injection) of corpus luteum collection. All heifers were injected intravenously with saline (2 ml) or $PGF_{2\alpha}$ (cloprostenol) on day 8 of the estrous cycle (estrus = day 0). Jugular blood was collected at 0, 1, 2, 3, 4 and 20, 21, 22, 23, and 24 h after injection. Resulting sera were analyzed for P_4 by use of radioimmunoassay. Luteal tissue was analyzed by gas chromatography/mass spectrometry for P_4, 20β-hydroxyprogesterone, pregnenolone, and allopregnanolone (3β-hydroxy-5α-pregnan-20-one). Treatment with $PGF_{2\alpha}$ reduced serum concentrations of P_4 as early as 1 h after injection ($P < 0.005$) and steroid levels remained low over 24 h. Similarly, administration of $PGF_{2\alpha}$ caused a decline in luteal P_4 ($P < 0.005$), 20β-hydroxyprogesterone ($P < 0.10$), and pregnenolone ($P < 0.05$). In contrast, treatment with $PGF_{2\alpha}$ caused an increase in luteal allopregnanolone over time (time × treatment interaction; $P < 0.05$). These data are interpreted to suggest that $PGF_{2\alpha}$ promotes conversion of P_4 to the metabolite allopregnanolone.

Keywords: Bovine; Progesterone; Allopregnanolone; Prostaglandin $F_{2\alpha}$; Corpus luteum

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doi:10.1016/j.domaniend.2004.08.001

1. Introduction

Prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) has been identified as the natural luteolysin in a number of mammalian species [1]. Administration of $PGF_{2\alpha}$ to pseudopregnant rats has been shown to cause a rapid reduction in luteal and blood concentrations of progesterone [2,3]. In the rat, this $PGF_{2\alpha}$-induced decrease in luteal function is accompanied by an increase in the activity of 20α-hydroxysteroid dehydrogenase [4,5]. This enzyme converts progesterone to 20α-hydroxyprogesterone (20α-hydroxy-4-pregnen-3-one), a metabolite with one-third to one-fifth the biological activity of progesterone as determined by the Clauberg bioassay [6]. Thus, in the rat, the $PGF_{2\alpha}$-induced reduction in blood levels of progesterone may be due, at least in part, to luteal tissue accumulation of 20α-hydroxyprogesterone. Administration of $PGF_{2\alpha}$ to ruminant species such as the cow or ewe during the mid-luteal phase of the estrous cycle causes a similar reduction in luteal and blood concentrations of progesterone [7,8]. However, changes in progesterone synthesis and metabolism that occur in response to $PGF_{2\alpha}$ during luteal regression in these species are not completely understood. Although the bovine corpus luteum can apparently produce negligible quantities of 20α-hydroxyprogesterone, it primarily synthesizes 20β-hydroxysteroid dehydrogenase (20β-HSD), which converts progesterone to 20β-hydroxyprogesterone (20β-hydroxy-4-pregnen-3-one) [9,10]. This metabolite has even less biological activity than 20α-hydroxyprogesterone as determined by the Clauberg bioassay [6]. Nevertheless, it was hypothesized that administration of $PGF_{2\alpha}$ to cows would stimulate luteal 20β-HSD resulting in increased luteal concentrations of 20β-hydroxyprogesterone. To test this hypothesis the present experiment was conducted to examine time-course changes in bovine luteal tissue and serum concentrations of progestins in response to exogenous $PGF_{2\alpha}$.

2. Methods and materials

2.1. Treatment

Sixteen beef heifers were assigned randomly in equal numbers to one of four groups in a 2×2 factorial arrangement of treatments. Heifers were observed twice daily for behavioral estrus, which was detected by use of a vasectomized bull. The first day of detected estrus was considered to be day 0 of the estrous cycle. On day 8 of the estrous cycle, a blood sample was collected from the jugular vein in order to establish baseline progesterone levels. Heifers were then immediately given an i.v. injection of either saline ($n = 8$) or 500 μg of $PGF_{2\alpha}$ analog (cloprostenol, Bayer Corporation, Shawnee Mission, KS; $n = 8$). Additional blood samples were collected at 1, 2, 3, and 4 h after injection from four control and four treated heifers. At 4 h after injection, the corpus luteum was removed from these control and treated animals by colpotomy [11]. Blood samples were also collected from the remaining eight heifers (control, $n = 4$; treated, $n = 4$) at 20, 21, 22, 23, and 24 h after injection. At 24 h after injection, the corpus luteum was removed from these eight remaining heifers. All experimental procedures involving animals were performed in accordance with the Institutional Animal Care and Use Committee guidelines at Oregon State University.