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Changes in steady-state concentrations of messenger ribonucleic acids in luteal tissue during prostaglandin F2α induced luteolysis in mares

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Abstract

Transvaginal ultrasound-guided luteal biopsy was used to evaluate the effects of prostaglandin (PG)F2α on steady-state concentrations of mRNA for specific genes that may be involved in regression of the corpus luteum (CL). Eight days after ovulation (Hour 0), mares ($n = 8$/group) were randomized into three groups: control (no treatment or biopsy), saline + biopsy (saline treatment at Hour 0 and luteal biopsy at Hour 12), or PGF2α + biopsy (5 mg PGF2α at Hour 0 and luteal biopsy at Hour 12). The effects of biopsy on CL were compared between the controls (no biopsy) and saline + biopsy group. At Hour 24 (12 h after biopsy) there was a decrease in circulating progesterone in saline group to 56% of pre-biopsy values, indicating an effect of biopsy on luteal function. Mean plasma progesterone concentrations were lower ($P < 0.001$) at Hour 12 in the PG group compared to the other two groups. The relative concentrations of mRNA for different genes in luteal tissue at Hour 12 was quantified by real time PCR. Compared to saline-treated mares, treatment with PGF2α increased mRNA for cyclooxygenase-2 (Cox-2, 310%, $P < 0.006$), but decreased mRNA for LH receptor to 44% ($P < 0.05$), steroidogenic acute regulatory protein to 22% ($P < 0.001$), and aromatase to 43% ($P < 0.1$) of controls. There was no difference in mRNA levels for PGF2α receptor between PG and saline-treated groups. Results indicated that luteal biopsy alters subsequent luteal function. However, the

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biopsy approach was effective for collecting CL tissue for demonstrating dynamic changes in steady-state levels of mRNAs during PGF2α-induced luteolysis. Increased Cox-2 mRNA concentrations suggested that exogenous PGF2α induced the synthesis of intraluteal PGF2α. Thus, the findings are consistent with the concept that an intraluteal autocrine loop augments the luteolytic effect of uterine PGF2α in mares.

Keywords: Corpus luteum; Gene regulation; Mare; Progesterone

1. Introduction

Prostaglandin (PG)F2α is considered to be the luteolysin in most mammals (reviewed in Arosh et al., 2004). Surgical removal of the uterus prolongs the life span of the corpus luteum (CL) in sheep, cattle, pigs, horses and some laboratory animals, indicating that luteolytic PGF2α is of uterine/endometrial origin in these species (Wiltbank and Casida, 1956; Anderson et al., 1961; Moor and Rowson, 1966; Ginther and First, 1971). Endometrial PGF2α reaches the CL by local, systemic, or a combination of both routes depending on the species (Bonnin et al., 1999). In mares, several experimental approaches have indicated that the pathway from uterus to ovaries for uterine-induced luteolysis is systemic (reviewed in Ginther, 1998). In contrast, in primates including women uterine PGF2α is not the initiator of luteolysis as hysterectomy does not prolong the lifespan of CL (Neill et al., 1969; Beling et al., 1970), and it has been postulated that autocrine and paracrine actions of intraluteal PGF2α may be involved in initiation of luteolysis (Arosh et al., 2004). The CL of primates has the capacity to synthesize PGs, and luteal PG synthesis increases near the time of normal luteolysis (reviewed in Wiltbank and Ottobre, 2003). Luteal PG production also has been demonstrated in a number of species in which uterine PGF2α has a primary role in luteolysis (Wiltbank and Ottobre, 2003). In this regard, production of PGF2α by luteal tissue has been reported in cattle (Milvae and Hansel, 1983), sheep (Rexroad and Guthrie, 1979), pigs (Guthrie et al., 1978) and horses (Watson and Sertich, 1990). Luteal PGF2α increases after treatment with PGF2α (Rexroad and Guthrie, 1979; Guthrie and Rexroad, 1980; Diaz et al., 2000) consistent with a role for luteal PGF2α in regression of the CL in cattle, sheep and pigs but apparently has not been studied in horse.

The biochemical events occurring during PGF2α-induced luteolysis have not been fully described. One of the hallmarks of luteolysis is a decrease in luteal progesterone production with an associated decrease in expression of steroidogenic acute regulatory protein (StAR). StAR facilitates the rate-limiting step in steroidogenesis, transport of cholesterol from the outer to inner mitochondrial membrane (Watson et al., 2000). After PGF2α treatment there is a decrease in mRNA and protein for StAR that corresponds closely to the PGF2α-induced decrease in circulating progesterone (Juengel et al., 1995; Tsai et al., 2001). In contrast, treatment with PGF2α increases a key enzyme in the PG biosynthesis pathway, cyclooxygenase (Cox) (Tsai and Wiltbank, 1997, 1998). The Cox enzymes catalyze the conversion of arachidonic acid to PGH2 which is the first committed step in PG synthesis (reviewed in Wiltbank and Ottobre, 2003). Attention has focused on the Cox-2 isoform of the enzyme because it