Available online at www.sciencedirect.com
SCIENCE DIRECT®
Domestic Animal Endocrinology 28 (2005) 172–189
DOMESTIC ANIMAL ENDOCRINOLOGY
www.journals.elsevierhealth.com/periodicals/dae

Acquisition of luteolytic capacity involves differential regulation by prostaglandin F2α of genes involved in progesterone biosynthesis in the porcine corpus luteum

Francisco J. Diaz, Milo C. Wiltbank*

Endocrinology-Reproductive Physiology Program, Department of Dairy Science, University of Wisconsin-Madison, 1675 Observatory Drive, Madison, WI 53706-1284, USA

Received 14 April 2004; accepted 10 August 2004

Abstract

Luteolytic capacity is defined as the ability of corpora lutea (CL) to undergo luteolysis after prostaglandin (PG) F2α treatment. The mechanisms causing acquisition of luteolytic capacity are not yet identified but CL without luteolytic capacity have PGF2α receptors and respond to PGF2α with some changes in gene expression. Inhibition of progesterone biosynthesis is a key feature of luteolysis and therefore we postulated that genes involved in progesterone biosynthesis would be regulated by PGF2α differently in CL with or without luteolytic capacity. Gilts on day 9 after estrus (lack luteolytic capacity) or day 17 of pseudopregnancy (with luteolytic capacity) were treated with saline or a PGF2α analog (cloprostenol) and CL were collected 0.5 (Experiment I) or 10 h (Experiment II) later. In Experiment III, large luteal cells from CL on day 9 or 17 were cultured for 1, 12 and 24 h with or without PGF2α. PGF2α decreased LDL receptor mRNA (27%), steroidogenic acute regulatory protein (StAR) mRNA (41%), StAR protein (75%), LH receptor mRNA (55%), and LH receptor protein (45%) at 10 h after treatment in day 17 but not day 9 CL. PGF2α increased DAX-1 mRNA at 0.5 h (43%) and 10 h (46%) after PGF2α in day 17 but not day 9 CL but decreased 3βHSD mRNA (∼20% at 10 h) in both days 9 and 17 CL. In vitro, PGF2α decreased StAR mRNA at 12 h only in day 17 luteal cells; however, continuous treatment with PGF2α for 24 h decreased StAR mRNA in both days 9

* Corresponding author. Tel.: +1 608 263 9413; fax: +1 608 263 9412.
E-mail address: wiltbank@calshp.cals.wisc.edu (M.C. Wiltbank).

0739-7240/$ – see front matter © 2004 Published by Elsevier Inc.
doi:10.1016/j.domaniend.2004.08.002

and 17 luteal cells. Thus, luteolytic capacity involves a critical change in responsiveness of DAX-1, StAR, and LH receptor to PGF2α that results in inhibition of luteal progesterone biosynthesis.

Keywords: Corpus luteum; Prostaglandin; Porcine; Luteolysis

1. Introduction

In many species, including swine, luteolysis is initiated by secretion of PGF2α from the uterus. In pigs, a single treatment with PGF2α causes luteolysis in pregnant, hysterectomized, or cycling animals after day 13 of the cycle but not prior to this time [1,2]. Thus, before day 13 porcine CL lack luteolytic capacity. Lack of luteolytic capacity prior to day 13 in pigs is not due to an absence of PGF2α receptors (FP receptors) on luteal cells [3,4] or lack of physiological response to PGF2α as indicated by similar PGF2α-induced decreases in mRNA for 3-β-hydroxysteroid dehydrogenase (3βHSD) and FP receptor in CL before or after acquisition of luteolytic capacity [5,6]. However after acquisition of luteolytic capacity, there is a dramatic change in regulation of several biosynthetic pathways by PGF2α such as luteal production of endothelin-1 (ET-1) [7], monocyte chemoattractant protein-1 (MCP-1) [8], intraluteal PGF2α [5,6], intraluteal estradiol production and signaling [9] and progesterone [6].

Two of the hallmark features of luteolysis are the rapid decrease in progesterone production by the CL [6,10,11] and programmed luteal cell death [12]. The progesterone biosynthesis pathway appears to be differentially regulated by PGF2α in CL with or without luteolytic capacity [2,6]; however, the mechanisms for this differential regulation remain undefined. Progesterone biosynthesis is regulated at multiple points by PGF2α including: inhibition of the LH stimulatory pathway, steroidogenic enzymes, and cholesterol transport. In vivo treatment with PGF2α decreases protein for the LH receptor in the pig CL [13,14]. In addition, the finding that hypophysectomy leads to a rapid decrease in progesterone secretion from aged CL [15] is consistent with the idea that inhibition of the LH stimulatory pathway may be important for changes in progesterone production during luteolysis. Maximal production of luteal progesterone is dependent upon delivery of exogenous cholesterol from lipoprotein. In pigs, LDL is the major circulating lipoprotein and the most stimulatory for luteal progesterone production [16]. Another key part of the cholesterol transport system is the movement of cholesterol from the cytoplasm to the inner mitochondrial membrane apparently mediated, at least in part, by steroidogenic acute regulatory protein (StAR) [17–21]. StAR protein is synthesized as a 37 kDa precursor that is processed to a 30 kDa mature form. Treatment with PGF2α inhibits both mRNA and protein for StAR in CL and luteal cells from many species [22–25]. In the rat, the StAR gene is regulated by two different transcriptional pathways. DAX-1, a member of the orphan nuclear receptor family and c-fos, a member of the AP-1 family of transcription factors, both appear to negatively regulate StAR mRNA in rat CL [25,26]. Thus, regulation of PGF2α-induced inhibition of cholesterol transport pathways, such as LDL receptor and StAR, as well as PGF2α regulation of transcription factors that control these pathways may be critical mechanistic aspects of the process of acquisition of luteolytic capacity.