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Short communication

Leptin infusion during the early luteal phase in ewes does not affect progesterone production

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Abstract

Infusion of leptin during the ovine follicular phase has been shown to increase progesterone secretion during the subsequent luteal phase. In this study, we have assessed the effects of infusing leptin during the early luteal phase. Infusion of leptin (2.5 μg/h) into the ovarian artery of ewes with ovarian autotransplants ($n = 5$) on day 3 of the luteal phase for 12 h did not affect progesterone estradiol or LH concentrations compared to control ewes ($n = 5$). These results suggest no direct effect of leptin on ovarian function at this stage of the estrous cycle.

Keywords: Corpus luteum; LH; Sheep

1. Introduction

Numerous studies have reported effects of leptin on steroidogenesis in a number of in vitro culture systems, establishing the hypothesis that leptin may have a direct role in controlling ovarian function, as well as its central action on the hypothalamo–piuitary axis

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[1]. More recent studies have demonstrated an effect on ovarian steroidogenesis of infusing physiological quantities of either recombinant ovine [2] or recombinant human [3] leptin. In one study [2], infusion of leptin during the follicular phase caused an inhibition of estradiol during the infusion period followed by an increase in progesterone during the subsequent luteal phase. Thus, leptin-induced effects on the developing ovulatory follicle can influence subsequent luteal function. Furthermore, leptin receptors have been detected on the bovine corpus luteum [4].

The aim of the present study was to determine whether leptin can act directly on the developing corpus luteum to stimulate progesterone secretion.

2. Materials and methods

The study was undertaken in 12 mature Finn-Merino ewes with ovarian autotransplants [5] during the breeding season. Initiation and synchronisation estrous cycles was achieved with two injections of the $PGF_{2\alpha}$ analogue cloprostenol (125 μg i.m. Estrumate; Schering-Plough Animal Health, Harefield, UK), given 17 days apart.

Ewes were randomly assigned to receive a continuous intravenous infusion of either saline (3 ml/h; control group, $n = 6$) or recombinant human leptin (supplied by Professor J.W. Goding, Monash University Medical School, Australia) (2.5 μg/h; treatment group; $n = 6$). This dose was selected, based on results from a previous study [2], to generate concentrations of leptin within the physiological range. Animals were infused on day 3 of the estrous cycle, directly into the carotid ovarian artery for 12 h.

Jugular blood samples were taken twice daily until day 12 of the estrous cycle with additional samples collected at 10 min intervals from hour 4 to hour 8 of infusion for LH analysis. During the infusion period ovarian venous blood samples were collected at hourly intervals. All samples were centrifuged at $3000 \times g$ for 20 min at 4 °C and plasma stored at −20 °C. Following the infusion period, animals were scanned daily (real time Aloka 500 ultrasound scanner with a linear 7.5 MHz transducer probe, Dynamic Imaging, Livingston, UK) to confirm the presence of a corpus luteum.

Progesterone concentrations were measured by radioimmunoassay [6] with a sensitivity of 0.11 ng/ml and intra- and inter-assay coefficients of variation of 8.8 and 9.2%. Leptin concentrations were determined in both ovarian and jugular plasma samples by radioimmunoassay [7] (antibody supplied by Dr. D Blache, University of Perth, Australia) with a sensitivity of 0.37 ng/ml and intra- and inter-assay coefficients of variation of 7.4 and 8.4%. LH concentrations were determined by radioimmunoassay [8] with a sensitivity of 0.13 ng/ml and the intra- and inter-assay coefficients of variation of 6.0 and 7.5%. Plasma samples collected from ovarian venous blood were assayed for estradiol by double antibody radioimmunoassay [9] with a sensitivity of 12.1 pg/ml and the intra- and inter-assay coefficients of variation of 12.9 and 13.1%.

Progesterone, estradiol and leptin concentrations were analysed by repeated sample analysis of variance on data that had been log-transformed using the general linear model (SPSS 11.0 software) with data partitioned on the basis of treatment and time. The characteristics of pulsatile LH secretion were determined using the Munro Pulse analysis programme (Zaristow software, Haddington, UK). An LH pulse was defined as a value that was greater