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Plasma Levels of Progesterone and Cortisol after ACTH Administration in Lactating Primiparous Sows

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Tsuma VT, Einarsson S, Madej A, Forsberg M, Lundeheim N: Plasma levels of progesterone and cortisol after ACTH administration in lactating primiparous sows. Acta vet. scand. 1998, 39, 71-76. – The effect of adrenocorticotropic hormone (ACTH) administration on progesterone and cortisol concentrations was determined in lactating primiparous sows. Physiological saline and 50 IU ACTH were administered on days 20 and 21 of lactation at 0900 hours via an indwelling jugular catheter. Blood samples for hormone analysis were collected via indwelling jugular catheters every 15 min (0800 to 1200 hours) and every 60 min (1300 to 1500 hours). Saline administration had no effect on progesterone nor cortisol concentrations in the lactating sows. Progesterone and cortisol concentrations increased ($p<0.001$) within 15 min after ACTH administration. Progesterone and cortisol concentrations peaked ($p<0.01$) within 45 min and had returned to pretreatment values within 120 min after ACTH treatment.

lactation; stress; hormone.

Introduction

Serum glucocorticoids increase dramatically after stress (*Becker et al.* 1985). Stressors activate the hypothalamic-pituitary-adrenal (HPA) axis, resulting in the release of adrenocorticotropic hormone (ACTH) which stimulates glucocorticoid secretion from the adrenal glands of stressed animals (*Dantzer & Mormede* 1983). During stress, a rise in plasma progesterone concentrations has also been observed in white-tailed deer (*Wesson et al.* 1979), calves (*Cooper et al.* 1995) and even in pregnant pigs (*Tsuma et al.* 1996). In white-tailed deer, it was proposed that increased progesterone during stress was from the adrenals in response to endogenous ACTH released during stress (*Plotka et al.* 1983). Adrenal stimulation induced by administration of ACTH has been shown to elevate progesterone in various animals (cattle: *Gwazdauskas et al.* 1972, sheep: *De Silva et al.* 1985, *Sheikheldin et al.* 1988) including ovariectomized sows (*Scholten & Liptrap* 1978), prepuberal (*Fonda et al.* 1984) and pregnant (*Sulong* 1985) gilts. The aim of the present study was to evaluate the effect of ACTH administration during lactation on progesterone and cortisol concentrations in primiparous sows.

Materials and methods

Three lactating crossbred (Swedish Landrace × Swedish Yorkshire) primiparous sows were used. The sows were housed in individual pens at the Department of Obstetrics and Gynaecology, and fed according to the Swedish breeding stock standard (*Göransson* 1984). All sows

were fitted with jugular vein catheters under general anaesthesia (*Rodriguez & Kunavongkrit* 1983). Lactating sows were fitted with jugular vein catheters on day 14 of lactation. The sows nursed 10 piglets each. Two ml physiological saline was administered at 0900 hours on day 20 of lactation via the indwelling jugular catheter. On the next day (day 21 of lactation) 50 IU ACTH (Acton prolongatum®, Ferring AB, Sweden) was administered at 0900 hours via the indwelling jugular catheter.

The experimental design was approved by The Ethical Committee for Animal Experiments, Uppsala, Sweden. On the day of the experiment, blood was collected every 15 min from 0800 to 1200 hours, and then every 60 min until 1500 hours. Blood samples were collected in heparin tubes, centrifuged and plasma collected and stored at –20 °C until assay. All samples were analysed for concentrations of progesterone and cortisol .

Progesterone concentrations were determined by an enzyme immunoassay (Amerlite®, Kodak Clinical Diagnostics Ltd., Amersham, England). The kit was used according to the manufacturer's instructions with modifications as described by *Rojkittikhun et al.* (1993). Sensitivity of the assay was 0.5 nmol/l. The intra-assay coefficient of variation, calculated from the precision profile of 5 assays, was below 2.1% for concentrations of progesterone between 2.0 and 160 nmol/l. The corresponding inter-assay coefficients of variation were 7.5% and 11.6% respectively for low and high assay controls.

Plasma cortisol was determined by a luminescence immunoassay (Amerlite®, Kodak Clinical Diagnostics Ltd., Amersham, England) according to a method previously described (*Magnusson et al.* 1994). The intra-assay coefficient of variation, calculated from the precision profiles of 5 assays, was below 9.8% for concentrations of cortisol between 11.6 and 1125.0 nmol/l. The corresponding inter-assay coefficients of variation for 3 quality control samples were 20.7% (mean = 13 nmol/l), 14.9% (mean = 125 nmol/l) and 18.3% (mean = 389 nmol/l).

Data were examined by analysis of variance using the General Linear Model procedure of Statistical Analysis System (*SAS Institute Inc.* 1987). Probabilities less than 0.05 were considered significant.

Results

Physiological saline given intravenously to the lactating sows did not alter progesterone nor cortisol secretion, which ranged from 0.2 to 0.4 nmol/l and from 20 to 54.7 nmol/l, respectively (Fig. 1). Plasma progesterone concentrations increased ($p<0.001$) within 15 min after ACTH administration in the lactating sows (Fig. 2). Progesterone concentrations ranged from 0.3 to 0.8 nmol/l prior to ACTH administration, and increased to maximum levels of 3.7 nmol/l within 45 min after ACTH administration. Progesterone concentrations returned to basal levels within 120 min after ACTH administration. Plasma cortisol concentrations increased from 47.7 to 198.3 nmol/l ($p<0.001$) within 15 min after ACTH administration in the lactating sows. Cortisol concentrations rose to a peak, i.e. 243.3 nmol/l, 30 min after ACTH administration (Fig. 2), and returned to pre-treatment levels within next 90 min.

Discussion

In the present study, the dose of ACTH was chosen according to suggestion by *Hennessy et al.* (1988) who reported that 50 IU of ACTH provided maximal stimulation of the adrenal cortex and reflected the potential response of the individual pig. Adrenal release of cortisol secretion following ACTH stimulation is well

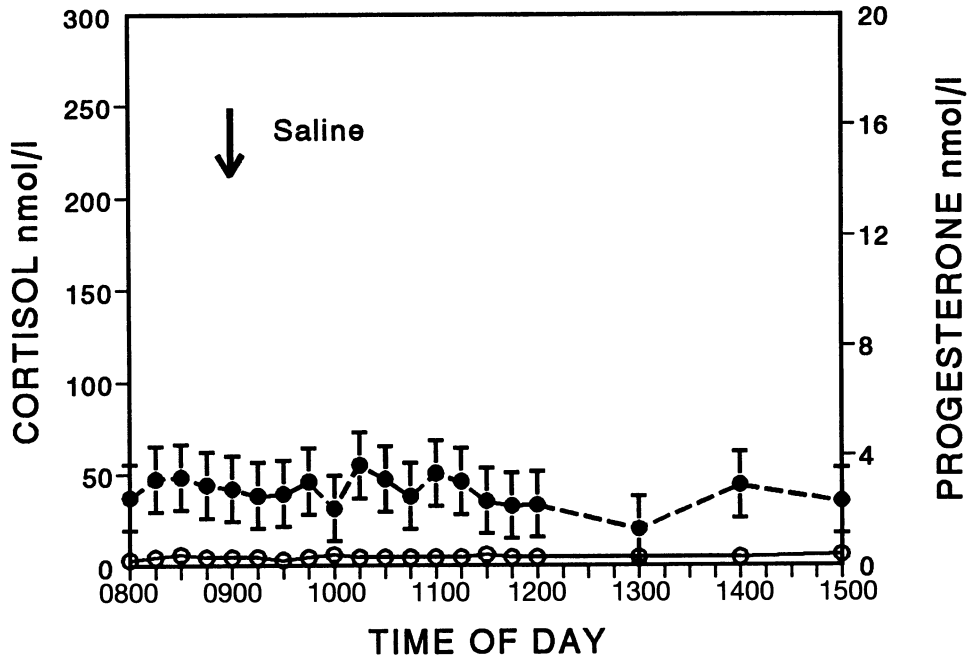

Figure 1. Cortisol (●——●) and progesterone (○——○) concentrations (LSmeans ± SEM) in lactating sows given physiological saline intravenously. Note: In the case of progesterone standards errors were 0.2 nmol/l.

established in the pig (*Rafai & Fodor* 1980, *Baldi et al.* 1989). The adrenal response to ACTH challenge may be influenced by the experiences of an individual during the preceding few weeks (*Mendl et al.* 1992). An adrenal previously exposed to elevated endogenous ACTH, for example through chronic stress, has been found to have enhanced adrenocortical reactivity to ACTH in pigs (*von Borrell & Ladewig* 1989).

Increased progesterone following ACTH administration has been shown in various animals (cattle: *Gwazdauskas et al.* 1972, sheep: *De Silva et al.* 1985, *Sheikheldin et al.* 1988). *Scholten & Liptrap* (1978) suggested that glucocorticoids and progesterone of adrenal origin may be involved in the onset of cystic ovaries in the sows. The increase in plasma progesterone concentration after ACTH injection on day 21 of lactation in the present study confirms previous results in lactating sows (*Benjaminsen & Lunaas* 1980). The adrenal cortex is the target tissue of ACTH, and therefore the ACTH-induced progesterone elevation in the present study, was likely from the adrenal glands. Plasma progesterone concentrations were low in the lactating sows in the current study, and there was no progesterone increase following saline administration. Progesterone is low during lactation in the pig as active luteal tissue is unlikely to be present (*Ash & Heap* 1975, *Duggan et al.* 1982, *Kunavongkrit et al.* 1982), and hence the ACTH-induced increase in progesterone concentration in lactating animals was most likely adrenal in origin. This conclusion is also supported by findings of *Fonda et al.* (1984). These authors found that ACTH treatment elevated progesterone concentrations only

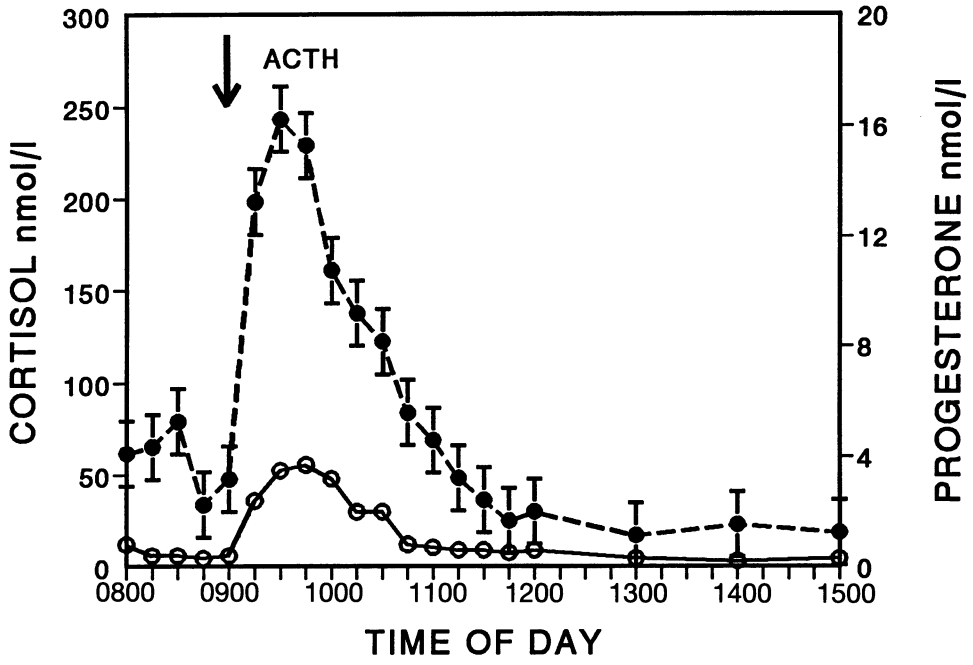

Figure 2. Cortisol (●——●) and progesterone (○——○) concentrations (LSmeans ± SEM) in lactating sows given ACTH intravenously. Note: In the case of progesterone standards errors were 0.2 nmol/l.

in ovariectomized gilts but not in gilts, which were both ovariectomized and adrenalectomized. Recently, *Bolaños et al.* (1997) reported that the adrenal gland could be an extra-ovarian source of progesterone during stress in Zebu cows.

In a previous study we observed an elevation in progesterone and cortisol concentrations during food deprivation in primiparous sows that were fasted during early pregnancy (*Tsuma et al.* 1996). Stress increases endogenous ACTH secretion, which in turn may stimulate adrenal production of hormones such as progesterone. The results in the present study indicate that in lactating sows, as in several domestic species, the adrenal gland may be a significant source of plasma progesterone, a factor which may be relevant in the interpretation of plasma hormone profiles during stress.

Acknowledgements

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Sammanfattning

Blodplasmakoncentrationerna av kortisol och progesteron efter ACTH injektion hos lakterande primipara suggor.

Effekten av en ACTH injektion på blodplasmakoncentrationerna av kortisol och progesteron bestämdes

hos lakterande suggor. Fysiologisk koksaltlösning och 50 IE ACTH injicerades klockan 09.00 på dag 20 respektive dag 21 av laktationen via en permanent inlagd jugularvenkateter. Blodprover för hormonanalyser uppsamlades via venkatetern var 15:e minut under perioden 08.00–12.00 och var 60:e minut under perioden 13.00–15.00. Koksaltinjektionen hade ingen inverkan på vare sig progesteron- eller kortisolkoncentrationerna. Progesteron- och kortisolkoncentrationerna steg ($p<0.001$) inom 15 minuter efter ACTH-injektionen. Progesteronkoncentrationen var högst ($p<0.01$) inom 45 minuter och hade återgått till ursprungsvärdena inom 120 min efter ACTH-behandlingen. Den högsta kortisolkoncentrationen uppmätes 45 minuter efter ACTH behandlingen och förhöjda kortisolkoncentrationer ($p<0.01$) uppmättes under sammanlagt 120 minuter.

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