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Human chorionic gonadotrophin in early gestation induces growth of estrogenic ovarian follicles and improves primiparous sow fertility during summer

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ABSTRACT

Reduced summer farrowing rates may be due to inadequate corpora luteal (CL) support. Porcine CL become dependent on LH from 12 d of pregnancy and the embryonic estrogen signal for maternal recognition of pregnancy (MRP) is initiated at about 11–12 d after insemination. We hypothesised that injection of the LH analogue human chorionic gonadotropin (hCG) would induce growth of estrogenic follicles and, by mimicking the signal for MRP and stimulating progesterone secretion, increase primiparous sow fertility. In Experiment 1, during a 28 d lactation 53 mixed parity sows were full-fed either throughout lactation (n = 16) or until 18 d and then feed restricted during the last 10 d of lactation (n = 36). At 12 d after mating restrict-fed sows were injected with 1000 IU hCG (n = 17) or were not injected (n = 19); the full-fed sows acted as non-treated positive controls. Transrectal ovarian ultrasound exams were performed on days 12, 16, 20, 24, and 28; blood samples were obtained on days 12, 14, and 15 for estradiol and progesterone assay. For Experiment 2, during the summer months primiparous sows received 1000 IU hCG 12 d after mating (n = 28) or were non-injected controls (n = 27). Pregnancy status was determined at 28 d and sows allowed to go to term to determine farrowing rates and litter sizes. In Experiment 1, injection of hCG increased ($P < 0.001$) follicle diameter and serum concentrations of estradiol ($P < 0.01$) and progesterone ($P < 0.05$). There were no effects of lactation feeding level on wean-estrus interval, farrowing rate or subsequent litter size. In Experiment 2, hCG injection was associated with a higher pregnancy rate ($P < 0.05$) and farrowing rate ($P < 0.08$). There was no effect on litter size. These data confirm that hCG stimulates growth of estrogenic follicles and CL function, and improves primiparous sow fertility during the summer months.

1. Introduction

The underlying cause of seasonal infertility of sows must involve an adverse effect on corpora luteal (CL) function. The net effect is that the CL of a sub-population of sows become more sensitive to adverse environmental conditions. The trigger for seasonal infertility in these susceptible sows is controversial, with arguments made for each of elevated temperatures and long/decreasing photoperiods, or more likely both (Prunier et al., 1994). It is established that higher temperatures will reduce appetite and that reduced lactation nutrient intakes are associated with reduced sow fertility (eg. Aherne and Kirkwood, 1985; Kirkwood et al., 1990). Reduced lactation nutrient intakes results in an

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attenuated preovulatory LH surge (Baidoo et al., 1992) and in lower circulating basal gonadotrophin concentrations in early gestation (Kirkwood et al., 1990). The significance of an attenuated LH surge for sows is not known but an adverse effect on luteinization of the ovulated follicles was previously suggested (Aherne and Kirkwood, 1985). In support of this suggestion, short lactations and exogenous growth hormone are also associated with both a smaller LH surge and reduced sow or gilt fertility (Kirkwood et al., 1984, 1988). The role of reduced basal LH concentrations in seasonal infertility is also not known. However, lower post weaning serum LH concentration may limit ovarian follicle growth and so extend the wean-to-estrus interval since LH is the primary stimulus of follicle growth, and consequent estrogen production, from about the 4 mm to ovulatory size (Driancourt et al., 1995). We are not aware of data concerning the impact of nutrient restriction during lactation on ovarian LH receptors, although an adverse effect seems likely. LH does stimulate luteal progesterone production from about 12 d of pregnancy and adverse effects of poor nutrient intakes in lactation on reproductive performance can to some extent be remedied by increased feed intakes in early gestation which was also associated with increased basal LH concentrations (Kirkwood et al., 1990; Love et al., 1993). Reduced feed intakes may also interact with photoperiod as, interestingly, feed restriction to 60% of ad libitum caused a marked increase in circulating melatonin concentrations in pigs subjected to a long photoperiod (ie. summer) but not in those subjected to a short photoperiod (Love et al., 1993).

Other than attempting to stimulate lactation feed intake, we are unaware of commercially established methods to protect pregnancy when factors such as low lactation nutrient intake or long photoperiods have a negative impact on reproduction. Under normal conditions, CL maintenance is promoted by embryonic estrogen secretion starting around days 11–12 of pregnancy, which is the first signal for maternal recognition of pregnancy. The estrogen serves to redirect endometrial PGF2α from an endocrine to an exocrine direction, and also increases luteotrophic PGE (Christenson et al., 1994). Interestingly, a role for LH in pregnancy maintenance has also been proposed, with administration of hCG stimulating in vitro endometrial PGE2 production (Ziecik et al., 2000), with the signal being further amplified by endometrial positive feedback further increasing the PGE2:PGF2α ratio (Ziecik et al., 2011). Failure or weakness of this first signal for maternal recognition of pregnancy will result in luteolysis and a return to estrus.

The administration of exogenous estrogen to cyclic gilts to mimic the signal for maternal recognition of pregnancy has been shown to induce pseudopregnancy (Cushman et al., 1999) and, therefore, would also likely support pregnancy. There is no label indication for estrogen administration to pigs but if ovarian follicular growth was stimulated in early pregnant females it could provide an endogenous source of estrogen. In female pigs, follicle growth from about 4 mm to ovulation has been shown to be primarily under LH control (Driancourt et al., 1995). Further, the LH analogue human chorionic gonadotrophin (hCG) has been shown to stimulate follicle growth in gilts (Guthrie and Knudsen, 1984; Soede et al., 2001) and sows (Ogasa et al., 1992), and when injected on day 12 of pregnancy has been shown to stimulate production of estradiol and progesterone (Tilton et al., 1989). The aim of the present study was to examine the hypothesis that injection of hCG on day 12 of pregnancy will induce growth of estrogenic follicles and, by supporting luteal function, increase pregnancy and farrowing rates.

2. Methods

The experiments were conducted at the University of Adelaide Roseworthy piggery in accordance with the Australian Code of Practice for the Care and Use of Animals for Scientific Purposes (NHMRC 2013) and approved by the University of Adelaide Animal Ethics Committee.

2.1. Experiment 1

This study was conducted during autumn and winter (March to November, 2015) with 52 Large White × Landrace mixed parity sows. During their 28 d lactation, sows were fed to-appetite a standard commercial lactation diet formulated to provide 14 MJ DE/kg and 1% total lysine. For the final 10 d of lactation 36 of the sows were feed restricted (4 kg/d for primiparous, and 5 kg/d for parity 2 and 3). This was done in an attempt to simulate summer feed intakes since it has been shown that nutrient restriction during this period of lactation is associated with less follicular growth and poorer embryo development (Zak et al., 1997). Remaining sows (n = 16) remained on full feed to act as positive controls. From weaning to mating and during gestation, sows were fed approximately 2.5 kg/d of a dry sow diet formulated to provide 13 MJ DE/kg and 0.69% total lysine. After weaning sows were moved into a breeding shed and housed in groups of 5–7 per pen until 12 d after mating and were then moved to a gestation barn and housed in individual stalls until 28 d after mating. Following pregnancy confirmation at 28 d, sows were rehoused into a pregnant sow ecoshelter for the remaining gestation period.

For estrus detection, sows had daily fenceline boar contact from the day after weaning in a detection mating area. At the detection of estrus and at 24 h intervals while still exhibiting estrous behaviour, sows were inseminated with 3×10^9 sperm in 80 mL Androstar^{TM} extender (SABOR, Clare, SA).

At 12 d after initial insemination, restrict-fed sows were assigned on the basis of parity to receive an intramuscular injection of 1000 IU hCG (Chorulon, MSD Animal Health; n = 17), or serve as non-injected controls (n = 19). The hCG dose was based on previously documented efficacy for sows (Tilton et al., 1989). The full-fed sows (n = 16) were not injected, serving as positive controls. To minimise variation in the fertilisation to treatment interval, day 0 was first day of estrus for sows mated once or twice (n = 31), or the second day of estrus for sows mated three times (n = 21).

Follicle size was measured on 12, 16, 20, 24, and 28 d after mating by transrectal real time ultra-sound using a 7.5 MHz sector probe (MyLabOneVet, Esaoate Europe B.V., Maastricht, The Netherlands). At each scan, the