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Increasing feed intake in late gestation does not affect plasma progesterone concentration in the sow

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Abstract

Rate of decline in plasma progesterone concentration may influence the success of lactogenesis in the sow. The aim of this experiment was to investigate whether progesterone concentration and rate of decline of progesterone in the periparturient sow could be manipulated by changing her feeding level. Forty-two sows received either 1.15 or 2 times maintenance energy daily from day 100 of gestation up until and including the day of farrowing. Blood samples were taken on days 98 (pre-treatment baseline) and 109 of gestation, during farrowing, 6 h after farrowing and at 09:00 h for the 3 days following farrowing. Plasma progesterone concentration was determined and progesterone half-life was calculated for each sow. High intake feeding had no effect on plasma progesterone concentration at any time of sampling. Progesterone half-life averaged 41.2 ± 3.81 h and did not differ between treatments. There was no relationship between progesterone concentration, or half-life, and litter weight gain, although there was a weak correlation between decline in progesterone in the first 6 h after birth and piglet growth rate from birth to 6 days of age ($R^2 = 0.109, P < 0.05$). It was concluded that increasing feed intake in late gestation cannot be used to increase progesterone clearance rate and hasten the onset of lactogenesis in sows.
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Keywords: Progesterone; Sow; Food intake; Late gestation

1. Introduction

There are two periods in the reproductive cycle of the sow when it might be advantageous to manipulate progesterone concentrations. The first of these is immediately following conception in order to maximise embryo survival [1]. The second period is in late

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pregnancy as the sow prepares for farrowing and lactation. The sow has maintained high progesterone concentrations throughout pregnancy. Progesterone is lipophilic; cycling gilts have been shown to have 10 times greater concentration of progesterone in fat than in blood [2]. Therefore, sows approaching the end of pregnancy are likely to have a considerable quantity of progesterone stored in their body fat. Progesterone withdrawal is necessary to allow parturition [3] and has also been implicated in lactogenesis in the sow. de Passillé et al. [4] found that there was a negative correlation between sow plasma progesterone concentrations during the first 48 h after farrowing and piglet growth rates in the first 3 days of life.

It has been clearly demonstrated in the progesterone infused ovariectomised gilt that increasing feed intake level increases metabolic clearance rate of progesterone [5,6]. How well does this model reflect the impact of feeding level in the intact female pig? There is evidence of an inverse relationship between feed intake and plasma progesterone concentrations during the first half of pregnancy [1,7], however, the effect of increasing feed intake as a means of increasing the rate of decline of progesterone prior to parturition has not been reported. The aim of this experiment was to investigate whether we could manipulate progesterone concentration and rate of decline of progesterone in the peri-parturient sow simply by changing her feeding level. We hypothesised that increasing feed intake in late gestation would reduce progesterone concentration in the peri-parturient sow.

2. Materials and methods

All procedures used in this experiment were approved by the University of Alberta Animal Care Committee to ensure adherence to Canadian Council of Animal Care Guidelines.

Forty-six Camborough sows (Pig Improvement (Canada) Ltd., Acme, AB, Canada), parities 1 to 3, were fed $1.15 \times$ maintenance energy levels until day 100 of gestation (normal). From day 100 of gestation until farrowing the sows were randomly allocated within parity either to remain on normal feed intake level ($1.15 \times$ maintenance energy—N sows), or to receive a high feed intake (twice maintenance energy—H sows). The high level of intake was set at twice maintenance rather than twice the normal intake because preliminary trials experienced difficulties in getting sows to consistently eat the greater amount of feed. There were 23 H sows ($9 \times$ parity 1, $10 \times$ parity 2 and $4 \times$ parity 3) and 23 N sows ($10 \times$ parity 1, $8 \times$ parity 2 and $5 \times$ parity 3), unfortunately four of the parity 1 H sows refused to eat their allocated ration in the last week of gestation and were removed from the trial. Reported results are therefore based on the remaining 42 sows. All sows were weighed on day 98 of gestation and within 24 h of farrowing. Backfat thickness was measured at these same times using an ultrasonic probe (Scanoprobe II, Scanco, Ithaca, NY) at the last rib and 65 mm from the midline (P2).

Maintenance requirement was assumed to be 460 kJ DE/kg $BW^{0.75}$ [8]. The daily ration was fed once daily at 8 a.m. The gestation diet contained 12.6 MJ DE/kg, 13.7% crude protein and 0.56% lysine. Sows on each treatment had similar weight and fatness at day 98 of gestation, averaging 199.7 ± 4.93 kg live weight and 17.7 ± 0.46 mm P2 backfat. During gestation the sows were housed in individual stalls at a room temperature of $20 \pm 2\,^{\circ}$C. On day 109 of gestation the sows were moved into individual farrowing crates

in the farrowing room and from this time until the end of lactation they received an appropriate amount of the lactation diet (13.7 MJ DE/kg; 15.4% crude protein: 0.74% lysine). Farrowing stalls were totally slatted and had covered creep areas containing heat lamps and overlays. Room temperature was maintained at 18 ± 2 °C. After farrowing all sows were fed ad libitum throughout a 26 ($\pm$0.3) day lactation. Feed intake was recorded daily. Sows had access to water at all times.

Litter size was standardised across treatments within 24 h of parturition. On the day of birth, piglets received an iron supplement, their teeth and tails were clipped and their ears were notched. Male piglets were castrated at 7 days of age. Piglets were weighed within 6 h of birth and then at 1, 2, 6 and 20 days of age and at weaning. Piglet weight change in the first 2 days of life was used as an indicator of the onset of lactogenesis. Piglets had access to creep feed from 20 days of age and to water at all times. Intake of creep feed was not recorded.

2.1. Blood sampling

Blood samples were taken on day 98–2 h after feeding; day 109—immediately before and 2 h after feeding; during farrowing, 6 h later and at 9 a.m. on the next 3 days. Blood samples were taken by ear vein puncture without sow restraint. All blood samples were centrifuged at $1500 \times g$ for 15 min at 4 °C within 20 min of sampling and plasma was stored at -30 °C until analysis.

2.2. Progesterone analysis

Plasma samples were analysed for progesterone by radioimmunoassay as described by Beltranena et al. [9]. Sensitivity of the assay was 0.02 ng/100 μL. No significant deviation from parallelism was apparent from assaying 100, 50 and 25 μL of a standard plasma pool. The intra- and inter-assay coefficients of variation for the progesterone assays were 4.1 and 5.2%, respectively.

The disappearance rate constant (k is the fraction of total hormone that disappears per unit time) of progesterone after farrowing was determined by regression of the natural logarithm of plasma progesterone concentrations from during farrowing until 3 days postpartum against time. The resulting regression fits the equation $X = A\,e^{-kt}$, where k is the slope of the curve. Only sows for which this regression was significant at the 5% level were included in the analysis. Progesterone half-life was calculated from the following equation:

$$\text{Half life (h)} = \frac{0.693}{k}$$

2.3. Statistical analyses

Data for pre-treatment plasma progesterone concentration, disappearance rate constant, half-life, piglet number, BW and growth rate were analysed using analyses of variance. Sources of variation were treatment (high or normal feed intake during the last 2 weeks of gestation), parity ($p = 3$), interaction between feed intake and parity and sow within feed

intake by parity (error term). Preliminary analyses indicated no significant feed intake by parity interactions and therefore only main effect least square means are presented. Comparisons among least square means were made using Fisher's protected least significant difference [10]. All computations were made using MANOVA operation of Systat [11]. Data for plasma progesterone concentrations during the treatment period and at farrowing were analysed according to the procedure described above plus a covariate of pre-treatment plasma progesterone concentration. Comparison between progesterone concentration of post-prandial samples before treatment (day 98) and during treatment (day 109) was computed as a split-plot addition to the model given above for pre-treatment progesterone concentration. Likewise comparison between progesterone concentration of pre-prandial and post-prandial samples during treatment (day 109) were also computed as a split-plot addition to the model given above for pre-treatment progesterone concentration.

3. Results

There were no significant interactions between treatment and parity for any of the variables measured.

From day 100 of gestation until farrowing mean daily intakes of H and N sows were 3.9 ± 0.09 kg/day and 2.4 ± 0.07 kg/day, respectively ($P < 0.001$). After farrowing there was no difference in feed intake between the two groups, mean feed intake over the whole lactation was 6.5 ± 0.26. There was no difference in P2 backfat thickness at farrowing between the treatments which averaged 16.8 ± 0.95 mm for H sows and 16.6 ± 0.85 mm for N sows.

There was no clinical incidence of agalactia or mastitis in this experiment.

3.1. Plasma progesterone

There was no difference between plasma progesterone concentrations of H and N sows at any stage measured in late gestation or early lactation, nor in the decline in progesterone in the first 6 h after farrowing (see Table 1 and Fig. 1). Pre-treatment plasma progesterone

Table 1
Plasma progesterone concentrations during late gestation and early lactation in sows fed high or normal intakes in late gestation

	High ($n = 19$)	Normal ($n = 23$)	Significance
Plasma P4 (ng/mL)			
Pre-treatment (day 98 of gestation)	24.4 ($\pm$1.25)	25.8 ($\pm$0.98)	N.S.
During treatment (day 109)—pre-prandial[1]	26.1 ($\pm$0.95)	25.1 ($\pm$0.81)	N.S.
During treatment (day 109)—post-prandial[1]	25.7 ($\pm$0.88)	24.8 ($\pm$0.71)	N.S.
At farrowing[1]	8.3 ($\pm$0.70)	8.4 ($\pm$0.57)	N.S.
6 h post-farrowing	5.9 ($\pm$0.56)	6.2 ($\pm$0.45)	N.S.
Disappearance rate constant	0.019 ($\pm$0.003)	0.025 ($\pm$0.002)	N.S.
Half-life (h)	42.3 ($\pm$5.32)	31.4 ($\pm$4.44)	N.S.

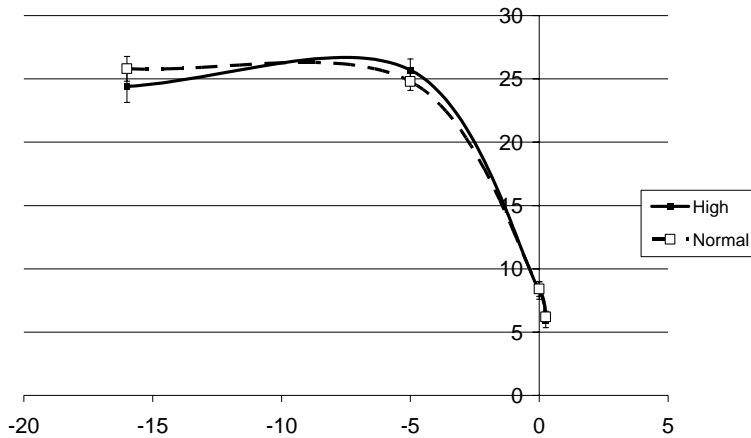[1] Pre-treatment value used as covariate.

Fig. 1. Plasma progesterone concentrations in late gestation and early lactation for sows which received normal or high levels of feed intake in late gestation. *X*-axis: time from farrowing (days). *Y*-axis: progesterone concentration (ng/mL).

concentrations on day 98 of gestation varied considerably between sows and were correlated to sow liveweight ($R^2 = 0.221$, $P < 0.001$). Plasma progesterone on day 98 of gestation was not related to the number of piglets in the litter. Parity 1 sows had lower plasma progesterone concentrations then sows of parities 2 and 3 on day 98 of gestation ($P < 0.05$, Table 2) but thereafter there were no differences in progesterone concentration between sows of different parities.

Plasma progesterone concentrations of high intake sows did not decline between days 98 and 109 of gestation in response to increased feeding and were not different from those of normal intake sows. On day 109 of gestation, progesterone concentrations were similar before and after feeding. Progesterone concentrations at farrowing were best predicted

Table 2
Plasma progesterone concentrations during late gestation and early lactation in sows of parities 1, 2 and 3

	Parity 1 (*n* = 15)	Parity 2 (*n* = 18)	Parity 3 (*n* = 9)	Significance
Plasma P4 (ng/mL)				
Pre-treatment (day 98 of gestation)	21.9[a] (±1.42)	25.7[b] (±1.12)	27.7[b] (±1.57)	$P < 0.05$
During treatment (day 109)—pre-prandial[1]	24.4 (±1.16)	25.8 (±0.89)	26.5 (±1.26)	N.S.
During treatment (day 109)—post-prandial[1]	24.8 (±1.07)	24.9 (±0.81)	25.1 (±1.13)	N.S.
At farrowing[1]	8.4 (±0.88)	7.8 (±0.65)	9.0 (±0.93)	N.S.
6 h post-farrowing	5.8 (±0.67)	5.3 (±0.53)	7.0 (±0.72)	N.S.
Disappearance rate constant	0.025 (±0.003)	0.022 (±0.003)	0.020 (±0.003)	N.S.
Half-life (h)	30.5 (±6.65)	39.3 (±5.12)	40.7 (±6.57)	N.S.

Values with different superscripts within rows are significantly different.

[1] Pre-treatment value used as covariate.

from the inherent progesterone concentration of the sow (on day 98 of gestation) and the total number of piglets born:

$$P4_f = -0.57 \pm 2.05 + 0.23 \pm 0.086\,P4_{d98} + 0.28 \pm 0.122\,LS_b$$
$$(R^2 = 0.363,\ P < 0.001) \tag{1}$$

where $P4_f$ is sow plasma progesterone concentration at farrowing (ng/mL). $P4_{d98}$ is sow plasma progesterone concentration on day 98 of gestation (ng/mL). LS_b is total number of piglets born.

Disappearance rate constants could only be calculated for 34 of the 42 sows and were not different between treatments. Progesterone half-life averaged 41.2 ± 3.81 h. Regression analysis identified a positive relationship between disappearance rate constant (k) and plasma progesterone at farrowing but a negative relationship to litter size at birth and to sow backfat thickness at farrowing. Therefore, half-life was shorter when progesterone at farrowing was higher, but became longer as the number of piglets in the litter, or the fatness of the sow at farrowing, increased;

$$k = 0.047 \pm 0.010 + 0.002 \pm 0.001\,P4_f - 0.002 \pm 0.001\,B_f - 0.001 \pm 0.001\,LS_b$$
$$(R^2 = 0.401,\ P < 0.01) \tag{2}$$

where k is progesterone disappearance rate constant. B_f is sow P2 backfat thickness at farrowing.

There was no relationship between progesterone concentrations during and after farrowing, nor the rate of decline of progesterone, with piglet weight gain in the first 2 days of life. There was a significant although weak correlation between decline in progesterone in the first 6 h after birth and piglet growth rate from birth to 6 days of age ($R^2 = 0.109$, $P < 0.05$). The disappearance rate constant was not correlated to any measure of piglet growth.

3.2. Piglet performance

Piglet birthweight was not affected by feed intake in late gestation and there were no significant differences in any other aspect of piglet performance between the two treatment

Table 3
Piglet performance data for sows fed either high or normal feeding levels in late gestation

	High ($n = 19$)	Normal ($n = 23$)	Significance
Total born alive	10.3 ($\pm$0.75)	9.8 ($\pm$0.65)	N.S.
Stillborn	0.8 ($\pm$0.18)	0.6 ($\pm$0.16)	N.S.
Birthweight of liveborn piglets (kg)	1.5 ($\pm$0.07)	1.6 ($\pm$0.06)	N.S.
Weight gain in first 2 days of life (kg)	0.159 ($\pm$0.0449)	0.240 ($\pm$0.0389)	N.S.
Litter size after cross-fostering	9.6 ($\pm$0.27)	9.3 ($\pm$0.25)	N.S.
Daily piglet liveweight gain to 20 days (kg/day)	0.243 ($\pm$0.008)	0.244 ($\pm$0.008)	N.S.
Number of pigs weaned	8.6 ($\pm$0.59)	8.7 ($\pm$0.47)	N.S.
Mean piglet weight at weaning (kg)	7.9 ($\pm$0.19)	8.0 ($\pm$0.16)	N.S.
Daily piglet liveweight gain to weaning (kg/day)	0.256 ($\pm$0.006)	0.257 ($\pm$0.005)	N.S.
Mortality	13.7 ($\pm$2.10)	17.0 ($\pm$1.93)	N.S.

groups (see Table 3). Sows produced an average of 9.9 ± 0.44 live piglets per litter. After cross-fostering to balance litter size, sows had an average of 9.4 ± 0.36 piglets. Weight gain in the first 2 days of life averaged 101 ± 12.8 g/day per piglet, 239 ± 6.5 g/day over the first 20 days and 236 ± 6.6 g/day to weaning. Sows weaned an average of 8.6 ± 0.35 piglets with a mean weight of 7.8 ± 0.22 kg at 26 days of age.

4. Discussion

4.1. Plasma progesterone concentration

In earlier work, we have demonstrated a significant increase in MCR of progesterone with consequent lower plasma progesterone concentrations in response to doubling the feed intake of ovariectomised gilts [6]. Therefore, we expected to see a comparable reduction in plasma progesterone concentration in high intake pregnant sows between pre-treatment values taken on day 98 of gestation and those on day 109 of gestation, particularly in comparison to the concentrations in N sows. Surprisingly this was not observed. Instead there was a trend towards an increased progesterone concentration on day 109 in the H sows. Increased progesterone clearance rate in response to increased feeding level is thought to result primarily from increased blood flow through the liver [5]. If the same mechanism occurred in pregnant sows in the current experiment then there must have been a corresponding increase in production rate since there was no decline in plasma progesterone concentration. This could occur as the result of negative feedback, although this was not observed in studies with rats [12], or through increased hormonal stimulation. Both insulin and IGF-1 have been shown to increase progesterone secretion in a variety of species [13] and both increase with increasing plane of nutrition. Therefore, high intake feeding of sows in late gestation may result in increased progesterone production as well as increased clearance. However, it may be that no change in plasma progesterone concentration was observed because there was no change in clearance rate in response to increased feed intake in pregnant sows.

In the ovariectomized gilt, progesterone concentrations decreased post-prandially in response to increased clearance, presumably via increased splanchnic blood flow in response to feed intake. The sows in this experiment were fed only once daily and therefore feeding might be expected to have a dramatic effect on progesterone clearance rate with a resulting depression in plasma progesterone concentrations measured 2 h after feeding on day 109 of gestation when compared to the pre-feeding value. This was not observed and again there are two possible explanations. Either there was no increased clearance in response to feeding or secretion of progesterone increased proportionally, perhaps in response to the feeding-induced surge of insulin.

Plasma progesterone concentration in late gestation was not related to resultant litter size but plasma progesterone concentration during farrowing was positively correlated to this parameter. This suggests that there was some residual progesterone production at farrowing related to the litter itself. This is almost certainly due to feto-placental production [14] which will be directly related to fetal number and placental mass. The disappearance rate

constant of progesterone and its half-life in the circulation of sows following farrowing were of the same order of magnitude as those measured in ovariectomized gilts [6]. The disappearance rate constant was positively correlated to plasma progesterone concentration during farrowing, therefore, the lower the plasma progesterone concentration during farrowing, the lower the disappearance rate constant and the longer the half-life of progesterone.

In this experiment disappearance rate constant was negatively related to sow backfat thickness and therefore fatter sows had longer progesterone half-lives than thinner sows. The concentration of progesterone in adipose tissue is more than 200 times greater than that in plasma [2], therefore, following 115 days of elevated plasma progesterone in pregnancy, we would expect progesterone concentrations in fat to be high and similar per unit of fat. In this case, fatter sows would have a greater total body content of progesterone than thinner sows because of their greater proportion of fat. Hence, we might expect progesterone to be released at a greater rate in fatter sows than in thinner, and possibly over a longer time period, thus sustaining higher levels of progesterone in plasma following farrowing. Progesterone would therefore have a longer half-life in such animals as was observed in this experiment, surprisingly this was not observed in ovariectomised gilts [2,6]. However, it does appear to make biological sense.

Disappearance rate constant was also negatively correlated to litter size at birth, presumably because sows giving birth to larger litters had greater feto-placental production of progesterone [14]. Hence, plasma progesterone will decline more slowly in sows giving birth to larger litters.

4.2. Piglet performance

There was no correlation between the disappearance rate constant of progesterone, or sow plasma progesterone concentration per se, and the onset of lactogenesis as determined by litter weight gain in the first 2 days of life. This contrasts with the work of de Passillé et al. [4] who observed a positive correlation between plasma progesterone concentration in sows in the 48 h following farrowing and in 3 days weight gains of piglets. The only correlation between progesterone and piglet weight gain in this experiment was that between the decline in plasma progesterone concentration in the 6 h following farrowing and piglet weight gain to 6 days of age. This does suggest that the more rapidly progesterone declines immediately after farrowing, the better the establishment of lactation. However, this effect ceased to be important as the piglets grew to heavier weights.

5. Conclusions

Increased feed intake in late gestation did not change progesterone concentrations in sows nor increase the rate of decline of progesterone at farrowing. Rate of decline in progesterone post-farrowing was negatively related to sow fatness. These observations are in direct contrast to findings with ovariectomised gilts and therefore indicate that the progesterone infused ovariectomised gilt is an inappropriate model in which to study progesterone metabolism in the periparturient sow.

Acknowledgements

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