Effect of Uterine Environment and Fetal Genotype on Placental Size and Efficiency

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ASL-R1491

Summary and Implications

Optimum conceptus (fetal and placental) growth appears to be achieved through the combination of both uterine and fetal-directed mechanisms. The uterus, in which a litter of conceptuses develops, has the major impact on limiting the size each conceptus ultimately attains; however, the genotype of each conceptus can differentially resist this effect, resulting in littermate conceptuses of different sizes. In contrast, the genotype of the conceptus modulates placental vascular density and thus placental efficiency. The ability to both limit placental size while at the same time increase placental vascular density of conceptuses of U.S. pig breeds would allow pork producers the potential of achieving an optimal litter size and increasing profitability.

Introduction

The number of piglets weaned per sow per year is one of the most economically important factors for pork producers today. In Iowa, the average farrow to finish pork producer farrowed 9.7 piglets per sow per litter in 1996, netting a profit of ≈$300 per sow. However, this litter size of 9.7 piglets is far from optimal as domestic sows have an ovulation rate that surpasses 15 ova and a fertilization rate exceeding 95%. These data indicate that prenatal mortality in Iowa sows exceeds 30%. In contrast, the prolific Chinese Meishan pig farrows three to four more piglets per litter than U.S. pig breeds even though both the ovulation and fertilization rates are similar. Previous data has demonstrated that after day 30 of gestation, uterine capacity (i.e., the amount of uterine space) exerts the greatest limitation on litter size. Because uterine size is similar between the Meishan and U.S. pig breeds, the Meishan pig must have evolved a mechanism for mitigating this limitation to litter size.

We have previously demonstrated that the Meishan uterus exhibits a powerful inhibitory effect on conceptus development throughout gestation. Conceptuses were significantly smaller when recovered from Meishan compared with Yorkshire uteri as early as day 12 of gestation. The uterus-mediated difference in conceptus size continued through day 90 when conceptuses were dramatically smaller (>60% by weight) when recovered from Meishan versus Yorkshire uteri.

Additionally, the effects of fetal genotype were only observed in Yorkshire uteri, as Yorkshire conceptuses were markedly larger than their littermate Meishan conceptuses on day 90 of gestation. However, when a separate group of Yorkshire recipient females gestating both Meishan and Yorkshire conceptuses were allowed to farrow, littermate Meishan and Yorkshire fetuses exhibited similar birth weights. In contrast, placentae that were matched to Meishan piglets continued to be markedly smaller than littermate Yorkshire placentae. Further, these small Meishan placentae were much redder, suggesting a greater vascularity. More recently, we demonstrated that the vascular density of Meishan placentae doubles as gestation progresses (day 90 through day 110) whereas placental size remains relatively constant. In contrast, Yorkshire placentae increase in size by 50% from day 90 through day 110 of gestation with no measurable change in vascular density.

In an attempt to focus specifically on the uterine environmental effects on conceptus development (placental growth, placental vascularity, and fetal growth), Meishan gilts were bred only by Yorkshire boars and Yorkshire gilts were serviced only by Meishan boars. This resulted in F1 conceptuses of similar genotype (one-half Meishan:one-half Yorkshire) in uteri of both Meishan and Yorkshire females.

Materials and Methods

Meishan (n=6) and Yorkshire (n=6) gilts of similar reproductive age (2–5 postpubertal estrous cycles) were checked for estrus twice daily with a boar. When a Meishan gilt was found in estrus she was bred to a Yorkshire boar and when a Yorkshire gilt was found in estrus she was bred to a Meishan boar. At random, four of these bred gilts (two Meishan and two Yorkshire) were assigned to slaughter on day 70, 90, or 110 of gestation. The gravid uteri were recovered and transported to our laboratory for further processing.

Each uterine horn was separated from the cervix, weighed, and its length measured from tip to base. Each fetus was exteriorized through an opening on the antimesometrial side of the uterine horn. The umbilical cord of each conceptus was double ligated and tagged, and this cord was then severed between the ligations so that each fetus and placenta could be matched later. The weight and crown rump length (CRL) of each fetus were then determined. The uterine horn was opened longitudinally along its antimesometrial side. An intact section (1×2 cm) of the placental-endometrial attachment site was removed from each day 90 and day 110 conceptus at a site 2–3 cm from the origin of the umbilical cord and containing no large caliber blood vessels. These endometrial-placental sections were immediately fixed in formalin, and later sectioned and stained for the visualization of placental and endometrial blood vessels. An image analysis system quantified the areas occupied by placental tissue, endometrial tissue, placental blood vessels, and endometrial blood vessels in the stained sections. The placental vascular density (placental blood vessel area/placental area) and endometrial vascular density (endometrial blood vessel area/endometrial area) were determined for each conceptus.

After marking both ends of each placental attachment site, individual placentae were then gently separated from the endometrium resulting in the recovery of an intact placenta. Each placenta was weighed and then spread out on a sheet of butcher's paper and it's perimeter traced. These tracings were allowed to dry and a planimeter was used to calculate its surface area.

Results and Discussion

Results are presented from six Yorkshire and five Meishan females as one Meishan female was found not to be pregnant.

The inhibitory effects of the Meishan uterine environment were evident as early as day 90 as both placental sizes and weights were markedly reduced for Meishan x Yorkshire conceptuses gestated in Meishan versus Yorkshire uteri (Table 1). Specifically, placental surface area was 50% less for Meishan x Yorkshire conceptuses recovered from Meishan uteri than those recovered from Yorkshire uteri. Additionally, this decreased placental size (weight and surface area) was maintained through day 110 for Meishan x Yorkshire conceptuses gestated in Meishan when compared with Yorkshire uteri. In contrast, the placental vascular density of Meishan x Yorkshire conceptus was similar, regardless of the uterine type in which they were gestated (data not shown).

Although weights of all fetuses increased progressively as gestation advanced, fetuses grew larger in Yorkshire compared with Meishan uteri (Table 2). Specifically, fetal weight was similar in both uterine environments at day 70; however, by day 90, fetuses gestating in Yorkshire uteri were 30% heavier than fetuses gestated in Meishan uteri. This difference in fetal weight was maintained through day 110. Additionally, these larger fetuses gestating in Yorkshire uteri exhibited a greater CRL (≈10%) than fetuses gestated in Meishan uteri on days 90 and 110 (Table 2).

By eliminating the confounding effects of fetal genotype through crossbreeding, the specific effects of both the Meishan and Yorkshire uterine type become evident. A pronounced uterine environmental effect was observed on placental size (placental surface area) by day 110 of gestation when Meishan x Yorkshire conceptuses were gestated in Meishan versus Yorkshire uteri. Additionally, fetal weights reflected the differences observed in placental size. Fetuses weighed markedly less on day 110 when gestating in a Meishan uterus than when gestating in a Yorkshire uterus. The Meishan uterus appears to effectively limit placental size, which results in a proportional reduction in the size of the corresponding fetus. This reduction in total conceptus size in a Meishan uterus results in a decreased space requirement by each conceptus for nutrient uptake and waste product removal, potentially increasing the number of conceptuses that can be maintained until term (day 114). The failure of the uterine environment (Meishan versus Yorkshire) to impact placental vascular density in this study supports the role of the fetal genotype as the sole regulator of placental vascularity.

Placental efficiency can be defined as the capture of maternal nutrients and oxygen and their transport to the fetus. Increased placental efficiency can be achieved by two principle mechanisms: (1) placental growth or increasing the surface area for absorption or (2) increasing the density of blood vessels per unit area of placental:endometrial interface.

The results of this study help to clarify the results of previous experiments conducted in our laboratory. Figures 1a and 1b combine data obtained previously with those of the current study to illustrate several points. Figure 1a demonstrates that placental growth is restricted by the Meishan uterus, regardless of fetal genotype. However, fetal growth appears to be determined by the conceptus' ability to vascularize its placenta once placental size limits are defined by the uterine environment (Figure 1b). Thus, although Meishan x Yorkshire conceptuses exhibited placental sizes similar to Yorkshire conceptuses in each uterine environment, their associated fetal weights were significantly reduced. This supports the concept that although Meishan x Yorkshire conceptuses develop placentae that are equivalent in size to the Yorkshire conceptus, they suffer a reduction of placental vascularity due to their Yorkshire genotype.

These data suggest that the uterus functions to limit placental growth in a breed specific manner, whereas the conceptus attempts to compensate by altering its placental vascular development. Additionally, it must be remembered that each conceptus in a litter interacts with the uterine environment to set its placental size and vascularity. In this way, each conceptus sets its own placental efficiency to assure adequate nutrient and waste product exchange. It is logical to assume that different U.S. pig breeds differ in the intensity of these uterine and/or fetal genotype effects resulting in placentae of different sizes and/or vascularity.

Further work is needed to define the inhibitory factor(s) in the Meishan uterine environment that limit placental size and fetal growth. Additionally, the fetal angiogenic factor(s) and growth factor(s) that drive differences in placental vascular development and placental growth have yet to be determined.

Table 1. Placental weight and surface area of Meishan x Yorkshire conceptuses in Meishan or Yorkshire uteri.

Day of gestation	Placental weight (g) Uterine type		Placental surface area (cm^2) Uterine type	
	Meishan	Yorkshire	Meishan	Yorkshire
70	206.1 ± 16.5^{a}	242.8 ± 18.4^{b}	1114 ± 66^{a}	1019 ± 31^{a}
90	189.5 ± 9.8^{a}	279.6 ± 15.2^{b}	1190 ± 35^{a,b}	1642 ± 63^{c}
110	207.4 ± 13.1^{a}	264.3 ± 10.1^{b}	1255 ± 61^{b}	1520 ± 42^{c}

^{a,b,c}Means ± SEM within a measurement differ ($P<.001$).

Table 2. Fetal weights and CRL of Meishan x Yorkshire conceptuses in Meishan or Yorkshire uteri.

Day of gestation	Fetal weight (g) Uterine type		Crown rump length (cm) Uterine type	
	Meishan	Yorkshire	Meishan	Yorkshire
70	227.9 ± 7.3^{a}	232.7 ± 5.9^{a}	17.3 ± .1^{a}	17.0 ± .2^{a}
90	561.6 ± 17.4^{b}	734.6 ± 19.4^{d}	23.2 ± .2^{b}	25.0 ± .2^{d}
110	935.6 ± 52.1^{c}	1248.1 ± 41.2^{e}	27.7 ± .5^{c}	29.6 ± .3^{e}

^{a,b,c,d,e}Means ± SEM within a measurement differ ($P<.005$).

Figure 1. Placental size (a) and associated fetal weight (b) of different conceptus types in Yorkshire or Meishan uteri on day 110 of gestation.