Effect of Porcine Somatotropin and Insulin on Prenatal Survival and Uteroplacental and Umbilical Cord Development in Gestating Gilts

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ABSTRACT : Pregnant Yorkshire gilts were utilized to investigate the efficacy of exogenous administration of pST and/or insulin in enhancing prenatal piglet survival, uteroplacental and umbilical cord growth and development. Gilts were randomly assigned in a 2×2 factorial arrangement to four treatment combinations consisting of either daily i.m. injections of 5 mg pST (P, n=23); 0.50 IU/kg of insulin (I, n=23); combination of pST and insulin (P+I, n=23); or 1 ml of saline as control (C, n=23) from gestation Day 30 to 70. All gilts were sacrificed on gestation d 113 to evaluate piglet survival and uteroplacental or umbilical cord development Uteri were longer (346.3 vs 325.7 cm; $p<0.05$), and heavier (3122.8 vs 2940.7 g; $p<0.05$) in insulin treated gilts. Only placental macroscopic surface area was enhanced by maternal insulin injections ($p<0.05$) Incidence of umbilical cord abnormalities were low (14.3%), and they were independent of maternal treatment, occurring more in short cords than in long ones (21 vs 12%; $p<0.05$). A 6% increase in cord length (53.2 vs 48.6 cm; $p=<0.05$) was observed in piglets from treated gilts compared with controls. Significant sex differences (in favour of males) were observed in piglet weight, crown rump length and for most umbilical or placental parameters. Gilt weight gains from breeding to Day 113 of gestation were 10% and 15% greater in pST and insulin treated gilts compared with controls. These data indicate that prepartum injections of pST and/or insulin to gestating gilts seem to have a beneficial effect on uteroplacental or umbilical cord development and promote conditions conducive for perinatal piglet survival. (*Asian-Aus. J. Anim. Sci. 1999. Vol. 12, No. 3 : 341-347*)

Key Words : pST, Insulin, Piglets, Uteroplacental, Umbilical Cord

INTRODUCTION

Before or during parturition in swine, the structural integrity of the placenta and umbilical cord of piglets can be severely compromised, leading to death by asphyxiation. In addition, many of the live born piglets that subsequently die (12 to 14%) have reduced viability due to birth asphyxia. Attempts to reduce stillbirth rate and improve neonatal piglet viability have focused on management of birth asphyxia via oxygen supply treatment or reducing the duration of exposure to asphyxia by decreasing the birth intervals between piglets with parasympathomimetic drugs or oxytocin (Curtis and Safarnsky, 1988; Bilkei, 1991; Zaleski and Hacker, 1993a,b) However, emerging evidence tends to support the concept that enhancing placental development can make piglets less prone to birth asphyxia. Increasing the length, strength or elasticity of the umbilical cord may reduce the incidence of premature rupture during parturition (Curtis, 1974; Randall, 1989; Whitely, 1990). Because the variability in perinatal survival, and neonatal piglet viability results from inadequate uterine size, differences in placental development, and structurally unsound umbilical cord, an alternative, more effective approach for enhancing piglet survival may be stimulating uteroplacental and umbilical cord development during gestation.

Recently, Gerrard et al. (1994) and Ramirez et al. (1994) reported data which show that porcine somatotropin (pST) or insulin administration to pregnant gilts have the potential to alter fetal growth and the composition and growth characteristics of fetal membranes However, the mechanism involved in this modified development remains to elucidated. The primary objective of the experiment described herein was to investigate if daily administration of pST, insulin or a combination of pST and insulin to pregnant Yorkshire gilts from gestation d 30 through d 70 influences, uteroplacental, umbilical cord development and prenatal piglet survival by d 113 of gestation.

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MATERIALS AND METHODS

Animal management and experimental design

Pubertal Yorkshire gilts were obtained and housed at, the Arkell Swine Research Station, Guelph, Ontario. Gilts were mated twice within 24 h after detection of estrus. Four boars were used with equal frequency for natural mating. At breeding time, experimental animals averaged 118.6±14 kg in weight and were 173.4±15.3 d of age. Gilts were moved to individual gestation stalls (2.1×0.66 m) soon after breeding. Each animal was limit fed 2.5 kg.d standard 15.2% crude protein diet consisting of corn, barley, and soya bean meal (table 1), with ad libitum access to water. Gestation weight on d 0, 30, 70 and 113 were recorded. Care of animals and procedures used were in accordance with the guidelines of the Canadian Council on Animal Care.

This study was set up as a randomized complete block design (RCBD), blocked on date of breeding. A total of 92 gilts were assigned to 23 blocks of 4 animals each. Within each block, pregnant gilts (gestation Day 30) were randomly allotted to one of four treatment combinations in a 2×2 factorial arrangement. The factors were dose of porcine somatotropin (0 and 5 mg/d; Lot V202-202/CP115409/150 mg/vial), generously donated by Monsanto, Canada, Inc., Miss., Ont., and dose of porcine pancreas insulin (0 and 0.50 IU/kg/d), purchased from ICN Biomedical Canada Inc., St-laurent, Que. Treatment combinations

were as follows: 1 ml of sterile water for injections (Baxter, Corporation, Miss., Ont. Canada; C, n=23), as control; 5 mg pST (P, n=23); 0.5 IU/kg of insulin (I, n=23); and a combination of 5 mg and 0.5 IU/kg insulin (P+I, n=23). Gilts were injected daily for 40 d, from d 30 to 70 of gestation. This window represents the in utero period of exponential fetal growth, as well as a period of maximal umbilical cord development. Either hormone or saline was administered in the extensor muscle of the neck contralateraly on alternate days between 0800 to 1000 h.

Table 1. Composition of diets, % (as fed basis)

Ingredient	%
Corn	40.25
Barley	40.00
Soybean meal, 48% CP*	16.4
Dicalcium Phosphate	1.50
Ground limestone	1.00
Salt	0.50
Vitamin premix**	0.25
Trace Mineral premix***	0.10

* CP=Crude protein.

** Vitamin mix provided per kg of diet: vitamin A, 10,000 IU; vitamin D_3, 1,500 IU; vitamin E, 30 IU; vitamin K, 2.2 mg; riboflavin, 5 μg; biotin, 0.2 mg; pantothenic acid, 16 mg; niacin, 25 mg; choline, 300 mg; vitamin B_{12}, 15 μg; pyridoxine, 1.5 mg; thiamine, 1.5 mg; folic acid, 1.0 mg.

*** Trace mineral mix provided per kg of diet: Selenium, 0.3 mg; Manganese, 59.9 mg; Iron, 70.0 mg; Zinc, 100.0 mg; Copper, 10.1 mg.

Data collection procedures

At d 113 of gestation, gilts were transported to the animal physiology wing in the Department of Animal and Poultry Science, University of Guelph, where they were stunned with a captive bolt pistol and exsanguinated. This method of slaughter was chosen because of it's lack of effect on piglets and their placental or umbilical tissues A mid abdominal incision was made and the entire reproductive tract was removed. A cut was made along the antimesentric border from the ovarian end of the horn across the uterine body to the ovarian end of the second horn, thus, enabling quick exteriorization of piglets, while still attached to their respective placenta via umbilical cord. Before a piglet was detached from the uterus, its corresponding placenta and umbilical cord were identified via two numbered cord clamps. Information on piglet development parameters (piglet weight, crown-rump length and sex) were recorded. Piglet survival rate was determined by expressing the number of live pigs as a percentage of the number of corpora lutea. The ovaries were weighed and the number of corpora lutea on each ovary enunciated and assumed to represent the number of potential embryos. The length of each uterine horn from the utero-tubal junction to the junction of the uterine body and cervix, along the mesimetrial border was determined with flexible tape measure. The length of both horns were added together to determine total uterine length.

Umbilical cord length was defined as the distance from the junction of the piglet abdominal wall and cord tissue to the point of insertion into the allantochorion, and was measured with flexible tape. The absolute strength of the umbilical cord was assessed by applying increasing tension on individual cord samples (20 cm/cord) until the cord broke, and using the maximum tensile force as an index of cord strength. Nene Test Equipment (Nene Instruments, Ltd., Wellingborough, England) was used in conjunction with a Nene Software Package. To apply tension evenly without tearing the cord tissues at the point of restraint, portions of the cord were held within a padded moveable clamp. One clamp was secured to a strain gauge and the other to a gear drive, the upper clamp was then set in motion with direct upward velocity of 100 mm/min. This upward movement of the clamp gradually broke the cord. The Nene software package coupled to the machine automatically performed the following calculations : *Load at end* = the ultimate tensile force required to break samples of the cord (kN); *Elongation at yield point* = the maximum displacement reached at yield point, an index of cord elasticity (mm); and *Time to break* = the maximum time to reach break point (sec). Cord abnormalities like excessive torsion, single umbilical artery or vascular occlusion were recorded based on gross examination of tissues. The presence, frequency, location, and the degree or direction of cord twist were also determined. Placental length or surface area was determined as described by Dalton and Knight (1983) and Whitely (1990) i.e. by spreading a transparent plastic sheet large enough to cover the spread placentas, and by cutting around each placenta with a pair of scissors. From these cuttings, surface area (cm^2) was measured by tracing outlines on a digitalized tablet interfaced with a computer program. Individual placentas were then stripped from the uterus and weighed.

Statistical analyses

Statistical analyses were performed according to the GLM procedures of SAS (1989). The model used to evaluate gilt and piglet parameters included P, I, P×I and block as main factors, gilt gestation d 30 body weight was used as covariate where applicable. The residual error term of the model was used as the error term for the various factors. Data were expressed as least square means and where appropriate, the differences among treatment means were compared by least significant difference using the predicted difference option (SAS, 1989). However, in most tables the actual probability level has been reported to indicate similarities or differences among treatments. The P×I interactions were not significant ($p>0.05$) and are not presented in the results. Pearson correlation coefficients were determined on all possible combinations of gilt and piglet parameters, using SAS (1989) correlation

Table 2. Main effects of pST or insulin adminstration to gestating gilts on uterine, placental and umbilical cord development*

Item	Treatment					P values		
	pST		Insulin					
	0	5 mg	0	0.5 IU	SE	P	I	P×I
No. of gilts	46	46	46	46				
Uterine length, cm	329.1	342.2	325.7	346.1	6.7	0.17	0.02	0.16
Uterine weight, g	2991.7	3071.7	2940.7	3122.8	53.1	0.29	0.001	0.89
Placental weight, g	266.1	268.0	265.2	268.7	1.9	0.40	0.20	0.50
Placental length, cm	60.6	61.7	60.1	61.8	0.46	0.08	0.06	0.21
Placental surface area, cm^2	1044.8	1057.3	1051.4	1051.7	4.7	0.40	0.80	0.23
Umbilical cord length, cm	51.3	53.8	51.3	54.6	0.45	0.07	0.01	0.45
Umbilical cord strength, kN	0.009	0.010	0.010	0.009	0.002	0.16	0.30	0.19
cord elasticity, cm	9.35	9.39	9.11	9.63	0.15	0.85	0.01	0.39

* Values are least square means.

procedures. The distribution of long versus short umbilical cords and normal versus abnormal cords was analyzed using the Chi-squared test.

RESULTS

Uterine and placental development

Least square means and pooled standard errors for uterine, placental and umbilical cord parameters measured at gestation Day 113 are shown in table 2. The mean length of combined empty uterine horns was 335.6±54.8 cm, with a range of 210 to 427 cm (CV = 13.04%), mean empty uterine weight was 3032.3±423.1 g, with a range of 2001 to 3932 g (CV = 10.87%). Uteri were significantly (p=<0.05) longer and heavier for insulin treated gilts (346.1 vs 325.7 cm; and 3122.8 vs 2940.7 g respectively. The pST treated gilts showed a tendency for longer (342 2 vs 329.1; p<0.05) and heavier (3071.7 vs 29991.1; p<0.05). When gilt body weights at gestation d 30 were included as covariates in the model, values of both dimensions were still higher than in controls. This suggests that morphological development of the uterus was beneficially enhanced by insulin, or pST treatments. Neither placental length or weight differed significantly between treated and control groups of gilts (p>0.05). However, placental macroscopic surface area was significantly enhanced in pST treated gilts (1057.3±4.3 cm^2) compared to insulin (1051.44± 4.6 cm^2) and saline treated gilts (1035.23±2.3 cm^2) (p=<0.05).

Umbilical cord development

Of 802 cords, 626 (78%) were twisted, while 176 (22%) showed no twist. There were no treatment effects on either direction, frequency, or location of cord twist (p>0.05). Incidence of cord abnormalities was low and independent of maternal treatment (14.3%; p>0.05). Specific cord abnormalities observed included: Excessive twisting (more than five 360° twist/cord, n=73; 9.1%), this appears to threaten the cord vessels; Single umbilical cord artery (n=7; <1%); and Haematoma/ Vascular oedema (n=35; 4.3%), obstruction to vessels as a result of local oedema of vessel walls. The mean force required to break a cord was 0.010±0.05 kN. There were no significant treatment effects on either cord strength (p>0.05) or the time required to break portions of tested cords (p>0.05). Maternal treatment with insulin had significant effect on cord elasticity (p<0.05). Cord length recorded on gestation Day 113 ranged from 19.0 to 75 cm, (CV=18.2%) with a mean of 53.2±11.04 cm. Cord length was longer (54.6 vs 51.31 cm; p<0.05) in piglets from insulin treated gilts compared to control and there was a noticeable trend for longer in piglets from pST treated gilts (table 2). Cord length values were later classified into one of the two cord length groups (short and long) to examine the relationship between cord length and incidence of cord abnormalities. Results showed short umbilical cords to be more associated with specific abnormalities than long umbilical cords (21 vs 12%; p<0.05) (table 3).

Table 3. Relationship between umbilical cord length and incidence of cord abnormalities

		Umbilical cord length, cm	
		Short (<29)	Long (30-70)
Number of cords		54	747
Cord abnormalities[1]			
	No	43 (80%)	661 (88%)
	Yes	11 (22%)**	86 (12%)

[1] Excessive torsion (9.1%), vascular edema (4.5%) and single umbilical cord artery (<1%).

** (Chi-squre=2.68; df=1) (p<0.01).

Piglet development and survival

Exogenous pST and insulin administrations did not have a significant effect on either piglet weight or crown rump length (p>0.05) (table 4). Piglet weight showed a significant correlation with crown-rump length (r=0.84), placental weight (r=0.83), length surface area

Table 4. Main effects of pST or insulin adminstration to gestating gilts on gestation weight gains, piglet development and survival[1]

Item	Treatment					P values		
	pST		Insulin					
	0	5 mg	0	0.5 IU	SE	P	I	P×I
No. of gilts	46	46	46	46				
Gestation weight, kg								
Day 30	134.9	136.9	136.3	135.5	2.0	0.53	0.80	0.34
Day 70	155.3	160.3	154.4	161.6	3.1	0.25	0.31	0.61
Day 113	181.7	189.7	183.9	185.5	4.0	0.03	0.10	0.89
Piglet weight, g	1,218.7	1,201.5	1,202.3	1,218.2	2.02	0.27	0.37	0.005
Crown rump length, cm	31.2	30.8	31.4	31.0	0.22	0.42	0.35	0.79
Litter size (Total)	8.7	9.3	8.7	9.1	0.48	0.49	0.49	0.74
Litter size (Alive)	8.5	8.7	8.5	8.8	0.41	0.53	0.53	0.83
Piglet Survival rate %	56.0	60.9	56.3	60.6	2.36	0.14	0.20	0.76

[1] Values are least square means.

Table 5. Correlation coefficients (r) among selected fetal, placental and umbilical cord parameters

Item	FWT	UBL	UBS	UBE	UBT	PLL	PLW	PLSA	CRL	PVIA	F:P
FWT	1.00	0.81**	0.30**	0.77**	0.71**	0.80**	0.83**	0.75**	0.84**	0.66**	0.69**
UBL		1.00	0.28**	0.76**	0.81**	0.77**	0.84**	0.76**	0.57**	0.39**	0.39**
UBS			1.00	0.33**	0.32**	0.34**	0.29**	0.36**	0.35**	0.21*	0.18NS
UBE				1.00	0.86**	0.78**	0.79**	0.71**	0.79**	0.45**	0.34**
UBT					1.00	0.77**	0.82**	0.74**	0.80**	0.50**	0.30**
PLL						1.00	0.87**	0.75**	0.77**	0.48**	0.30**
PLW							1.00	0.83**	0.84**	0.56**	0.17**
PLSA								1.00	0.78**	0.54**	0.26**
CRL									1.00	0.53*	0.41**
PVIA										1.00	0.18NS
F:P											1.00

* =p<0.05; ** =p<0.01; NS=Not significant.
FWT=piglet weight, UBL=umbilical cord length, UBS=cord strength, UBE=cord elasticity, UBT=cord break point time, PLL=placental length, PLW=placental weight, PLSA=placental surface area, CRL=crown rump length, PVIA=piglet viability score, F:P=piglet vs placental weight ratio.

(r=0.75), and Umbilical cord length (r=0.81) (table 5). Most piglets (785/95%) were determined to be alive at d 113 of gestation, 13 piglets (1.6%) were recovered dead and 14 (1.8%) necrotic or mummified fetuses were observed. Correlation coefficients between number of live piglets and piglet survival rates were significant (p<0.05 and ≥0.50). Piglet measurements were also partitioned by sex to examine the differences due to sex or treatment of dam. The ratio of male to female piglets was 384:417, which translates into 48.8% males. Sex differences (in favour of males) were detected for placental weight (p<0.05), length (p<0.01), surface area

Table 6. Effects of sex and treatment on selected piglet, placental and umbilical cord parameters[1]

Item	Male	SE	Female	SE	P values		
					Sex	Trt.[2]	SEX×Trt.
No. of piglets	384		417				
Crown rump length, cm	31.4	0.42	29.5	0.22	0.01	0.68	0.80
Piglet weight, g	1,184.3	15.9	1,132.2	16.8	0.04	0.09	0.06
Placenta							
Weight, g	267.1	2.5	257.7	2.6	0.02	0.70	0.50
Length, cm	60.5	0.60	58.7	0.65	0.008	0.40	0.62
Surface area, cm^2	1,061.3	6.4	1,042.2	6.1	0.009	0.04	0.64
Umbilical cord							
Length, cm	52.1	0.69	50.8	0.65	0.08	0.30	0.70
Strength, kN	0.010	0.003	0.009	0.08	0.08	0.43	0.54
Elasticity, mm	9.0	0.21	8.6	0.22	0.12	0.60	0.70

[1] =Values are least square means. [2] =pST, insulin and pST+insulin.

($p<0.01$); piglet weight ($p<0.05$) and length ($p<0.05$) (table 6). This is interpreted to mean that male piglets possessed in utero size or growth advantage which persisted until d 113 of gestation.

DISCUSSION

One of the major objectives of the present study was to determine the effects of pST and or insulin injections on the morphological development of the uteroplacental unit in gestating gilts. Uteri were significantly longer and heavier in insulin treated gilts. Similarly, pST treated gilts, demonstrated tendency for longer and heavier uteri compared to control gilts (table 2). It is apparent from these results, that the functional integrity of the uterus, as measured by its ability to support the survival and normal development of conceptuses, were beneficially enhanced by maternal pST or insulin treatment from gestation d 30 to 70. Although exogenous administration of pST is known to increase organ weights in growing/finishing pigs, data on direct effects of this hormone on uterine morphology during gestation are scarce. No treatment effects on uterine mass were detected in prepubertal gilts given 5 mg pST /d for 42 d (Bryan et al., 1992). Kelly et al. (1992) and Andres et al. (1993) also reported no significant differences in uterine dimensions in gilts that were injected twice daily with 30 μg/kg pST from d 28 through 38 of gestation. Only limited information regarding direct effects of maternal insulin administration on reproductive tract development in swine, although growth promoting effects of insulin in the preimplantation gravid uterus have been reported in mice (Harvey and Kaye, 1991). The pronounced increases in uterine weight and length in gilts treated with pST or insulin presents one of the more novel aspects of the present study, since it is widely acknowledged that the uterus imposes physical limitations on fetal survival in the pig (Knight et al., 1977; Wu et al., 1987; Chen and Dzuik, 1993).

However, the above results do not allow decisive conclusions as to the mechanisms involved in this modified uterine development, but may be mediated through changes in local production of insulin-like growth factors -I (IGF-I). The IGFs were first identified as circulating mediators of the action of growth hormone. Subsequently they were shown to be highly expressed in many tissues, especially the ovary and the uterus (Murphy and Ballejo, 1994). IGF-I protein is present in uterine lumenal fluid and endometrium of pigs (Letcher et al., 1989; Simmen et al., 1990, 1992). The mRNA for IGF-I is also present in endometrium and was highest on d 12 of gestation and between d 30 and 60, coincident with maximum growth of the uterus (Geisert et al., 1991; Hofig et al., 1991). Together, these observations fulfil many necessary criteria for considering possible IGF-I involvement in pST or insulin mediated enhanced uterine development.

The significant maternal treatment effect in placental measurements was on placental macroscopic surface area, although there was a noticeable trend for placental weight, and length to be higher in treated gilts. The lack of significant treatment effect on placental length was not unexpected, because previous studies by Knight et al. (1977) and Wigmore and Strickland (1980) have provided data that suggest that placental length is probably determined early in gestation, i.e., prior to d 30 in pigs. A significant and positive correlation was calculated between placental surface area and piglet weight or crown-rump length (table 6). These coefficients indicate that the surface area of placental tissues supporting a piglet is significantly related to the growth of that piglet in utero. There is little information in available on the effects of either maternal pST or insulin treatment on porcine placental development, although, Gerrard et al. (1994) provided data which showed weights of individual placenta to be greater in pST compared to saline treated gilts.

The incidence of specific cord abnormalities (excessive torsion, single umbilical cord artery or vascular oedema) was low (14.3%) and independent of treatment, thus, are regarded as a normal physiological phenomenon. However, cord abnormalities occurred more in short umbilical cords than in long ones ($p<0.01$; table 3). This study has demonstrated for the first time that short cords were more commonly associated with specific cord abnormalities in the fetal pig. The reason for this remains to be determined. However, it is tempting to speculate that excessive traction on short cords, as a result of in utero fetal activity, could cause transient cord torsion and vascular oedema, which were the more common forms of cord abnormalities observed. When cord length data from treatment (P, I, & P+I) groups were pooled an contrasted with control group, a significant 6% increase (53.2 vs 49.6 cm; $p<.05$) in cord length was detected.

The exact mechanisms by which pST and or insulin treatment stimulated umbilical cord longitudinal development remains to be determined. The stimulus for increased cord length is yet to be determined for any species, although, Miller et al. (1981) had proposed a "stretch hypothesis" which states that cord length relates to the stretch placed on it by the developing fetus, thus, an index of fetal motor activity. Studies in the pig tend to support this concept, because the length of umbilical cord was significantly shortened in hypophysectomized fetuses compared to their intact litter mates (Randall, 1989). Following the above hypothesis, we speculate that the significantly longer uteri observed in pST or insulin treated gilts (table 2), resulted in less restricted intrauterine space and movement of fetal pigs, increased tension on the cord, thereby providing the biologic force that caused linear cord growth.

This insulin and or pST mediated increases in cord longitudinal development is regarded as an original contribution of the present study. Because for a wide variety of species, short cords have been associated with increased risk of premature cord rupture during delivery

in man (Bruce et al., 1978), in swine (Curtis, 1974; Randall, 1989), and in rodents (Ballantyne et al., 1978). Nonsignificant differences in cord strength, measured by tension necessary to break a portion of the cord, were detected among and within treatments. It is not clear from the present study or from any other work in the literature, as to what contributes to umbilical cord strength in fetal pigs. Cord elasticity was equally improved by insulin treatment. Because of the significant correlations between cord length and elasticity (r=0.78), and because both parameters were enhanced by maternal insulin treatment, it is suggested that conditions that are favourable to linear cord growth are equally favourable for cord elasticity.

In contrast to the apparent beneficial effect of exogenous insulin administration on piglet survival reported in this study, Cox et al. (1987) and Kirkwood and Thacker (1991) reported a lack of effect of exogenous insulin on litter size as well as embryo or fetal pig survival. As evident in table 4, no differences in piglet weight or crown to rump length were observed between control and treated gilts. Male piglets had growth advantages over females regardless of maternal treatment. There was also a significant sex effect on placental development in favour of males (table 6). Thus, while exogenous pST and or insulin may not have significantly affected fetal pig weight or crown-rump length, the present study has provided supporting evidence that male fetal pigs have growth superiority resulting from discernable differences in placental development.

CONCLUSION

This study has elicited some of the responses of fetal, uteroplacental, umbilical cord parameters to parenteral injections of porcine somatotropin and or insulin to gestating gilts. The result of this study with regard to in utero piglet development were not particularly dramatic, despite the compelling evidence in the literature that insulin and to lesser extent somatotropin controls fetal development in a wide variety of mammalian species including the pig. Therefore, attention should be shifted away from regulation of fetal pig growth per se and focused on methods of stimulating uteroplacental and umbilical cord development during gestation. Also, these data have provided a better understanding of the roles of hormones of the somatotrophic axis in regulating uterine, placental, umbilical cord development and fetal survival in swine, and can function as a direction for future research

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