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EFFECTS OF L-CARNITINE ON FETAL GROWTH AND THE INSULIN-LIKE GROWTH FACTOR SYSTEM IN PIGS[1]

A.T. Waylan, B.J. Johnson, J.P. Kayser, D.P. Gnad[2], J.D. Dunn, E.K. Sissom, J.J. Higgins[3], and J.C. Woodworth[4]

Summary

Twelve sows were used to examine the effects of feeding L-carnitine from artificial insemination to mid-gestation on maternal circulating IGF-I and carnitine concentrations and fetal growth. Supplementing L-carnitine did not influence the serum concentration of IGF-I. However, sows that were fed carnitine had increased circulating plasma free carnitine. Litters from sows fed L-carnitine were heavier and had more fetuses. The increase in litter fetus number was not detrimental to other growth traits such as individual fetal weight or crown to rump length. Our study suggests that feeding L-carnitine to gestating sows is beneficial for fetal growth and development.

(Key Words: Sows, Carnitine, Insulin-like Growth Factor)

Introduction

L-carnitine is a water-soluble amine that is naturally synthesized in liver, kidney, and brain. This compound plays an important role in lipid metabolism where it serves as a co-factor in mitochondrial transport and oxidation of long-chain fatty acids. Carnitine has also been found to regulate carbohydrate metabolism. Fatty acids and carbohydrates are essential nutrients for the development of tissue, including skeletal muscle in mammals.

Insulin-like growth factors (IGF) –I and –II are proteins that have potent proliferative and differentiation-promoting effects on cultured muscle cells, and the interactions of these growth factors with muscle cells play a significant role in regulating growth and differentiation of muscle tissues *in vivo*.

Previous research has shown that feeding L-carnitine to gestating sows increased circulating IGF-I and free carnitine at mid-gestation. Additionally, supplemented L-carnitine fed to sows during gestation resulted in piglets with a larger cross-sectional area of semitendinosus muscle. These data suggest that feeding L-carnitine to gestating sows will positively affect muscle growth and development in subsequent offspring. However, the exact mechanism of L-carnitine's affect on muscle growth has not been determined. Therefore the objectives of this experiment were to: 1) further evaluate the circulating concentration of IGF-I and carnitine in sows fed a diet with or without carnitine and 2) evaluate fetal growth characteristics of fetal

[1]The authors would like to thank Lonza, Inc., Fair Lawn, New Jersey, for their financial support.
[2]Lonza, Inc., Fair Lawn, New Jersey.
[3]Department of Statistics.
[4]Agricultural Practices, College of Veterinary Medicine.

pigs at mid-gestation from sows fed L-carnitine as compared to control-fed sows.

Procedures

All animal procedures were reviewed and approved by the Kansas State University Animal Care and Use Committee. Twelve fourth-parity sows (PIC, Franklin, Kentucky; C 22 sows; BW = 552.6 lb) were inseminated (PIC; 327 MQ) artificially 12, 24, and 36 hours after the onset of estrus. Sows were housed in individual crates (6 × 1.8 ft) in an environmentally controlled gestation barn at the Kansas State University Swine Teaching and Research Center from breeding to mid-gestation. Sows were randomly allotted to one of two dietary treatments based on weight at breeding. All sows were fed 4.5 lb/d of a corn-soybean meal based gestation diet and received a 50 g top dress containing either 0 (control, n= 6) or 100 mg L-carnitine from d 1 to approximately d 57 of gestation. Day 1 was considered 12 hours after the first insemination. Sows were allowed *ad libitum* access to water.

At d 0, 28, and 57 of gestation, blood samples were collected 7 hours after feeding by puncture of the vena cava for determination of total and free carnitine and IGF-I. Blood samples were collected in both heparinized and non-treated tubes and were placed on ice until centrifuged (2,500 x *g* for 20 minutes at 39°F) or refrigerated (39°F) 48 hours before centrifugation, respectively. Plasma or sera was then separated and frozen (-4°F) until analysis. Microdetermination of carnitine concentrations in plasma and a two-sided immunoradiometric assay was used to determine IGF-I concentrations in sera.

Sows were anesthetized intravenously with sodium thiopental (8 mg/kg) before surgery, and the surgical plane of anesthesia was maintained by inhalation of halothane (2 to 5%). Additionally atropine sulfate (0.04 to 0.08 mg/kg) was administered intramuscular to decrease salivation. Sows underwent Caesarean section on d 54.5 to 59 of gestation. A mid-ventral incision was made and all blood flow to the uterus was ligated with ligatures on the ovarian stump and cervix. The uterus was removed and the abdominal layers were closed with absorbent sutures. Number and sex of fetuses were determined and recorded after the removal of the uterus from the sow. Fetal pigs were then removed and individually weighed and measured (crown to rump length). To calculate total litter weight, the sum of individual fetus weights was determined.

Statistical analyses for blood concentrations were performed with the MIXED procedure of SAS (SAS, 2000; SAS Inst. Inc., Cary, North Carolina). A split-plot analysis was conducted to account for repeated measurements that included the fixed effects of treatment and day of bleeding as the repeated measure. Satterthwaite adjustment was used for the degrees of freedom. Gestational growth data were also analyzed using the MIXED procedure of SAS. The model included treatment and feeding period with gestation day as a covariate. All treatment means were separated ($P<0.05$) using the Least Significance Difference (LSD) procedure when the respective F-tests were significant ($P<0.05$) unless otherwise stated.

Results and Discussion

No treatment by day interaction ($P>0.20$) was observed for circulating IGF-I or free carnitine (Figure 1). A day effect ($P<0.0001$) was detected for IGF-I (Figure 2) with circulating IGF-I higher ($P<0.05$) at d 0 of gestation than at d 28 or 55. Furthermore, as the number of gestation d increased from d 28 to 55, IGF-I concentrations numerically decreased. A treatment by day interaction ($P<0.05$) was observed for total carnitine (Figure 3). Sows fed L-carnitine had a higher ($P<0.05$) concentration of total carnitine at d 55 than did the control sows.

For the growth parameters, litter weights tended ($P=0.07$; Table 1) to be heavier in sows

fed L-carnitine compared to the controls. However, individual fetus weight did not differ ($P>0.05$) between the two treatments. Supplementing sows with L-carnitine resulted in larger ($P<0.05$) litters compared to litters from control fed sows. There was no affect ($P>0.05$) on fetus crown to rump length between treatments.

These results suggest that circulating IGF-I levels of gestating sows fed with or without L-carnitine are similar. Previous research has indicated that feeding sows L-carnitine during gestation had increased circulating IGF-I levels on both d 60 and 90 of gestation. These findings may explain why pigs farrowed from sows fed carnitine had heavier-muscled carcasses at slaughter compared to those from sows fed a control diet. The researchers suggested that the improvement observed in muscling of offspring from L-carnitine fed sows was a result of increased number of muscle fibers compared to the controls. Because IGF-I acts as a promoter of muscle growth it was suggested that the elevated IGF-I was having a proliferative affect on muscle cells allowing for improved carcass muscling. However the results of the current study suggest that the mode of action for L-carnitine improving muscling is not an endocrine effect by maternal IGF-I.

Feeding L-carnitine to gestating sows was beneficial for maintenance of fetal growth and development. The observed increase in total litter weight from sows fed L-carnitine suggests that L-carnitine affects growth by mid-gestation. Furthermore, individual fetus weight was unchanged between the two treatments, but the number of fetuses in the litters increased from 11 to 16 for control and carnitine fed sows, respectively. The carnitine was fed after ovulation and hence may increase the availability of nutrients to sustain more embryos and resulting in the observed increase in fetus number at mid-gestation. In addition to individual fetal weight, fetus crown to rump length was not affected by feeding L-carnitine, even though there was an increase in total litter weight. Therefore, the increased fetus number was not at the expense of fetal growth performance, a relationship that is normally inversely related.

Feeding L-carnitine resulted in greater variation of the relation of fetus number per litter to individual fetus weight compared to diets not containing carnitine (Figure 4). Even though there were more fetuses per litter from the sows supplemented L-carnitine, individual fetal weight was not negatively affected. In the litters from control fed sows, the range was smaller for both fetal weight and fetus number per litter. This suggests that the observed variation from feeding L-carnitine may be influenced by both the growth factor system and nutrient availability.

Due to the insemination of multiple sows on the same day, hysterectomies were completed on differing days of gestation. For both treatments, on average, litter weight increased as the number of gestation days increased (Figure 5). This suggests that mid-gestation is a time of rapid fetal growth and development. Interestingly, feeding L-carnitine resulted with heavier litters on each evaluated gestation d except d 59.

Feeding gestating sows L-carnitine increased number of piglets and total litter weight. Since, muscle development occurs before adipose tissue, the increase in litter weight indicates that fetal muscle mass may be increased in fetuses obtained from sows fed L-carnitine. In conclusion, producers can feed L-carnitine to gestating sows to take advantage of enhanced performance traits without negatively affecting fetal growth and development. More research should be conducted to further define the mechanisms that are affected by carnitine and that are responsible for the increased muscling in carcasses.

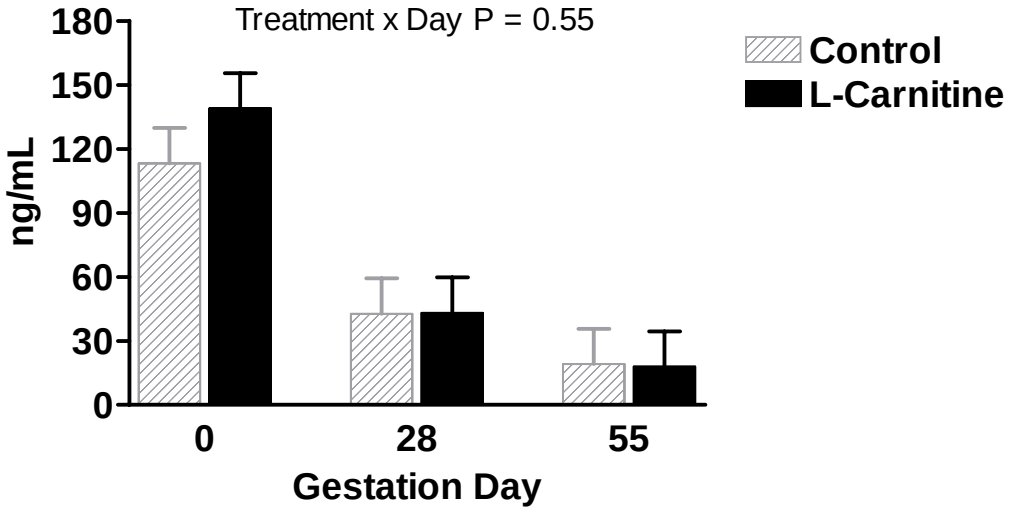

Figure 1. The influence of feeding sows L-carnitine on serum IGF-I concentrations.

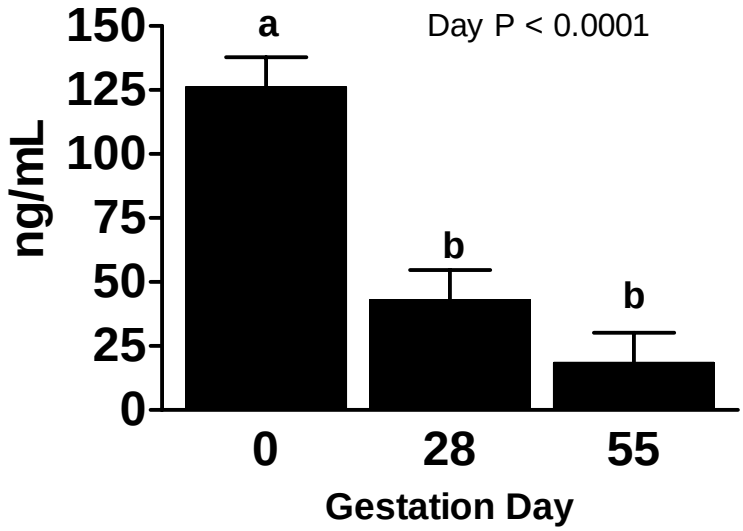

Figure 2. The influence of gestation day on maternal serum IGF-I concentrations.

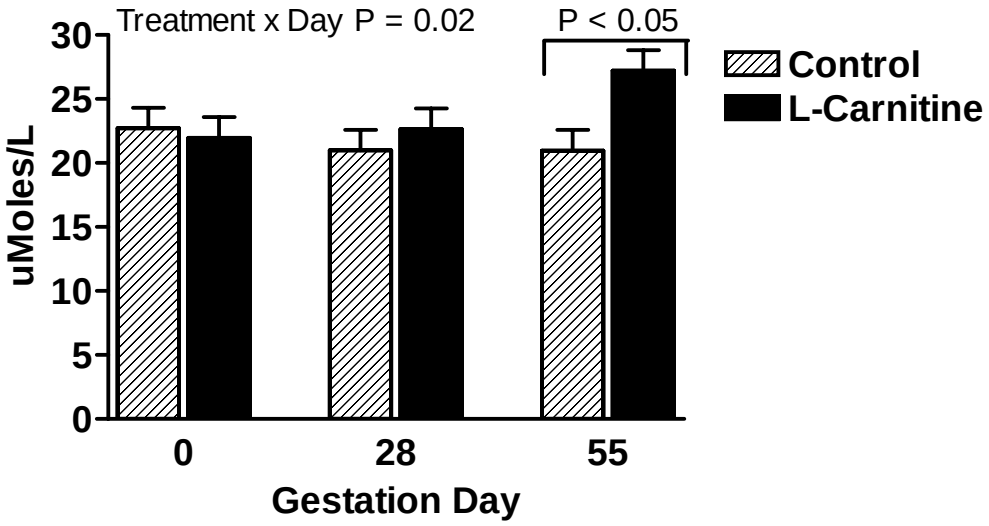

Figure 3. The influence of feeding sows L-carnitine on plasma total carnitine concentrations.

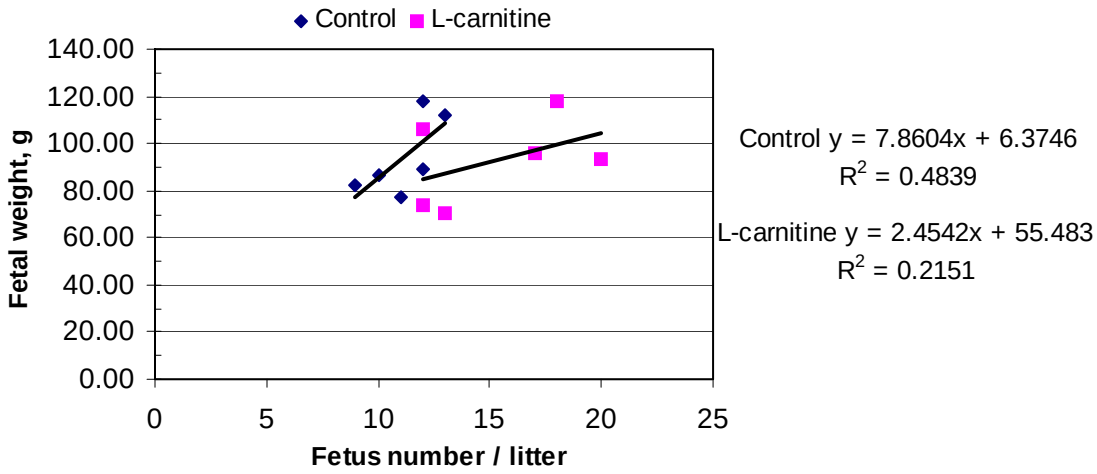

Figure 4. Relationship between the number of fetuses per sow and average fetal weight.

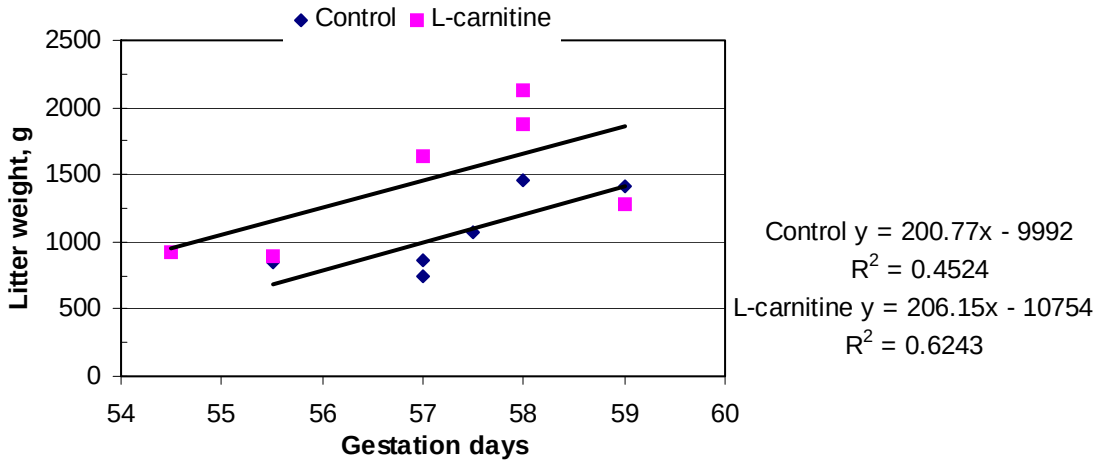

Figure 5. Relationship between number of gestation days on total litter weight.

Table 1. Effects of Feeding Gestating Sows L-carnitine on Fetal Growth Traits

	Control	L-carnitine	P-value
Initial sow weight, lbs	552.3	553.5	--
Number of fetuses	67	92	--
Gender of fetuses (75 female & 84 male)	--	--	--
Fetus number per litter	10.8[y]	15.5[x]	.019
Litter weight, g[a]	989.4[y]	1,449.6[x]	.068
Fetus weight, g	91.4	92.4	.880
Fetus crown to rump length, in	5.4	5.2	.085

[a]Litter weight was calculated by summing each individual fetus weight per litter.

[x,y]Means in the same row without a common superscript letter differ (P<0.05).