Effects of Dietary Supplementation of Creatine-Monohydrate on Fetal-Placental Development in Mid- and Late-Gestating Gilts

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The creatine-creatine kinase-phosphocreatine (Cr-CK-PCr) system maintains intracellular ratios of ATP/ADP for support of metabolism and multiple cellular functions. Postnatally, Cr synthesis begins in the kidneys with arginine and glycine converted into guanidinoacetate (GA) by arginine-glycine amidinotransferase. GA is released from the kidneys into vasculature and transported to the liver for methylation by guanidinoacetate-n-methyltransferase to form Cr which is released into vasculature for uptake by target cells and tissues. Within target cells and tissues, CK converts Cr into PCr, which rapidly regenerates ATP. The Cr-CK-PCr system has been characterized at the placental-uterine interface of rodents, primates, and sheep, and is hypothesized to support fetal-placental development. The ATP buffering capacity of the Cr-CK-PCr system is important for muscle cell function and may be involved in fetal muscle development. This study aimed to determine effects of dietary supplementation of creatine to gestating gilts on fetal-placental growth and development and on number and ratio of primary and secondary muscle fibers, respectively in fetal pigs at Days 60 and 90 of gestation. Reproductively mature gilts were synchronized to estrus using Matrix and observed for estrus (Day 0) in the presence of a fertile boar and were artificially inseminated 12h and 24h later. Gilts were individually housed from Day 9 and fed 2 lbs of a 14% crude protein diet twice daily that meets the nutrient requirements for pregnant gilts. Gilts were assigned to either control (CON) (n=9 gilts/Day of gestation) or creatine (Cr) (n=10 gilts/Day of gestation) treatment groups. Creatine (15g twice daily) was provided to gilts assigned to Cr treatment group from Day 10 to either Day 60 or Day 90 of gestation, whereas CON gilts were unsupplemented. Gilts were euthanized and hysterectomized on Day 60 or 90 of gestation. These protocols were completed in replicates, in which gilts were synchronized in spring then euthanized in summer or synchronized in fall then euthanized in winter. Litter size, fetal crown-rump length, fetal sex, and fetal body weight was recorded. Three female and male fetuses closest to mean body weight within each litter was selected and mean fetal brain, kidney, liver, spleen, and biceps-femoris muscle weight was recorded. Data were analyzed to determine effects of treatment, Day of pregnancy, season, and fetal sex on litter size, fetal measurements, and incidence of intrauterine growth restriction. There was significant treatment effect of greater mean kidney weight for fetuses from Cr-treated than CON-treated gilts in both Days 60 ($P<0.0001$) and 90 ($P=0.0410$) of gestation. Fetuses from CON gilts tended ($P=0.0609$) to have heavier brains than fetuses from Cr gilts on Day 60 of gestation. Mean weights of fetal body weight, kidney, liver, and biceps-femoris from winter euthanized replicates on Day 60 of gestation were significantly greater ($P<0.0001$) than those of summer euthanized replicates. Mean fetal spleen and liver weights were significantly greater ($P<0.001$) in summer euthanized replicates than winter euthanized replicates from Day 90 of gestation. Results of this study suggest that dietary supplementation of creatine in gestating gilts had limited effects on fetal organ development. Studies on treatment effects on placental and fetal muscle fiber development are ongoing and further mechanistic analyses should be performed to investigate the observed effects on organ development.

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