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Growth, intake, and health of Holstein heifer calves fed an enhanced preweaning diet with or without postweaning exogenous estrogen

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ABSTRACT

Research has shown that changes in nutrition both before and after weaning can affect mammary development. Additionally, estrogen is known to be a potent mammogenic stimulant. Our objectives were to determine effects of altered preweaning feeding and exogenous estradiol postweaning on growth, intake, and health. Thirty-six Holstein heifer calves were reared on (1) a restricted milk replacer (MR) diet fed at 0.44 kg powder dry matter (DM)/day [R; 20.9% crude protein (CP), 19.8% fat, DM basis], or (2) an enhanced MR fed at 1.08 kg powder DM/d (EH; 28.9% CP, 26.2% fat, DM basis). The MR feeding was reduced 50% during wk 8 to prepare for weaning. Starter was offered after wk 4 but balanced between treatments. Body weight and frame were measured weekly with intakes and health monitored daily. At weaning, a subset of calves were slaughtered ($n = 6$ /diet). Enhanced-fed calves had greater carcass, thymus, liver, spleen, and mammary gland (parenchyma and mammary fat pad) weights. The EH calves also had greater average daily gain (ADG) starting during wk 1 (0.36 vs. -0.06 kg/d) and lasting through wk 7 (1.00 vs. 0.41 kg/d). Remaining calves received estrogen implants or placebo and were slaughtered at the end of wk 10, creating 4 treatments: (1) R, (2) R + estrogen (R-E2), (3) EH, and (4) EH + estrogen (EH-E2). Postweaning ADG was similar between R, EH, and EH-E2 calves, but greater in R-E2 calves than E calves. The EH-E2 calves had the heaviest mammary glands, and R-E2 calves had heavier mammary glands than R calves. The EH calves consumed more MR DM, CP, and fat preweaning. The R-fed calves consumed more starter DM preweaning. Fecal score was greater for EH calves (1.74 vs. 1.50) preweaning, but days medicated did not differ. Fecal scores were lower for R-E2 calves postweaning. Improved preweaning feeding of calves increased body weights and frame measures.

Differences in body weights remained postweaning. Enhanced-fed calves showed greater ADG during the preweaning period but not postweaning. Exogenous estrogen may elicit diet-dependent growth responses. Analysis of collected samples will allow determination of cellular and molecular processes responsible for the marked differences in mammary development observed. **Key words:** mammary gland, milk replacer, estradiol, calf

INTRODUCTION

Some research has shown that greater prepubertal ADG decreases mammary gland development and subsequent milk yield. Radcliff et al. (2000) fed Holstein heifers either a diet targeting a BW gain of 0.8 or 1.2 kg/d beginning at 125 kg of BW. Calves fed for a greater rate of gain had greater prebreeding BW gains and were approximately 90 d younger at first insemination. However, these heifers produced 14% less milk during their first lactation. These data correspond with others (Sejrsen et al., 1982; Sejrsen, 1984) reporting that mammary parenchymal (PAR) tissue mass and DNA content decreased by 23 and 32%, respectively, when prepubertal heifers were fed for greater weight gain beginning after weaning. However, the mechanisms involved are still not well understood (e.g., failed cell proliferation or cellular differentiation, premature puberty, blunting of normal waves of allometric mammary growth with each estrus cycle, and so on; Meyer et al., 2006a,b).

Recent data (Soberon et al., 2012), however, have indicated that the negative correlation between gain and mammary development may not be the same throughout the entire prepubertal period. Specifically, a greater rate of gain during the preweaning period may be beneficial to mammary gland development. Historically, it was generally thought that mammary PAR growth was largely quiescent until the onset of allometric mammary growth at approximately 2 to 3 mo of age. Recent reports (Capuco and Akers, 2010; Esselburn et al., 2015) show that allometric growth begins much earlier (i.e., a 60-fold increase in mammary

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PAR mass from birth until approximately 90 d of age). During this same period, a doubling of BW typically occurs (Capuco and Akers, 2010).

A limited number of studies have focused on the effect of preweaning milk replacer (MR) feeding on mammary development (Brown et al., 2005; Meyer et al., 2006a,b; Daniels et al., 2009). Results indicate that preweaning plane of nutrition can alter mammary fat pad weight, DNA content of the mammary PAR, total mammary PAR, and total mammary PAR DNA without negatively affecting PAR, lipid, or protein concentration (Brown et al., 2005; Meyer et al., 2006a). Additionally, recent data have shown that increasing preweaning ADG by 1 kg/d is associated with an increase of 1,000 kg or more in first lactation milk yield (Soberon et al., 2012). Mechanisms responsible for this increase remain unknown.

We hypothesized that enhanced preweaning nutrition positively alters mammary gland development by creating mammary cells that are primed to better respond to mammogenic stimuli. The most commonly recognized mammogenic agent at this point in development is estradiol (Akers, 2000). Indeed, removal of estradiol in early life severely impairs mammary gland development, and this impairment can be attributed to lack of estradiol, altered estrogen receptor expression, or both (Tucker et al., 2016). We hypothesized that calves fed a higher plane of nutrition preweaning would show an enhanced response to exogenous estradiol supplementation. Our first objective was to create 2 distinct groups of calves via dietary alterations and to assess the effects of plane of nutrition on body and organ growth and overall mammary development. A second objective was to determine if animals fed a higher plane of nutrition responded differentially to exogenous estrogen administration. To do this, tissue samples were collected and will be analyzed to discover cellular and molecular mechanisms involved in producing the effects of enhanced preweaning nutrition and estrogen treatment on heifer mammary development. In this report, we provide details of animal body and organ growth, performance, and health, and general mammary development as influenced by preweaning nutrition and treatment with exogenous estradiol postweaning. Subsequent reports will provide information regarding the mammary gland and its development.

MATERIALS AND METHODS

This experiment was conducted under the review and approval of the Virginia Polytechnic Institute and State University Institutional Animal Care and Use Committee (#14-045-DASC).

Animal Handling and Experiment Design

Thirty-six Holstein heifer calves were purchased from a single commercial producer (located ~90 miles from campus) and brought to the Virginia Polytechnic Institute and State University Dairy Farm between May and June of 2014. Three batches ($n = 12/\text{batch}$) of heifers were acquired. The heifers were approximately 1 wk old (6.0 ± 2 d) and weighed 39.0 ± 4.4 kg at the time of arrival. Only calves with total serum protein concentrations ≥ 5.5 mg/dL were purchased. Heifers were randomly assigned to treatments, individually housed in outdoor hutches on crushed rock without bedding, and quarantined from the Virginia Tech Dairy herd. Heifers were given ad libitum access to water.

Calves were assigned to 1 of 2 experimental MR ($n = 18/\text{MR}$): (1) a restricted MR diet (R; 20.9% CP, 19.8% fat, DM basis; Southern States Cooperative Inc., Richmond, VA) fed at 0.44 kg of MR powder/animal per d, DM basis, or (2) an enhanced MR (EH; 28.9% CP, 26.2% fat, DM basis; Land O'Lakes Animal Milk Products Co., Shoreview, MN) fed at 1.08 kg of MR powder/animal per d, DM basis. Milk replacers had similar fatty acid profiles due to edible lard being the main fat source, and were fed at 15% solids. Milk replacer was fed in 2 equal portions twice daily at 0600 and 1700 h for the first 7 wk of trial. At wk 8, heifers were fed half the usual amount $1\times$ daily at 1700 h to prepare for weaning. Weaning occurred at the end of wk 8. Starter (25.6% CP, 4.0% fat, 19.8% NDF, DM basis; Southern States Cooperative Inc., Richmond, VA) was offered at the end of wk 4 of the trial. In an effort to keep starter intakes similar between treatments, starter was pair fed between R and EH calves. Simply put, R-fed calves were offered starter in the amount of what was consumed by EH-fed calves on the previous day. For example, on d 1, all EH-fed calves were offered starter ad libitum. Their starter intake was then averaged, and that average intake amount was offered to R-fed calves the following day. This was done daily as it was assumed R-fed calves would consume more starter than EH-fed calves if offered ad libitum.

A subset of calves ($n = 6/\text{diet}$) was slaughtered upon weaning to assess dietary effects on organ and tissue development. The remaining calves ($n = 24$) were either given an estradiol implant (Compudose, Elanco Animal Health, Greenfield, IN) or a placebo implant on the day of final milk consumption (weaning). The placebo consisted of the silicon material of the estradiol implant without the hormone content. Estradiol implant selection and implantation was conducted similarly to previous research (Lammers et al., 1999). Implants were administered at the base of the left ear. This produced the following treatment groups ($n = 6/\text{treatment}$):

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