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The degree of maternal nutrient restriction during late gestation influences the growth and endocrine profiles of offspring from beef cows

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ABSTRACT

Context. Cow–calf operations in Argentina are managed under extensive grazing condition and the quality of forages is often poor during the second half of gestation. The severity of nutrient restriction in bovine gestation, caused by seasonal pasture production, often results in poor production traits in progeny. **Aims.** The objective of the current study was to determine whether different levels of maternal nutrient intake in beef cows during late gestation affect fetal and postnatal growth, glucose metabolism, and insulin-like growth factor 1 (IGF1) concentrations in offspring of beef cattle. **Methods.** At 180 ± 4 days of gestation, multiparous Angus cows (n = 56) were blocked by bodyweight (BW) and expected calving date, and assigned to pens (2 or 3 cows/pen). Pens (n = 8 per treatment) were then randomly assigned to the following treatments: severely restricted (SR; 50% of net energy and 58% of CP requirements), moderately restricted (MR; 75% of net energy and 85% of CP requirements), or control (CON; 100% of net energy and 116% of CP requirements). Pen was the experimental unit and data were analysed by ANOVA or repeated measures analysis, as appropriate. After calving, all cows were managed in a single group until weaning. **Key results.** Cow BW and body condition score decreased as nutritional restriction increased ($P < 0.05$). At parturition, birth weight of calves from SR dams and MR dams was lower than that of calves from CON dams ($P = 0.05$; 4.9 kg and 2.1 kg respectively). Average daily gain of calves from birth to 24 days of age was higher ($P = 0.01$) in calves from SR dams than in calves from CON and MR dams. Calves from MR dams were lighter ($P = 0.04$) than were calves from SR and CON dams at weaning. Treatments did not affect milk production or composition ($P > 0.10$) or glucose–insulin metabolism of offspring during lactation ($P > 0.10$). Concentration of IGF1 tended to be lower in MR progeny than in SR and CON progeny during lactation ($P = 0.09$). **Conclusions.** Late gestation maternal nutrient restriction, irrespective of the severity of the restriction, decreased birth weight of offspring; however, severe nutrient restriction induced early postnatal compensatory growth. **Implications.** The severe nutritional restriction produced calves with weaning weights indistinguishable from the control cows due to early postnatal compensatory growth. However, the longer-term effects of nutritional restriction of the dam in the second half of pregnancy on metabolic and reproductive performance in replacement heifers or meat production/quality in steers is yet to be determined.

Key words: beef cattle, calves growth, endocrine perfiles, fetal programming, late gestation, milk production, nutrient restriction, offspring performance.

Introduction

Beef cows within Argentinian commercial herds often receive inadequate nutrition during late gestation as this stage of pregnancy often coincides with the end of winter season, a period of decreased forage quality and availability. Inadequate maternal nutrition during late gestation may lead to intrauterine growth restriction of bovine fetuses with long-term consequences on offspring growth and physiology (Funston *et al.* 2010; Long *et al.* 2010; López Valiente *et al.* 2019; Maresca *et al.* 2019). Previous experiments in beef cattle evaluating nutrient restriction from mid- to late gestation have reported decreased birth weight (Corah *et al.* 1975; Houghton *et al.* 1990; Freetly *et al.* 2000) and weaning weight (Corah *et al.* 1975; LeMaster *et al.* 2017) of calves born from both primiparous and multiparous dams when nutrients have been restricted during the last 100 days of gestation. Conversely, experiments that applied nutrient restriction regimes on cows during late gestation observed lowered birth weight but no effect on weaning weight in offspring (Spitzer *et al.* 1995; Freetly *et al.* 2000; Wilson *et al.* 2016).

Nutrient availability during fetal development may play a role in altered glucose–insulin homeostasis during early postnatal growth and development in cattle. These responses have been observed when total nutrient (Gardner *et al.* 2005; Ford *et al.* 2007; Long *et al.* 2010) or specific component of the diet, such as protein, are restricted (Maresca *et al.* 2018). Thus, low dietary protein concentration during late gestation generates hyperglycemia in the calves during the first 60 days of life but does not alter growth rate until weaning (Maresca *et al.* 2018). Conversely, LeMaster *et al.* (2017) reported that late-gestation nutrient restriction or restriction with supplementation with 0.45 kg of soybean meal 3 days/week reduced birth weight and postnatal plasma glucose concentrations compared with control cows. Insulin-like growth factor I (IGF1) is essential for regulation of animal growth and nutritional restriction on fetal development, which may result in permanent alterations of the IGF axis (Bauer *et al.* 1995; Brameld *et al.* 2000). Maternal protein restriction in mid- to late gestation decreases concentrations of IGF1 in offspring, including changes in the development of muscle and adipose tissues (Maresca *et al.* 2018; López Valiente *et al.* 2019). Inconsistencies in the literature may be attributed to differences in the severity of nutrient restriction induced in animals and the factors that were being evaluated in offspring. Therefore, the degree of bodyweight or body condition loss during treatments and subsequent lactation performance in beef cows vary greatly. Few studies have examined the relationship between postnatal growth and milk performance following late-gestation nutrient restriction in beef cows (Corah *et al.* 1975; Marston *et al.* 1995; Radunz *et al.* 2010).

We hypothesise that the level of severity of maternal nutrient restriction exhibits a linear effect on growth and metabolic function of offspring. The objective of the current study was to determine whether altered levels of maternal nutrient intake during late gestation affect fetal and postnatal growth, glucose metabolism, and IGF1 concentrations in offspring of beef cattle.

Materials and methods

Cow and calf management

The experiment was conducted at Experimental Farm Cuenca del Salado INTA (Buenos Aires, Argentina). All procedures were approved by CICUAE INTA-CERBAS (Institutional Committee for Care and Use of Experimental Animal of South Buenos Aires Region), approval No. 92. Multiparous Angus cows (n = 56) with an initial bodyweight (BW) of 497 ± 8 kg and initial body condition score (BCS: 1 = emaciated to 9 = obese; Wagner *et al.* 1988) of 5.2 ± 0.4 were synchronised for estrus by using a controlled internal progesterone-releasing device (Cronipres®, Biogenesis-Bago, Argentina) for 7 days. On removal of the device, 500 μg of cloprostenol (Ciclase DL®, Syntex, Argentina) and 1 mg of oestradiol benzoate (Benzoate de oestradiol Syntex®, Argentina) were injected intramuscularly. Timed artificial insemination (AI) was conducted 48 h after oestradiol injection, using semen from a single Angus sire. Ten days after AI, a single Angus bull was used for 15 days for natural breeding period. Thirty days after the end of the natural breeding period, singleton pregnancy was confirmed and fetal age was determined *via* transrectal ultrasonography (6.5-MHz probe; Aquila pro, Esaote Europe B.V. Maastricht, Netherlands). Pregnant cows that were to be enrolled in the study were managed on fescue pastures from early to mid-gestation (63.1% *in vitro* dry-matter digestibility (DMD); 13.9% crude protein (CP). On the 113th day before the expected calving date, all cows were placed in pens and fed total mixed ration (TMR) diet (100% of NRC recommendations for middle-gestation cows). Cows were assigned into four blocks by bodyweight (BW) and the expected calving date and randomly assigned into 24 pens (2 or 3 cows/pen). Pens (n = 8 per treatment) were randomly assigned to one of the following three treatments for the last 103 ± 4 days of gestation: severely restricted (SR; 50% of requirement for net energy (NE) and 58% of requirement of CP), moderately restricted (MR; 75% of requirement for NE and 85% of requirement of CP), or control (CON; 100% of requirement for NE and 116% of requirement of CP). Ration was fed in feeders as a TMR daily at 0900 hours, and the DMI was measured all days by the difference between feed offered and orts. In all cases, the requirement was taken as maintenance and gestation (National Research Council 2000). Composition and nutrient analysis of the ration are given in Table 1.

Following parturition, cow–calf pairs were moved and maintained as a single group on grazed oats grass (81.7% DMD; 16.2% CP) and mixed grass pasture (51.4% DMD; 10.1% CP) until weaning of calves at 150 days of age. Except in the case of the birth of the calves, all BWs were registered after 12 h of fasting from feed and water. BCS was assigned by a single trained technician throughout the experiment. Maternal BW and BCS were recorded on the

Table 1. Ingredients and diet composition for cows fed diets that were severely restricted (SR, 50% of NE and 58% of CP requirements), moderate restricted (MR, 75% of NE and 85% of CP requirements) or not restricted (CON, 100% of NE and 116% of CP requirements; National Research Council 2000) for the last 103 days of gestation.

Parameter	Value
Ingredient (% DM)	
Corn silage	98.3
Urea	0.6
Mineral supplement	1.1
Diet composition[A]	
DM (%)	25.9
CP (% of DM)	10.3
NDF (% of DM)	64.8
DMD (% of DM)	67.3
ME (MJ/kg DM)	10.1
DMI per treatment (kg/day)	
SR	4.55
MR	6.64
CON	9.04

Note: requirements refer to maintenance and gestation.
[A]All values are from laboratory analyses and are presented on a 100% DM basis.

first day of the trial (Day –103), at parturition (Day 0), and at weaning (Day 150). Calf BW was recorded at parturition, and every 30 days until weaning (Day 150). Average daily gain (ADG) was calculated as BW gain divided by days on study. The gestation length was determined only in AI pregnancy cows because date of breeding was accurately recorded (SR: 12 cows, MR: 12 cows; CON: 12 cows).

Newborn body measurement

At the time of parturition, calves were examined within the first 12 h of life to determine sex, and measure birth weight and the following morphometric measurements: height (linear distance from floor to trochanter major of femur), body length (linear distance along vertebral column from first coccygeal vertebra to occipital bone), head circumference (encompass the head from mandible and parietal bone just posterior to eye orbits), heart girth (posterior to foreleg) and cannon bone circumference (narrowest point of metacarpus). Body mass index of newborn calves was calculated by dividing birth weight of each calf by the square root of body length (Sharma *et al.* 2012).

Milk production and composition

Milk production and composition were measured on one cow per pen and thus eight cows per treatment on Days 29, 50, 80, 110 and 150 postpartum, by using the protocol previously established by Quintans *et al.* (2010). On the days of collection, cows to milk were separated from their calves at 1200 hours and then injected intramuscularly with 10 international units of oxytocin (Over®, Argentina) to facilitate milk letdown. Cows were milked using a portable milking machine equipped with a milk meter in line (TrueTest®, Auckland, New Zealand) 5 min after injection. Calves were fitted with nose plates to prevent suckling (San Miguel® Argentina) and returned to their dams in the same paddock. The following day, at approximately 0600 hours, cows were milked again. A sample of 125 mL of milk was taken from the milk meter (TrueTest®, Auckland, New Zealand) of each cow to determine the following components: milk protein, fat, lactose, total solid (IDF 141C:2000 Bentley Instruments, Chaska, MN, USA) and urea (Chemspec 150, Bentley Instruments, Chaska, MN, USA) in Dairy Laboratory LABVIMA, Buenos Aires, Argentina.

Blood collection

Maternal blood samples were collected every 30 days from the beginning of the trial to calving (Days –103, –73, –43, –13) from all cows. Maternal blood samples were collected after 12 h without access to food or water. Calf blood samples were collected from all calves, at parturition and every 30 days until weaning (Days 0, 30, 60, 90, 120, 150). After Day 0, calf blood samples were collected following separation from their dams for 12 h. Serum samples of cows and calves were collected in 6 mL collection tubes (Becton, Dickinson and Co. Franklin Lakes, NJ, USA) via jugular venipuncture. The tubes were placed in ice for <3 h and then centrifuged at 2500*g* for 15 min at 4°C. Serum was decanted and stored at –20°C until further analysis.

Metabolite and hormone analysis

Glucose concentrations were determined using a whole blood sample *via* a hand-held electronic glucometer (Abbott©, UK) immediately following collection (Wittrock *et al.* 2013) with an intra-assay CV of 3.3%, an inter-assay CV of 4.4% and sensitivity of 2.7 mg/mL. Serum insulin concentrations were determined by radioimmunoassay (RIA) in multiple assays through the use of anti-bovine insulin antibody (Sigma, St Louis, MO, USA) and standard human insulin provided by Laboratorios Beta (Buenos Aires, Argentina) with an intra-assay CV of 7.9%, an inter-assay CV of 10.4% and sensitivity of 0.05 ng/mL. Serum insulin-like growth factor 1 (IGF1) concentrations were determined in one assay *via* RIA through the use of an IGF1 antibody (UB2-495) of the NIDDK by using a previously validated acid ethanol extraction procedure (Lacau-Mengido *et al.* 2000) with an intra-assay CV of 7.7% and sensitivity of 2.5 ng/mL.

Statistical analyses

Initially, all cows were blocked according to BW and the expected calving date. Maternal BW, BCS, gestation length, date of calf birth, sex of the calf and offspring body measurements were analysed using the MIXED procedure of SAS (SAS Inst. Inc., Cary, NC, USA). Model statement included the fixed effects of maternal dietary treatment, block, sex, and all possible interactions. Random effect was pen nested into the block per treatment interaction. Maternal glucose, calf concentration of hormones, and metabolites and content of protein, fat, urea, total solids and lactose in milk were analysed as repeated measures using MIXED procedure of SAS (compound symmetry), with treatments, sampling times and their interaction in model. In all cases, pens were considered as experimental units and data are presented as least-square means and s.e.m. Statistical significance was declared at $P \leq 0.05$, while a tendency was declared at $0.05 < P \leq 0.10$.

Table 2. Effect of maternal nutritional status during late gestation on bodyweight and body condition score on cows.

Item	Treatment			s.e.m.	P-value
	SR	MR	CON		Treatment
N	8	8	8	–	–
Body weight (kg)					
Start of treatment	495	496	501	8	0.62
Calving	442c	463b	495a	11	0.01
Change during treatment	−53c	−33b	−6a	8	<0.01
Weaning	458	451	446	12	0.50
Change during lactation	16a	−12b	−49c	10	<0.01
Body condition score					
Start of treatment	5.1	5.3	5.1	0.4	0.84
Calving	3.8c	4.5b	5.0a	0.2	0.01
Change during treatment	−1.3c	−0.8b	−0.1a	0.2	<0.01
Weaning	4.7	4.4	4.5	0.4	0.58
Change during lactation	0.9a	−0.1b	−0.5c	0.2	<0.01

Note: treatments were applied for the last 103 days of gestation, until partum. Start of treatment was at 180 days of gestation (Day −103). Calving/parturition (Day 0); end of the treatment. Duration of treatment approximately the last 103 days of gestation. Weaning was performed on Day 150. Duration of lactation from the time of calving (Day 0) to the time of weaning (Day 150). Body condition scores are as per Wagner et al. 1988.
Means within a row followed by different letters are significantly different at $P = 0.05$.
SR, severely restricted, 50% of NE and 58% of CP requirements; MR, moderately restricted, 75% of NE and 85% of CP requirements; CON, not restricted, 100% of NE and 116% of CP requirements for maintenance and gestation.

Results

Data for maternal BW and BCS are reported in Table 2. Maternal BW and BCS were not different ($P = 0.62$ and $P = 0.84$ respectively) among the treatments at the start of the trial (Day −103). By parturition, BW of dams was different among the treatments ($P = 0.01$). Maternal BW decreased 11% in SR dams and 7% in MR dams, while CON dams lost only 1%. Similarly, maternal BCS decreased 26% in SR dams and 15% in MR dams, while CON dams lost only 2% ($P = 0.01$). During the lactation period from parturition to weaning, SR dams gained BW ($P < 0.01$) compared with MR and CON dams, which lost BW. Similarly, during the lactation period, SR dams gained BCS ($P < 0.01$) compared with MR and CON dams, which lost BCS. Maternal BW and BCS were not different ($P = 0.50$ and $P = 0.58$ respectively) among the treatments at the time of weaning.

Data for maternal glucose concentrations are shown in Fig. 1. A treatment by time interaction ($P = 0.03$) was observed for glucose concentrations during the treatment period. Glucose concentrations were decreased ($P = 0.04$) in SR and MR dams compared with CON dams at 45 and 68 days before calving, were increased ($P = 0.03$) in SR dams compared with MR dams at 13 days before calving, and decreased ($P = 0.02$) in MR dams compared with CON dams at 13 days before calving.

Data for maternal milk production are shown in Fig. 2. Maternal milk production was not different (SR = 6.1, MR = 6.0, CON = 5.6 ± 0.3 L/day, $P = 0.26$) among the treatments or across days ($P = 0.11$).

Data for maternal milk composition are reported in Table 3. Milk composition components (fat, urea, lactose and total solids) were not different ($P > 0.20$) among the treatments. A trend for the interaction time by treatment was observed ($P = 0.06$) in which SR cows tended to produce more protein ($P = 0.07$) than did CON cows at Day 157 postpartum, while MR was intermediate between the SR and CON treatments.

No sex effect ($P > 0.32$; data not shown) or treatment × sex type interaction ($P > 0.24$; data not shown) was observed for any calf variables. Data for calf morphometric measurements at birth are reported in Table 4. Calves from SR dams had smaller ($P = 0.03$) head circumference at parturition than did calves from MR and CON dams. Heart girth ($P = 0.16$), cannon circumference ($P = 0.87$) and height ($P = 0.52$) were not different among the treatments. Calves from MR and SR dams had shorter body length ($P = 0.01$) than did calves from CON dams. Body mass index at birth tended to be reduced ($P = 0.08$) in calves from SR dams compared with those in calves from CON dams, while calves from MR dams were intermediate between the two other treatments. No effect of late-gestation nutritional status on gestation length was found ($P = 0.55$; data not shown), as measured between the day of calf birth and the moment from timed AI (Day –284), and the date of birth was not modified ($P = 0.45$, Table 5).

Data for calf BW from birth until weaning is reported in Table 5. Calves born from SR dams were 4.9 kg lighter than

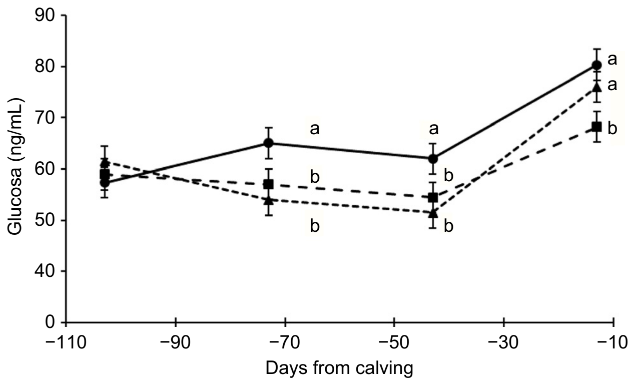

Fig. 1. Glucose concentrations (ng/mL) of cows fed diets that were severely restricted (SR; 50% of NE and 58% of CP requirements; -----), moderately restricted (MR; 75% of NE and 85% of CP requirements; – – –) or met requirements (CON; 100% of NE and 116% of CP requirements; —) according to National Research Council (2000) for maintenance and gestation for the last 103 days of gestation. Values are reported as means ± s.e.m. Different letters indicate a significant ($P \leq 0.05$) difference; treatment, $P = 0.25$; time, $P < 0.001$; treatment × time, $P = 0.03$.

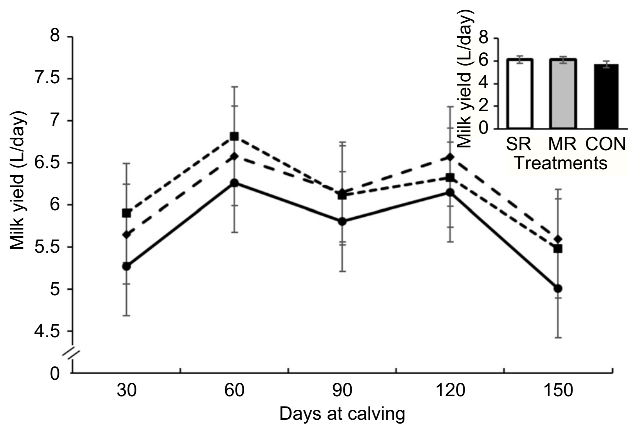

Fig. 2. Maternal milk production (L/day) of cows fed diets that were severely restricted (SR; 50% of NE and 58% of CP requirements; -----), moderately restricted (MR; 75% of NE and 85% of CP requirements; – – –) or met requirements (CON; 100% of NE and 116% of CP requirements; —) according to National Research Council (2000) for maintenance and gestation for the last 103 days of gestation. Values are reported as means ± s.e.m. Treatment, $P = 0.26$; time, $P = 0.11$; treatment × time, $P = 0.76$.

calves born from CON dams, and calves from MR dams were 2.1 kg lighter than calves from CON dams ($P = 0.05$). At 24 days of age, BW of calves from MR dams tended to be decreased ($P = 0.07$) compared with BW of calves from SR and CON dams. By weaning, BW of calves from MR dams was decreased ($P = 0.04$) compared with that of calves from SR and CON dams. The ADG of calves from SR dams from birth to 24 days of age was greater ($P = 0.01$) than that of calves from MR and CON dams. From 24 days of age until weaning, ADG was not different ($P = 0.13$) among the treatments. Overall, ADG from birth to weaning tended to be decreased ($P = 0.09$) in calves from MR dams compared with that in calves from SR and CON dams.

Data for glucose, insulin, and IGF1 concentrations of calves are reported in Fig. 3. Calf glucose and serum insulin concentrations were not different among the treatments ($P = 0.92$ and $P = 0.36$ respectively; Fig. 3*a, b*). Glucose and serum insulin concentrations decreased over time during the lactation period ($P < 0.001$; Fig. 3*a, b*). Serum IGF1 concentrations tended to be decreased in calves from MR dams ($P = 0.09$) compared with those incalves from SR and CON dams (Fig. 3*c*). Serum IGF1 concentrations changed over time during the lactation period ($P < 0.001$; Fig. 3*c*).

Discussion

In the current study, nutrient restriction during late gestation led to progressive reduction in BW and BCS of cows as the level of restriction became more severe. The decreased BW observed in non-restricted dams was possibly due to a loss of gut fill and splanchnic tissue mass due to a change from full grazing forage to the experimental TMR diet. Throughout late gestation, observed BCS loss in restricted treatments was more drastic, percentage-wise, than was BW loss, in which severely restricted cows lost 25% of BCS while moderately restricted cows lost 15% of BCS. BCS serves to better indicate overall long-term nutrition than does change in BW (Wagner *et al.* 1988). In the current study, nutrient restriction treatments decreased maternal blood glucose concentrations. Similar results have been observed in beef cows (Richards *et al.* 1989; LeMaster *et al.* 2017) and sheep (Ford *et al.* 2007), in which plasma glucose concentrations were reduced when nutrient supply was restricted.

In the current study, BW of calves at birth decreased as the degree of nutrient restriction increased. Gestation length was similar among the treatments, thus, alteration of fetal development can be attributed completely to maternal nutritional restriction. At parturition, calves from severely and moderately restricted dams weighed 14% and 6% less than did calves from control dams. Decreased birth weight in calves from dams that received nutrient restriction diets during late gestation has been well documented in beef cattle (Corah *et al.* 1975; Warrington *et al.* 1988; Houghton *et al.* 1990; Spitzer *et al.* 1995; Freetly *et al.* 2000). However, calf birth weight was not affected when cows were fed a diet deficient only in protein during late gestation (Stalker *et al.* 2006; Larson *et al.* 2009; Maresca *et al.* 2018). Fetal growth restriction was associated with various morphometric alterations, regardless of no change observed in birth weight (Harding and Johnston 1995; Barker 1998). In the current experiment, head circumference and body length were greatest in calves from dams that did not undergo nutrient restriction while body

Table 3. Effect of maternal nutritional status during late gestation on milk composition.

Item	Treatment			s.e.m.	P-value		
	SR	MR	CON		Treatment	Time	Treatment × Time
N	8	8	8	–	–	–	–
Fat (g/100 mL)	2.29	2.53	2.66	0.37	0.23	<0.001	0.85
Protein (g/100 mL)	3.18	3.37	3.29	0.08	0.44	<0.001	0.06
Urea (mg/dL)	10.26	10.58	10.62	0.23	0.49	0.01	0.24
Lactose (g/100 mL)	4.89	4.98	4.94	0.07	0.69	<0.001	0.16
Total solids (g/100 mL)	11.33	11.69	11.23	0.18	0.20	<0.001	0.52

Treatments were applied for the last 103 days of gestation, until partum. SR, severely restricted, 50% of NE and 58% of CP requirements; MR, moderately restricted, 75% of NE and 85% of CP requirements; CON, not restricted, 100% of NE and 116% of CP requirements for maintenance and gestation.

Table 4. Effect of maternal nutritional status during late gestation on morphometric measurements of calves at birth.

Item	Treatment			s.e.m.	P-value
	SR	MR	CON		Treatment
N	8	8	8	–	–
Head circumference (cm)	45.1b	47.1a	48.2a	0.7	0.03
Heart girth (cm)	73.7	74.4	78.0	1.6	0.16
Cannon circumference (cm)	11.6	11.7	11.8	0.3	0.87
Body length (cm)	76.7b	74.8b	81.8a	1.7	0.01
Height (cm)	66.5	65.8	68.5	1.8	0.52
Body mass index (kg/m^2)	3.46x	3.80xy	3.98y	0.15	0.08

Note: treatments were applied for the last 103 days of gestation until partum. Weaning (150 days of age).
Means within a row followed by different letters (a, b) differ significantly ($P < 0.05$), and means followed by different letters (x, y) tend to differ ($P < 0.10$).
SR, severely restricted, 50% of NE and 58% of CP requirements; MR, moderately restricted, 75% of NE and 85% of CP requirements; CON, not restricted, 100% of NE and 116% of CP requirements for maintenance and gestation.

Table 5. Effect of maternal nutritional status during late gestation on bodyweight of calves from birth to weaning.

Item	Treatment			s.e.m.	P-value
	SR	MR	CON		Treatment
N	8	8	8	–	–
Bodyweight (kg)					
Birth	30.4c	33.2b	35.3a	0.85	0.05
24 days of age	57.5x	50.3y	57.3x	2.68	0.07
Weaning	163.7a	151.4b	168.4a	5.96	0.04
Average daily gain (kg/day)					
Birth to 24 days of age	1.18a	0.75b	0.85b	0.11	0.01
24 days of age to weaning	0.81	0.77	0.87	0.03	0.13
Birth to weaning	0.84xy	0.78y	0.87x	0.03	0.09

Note: treatments were applied for the last 103 days of gestation until partum. Weaning (150 days of age).
Means within a row followed by different letters (a–c) differ significantly ($P < 0.05$), and means followed by different letters (x, y) tend to differ ($P < 0.10$).
SR, severely restricted, 50% of NE and 58% of CP requirements; MR, moderately restricted, 75% of NE and 85% of CP requirements; CON, not restricted, 100% of NE and 116% of CP requirements for maintenance and gestation.

mass index decreased as the level of nutrient restriction increased. Previous experiments have suggested that smaller body dimension and reduced body mass index at birth are indicators of intrauterine growth retardation (Long et al. 2009; Maresca et al. 2018). Reduced body mass index observed in calves from severely and moderately restricted dams supports the notion that they have experienced an onset of intrauterine growth restriction.

Impaired maternal nutrition during late gestation may have carryover effects on lactation performance of beef cows. Thus, consequences of fetal undernutrition could be confounded by altered maternal milk production and composition during postnatal growth (Robinson et al. 2013). In the current study, decreased BCS and BW observed during late gestation due to altered levels of nutrient provided during late gestation did not affect subsequent milk production or composition. Few studies have reported that maternal nutrient restriction during gestation affects milk production or quality in beef cows. Lake et al. (2005) and Radunz et al. (2010) observed similar milk production (8.6 kg/day to 8.8 kg/day and 8.9 kg/day to 10.3 kg/day respectively) in beef cows with thin to moderate BCS at the time of calving. Similar results were observed when mature beef cows were fed fescue pasture or fescue pasture and 2.1 kg DM dried distillers grains soluble (5.4 kg/day and 5.6 kg/day respectively, Wilson et al. 2016). In addition, milk production and quality did not differ when cows were fed various levels of protein during late gestation (Larson et al. 2009; López Valiente et al. 2018). Previous studies have suggested that high nutrient quality and increased BCS during lactation could potentially mitigate the negative consequences imposed by nutrient restriction during gestation on subsequent milk production (Bell et al. 2000; Lalman et al. 2000). In our experiment, cows were grazing oats grass (81.7% DMD; 16.2% CP) and mixed grass pasture (51.4% DMD; 10.1% CP)

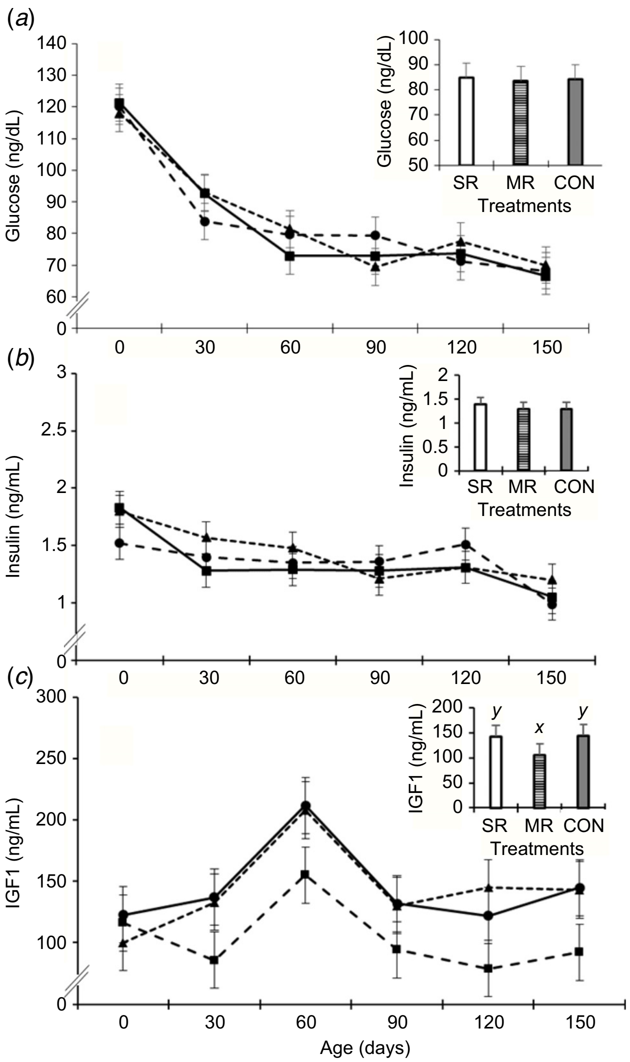

Fig. 3. (*a*) Glucose concentrations (ng/dL), (*b*) serum insulin concentrations (ng/mL), and (*c*) serum IGF1 concentrations (ng/mL) in calves born to cows fed diets that were severely restricted (SR; 50% of NE and 58% of CP requirements; -----), moderately restricted (MR; 75% of NE and 85% of CP requirements; – – –), or met requirements (CON; 100% of NE and 116% of CP requirements; —; National Research Council 2000) for maintenance and gestation for the last 103 days of gestation. Values are reported as means ± s.e.m. *x*, *y* letters signify a tendency to differ ($P < 0.10$). For glucose: treatment, $P = 0.92$; time, $P < 0.001$; treatment × time, $P = 0.75$. For serum insulin: treatment, $P = 0.36$; time, $P < 0.001$; treatment × time, $P = 0.31$. For serum IGF1: treatment, $P = 0.09$; time, $P < 0.001$; treatment × time, $P = 0.82$.

during the lactation period, and that high-quality diet could have mitigated the effects of several nutrient restrictions during prepartum period on milk production. Therefore, additional studies are necessary to understand the effects of prepartum maternal nutrition on subsequent lactation performance in beef cows.

The current experiment provided evidence of differential response on offspring growth performance due to different levels of intensity of nutrient restriction during late gestation. During the first month of postnatal life, calves from severely restricted dams had a greater ADG than did those from moderately restricted or control dams. The performance of MR calves in the present study was similar to that in other experiments when the effect on BW or BCS on restricted cows was moderated (Larson *et al.* 2009; Funston *et al.* 2010; Underwood *et al.* 2010; Gunn *et al.* 2014; López Valiente *et al.* 2014). Underwood *et al.* (2010) observed that calves from dams grazing native range, with a moderate nutritional restriction, had a lower total BW gain and weaning BW than did calves from dams grazing improved pasture during late gestation. Performance of calves from severely restricted dams in the current experiment was similar to the results reported by other researchers when maternal BW loss of restricted cows was of a similar magnitude. Long *et al.* (2010) reported that primiparous beef cows that underwent a severe BW loss (16%) during early gestation produced heavier steers than did non-restricted cows. In sheep, Ford *et al.* (2007) reported that wethers from ewes fed 50% of nutritional requirements (10.5% BW loss) during early to mid-gestation were heavier at 9 months of age than were wethers from non-restricted ewes. Additionally, ewes with impaired placental growth and function produced lambs that were lighter at birth, but by 43 days of age were of a similar weight as lambs from control ewes (De Blasio *et al.* 2007). The calves from severely restricted dams exhibited a strong compensatory growth. This supports the thrifty phenotype hypothesis proposed by Hales *et al.* (1996), in which fetal malnutrition imposes mechanisms of nutritional savings on the growing calf. Nutrient-restricted cows produce calves that are more efficient in converting food into BW than are calves from unrestricted dams (Tudor *et al.* 1980).

Several studies have proposed a strong connection between intrauterine growth restriction, early compensatory growth and metabolic diseases (Desai and Hales 1997; Soto *et al.* 2003). Ford *et al.* (2007) demonstrated that undernutrition during early to mid-gestation in sheep increased offspring BW, fat deposition and dysregulated glucose uptake. A recent study demonstrated that heifers born from restricted dams exhibited compensatory growth associated with an increased DMI followed by an inability to regulate circulating glucose levels (Tipton *et al.* 2018). In contrast, different levels of nutrient restriction applied to cows during late gestation in the current study did not affect offspring glucose concentrations. Lack of differences could be due to low blood sampling frequency during the first month of life, the time at which compensatory growth of calves from severely restricted dams was observed. Gardner *et al.* (2005) found that baseline plasma glucose and insulin were similar between lambs from undernourished and control dams; however, plasma glucose and insulin concentrations were greater in lambs from restricted ewes during an intravenous glucose tolerance test. Thus, a glucose tolerance test may help find altered glucose homeostasis in progeny from restricted dams.

Particularly for developing offspring, IGF1 is essential for animal growth regulation, and nutritional restriction during fetal development may induce permanent alterations of the IGF axis (Bauer *et al.* 1995; Brameld *et al.* 2000). Maternal nutrient restriction during mid- to late gestation produced altered circulating levels of IGF1 associated with changes in muscle and adipose tissue development of the progeny (Maresca *et al.* 2018; López Valiente *et al.* 2019). In this experiment, calves from severely restricted dams grew at a faster rate during early postnatal life and tended to have greater IGF1 serum concentrations than did calves from moderately restricted dams. Increase in BW due to compensatory growth in early postnatal life may be due to alterations in the IGF1 system, as IGF1 concentrations increased rapidly from birth onward (Mericq *et al.* 2005; Iñiguez *et al.* 2006). Compensatory growth immediately following parturition, similar to that in progeny of restricted dams, has also been reported in humans (Karlberg and Albertsson-Wikland 1995; Albertsson-Wikland *et al.* 1998). Rustogi *et al.* (2018) observed a positive correlation between circulating concentrations of IGF1 and increased weight gain in the first few months of life in humans. Results of the current study indicated that moderate restriction during late pregnancy is a sufficient stimulus to reduce calf IGF1 concentrations postnatally. Interestingly, calves from dams that underwent severe nutrient restriction were observed to have similar concentrations of IGF1 as did calves from non-restricted dams by the time of weaning. However, further investigation is required to elucidate the physiological mechanism involved in differential response between restricted groups.

Conclusions

In recent years, various experiments have been designed to determine the effect of cow nutrient restriction during gestation on progeny growth and development. Inconsistencies in the literature may be attributed to differences in the severity of nutrient restriction induced in animals. To the authors' knowledge, this is the first experiment to demonstrate that different levels of nutrient restriction during late gestation induce a differential response in growth of offspring in beef cattle. Moderate nutrient restriction (75% of the energy requirements) resulted in moderate maternal BW and BCS loss during gestation, decreased calf BW at parturition and weaning, and tended to decrease IGF1 concentrations in calves. Severe nutrient restriction (50% of the energy requirements) decreased BW of calves at parturition, but compensatory growth during early lactation was observed. Calves from severely nutrient restricted dams reached BW and IGF1 concentrations at weaning similar to those of calves from control dams. The degree of nutrient restriction applied in dams did not affect milk production and composition; thus, differential calf performance may have been due to a programming effect. Further studies are needed to elucidate a potential mechanism at which the differential response is occurring when levels of nutritional restriction vary.

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Data availability. The data that support this study will be shared upon reasonable request to the corresponding author.

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