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THE ALVEOLAR-ARTERIAL OXYGEN PRESSURE GRADIENT OF PRE-WEANED BEEF CALVES IS NEGATIVELY ASSOCIATED WITH THE CROSS-SECTIONAL AREA OF THE LONGISSIMUS DORSI MUSCLE

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ABSTRACT: An alveolar-arterial oxygen (A-a O_2) pressure gradient is a measure of O_2 diffusion inefficacy from lung alveoli into pulmonary blood. Gradients can be calculated from arterial blood-gas tensions. Variation in A-a O_2 gradients among calves may be explained by the presence of pulmonary lesions. Pneumonia has been associated with long-term detrimental effects on productivity, such as growth rate. This may be because cattle have very little pulmonary reserve. Therefore, lesions that reduce the gaseous exchange surface area or impede O_2 diffusion across the blood-gas boundary are likely to increase the A-a O_2 gradient. Skeletal muscle growth has a high O_2 requirement. *Longissimus dorsi* cross-sectional area is an indicator of total body muscling. We hypothesized that the A-a O_2 gradient is negatively associated with *l. dorsi* area. Beef calves, 102-280 days old, were randomly selected from two herds at 1,466m (Herd A, n=30) and 2,008m (Herd B, n=30) above sea level. Blood obtained from the coccygeal artery was analyzed using a handheld blood-gas analyzer. Height was measured from the ground to the iliac crest. *L. dorsi* area was obtained ultrasonically between thoracic vertebrae 12 and 13. Calves in herd A were sampled twice, 118 days apart. Complete sets of observations were analyzed using generalized estimating equations (n=81). A-a O_2 gradients ranged from 2.3-43.6 mmHg with a mean of 23.0 ± 0.9 mmHg. Calf age was not associated with *l. dorsi* area when controlling for height (P=0.40) and was eliminated from the model. *L. dorsi* area was negatively associated with A-a O_2 gradient (P=0.001) when controlling for ranch (P=0.74), sex (P=0.07) and hip height (P<0.001). An increase in the A-a O_2 gradient by 1 standard deviation (8.3 mmHg) was associated with a decrease in *l. dorsi* area of 1.3 ± 0.5 cm^2. It can be concluded that, in the calves sampled, inefficacious alveolar-arterial O_2 diffusion was associated with reduced *l. dorsi* muscle growth. This highlights the importance of minimizing the presence of pulmonary pathology in order to achieve optimal growth performance.

Key words: beef calves, muscle growth, oxygen

Introduction

Bovine respiratory disease (**BRD**) is a leading cause of morbidity and mortality (Loneragan et al., 2001). BRD has long-term detrimental effects on productivity. The occurrence of BRD in dairy calves less than 3 months old significantly reduces weight gain and first lactation milk production (van der Fels-Klerx et al., 2002). The presence of pulmonary lesions in feedlot steers has been associated with significantly reduced weight gain (Wittum et al., 1996). Cattle have limited pulmonary reserve due to their small total alveolar surface area available for gaseous exchange relative to O_2 demand (Veit and Farrell, 1978). The accumulation of pulmonary lesions may reduce the already limited gaseous exchange surface area. This may reduce the efficacy of O_2 transfer from the alveoli into the pulmonary circulation. The efficacy of O_2 transfer can be estimated from the alveolar-arterial O_2 (**A-a O_2**) pressure gradient. Efficacy of O_2 transfer is inversely related to the A-a O_2 gradient. Skeletal muscle is a major determinant of basal O_2 requirements (Zurlo et al., 1990). Therefore, efficacy of O_2 uptake may be a limiting factor for skeletal muscle growth. Live animal total muscling can be predicted ultrasonographically from the cross-sectional area of the *longissimus dorsi* muscle (Herve and Campbell, 1971). We hypothesized that the A-a O_2 gradient of pre-weaned beef calves is negatively associated with the cross-sectional area of the *longissimus dorsi* muscle.

Materials and Methods

The Colorado State University Animal Care and Use Committee approved of the animal handling and sampling procedures prior to sample collection.

Study site

Calves from 2 herds in northern Colorado were randomly selected for the study. Black Aberdeen Angus calves from herd A were sampled on 2 occasions. Calves from herd B were born to red Aberdeen Angus and Hereford composite cows bred to red Aberdeen Angus bulls. Due to herd management practices calves in herd B were tested only once (Table 1).

Table 1. Herd, altitude, date of sampling, number of calves sampled and age

Herd	Altitude, m	Date	n[1]	Mean age ± SD, days
A	1,466	07/01/2011	30	103.5 ±16.0
		10/27/2011	28	249.7 ± 15.9
B	2,008	09/27/2011	30	126.1 ± 13.0

[1] number of calves sampled

The dams of calves studied were given a pre-breeding and pre-calving vaccination offering protection against *Bovine herpesvirus 1* (infectious bovine rhinotracheitis [IBR]), BVDV, *Bovine respiratory syncytial virus* (BRSV), and *Bovine parainfluenza virus 3* (BPIV-3). Calves were vaccinated against the same respiratory pathogens at 4-8 weeks of age and 2-4 weeks prior to weaning. Herd A used a modified-live vaccine and herd B used a killed vaccine on both cows and calves. Calves on both ranches were administered a killed vaccine at 4-8 weeks of age offering protection against: *Cl. chauvoei, Cl. septicum, Cl. novyi, Cl. sordellii* and *Cl. perfringens* Type C and D. Vaccines were given according the manufacturers instructions. Herd A takes ear notch samples routinely from all calves kept as replacement heifers for *Bovine viral diarrhea virus* (BVDV) enzyme-linked immunosorbent assay testing. Herd B tests suspect animals based on the advice of a veterinarian. No calves persistently infected with BVDV have been detected in either herd to date. Communal grazing does not occur. Salt licks are provided year-round. Growth promotants were not used. Calves were born with minimal, if any, assistance.

Alveolar-arterial oxygen pressure gradient

The A-a O_2 pressure gradient is an indicator of the efficacy of O_2 transfer from the alveoli to the pulmonary blood. An A-a O_2 pressure gradient > 10 mmHg is an indicator of poor O_2 transfer due to ventilation-perfusion mismatching, diffusion impairment or right-to-left vascular shunt (Lekeux, 1993). The A-a O_2 pressure gradient is calculated using the following formulae:

$$\text{A-a } O_2 \text{ pressure gradient} = P_AO_2 - PaO_2$$

$$P_AO_2 = FiO_2(BP - pH_2O) - (PaCO_2/R)$$

where P_AO_2 = alveolar O_2 tension (mmHg); PaO_2 = arterial O_2 tension (mmHg); $PaCO_2$ = arterial CO_2 tension (mmHg); R = respiratory exchange ratio (0.9); FiO_2 = fraction of inspired O_2 (0.21); BP = barometric pressure (mmHg); and pH_2O= water vapour pressure at body temperature (52.4 mmHg at 39°C).

A study of 7 cows at least 2 years old reported a mean respiratory exchange ratio of 0.91 (±0.05) (Gallivan et al., 1989). A value of 0.9 was used in this study.

Sample collection

Blood was collected from the coccygeal artery using a 22 gauge, 2.54 cm (1") hypodermic needle. The bovine coccygeal artery is a suitable source for blood-gas analysis (Collie, 1991; Nagy et al., 2002). Arterial blood unlike venous blood can fill a heparinized syringe without applying suction. Therefore, minimal, if any, negative pressure was applied to the syringe chamber by drawing on the plunger when obtaining a sample. Approximately, 2 – 2.5 ml of blood was collected in a 3 ml syringe. Syringes were heparinized with approximately 0.25 ml of sodium heparin (1,000 IU/ml). The plunger of each syringe was pulled back to the 3 ml mark coating the inner chamber surface with heparin. Heparin was then expelled so that only the needle hub contained heparin. Collection of blood up to the 2 ml mark results in dilution of the blood sample by < 5 % (Hopper et al., 2005). Dilution < 10 % is sufficient to minimize pre-analytic error (Hutchison et al., 1983). The sample was discarded if during collection the flow of arterial blood was interrupted. Air bubbles within the blood were immediately expelled and the first several drops of blood discarded before analysis. Blood-gas analysis was performed using a handheld analyser (VetScan i-STAT 1, Abaxis, Union City, CA, USA). Results are automatically stored under the animal identification number. A temperature 'correction' algorithm was used to adjust blood-gas tensions according to rectal temperature (CLSI, 2001).

L. dorsi cross-sectional area was measured using…
Hip height was measured from the ground to the iliac crest.

Statistical Procedures

Statistical analyses were performed using STATA version 12 (Stata Corporation, College Station, Texas, USA). Generalized estimating equations were used to account for the repeated measures (Liang and Zeger, 1986; Zeger and Liang, 1986). An exchangeable correlation structure was used. Hip height was forced into the model to account for the functional maturity of the cardio-pulmonary system (Lekeux et al., 1984). Herd was included as a fixed effect to account for clustering.

Results

When controlling for hip height calf age was not significantly associated with *l. dorsi* area (P = 0.40) and was removed from the model. Herd (P = 0.74), sex (P = 0.07), hip height (P < 0.001) and A-a O_2 pressure gradient (P = 0.001) were included in the final model. No significant interactions were present. Bulls had a *l. dorsi* area 3.0 ± 1.4 cm^2 larger than heifers (P = 0.03) and 2.9 ± 2.1 cm^2 larger than steers (P = 0.06) when controlling for other variables in the model. *L. dorsi* area did not differ between steers and heifers (P = 0.57). A 1 cm increase in hip height was associated with a 0.6 ± 0.1 cm^2 increase in *l. dorsi* area (P < 0.001) when controlling for other variables in the model. An increase in the A-a O_2 pressure gradient of 1 mmHg was associated with a 0.22 ± 0.07 cm^2 decrease in *l. dorsi* area (P = 0.001) (Fig. 1). The mean A-a O_2 pressure gradient was 23.0 ± 0.9 mmHg and ranged from 2.3 - 43.6 mmHg. This range in A-a O_2 pressure gradients is associated with an absolute difference in *l. dorsi* area of 9.20 ± 2.73 cm^2 when controlling for herd, sex and hip height.

Discussion

Genetic selection for high productivity has produced cattle with small cardiopulmonary systems relative to metabolic O_2 requirements (Veit and Farrell, 1978). The limited pulmonary reserve means that pulmonary lesions are likely to impair the uptake of O_2 from the alveoli into the pulmonary circulation. The efficacy of O_2 transfer from the alveoli into the pulmonary blood can be estimated from the A-a O_2 pressure gradient. An A-a O_2 pressure gradient > 10 mmHg is considered to be abnormally high due to diffusion impairment, right-to-left vascular shunt or more commonly, ventilation-perfusion mismatching (Lekeux, 1993). Bovine A-a O_2 pressure gradients tend to exceed 10 mmHg (Gallivan et al., 1991; Lekeux et al., 1984).

Further studies are necessary to explain the physiological basis of high A-a O_2 pressure gradients in cattle. Due to the high prevalence of pulmonary lesions in young cattle (Wittum et al., 1996) it is reasonable to presume that some of the variation in pressure gradients can be explained by pulmonary pathology. If so, this highlights the importance of minimizing the presence of pulmonary lesions in calves associated with the occurrence of bovine respiratory disease (**BRD**). Perhaps A-a O_2 pressure gradients are influenced by environmental conditions during the neonatal period. For example, 'pruning' of the pulmonary vasculature of neonatal beef calves has been reported to occur in response to chronic hypoxia (Reeves and Leathers, 1967). Cattle have a lower density of pulmonary capillaries associated with alveoli than the mammalian average (Epling, 1964). Pulmonary vascular 'pruning' due to neonatal hypoxia may increase ventilation-perfusion mismatching. A-a O_2 pressure gradients may be genetically determined. Spirometric variables in Belgian Blue calves are genetically determined and have a favorable association with body muscling (Bureau et al., 2001). Low A-a O_2 pressure gradients are characteristic of human populations adapted to life in high altitude environments (Moore et al., 1998) suggesting a genetic influence. Genetic selection of cattle for efficacious alveolar-arterial O_2 uptake may reduce the deleterious effect of BRD on calf growth.

Implications

Studies have typically focused on the effects of clinically apparent BRD on growth. This subjective approach does not account for the high proportion of calves with subclinical pneumonia. The true effect of pulmonary pathology on productivity has likely been underestimated. Estimation of A-a O_2 pressure gradients provides a measure of O_2 transfer from the lung to the pulmonary circulation irrespective of the underlying cause or causes of impairment. Efficacy of O_2 transfer from the lung into the pulmonary blood may be a limiting factor for optimal muscle growth in calves. This may be particularly true in high altitude environments such as those associated with the Rocky Mountain range.

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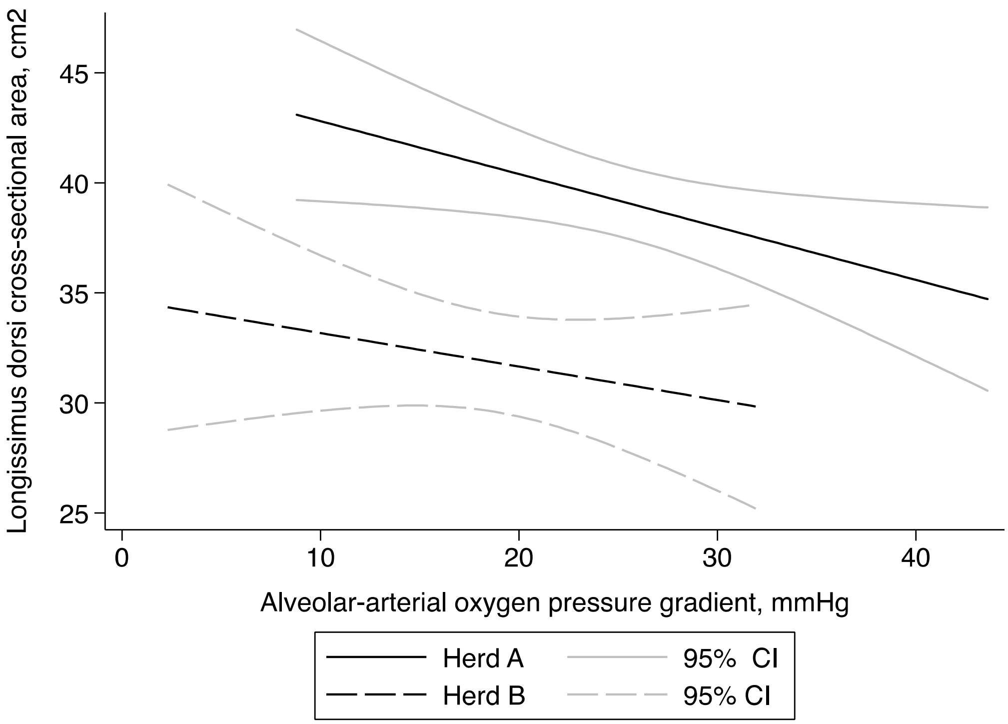

Figure 1. *Longissimus dorsi* cross-sectional area (cm^2) by herd and alveolar-arterial oxygen pressure gradient (mmHg). Regression lines are provided with 95% confidence intervals (95% CI). Calves in herd A and herd B were sampled at 1,466m and 2,008m, respectively.