High Energy Ration Feeding in Steers at Low Elevation: A Natural Animal Model of Irreversible Pulmonary Hypertension, Pulmonary Arterio-Venous Remodeling, and Heart Failure

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Rationale

1. Pulmonary hypertension (PH) is increasingly recognized in otherwise healthy obese individuals (BMI>30 kg/m2), in fast-growing broiler chickens, and in beef cattle transitioning through the finishing period of the life cycle when cattle are fed high-energy diets intended to maximize growth and weight gain.

2. Metabolic syndrome is associated with impaired lung function and is a risk factor for WHO Group II PH, the most common cause of PH.

3. Lipoatrophica arising from hyperlipidemia is associated with increased transcription factor activity regulating expression of inflammatory mediators.

4. Accumulating evidence suggests that obesity hypoventilation leading to pulmonary venous remodeling, increased pulmonary venous pressure and left heart dysfunction contributes to progression of PH and right heart failure (RHF).

5. Pulmonary capillary wedge pressure, an indirect measure of LV-EDP is elevated in finishing cattle exhibiting signs of RHF, suggesting that similar to humans with Group II PH, pulmonary venous hypertension due to LV insufficiency is a contributing factor.

Epidemiology of RHF in Beef Cattle

1. Incidence of RHF in finishing beef cattle is increasing.

2. Death loss attributed to PH in 2 Northern Colorado feedlots (2014) accounted for 7.1, 9.9, 6.5% of mortalities and death loss occurred late in the natural life cycle (12-18 months).

3. Majority of beef cattle are finished at low altitudes (800-1600 m).

4. Cattle treated for bovine respiratory disease (BRD) 3X more likely to die from RHF.

5. Average live market weight has increased 48% since 1944.

6. Cardiac mass as a proportion of hot carcass weight is smaller than almost a century ago.

7. Mean pulmonary arterial pressure (mPAP) increases with age and adiposity.

Hypothesis

In low elevation (<1600 m) finishing beef cattle, the interaction of obesity and components of metabolic syndrome during the finishing period, together with a persistent pro-inflammatory state drives progression to PH.

Methods

Using 2D echocardiography and right heart catheterization, cardiac imaging and pulmonary arterial testing was performed in two late-fed steers from the Eastern Colorado Research Center (ECRC) feedlot in Akron, Colorado (elevation 1400 m).

The steers presented with a history of BRD, severe brisket edema, jugular vein distention and muffled heart sounds. Based upon poor prognosis, the steers were euthanized and submitted for postmortem examination. Histopathology using routine H&E and Masson's Trichrome staining was performed by a veterinary pathologist (G. Krafl).

The steers were 11-month-old Angus steers, 880 lb. and 12-month-old Angus steers, 1000 lb.

Summary

Summary: Beef cattle fed high energy diets exhibit novel features of PH and RHF associated with LV dysfunction.

• Clinical signs of heart failure occur late in the natural life cycle and at low elevations in the absence of environmental hypoxia.

• Severe PH with right heart failure.

• Pathophysiological remodeling of both LV as well as RV.

• Structural remodeling of pulmonary veins as well as pulmonary arteries.

• Consistent evidence of global inflammatory remodeling.

Implications

• A Natural Large Animal Model of PH and RHF associated with LV dysfunction.

1. Finishing beef cattle serve as an effective large animal model to monitor the natural progression of PH-RHF associated with LV dysfunction and pulmonary venous remodeling, the largest and fastest growing form of PH in human patients.

2. Similar to obese human PH patients, adverse interactions between metabolic dysfunction and inflammation may play a role in the pathogenesis of pulmonary vascular remodeling, PH and heart failure.

3. These metabolic and inflammatory sequelae may predispose finishing cattle exhibiting signs of PH and RHF to develop bovine respiratory disease, accelerating disease progression and influencing disease outcome.