

CONTINUOUS FEEDING DOES NOT BLUNT SKELETAL MUSCLE PROTEIN SYNTHESIS, SATELLITE CELL ABUNDANCE, OR LEAN GROWTH IN A NEONATAL PIG MODEL OF PREMATURITY

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Background: Optimizing lean growth in preterm neonates may help prevent adverse chronic health outcomes. Skeletal muscle growth accounts for a considerable fraction of lean mass accretion in the postnatal period and requires the coordinated activation of muscle protein synthesis, satellite cell (SC; muscle stem cell) proliferation, and SC differentiation and fusion into muscle fibers. We have reported previously that prolonged intermittent bolus feeding stimulates muscle protein synthesis and promotes lean growth compared to continuous feeding in term neonatal pigs, but the impact of targeted nutritional interventions on SC function is poorly understood. The objective of this study was to determine the effect of feeding modality on skeletal muscle protein synthesis, SC abundance, and lean growth in preterm neonatal pigs.

Materials/Methods: Preterm pigs obtained by C-section (952 ± 205 g) were fitted with an umbilical artery catheter (later replaced with jugular vein catheter) and an orogastric tube for parenteral and enteral nutrition, respectively. Pigs were assigned to continuous (CONT; $n = 14$; 7.5 mL/[kg·h]) or intermittent bolus (INT; $n = 30$; 30 mL/kg every 4 h over 15 min) feeding for 21 d (210 kcal/kg and 16 g protein/kg per d). Pigs advanced from full parenteral to full enteral feeding over 6 d. At the end of the study, body composition was measured by DXA and muscle protein fractional synthesis rate was determined with an infusion of L-[ring-2H5]-Phe. After euthanasia, longissimus dorsi muscle was collected for analysis. Sublaminal and total Pax7+ SC per 1000 fibers in muscle cross-sections were quantified by immunofluorescence in a subset of animals.

Results: Body weight gain, lean mass, and fat mass did not differ between CONT and INT groups. Postprandial muscle protein synthesis did not differ between CONT and INT groups (16.4 vs. 16.1 ± 0.6 %/d). Sublaminal Pax7+ SCs per 1000 fibers was similar between CONT and INT groups (60.9 vs. 58.3 ± 6.0). The proportion of sublaminal relative to total Pax7+ SCs was similar between CONT and INT groups (78.8 vs. $78.8 \pm 2.2\%$).

Conclusions: Continuous feeding does not blunt lean growth in preterm pigs compared to intermittent bolus feeding. The lack of increased lean growth with intermittent bolus feeding is consistent with similar muscle protein synthesis rates and abundance of SCs between feeding modalities. Supported by NIH AR044474, HD072891, HD085573, USDA NIFA 2013-67015-20438, and ARS 6250-51000-055.