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TEMPORAL PATTERNS OF CHANGE IN NITROGEN METABOLISM, CIRCULATING IGF-I CONCENTRATIONS AND SKELETAL MUSCLE IGF-I mRNA ABUNDANCE IN RESPONSE TO ABOMASAL CASEIN INFUSION IN STEERS.

D.H. BEERMANN[1], A.P. MOLONEY[2], D. GERARD[3], T.F. ROBINSON[1], AND K.D. FINNERTY[1]. [1]Cornell University, Ithaca, NY, [2]Teagasc, Grange Research Centre, Ireland and [3]Univ. of Missouri, Columbia.

Key Words: Muscle growth, IGF-I expression, cattle

Background

Insulin-like growth factor I (IGF-I) is involved in the regulation of postnatal skeletal muscle growth, but whether IGF-I exerts its effects in a classical endocrine fashion or by autocrine or paracrine influence is not known. IGF-I stimulates satellite cell proliferation and differentiation in vitro (Allen, 1990), and IGF-I is considered an integral part of somatotropin-induced acceleration of skeletal muscle growth. Circulating IGF-I and the IGF-I binding proteins are also increased in association with increasing levels of energy or protein intake (Clemmons and Underwood, 1991). Increases in plasma IGF-I were observed with increases of protein intake in young pigs fed isocaloric diets (Campbell et al., 1990; Beermann et al., 1992), and in lambs receiving abomasal protein infusion (Beermann et al., 1993).

Work-induced hypertrophy increased muscle IGF-I mRNA abundance within 2d of tenotomy (DeVol et al., 1990), and increased abundance was observed in liver and adipose tissue, but not skeletal muscle in pigs administered porcine somatotropin for 7 or 14 days (Grant et al., 1991; Coleman et al., 1994). However, the time at which samples were collected relative to the time of pST injection may have precluded observing an increase. Ramsay and co-workers (1995) found that IGF-I mRNA abundance in liver, adipose and skeletal muscle was increased to the greatest extent between 12 and 16 hours after a single pST injection, and declined at different rates in different tissues to 24 hours post-injection.

Abomasal infusion of protein in growing lambs and Holstein steers increases whole-body nitrogen (N) balance 30 to 40% and this increase is strictly additive with the 25-30% increase caused by bST administration (Beermann et al., 1991; Houseknecht et al., 1992). We have shown that net appearance of amino acids in the mesenteric vein and amino acid uptake by the hind leg is increased in proportion to the rate of abomasal casein infusion. Results suggest that enhancing amino acid absorption and availability enhances skeletal muscle growth in ruminants fed conventional diets at or above NRC requirements, but the mechanism(s) by which muscle protein synthesis and deposition are increased are not known. We hypothesized that an autocrine or paracrine influence of IGF-I may be involved, and that a temporal increase in IGF-I mRNA abundance might be followed by return to a normal IGF-I mRNA:total RNA ratio.

Objectives

1. To determine if IGF-I mRNA abundance in skeletal muscle is increased in association with the increases in amino acid availability and whole-body N balance.

2. To determine the temporal pattern of change in IGF-I mRNA abundance in skeletal muscle, and to determine if circulating concentrations of IGF-I are altered in association with the increase in N retention.

Methods

Four Holstein steers (208 ± 8 kg BW) were surgically instrumented with an abomasal cannula and jugular catheters and allowed 2 wk recovery. Steers were offered hourly a 43:57% forage-concentrate diet at 95% of ad libitum intake supplemented with continuous abomasal infusion of glucose (to replace 12.5% of metabolizable ad lib energy intake) for 13 d prior to and throughout the abomasal infusion of 67 g casein N/d. Daily N balance collections were conducted for 6 d prior to initiating the abomasal infusion of casein. Biopsies of the liver and right and left semimembranosus muscles were removed and frozen in liquid N, and casein infusion was begun. Muscle biopsies weighing approximately 500 mg and daily N balance samples were collected at 8, 16, 24, and 48h after the initiation of casein infusion and on d7 and d14. Jugular blood samples were collected hourly for the first 24h after the initiation of casein infusion, every 6h for the next 24h, and daily for the remainder of the experiment. RNA was prepared using a CsCl cushion and ultracentrifugation, and IGF-I mRNA content was determined by solution hybridization analysis using the ribonuclease protection assay kit from Ambion. The cDNA probe used was a 150 base pair fragment of the coding sequence for bovine IGF-I.

Results

Nitrogen balance increased from 23.6 to 71.5 g/d ($P<.001$) within 24h, and remained elevated (mean = 58.4 g/d) during the 14 days of casein infusion. Plasma urea N increased from 4 to 9.5 mg/dL during the first 24h of casein infusion ($P<.01$) and remained constant to d14. Muscle IGF-I mRNA abundance was not different between the left and right legs at d0 (1.35) and at 8h (1.28), was higher ($P<.01$) at 16h (2.90), and increased to 3.30 at 24h after initiating the casein infusion. Abundance reached a maximum of 3.70 on d7 and then declined to near pre-infusion levels on d14 (1.77). Plasma IGF-I concentrations increased from 668 ng/ml to 785 and 841 ng/ml at 8h and 24h, respectively ($P<.01$), and subsequently declined to control levels on d7 and d14. Liver IGF-I mRNA abundance was approximately 100-fold that in skeletal muscle (158.0) before casein infusion, and was not significantly higher at 14d (154.3).

Conclusions

Results demonstrate that increased protein intake alone, at constant energy intake, is capable of inducing IGF-I gene expression in skeletal muscle. We conclude that enhanced amino acid availability alone may modulate skeletal muscle protein synthesis and accretion through a paracrine IGF-I influence. To what extent the modest transient increase in circulating IGF-I concentration influences skeletal muscle protein synthesis and deposition remains unknown.

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