Fetal Programming of Skeletal Muscle Development in Food Producing Animals—An Overview

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Abstract

Prenatal skeletal muscle development is a result of two waves of myogenesis in food producing animals. During the initial stages of embryonic life primary myofibers are formed which provide framework for the larger population of smaller secondary fibers. These fibers are formed from fetal myoblast during a second wave of differentiation. Studies shows that the level of maternal nutrition alters fetal skeletal muscle development with long term effects on offspring growth and performance, so called fetal programming. Maternal under-nutrition at fetal stage affects the proliferation of myogenic precursor cells and reduces the number of muscle fibers formed. Maternal over-nutrition results in impaired myogenesis and elevated adipogenesis. Fetal skeletal muscle development mainly involves myogenesis moreover also involves adipogenesis and fibrogenesis. These tissues in fetal muscle are mainly derived from mesenchymal stem cells (MSC). Shifting the commitment of MSC from myogenesis to adipogenesis increases intramuscular fat (i.e. marbling), improving the quality/grade of meats.

Keywords: Fetus, Maternal nutrition, Myogenesis, Marbling, Skeletal muscle.

1. Introduction

The early fetal environment plays a key role in development of skeletal muscle. The number of myofibers in muscle is largely determined during gestation and no net increase in the number of muscle fibres occurs after birth (Greenwood et al., 2000; Nissen et al., 2003) thus, numbers of prenatal muscle fibres have profound effects on muscle growth and development during later postnatal life. Proper management of animal nutrition during gestation can improve progeny performance and health. Skeletal muscle is a lower priority in nutrient partitioning compared with the brain, heart, or other organ systems (Bauman et al., 1982; Close and Pettigrew, 1990), making it particularly vulnerable to nutrient deficiency. Meat animals are raised for their skeletal muscle. Thus, a decrease in nutrient availability to the dam during gestation can result in a reduced number of muscle fibers through fetal programming, reducing muscle mass and impacting animal performance. Results of numerous studies have suggested that maternal under nutrition influences the physiology and development of fetuses, with long-term consequences that predispose to certain diseases such as diabetes, obesity and cardiovascular diseases during postnatal life (King, 2003).

Marbling (i.e., intramuscular fat) is crucial for meat palatability and fetal life is a major stage for generation of intramuscular adipocytes (Tong et al., 2008), which provide the sites for intramuscular fat accumulation or marbling during fattening. Thus, fetal programming also affects marbling in offspring of animals. Theme of this article is, understanding the basic principles of skeletal muscle development, intramuscular adipogenesis and effect of fetal programming on the growth performance and meat quality of offspring.

2. Basic Events of Myogenesis

During embryonic development, myoblasts develop from myogenic precursor cells which are of mesodermal in origin (Eurell and Brian, 2006). These cells are determined to enter the myogenic lineage; the determined myoblasts are able to proliferate and to divide which establish a pool of myoblasts. Special signals cause myoblasts to exit the cell cycle, to stop division and start differentiation. Muscle cells begin to express cell-specific proteins align with one another.
The multiple myoblasts fuse to form elongated myotubes. In the final stage, skeletal myotubule differentiation involves the production of specific myofilaments which mature into a myofiber (Fig 1).

3. Morphological Aspects of Myogenesis

Muscle does not just appear during prenatal development. Muscle fiber formation in food animals are multiphasic processes, occurs in early and late waves. During the early wave, primary fibers are generated by the fusion of embryonic myoblast and in later wave secondary fibers by fetal myoblast (Fig 2) and they respectively give rise to the primary and secondary muscle fibers. During myogenesis three populations of myoblasts i.e., embryonic, fetal and adult, appears sequentially and predominate at different stages of development (Dunglison et al., 1999). The existence of a third generation of fibers has been described in bovines, sheep, and pigs in the late fetal or early postnatal period (Picard et al., 2002). These fibers are closely associated with secondary myotubes like newly formed secondary myotubes with primary myotubes. They only exist in large animals where they could be part of the mechanisms leading to the larger muscle mass.

Duxson et al. (1989) reported that secondary fibers formed initially at site of innervations of the primary fibers and are surrounded by the same basal lamina as the primary fiber on which they lie. The secondary myotubes remain attached for a short period with primary fibers and subsequently elongated to become independent fibers, which can be distinguished from primary fibers, by their relative small size. Once muscle development completed primary and secondary fibers cannot be distinguished morphologically (Wigmore and Dunglison, 1998).

As previously described the secondary myofibers are derived from muscle precursor cells, which are initially maintained in a proliferating, undifferentiated state (Swatland, 1973). Because the availability of nutrients influences the proliferation of cells, it is hypothesized that the number of secondary fibers in prenatal muscles is influenced by maternal nutrients and that maternal nutrient restriction would have long-term consequences on muscle growth and development (Zhu et al., 2004). Another population of myoblasts does not form fibers but stays close to the myofibers; these are termed satellite cells (Fig 2) and they are able to divide and serve as the source of new myonuclei during postnatal growth. Satellite cells are dormant mononucleated cells, which are at the G0 phase of the cell cycle. Although the specific population dynamics of the cells are unknown, numerous subpopulations of these cells are found in skeletal muscle. After activation by various environmental stimuli related to growth, satellite cells undergo asymmetric proliferation with a portion of daughter cells replenishing the original pool and the remaining differentiating into myoblasts (Yan et al., 2013). These newly generated myoblasts fuse with existing muscle fibers to increase the muscle fiber size, as well as the number of nuclei in muscle fibers (Allen et al., 1979). They contribute to growth of the fibers and also participate in regeneration processes. However, recent studies indicate that a portion of satellite cells are also capable of differentiation into other cell types in addition to muscle cells, such as adipocytes and fibroblasts (Tong et al., 2008).

4. Influence of Maternal Nutrition on Fetal Skeletal Muscle Development

Studies on bovine fetal skeletal muscle development suggested that primary muscle fibers of the bovine fetus begin forming within the first 2 months of gestation. Very limited numbers of muscle fibers are formed at this stage; thus, maternal nutrition has little influence on primary muscle formation during this early time frame. During the second to eighth month of gestation, the majority of muscle fibers form; therefore, reduction of muscle fiber formation during this stage through any source of stimuli (e.g., maternal nutrition) has long lasting, irreversible consequences to the offspring (Du et al., 2010). Fig 3 depicts the effects of maternal nutrition on fetal skeletal muscle formation and control points in which maternal nutrition has been shown to impact fetal muscle development. The dates are estimated mainly based on data from studies in sheep, rodents, and humans and represent the progression through the various developmental stages. Nutrient restriction during mid gestation reduces muscle fiber numbers, whereas restriction during late gestation reduces both muscle fiber sizes and the formation of intramuscular adipocytes (Du et al., 2010).

Larson et al. (2009) reported increased progeny birth weights from protein supplemented dams, suggesting a potential alteration in fetal muscle growth. Greenwood et al. (2009) reported steers from cows nutritionally restricted during gestation had reduced body weight and carcass weight at 30 months of age compared to steers from adequately fed cows. Zhu et al. (2004) reported that ewes were fed to 50% nutrient-restricted of total digestible nutrients (National Research Council requirement) from days 28 to 78 of gestation showed retarded development of muscles and skeleton. Muscle from nutrient-restricted fetuses contained fewer secondary myofibers than muscle from control fetuses, and the average area of fasciculi was smaller (P < 0.05). The decreased number of secondary
myofibers in nutrient-restricted fetuses may result from the decreased mTOR (mammalian target of rapamycin) signaling. Lower activation of mTOR signaling in nutrient-restricted fetuses may reduce the proliferation of myoblasts and, thus, reduce the formation of secondary myofibers. This decrease in secondary myofibers in fetuses may predispose fetuses to metabolic diseases, such as diabetes and obesity, in their postnatal lives.

In pig, under nutrition in utero results in low birth weight and decreased numbers of muscle fibers. Results of the study indicate that the mean number of secondary fibers formed in a litter of pigs can be improved by increasing maternal feed intake during 25 to 50 day of gestation. This may have additional benefits in terms of improved growth rate and growth efficiency in the latter stages of pig growth to 80 kg (Dwyer et al., 1994). Similar results have been observed in guinea pigs (Ward and Stickland, 1991). In another study, Nissen et al. (2003) reported that ad libitum feeding of pregnant sows from day 25 to 50 or day 25 to 70 of gestation did not have any beneficial effect on muscle fiber number and area in the offspring. It seems that maternal ad libitum feeding from day 25 to 50 in gestation had a negative effect on postnatal muscle growth, with especially the lightest weight pigs being affected. While working with beef cattle scientist of Wyoming University fed three different diets to different groups like 100%, 70% of NRC (2000) and 70% of NRC (2000) plus supplementation of ruminal bypass protein from day 60 to 180 of gestation. Steer progeny from dams fed 70% NRC plus supplement had numerical decreases in marbling scores when compared to steers from dams fed 100% of requirements (Du et al., 2010).

Skeletal muscle matures during late gestation in sheep (approximately day 105 of gestation) and cattle (approximately day 210 of gestation), and nutrient restriction after this stage has no major impact on muscle fiber number. Maternal nutrient restriction during late gestation reduces fetal sheep muscle fiber size, but not number (Greenwood et al., 1999). Recent studies indicated that maternal nutrition can programs fetal development, especially skeletal muscle development as per schedule.

5. Effect of Developmental Programming on Steer Progeny Performance

Recent studies on steer reported improved muscle development from adequately fed dams when compared to progeny from nutrient restricted dam. Nutrient supplementation during early to mid gestation in steers has the potential to improve the muscle development and overall production efficiency of offspring. Underwood et al. (2008) conducted a study with steers were grazing either to improved pasture (n = 8) or to native range pasture (n = 7) from 120 to 150 day through 180 to 210 day of gestation. The native -
(Nutrient restriction reduces adipogenesis, decreasing marbling in fetus)

(Nutrient restriction reduces muscle fiber hypertrophy, decreasing birth weight)

(Nutrient restriction reduces myogenesis, decreasing muscle fiber number and muscle mass in offspring)

Muscle fiber Hypertrophy

Secondary Myogenesis

Primary Myogenesis

Adipogenesis

0 1 2 3 4 5 6 7 8 9

(Parturition)

(Conception)

(Embryonic stage)    (Fetal stage)

Fig 3: Effects of maternal nutrition on bovine fetal skeletal muscle development.

range pasture had an average CP (crude protein) of 6.7% and the improved pasture, consisting of irrigated pastures with increased forage production, had an average CP of 8.9%. The chemical ether extract (i.e., fat content) of the LM (Longissimus dorsi muscle) at the 12th rib was increased ($P = 0.06$) and adipose tissue cell numbers per field were greater ($P = 0.09$) in the steers born to mothers grazing improved pasture compared with the steers born to cows maintained on native range pasture. In another study, Underwood et al. (2010) reported increased weight gains, final weight, hot carcass weight and increased tenderness in steers from dams grazed on improved pasture from day 120 to 180 of gestation when compared to progeny from steers grazing native range during that same time. Radunz (2009) reported the effect of dietary energy source on progeny calf performance. Cows offered different diets during gestation beginning on approximately day 209 of gestation: hay (fiber), corn (starch), or distillers grains with solubles (fiber plus...
fat). Corn and distillers grains diets were limit fed to ensure isocaloric intake among treatments. Results showed reduced birth weights for calves from dams fed grass hay when compared to calves from the other two groups with an increase (\(P \leq 0.05\)) in calf body weight reported through weaning when comparing calves from corn fed dams to hay fed dams. Feedlot performance among treatments was not different; however, calves from hay fed dams required 8 and 10 more days on feed to reach a similar fat thickness when compared to calves from distillers and corn fed dams, respectively.

6. Molecular Mechanisms Associated with Fetal Programming of Skeletal Muscle and Adipose Tissue Development

As previously discussed, the fetal stage is critical for skeletal muscle development, as well as adipose and connective tissue development. These tissues in fetal muscle are mainly derived from mesenchymal stem cells (MSC). Shifting the commitment of MSC from myogenesis to adipogenesis increases intramuscular fat. Prenatal myogenesis is under the control of a panel of regulatory proteins, including Wingless and Int (Wnt), paired box gene (Pax) 3 and Pax 7 (Hyatt et al., 2008; Maroto et al., 1997). Studies indicate that Wingless and Int (Wnt)/β-catenin signaling regulates MSC differentiation. Upregulation of Wnt/β-catenin promotes myogenesis, and down regulation enhances adipogenesis (Du et al., 2010). Additionally, Wnt signalling may have a role in the regulation of body fat distribution and to a degree susceptibility to obesity (Christodoulides et al., 2009).

References


Du et al. (2010) also stated that Wnt signaling is crucial for both myogenesis and adipogenesis in fetal muscle. Because myogenesis occurs a little earlier than adipogenesis, it should be feasible to enhance both myogenesis and adipogenesis by enhancing Wnt signaling during early to midgestation, when myogenesis is occurring in ruminant animals, and by inhibiting Wnt signaling in late gestation, when adipogenesis is active. The expression of Pax 3 and Pax 7 in mesenchymal stem cells induces the expression of myogenic regulatory factors (MRFs) which leads to myogenic differentiation (Amthor et al., 1999). Recent studies indicate that microRNA is intensively involved in myogenic and adipogenic differentiation from mesenchymal stem cells and epigenetic changes such as DNA methylation are expected to alter cell lineage commitment during fetal muscle and adipose tissue development (Yan et al., 2013).

7. Conclusion

Available literature clearly shows that secondary fibers in prenatal muscle development are influenced by maternal nutrition and maternal nutrient restriction at this stage i.e., nutrition has long-term consequences on muscle growth and development. However, Proper nutrient supplementation improves fetal skeletal muscle development and adipogenesis in fetal skeletal muscle, thereby enhancing marbling in progeny. Additional studies on maternal nutritional supplementation at specific gestational age are required for marbling; improve growth efficiency of draught animals and the quality of meat in food animals.


King JC (2003). The risk of maternal nutritional depletion and poor outcomes increases in early or closely spaced pregnancies. *Journal of Nutrition*, 133: 1732S-1736S.


Nissen PM, Danielsen VO, Jorgensen PF and Okshjerg N (2003). Increased maternal nutrition of sows has no beneficial effects on muscle fiber number or postnatal growth and has no impact on the meat quality of the offspring. *Journal of Animal Science*, 81: 3018-3027.


