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PJBS

ISSN 1028-8880

Pakistan Journal of Biological Sciences

ANSInet
Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

Pakistan Journal of Biological Sciences 17 (3): 329-334, 2014
ISSN 1028-8880 / DOI: 10.3923/pjbs.2014.329.334

Nutrigenomics and its Role in Male Puberty of Cattle: A Mini Review

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Abstract: Nutrigenomics a novel era in genomics research is based on puzzling issue on how nutrition and genes re-interacts. Perusal of literature reveals that very few information are available in this field and especially when it is associated with puberty in cattle which is a multigenic trait of great economic importance. Thus it opens a new area of research interest. Various markers like-gonadotropin releasing hormone/GNRH (responsible for sexual differentiation and reproduction), interstitial growth regulating factor/IGF1 (having signal controlling reproduction function linked to somatic growth); circulating metabolic hormones viz., leptin apart from GnRH and IGF1 (having impact on testicular development in peripubertal bull) are proved to be associated with male puberty in cattle. Various minerals (copper, selenium, manganese, zinc, chromium, iron and molybdenum) and vitamins (Vit. A, D, E and C) are directly or indirectly linked to male puberty. But no research till today initiated how the nutrients effect on the transcriptome/proteome/ metabolome level of marker genes associated with male puberty in cattle. Application of nanotechnology to make food safer for promotion of good health has created much excitement and nanoparticles has been developed against infectious diseases (e.g., Campylobacteriosis) affecting puberty along with certain nanocarriers that can facilitate the uptake of essential nutrients associated with puberty. Much of nutrigenomics research is however in infancy and hence the present mini-review will allow building the concept among researchers and scientists to initiate research in this interesting area.

Key words: Genetic markers, GNRH, IGF1, macro components, nanodelivery, night blindness, nutragenomics, male puberty

INTRODUCTION

Increase in the demand of milk, meat and eggs globally, due to increased population density and requirements of feeds including Genetically Modified Crops (GMO) crops have also made pressure for enhancing the increase livestock population (Tayo *et al*., 2011; Mahima *et al*., 2012). With the advancement on genomics research various novel "omics" research has been raised up (Deb *et al*., 2012a, b). Gene expression is modified by dietary components i.e., macrocomponents (includes carbohydrates, proteins, fats and cholesterol), vitamins (e.g., A, B, E, D) minerals (e.g., Fe, Se, Ca) and phytocompounds such as flavonoids, isothiocyanates and indoles (Kaput and Rodriguez, 2004; Lander *et al*., 2001; Venter *et al*., 2001; Boss *et al*., 2012; Neibergs and Johnson, 2012). This has laid to a new era in science so called "nutrigenomics", literally means interaction between nutrition and genomics (Kaput *et al*., 2005). The primary focus of Nutrigenomics is on effect of diet on health, altered gene expression by compounds present in feed (Neibergs and Johnson, 2012). From a nutrigenomic point of view diet and nutrients directly/indirectly influence primarily gene (transcriptomics) and protein expression (proteomics) and ultimately metabolite production (metabolomics) (Muller and Kerten, 2003). Nutrition research has conventionally decisive on the fact that all individuals have the same nutritional needs, although nutritional professionals do recognise that children differing needs compared with adults, as well as

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males as compared with females. Advancement in nutritional science, 'Mypyramid' dietary tool (www.mypyramid.gov) were established for individual dietary requirements which indicate that personal eating plan can be prepared by entering physical activity along with age and sex, height and weight (Mahima *et al.*, 2013). Puberty is an important factor for differentiating among cattle breeds (Casas *et al.*, 2007; Kumar *et al.*, 2013). Puberty is a mutagenic trait and the study on human /mouse puberty indicate that there could be single genes with major effects involved for male puberty. Even though its economic importance, there are very few markers associated with male puberty. The association of receptor for Gonadotropin releasing hormone (GNRHR) polymorphisms and first service period after calving has been proved in dairy cattle (Derecka *et al.*, 2010) and also with the age of first CL in Brahman and Tropical cattle (Silveira *et al.*, 2010). Apart from this, other factors like cell adhesion, axon guidance, ErbB signalling and glutamate activity are also affecting GnRH release (Fortes *et al.*, 2011). However, these still remain to be investigated in bovine males which reinforce the importance of identifying genes that regulate puberty and polymorphisms thereby explaining these differences in bulls. Present mini-review, just a concept note for initiating research on nutrigenomics study on male puberty in cattle.

Genetic Markers and circulating hormones related to male puberty in cattle

GNRH: GNRH and its receptor having a major role for sexual differentiation as well reproduction in mammals by stimulating the secretion of Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH) for regulating gonadal function viz. steroid gametogenesis and synthesis of hormones. Fortes *et al.* (2010) reported that genetic polymorphisms within GNRHR add to the regulation of pubertal timing in human and mouse.

IGF1: Insulin like growth factor 1 (IGF1) has been reported as a signal controlling reproductive function links to somatic growth primly during puberty in mammals by influence on the activity of GNRH neurons, stimulating testicular growth, development of seminiferous tubules as well as Leydig cells. Interestingly, positive relations were observed in between serum concentrations of IGF1 and serum LH and testicular LH receptor (LHR) concentrations in bull calves (Bagu *et al.*, 2010). Some evidence suggests that via direct actions at the pituitary and gonadal levels, IGF1 can regulate the hypothalamic-pituitary-gonadal axis (Daftary and Gore, 2005). In this context, serum concentrations of pre-pubertal IGF-1 have been genetically correlated with the adult scrotal circumference as well as sperm motility in bulls (Yilmaz *et al.*, 2004). IGF1-SnaBI SNP has been reported to associate with IGF1 gene expression and IGF1 blood level in cattle (Maj *et al.*, 2008) and affect animal weight at different ages in cattle (Siadkowska *et al.*, 2006; Burns *et al.*, 2011) and with BMI in bovine and human (Elks *et al.*, 2010).

Circulating metabolic hormones: Brito *et al.* (2007) reported that, circulating concentrations of leptin, IGF-I and insulin associated with testes size, indicating their involvement in gonadotropin independent mechanism for regulation of development of testes in peripubertal bulls. Leptin is a recently discovered hormone produced by adipose tissue regulating feed intake and energy balance and restores fertility exogenously (Barb and Kraeling, 2004; Adam *et al.*, 2003; Zieba *et al.*, 2005). The IGF system has an autocrine regulatory mechanism in neuronal GnRH secretion. Treatment with IGF-1 increases GnRH secretion by GT 1-7 cells in vitro and increases LH secretion in castrated males in vivo (Adam *et al.*, 1998; Anderson *et al.*, 1999). Moreover, insulin and IGF-I receptors have been identified in leydig cells which causes proliferation of the leydig cells (Wang *et al.*, 2003; Wang and Hardy, 2004).

Nutrients and their effect on male puberty

Minerals

Copper (Cu): Copper act as cofactors of many enzymes like Cytochrome oxidase, which is necessary for electron transport in mitochondria for energy metabolism of ATP dependent biosynthetic reactions. It is required in the body for production of red blood cells, as it is essential for absorption as well as transportation of iron necessary for haemoglobin synthesis (Tuormaa, 2000). Deficiency of copper and cobalt may delay onset of puberty.

Selenium (Se): Selenium along with Vitamin E acts as antioxidant and inactivate the peroxidase formed during cell metabolism (Hine 1992; Puertollano *et al.*, 2011; Chaudhary *et al.*, 2010; Mahima and Mudgal, 2012; Mahima *et al.*, 2012). Testicular selenium is essential for testicular function. Low selenium leads to lower sperm production and motility with flagella defects localised primarily to the mid piece has been a consistent feature.

Manganese (Mn): Though the pathway of specific manganese involvement in reproductive functions remains unknown, some evidence suggests that it plays a role in the activity of certain endocrine organs. Mn functions as co factor during cholesterol synthesis, necessary for the synthesis of steroids viz., progesterone, estrogens and testosterone (Keen and Zidenberg-Cherr, 1990). In males the dietary deficiencies of Mn may leads to absences of libido, decreased motility of spermatozoa and reduced number of sperms in ejaculate.

Zinc (Zn): Zn deficiency has profound effect on reproductive cycle by interfering prostaglandin synthesis and delayed puberty (Kreplin and Yaremcio, 1992). Zn deficient male animals have lower FSH and LH (Boland, 2003). Zinc deficiency in male may leads to atrophy of semeniferous tubule, reduced testicular size, lack of libido and can adversely affect spermatogenesis (Kumar, 2003).

Chromium (Cr): Naturally occurring chromium is crucial for carbohydrate metabolism. Chromium supplementation may regulate the genes for insulin production and may be helpful in diabetes or obesity management (Lau *et al*., 2008). Lower sperm count associated with chromium deficiency.

Iron (Fe): Iron takes part in the function of transportation of oxygen to tissues, maintenance of oxidative enzyme system and is concerned with ferretin formation. All these are accomplished via haemoglobin and myoglobin as well as many enzymes viz., cytochrome enzymes of electron transport chain forms (Khillare, 2007). Deficiency in adult animals is rare due to its ubiquitous presence in the feed stuffs.

Molybdenum (Mo): Mo is interdependent with Cu with reference to body system of ruminants and thus proper balance of Cu and Mo in soil is very much essential for normal absorption (Randhawa and Randhawa, 1994). Molybdenum deficiency causes sex drive and spermatogenesis leading to sterility in males and is responsible for delayed puberty, reduced conception rate and anoestrous in females.

Vitamins: Some of the vitamins play role in puberty like vitamins E, A and D. Vitamin A (retinol) is the vitamin most likely to be deficient in diets of cattle. Normal vision, growth and reproduction along with maintenance of skin tissue and body cavity lining cell and bone development are all influenced by Vitamin A (Perrotta *et al*., 2003). The deficiency of this vitamin shows up as night blindness and excessive tear production, reduced feed intake and rough hair coat and even fluid accumulation in joints and brisket, diarrhea, seizures, poor (and slow) skeletal growth, reproductive problems, low quality semen and infections in cattle. Vitamin D is necessary for calcium and phosphorus absorption required for normal bone mineralization and calcium mobilization from bone and also it requires for puberty. Recent study demonstrated that there is a significant inverse relationship between obese Asian-Indian children between body fat indices and serum 25 (OH) D concentrations. Vitamin E serves as an antioxidant and is particularly important in protecting the immune system from damage during times of oxidative stress and infection of bacteria, virus or parasite. Deficiency of this vitamin increases the susceptibility to infections (Beck, 2007; Fondell *et al*., 2011). Selenium is closely linked with this vitamin and helps in testicular function. Vitamin C (L-ascorbic acid) an antioxidant; is present in high concentrations in the plasma and leukocytes rapidly decline during infections and stress and has got a significant impact on health status of bulls during exercise (Schwager and Schulze, 1998; Castellani *et al*., 2010; Puertollano *et al*., 2011; Khadgawat *et al*., 2012; Holmannova *et al*., 2012; Sahay and Sahaya, 2012; Braakhuis, 2012).

Nanofood and nanodelivery: Application of nanotechnology to make food safer for promotion of good health has created much excitement. Nanoparticles has been developed that latch on to *Campylobacter* a bacterium having no harmful effect on chicken but causes illness in human beings leading to even death. Nano-sized self assembled liquid structures (incorporated with lycopene as well as beta carotene and lutein); nanocochleates (containing vitamins and omega fatty acids) have also been widely used to enhance male puberty (Roco and Bainbridge, 2003; Wolbing, 2007; Maclurcan, 2005).

CONCLUSION AND FUTURE PERSPECTIVES

Puberty is a multigenic trait and endocrine patterns associated with puberty in cattle are governed to a greater extent by the nutrient requirements. It has been a prime focus of nutrition research to investigate how nutrition can optimize and maintain tissue as well as organ and whole body integrity having considerable effect on male puberty. In recent years it has shifted from epidemiology and physiology to molecular biology and genetics. This has increased the importance of nutrigenomics in the eye of the researchers as such dynamic arena of biological science is able to demonstrate the effect of bioactive food compounds on puberty and health status of bull affecting fertility. Study of genetic markers and hormones along with kinetics of utilization of essential vitamins and minerals that are essential to have better understanding of male puberty forms theme of nutrigenomic research. Identification of polymorphism in genes regulating puberty has also not been over looked. Nutrigenomics though is a rapidly developing science but still is considered in its infancy as far as management of puberty in bull is concerned. Uncertainty prevails regarding the use of the tools to study protein expression profile and metabolite production to such point of extent so as to enable efficient and reliable measurements. With the advent of nanotechnology it is not only easier to deliver essential nutrients to the animal in a better and safer way but also to prevent infectious diseases that affect puberty. There is however considerable debate regarding whether nano approaches will be used to increase the usability of the previously existing approaches or whether these two will complement each others. Such advanced technologies are still under development. Not only achieving success in the field of nutrigenomics but also further integrations together to produce dietary recommendations will be ultimately fruitful.

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