ROLE OF IGF 1 IN MALE AND FEMALE REPRODUCTION IN BOVINES: A REVIEW

Dr. Amit Kumar1*, Dr. N. Anand Laxmi2

1Ph.D. Scholar, 2Principal Scientist,
National Dairy Research Institute, Karnal, Haryana.

*Corresponding author

ABSTRACT

IGF 1 is an endocrine hormone which plays an important role in growth in calves and continues to have anabolic effects in adults. It plays a key role in reproduction because it has positive effect on cell proliferation, transformation and differentiation. IGF 1 supplementation to granulosa cell culture increased proliferation and functional activity of cells. Screening based on plasma IGF 1 level has been used as an indicator for improvement of breeding efficiency of either male or female bovines.

Key words: IGF 1, Reproduction, Female, Male, Bovines.

INTRODUCTION

Insulin like growth factor 1 (IGF 1) also called as somatomedin C, is a protein that is encoded by IGF 1 gene (Hoppener et al 1985). IGF 1 is a protein that cells use to communicate with other cells and their environment. IGF 1 belongs to a complex system which consists of two cell surface receptors (IGF 1R and IGF 2R), two ligands (IGF 1 and IGF 2 ), six IGF binding proteins (IGFBP 1 to IGFBP 6) as well as IGFBP degrading proteases. IGF 1 has high sequence similarity to insulin. Recently, a third form of IGF, termed as IGF 3, has been reported to exist. It is limited to fishes only and found in the gonads of male and female fishes (Berishvili et al. 2010). IGF 1 is a primary growth factor in adults while IGF 2 is a primary growth factor in fetus. The IGFs are synthesized by almost all the tissues and are important mediators of cell growth, differentiation and transformation. IGF 1 plays important role in both prenatal and post natal growth and act via binding to its receptor IGFR1 and the multiple IGFBPs play role in modulating its effects. GH, on binding to its liver receptors, stimulates the synthesis and release of IGF 1 peptide into circulation where it
binds with specific IGFBPs and circulates as endocrine form of IGF 1. IGF 1 produced by other organs has got lower affinity for IGFBPs and they are the autocrine form or paracrine form of IGF 1. IGF 1 by acting through IGF1r may produce its effects via multiple pathways including phosphatidyl inositol 3 kinase (PI3K), Akt and mitogen activated protein kinase (MApK) pathway. IGF 1 by acting through different pathways produces different type of effects like cell growth or differentiation, cell migration and survival etc. IGF 1 is an important parameter of somatotropic axis which includes growth hormone (GH) itself and its receptors. Most of the circulatory IGF 1 is released from the liver in response to GH. It has a negative feedback effect on pituitary to regulate the secretion of GH. The role of IGF-1 has been conserved during evolution of species and its heightened activity has been linked to fertile reproductive patterns. It plays a critical role in nutrient utilization and its metabolism in ruminants. They are regulated by lactation and energy balance (Rhoads et al., 2008). Differences in plasma IGF1 concentration has been reported to vary in different breeds (Jones et al., 1991). In humans the insulin like peptide family comprises ten members viz., insulin, IGF 1 and 2 (which are closely related) and the seven peptides related to relaxin. Insulin and IGFs bind to receptors from superfamily of receptor tyrosine kinases (RTKs) (Meyts et al., 2000). Bovine IGF1 is a 70 amino acid, basic, single chain polypeptide with a molecular mass of 7649 Daltons. The bovine cDNA for IGF 1 is 93% identical to the human sequence and the amino acid sequence is 96% identical. Three disulphide bridges maintain the tertiary structure of the molecule (Watson et al., 1999). Bovine, porcine and human IGF 1 is identical. The gene for IGF 1 in bovines is present on chromosome no. 5 and it is known in other species also. IGF 1 is known to act in all the three ways viz. endocrine (Butler et al. 2002) as well as paracrine and autocrine (Holly and Wass, 1989).

Normal reproductive activity for cows and bulls is an important event required for a sustainable cattle farming. Several hormones and metabolites are known to control the various reproductive events. IGF 1 is one such hormone belonging to IGF family that plays an important role in different mammalian reproductive events.

ROLE OF IGF 1 IN FEMALE REPRODUCTION

Sun et al. (2011) reported that brain IGF 1 receptors and estrogen receptors interact to regulate female reproduction and behavior. IGF 1 stimulates the estrogen sensitive neurons through IGF1 receptors thereby mediating the estrogen stimulation of GnRH neurons and subsequently GnRH release. In the cow, expression of IGF 1 receptors has been reported from different structures present on ovary (Nuttinck et al., 2004; Armstrong et al., 2001; Perks et al., 1999), different parts of oviduct (Fenwick et al., 2008), uterus (Robinson et al., 2000; Richterich et al., 2007), different stages of conceptus (Yaseen et al., 2001; Sawai et al., 2007).

Reproductive life of female can be divided into different phases viz. puberty, period of recurring estrous cycles, period of pregnancy, post partum period. IGF 1 is associated with all these different phases of female reproduction. Age at puberty is a major determinant of lifetime reproductive efficiency of ruminants. Season, age, nutrition and body weight of animals determine the age at puberty (Schillo et al., 1992). In the reproductive life of female cattle, puberty is that stage in which it shows the estrus behavior for the very first time which is also associated with subsequent ovulation and then, development of a persistent corpus luteum. IGF1 and somatotropin concentration are important factors in the initiation of puberty in cattle and buffalo heifers (Simpson et al., 1991; Anand Laxmi and Sehgal, 2014). Similar results have been reported by Lamberson et al. (1995) in pigs. Endocrine IGF 1 concentration has been a predictor of reproductive success and was suggested that future fertility of prepubertal female calves may be estimated by the measurement of circulatory IGF 1 (Taylor et al., 2004). Though IGF 1 is an important hormone bringing
about puberty, it’s not the sole factor for determining the onset of puberty (Moran et al., 1989; Vandehaar et al., 1995). The decrease in the concentration of plasma IGF1 had delayed puberty due to retardation in follicle growth, decrease in estradiol content and possibly resulting in delay in LH surge (Simpson et al., 1991; Armstrong et al., 1992). IGF1 is positively related with body weight gain and average daily gain (Anand Laxmi and Sehgal, 2014).

The estrous cycle of cattle involves the luteal and follicular phases. During these two phases, gonadotropins secretion influences gametogenesis, folliculogenesis, ovulation, corpus luteum function and steroidogenesis in the ovary. Gonadotropins secretion is regulated by a delicate balance between hormonal interactions in the hypothalamic- pituitary- ovarian axis, which in turn regulates development and regression of ovarian follicles and corpus luteum (Kojima, 2003). Beg and Ginther (2006); Spicer and Aad (2007) have suggested a role for IGFs in selection of follicles for development. In vitro studies have revealed that IGF 1 supplementation to culture medium, increased proliferation of granulosa cells and estradiol production (Glisteter et al., 2001). Regulation of activity of granulosa cells and increase in testosterone secretion by theca cells have been reported (Spicer et al., 2002). Intrafollicular IGF 1 acts in an autocrine and paracrine pathway leading to oocyte and follicular differentiation (Izadyar et al., 1997). Echternkamp et al. (2012) showed greater concentration of IGF 1 in blood of twinner cows and suggested that IGF system may prime the dominant follicle more towards LH than towards FSH (Hastie and Haresign, 2006; Echternkamp et al., 2004). The embryo must get implanted in the uterus following conception and should develop normally into a viable fetus for a successful pregnancy. Since IGF 1 receptors are present on uterus (Robinson et al., 2000; Richterich et al., 2007), embryo, morula and blastocyst (Yaseen et al., 2001), therefore, IGF 1 can affect the growth and development of embryo directly by acting on it or indirectly by acting on uterus. Matsui et al. (1997) reported that the addition of insulin and IGF1 to the in vitro culture of bovine embryos had positive effects on embryo development and favored the bovine embryos to develop to the morula stage. Einspanier et al. (1990) reported that IGF 1 is also luteotropic in action and stimulates progesterone production from the maternal corpus luteum. Appropriate plasma concentration of maternal progesterone, in turn, stimulates the production of Inf –tau by bovine embryos for the successful recognition of pregnancy. Moyes et al. (2003) reported a higher concentration of IGF 1 in plasma of pregnant cows as compared to non pregnant cows.

For a profitable dairy farming the cows are expected to yield a calf every year. For this, the dam should resume the estrous cyclicality along with normal ovulation as soon as possible, after calving. Though post partum anestrus is common in cattle, it becomes a problem in cattle management when it gets prolonged. Undernutrition and negative energy balance had been assigned as most important cause for the prolonged anestrus (Montiel et al., 2005). Zulu et al. (2002) reported that maternal plasma IGF 1 concentration plays an important role in the energy balance, average daily gain and nutritional regulation of post partum reproductive performance in cattle. Less concentration of IGF-1 in circulation of post partum cross bred heifers has led to anestrus condition (Anand Laxmi and Sehgal, 2014). Strauch et al. (2001) reported that the circulating plasma IGF 1 concentration is negatively correlated with the post partum interval to first ovulation. This may be due to the positive effect of plasma IGF 1 on the secretion of estradiol by the dominant follicle which in turn stimulates the LH secretion by the anterior pituitary (Beam and Butler, 1997). It had been observed that decrease in plasma concentration of IGF 1 and its gene expression in the early post partum period may have an impact on reproductive organs and early embryo development. The body should regain energy balance and optimum concentration of metabolic hormones like IGF1 to control the reduction in fertility (Wathes et al., 2007; Beam and Butler, 1999). Reports are available which state that supplements like fermented yeast culture can enhance the circulatory IGF 1 which has positive effect on reproductive functions (Anand Laxmi and Sehgal, 2014).
ROLE OF IGF 1 IN MALE REPRODUCTION

The hypothalamo-hypophyseal gonadal axis secretes certain hormones which in turn regulate the reproductive axis of the female and male. The GnRH-LH-FSH-estrogen/testosterone cascades of pathway regulate this axis. It has been observed that both LH and IGF1 had an effect on circulatory testosterone levels and on age at puberty. There is temporal association between LH secretion pattern and circulating IGF1 concentration regulating GnRH pulse generator. IGF1 receptors have been localized in leydig cells and sertoli cells in rats (Rouiller-Fabre et al., 1998). The report also suggests that IGF1 acts as a paracrine / autocrine factor in the differentiation and activity of fetal leydig cells also. In young bulls Lund-Larsen et al., (1977) observed an increase in concentration of IGF1 with advancing age. It has been observed that in bulls of different breeds, where IGF1concentration was more, even testosterone production was more as estimated in plasma and sexual maturity was also earlier in these bulls (Istasse et al., 1990).

The size of the testis in growing bulls has been shown to be dependent on the circulatory level of metabolic hormones (Brito et al., 2007 a, b). It has been suggested that the growth of the testis during peripubertal period is more independent of the level of gonadotropins than during the prepubertal period, where testis is more responsive to the action of gonadotropins. During prepubertal period the concentration of plasma IGF1 varied with age and severely feed restricted bulls had lower concentration of IGF1 and the concentration of gonadotropins also decreased, the effect was observed to be more on LH. The results of Yilmaz (2003) suggested that bulls can be screened based on plasma concentrations of IGF 1 which correlated well with scrotal circumference and percent motile sperms. Studies also indicated that serum IGF 1 concentrations are genetically correlated with reproductive traits. Flowers (2013) has stated that reproductive failure in beef cattle is attributed more to bulls whereas in dairy cattle it is attributed more to cows.

In vitro addition of IGF 1 at physiological concentrations increased the percentage of motile sperms of bovine semen. In boars no correlations could be observed (Hirai et al., 2001). Miah et al. (2008) reported that spermatozoa characteristics like progressive motility, induction of capacitation and acrosome reaction were increased by IGF 1. The local production of IGF 1 in the testis has been indicated by Hess and Roser, (2001). Roser (2001) has given its source as Leydig and Sertoli cells and Lejeune et al. (1996) have reported its regulation by gonadotropin hormones. Receptors for IGF 1 in testicular cells have been identified by Wang and Hardy (2004) and in spermatozoa (Henricks et al., 1998). The mentioned reports are confined to rats, human and stallion species. The source of seminal plasma IGF 1 is of epididymal or testicular origin (Glander et al., 1996). In ruminant nutrition, IGF 1 is the most powerful factor that regulates testicular function through neural and hormonal systems (Blache et al., 2000; Brito et al., 2007). Since IGF 1 receptors have been localized on spermatozoa of cattle and buffalo (Henricks et al., 1998; Namagirilakshmi, 2013), it suggests that this factor has an important role in regulating functions of bovine spermatozoa. Sortino and Canonico (1996) suggested that in neurons IGFs prevent mitochondrial dysfunction. It may also act as an antioxidant. Hence, IGF 1 may act through its receptors on spermatozoa and might stimulate spermatozoa functions.

CONCLUSION

Endocrine IGF 1 is an indicator of occurrence of successful reproductive events after attainment of proper nutritional conditions and body weight in bovines. It plays an important role in follicular development, fetal growth and spermatogenesis. Further research is required to fully understand the interactions between endocrine and paracrine- autocrine action of IGF 1.
REFERENCES


