Hormonal Control Of Infertility In Bovines

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The term fertility as applied to the cow denotes the desire and ability to mate, the capacity to conceive and to nourish the embryo and finally the power to expel a normal calf and fetal membranes. Sterility means an absolute inability to reproduce, whereas infertility is the temporary absence of fertility. Reduced fertility is denoted by the term subfertility. In simple words fertility can be defined as the ability to produce young ones and the ability to produce more number of young ones is fecundity. Healthy cattle give expression to normal fertility by producing one viable calf per year.

It is a general finding that as milk production potential of cattle increases, more and more infertility problems creep in. Corresponding to the increase in the milk production potential of crossbred animals, the incidence of infertility is also on an increase in Kerala.

The causes of bovine infertility can be broadly grouped under four main headings; anatomical factors, functional abnormalities, management problems and infectious causes. The most commonly encountered infertility condition in Kerala is nutritional infertility. Since the feeding of cattle in the rural areas is mainly based on crop residues, most of the farmers are not in a position to provide stationary conditions in feeding round the year. Next to poor nutrition, infectious causes contribute to infertility. Only a small proportion of infertile cases comes under true hormonal infertility. Hence hormonal preparations should not be the drug of choice in infertility until and unless it is specifically indicated. Since hormones are like double edged swords, they should be used judiciously.

Anatomical Factors

Both congenital and acquired abnormalities of the genital system can influence fertility. When compared to the congenital abnormalities, the incidence of acquired abnormalities is high. Most of the acquired abnormalities are encountered in parous animals and might occur at parturition and during the puerperium. Ovarian agenesis, ovarian hypoplasia, abnormalities of fallopian tubes, intersexuality and freemartinism, segmental aplasia of Mullerian ducts etc. are examples of congenital abnormalities that can cause infertility. The acquired abnormalities include ovaro-bursal adhesion, cirrhosis of cervix, tumours of ovary and cervix etc.

Management Problems

The common management problems encountered are undernutrition, poor heat detection, incorrect timing of breeding etc.

Infectious Causes

Infections of the bovine genital tract, both specific and non-specific affect fertility by altering its environment so that there may be impaired sperm transport, sperm death, embryonic or foetal death, stillbirth or birth of weak calves. Unhygienic practices during artificial insemination are also contributing to genital infection.

Functional forms of infertility

Usually the functional forms of infertility affect individual animals and when they affect a large number of animals in a herd, they frequently reflect some other problem, especially nutrition. Most functional aberrations occur because of some endocrinological abnormality which is frequently difficult to specify even with current methods of hormonal assay. The abnormalities occur as a result of inherited factors, nutritional deficiencies or excesses, social influences which may arise from modern husbandry methods and the stress of production.

After the onset of puberty, cyclic ovarian activity should be maintained continuously throughout the vow's life except during pregnancy and for a short period after calving in the puerperium. It is possible that there are signs but that they are not being observed: in this case it is a management problem. The three most important reasons for absence of oestrus are true anoestrum, anoestrum due to suboestrum and anoestrum due to persistent corpus luteum.

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True anoestrum: When this occurs the ovaries are quiescent with absence of cyclical activity. The reason for failure of cyclical activity may be insufficient release of production of gonadotrophin to cause folliculogenesis or it may reflect the failure of the ovaries to respond. Rectal palpation of such animals reveals small ovaries which are usually flat and smooth. The main feature will be the absence of corpus luteum, either developing, mature or regressing. Some cows resume cyclic ovarian activity within a few weeks of calving and then become anoestrous. True anoestrum is most frequently diagnosed in high yielding dairy cows and first calf heifers which are still growing. There are a number of factors which predispose to this condition. Suckling has a profound effect. The anterior pituitary appears to be refractory to stimulation with gonadotrophin releasing hormone (GnRH) in the immediate postpartum period. The refractory period is probably due to the duration of the progesterone induced negative feedback during pregnancy. The act of suckling stimulates bursts of prolactin secretion which may be responsible for the extension of the period of anoestrum. The effect of high milk yield on ovarian rebound is debatable. Some have demonstrated an effect whilst others suggest that it is not a direct effect but a result of a concomitant loss of body weight and nutritional deficiency. An energy deficit is particularly important, exerting its effect by suppressing the release of GnRH and LH, especially if there is excessive weight loss. Deficiency of P, Cu, Co, Mn and the ingestion of phyto-oestrogens can cause anoestrum. Debilitating diseases and metabolic diseases also have a similar effect.

Treatment: Improved feeding, particularly increasing the energy intake is important although it would be preferable to prevent the condition occurring by adequate feeding to maintain body weight. Temporary weaning and restricted suckling together with the use of progestogens during the time of calf removal may be helpful in reducing the time of the first ovulation postpartum.

Equine chronic gonadotrophin (eCG) can be used to stimulate ovarian activity. A dose rate of 3000 - 4500 IU will frequently cause superovulation and therefore it is not advisable to inseminate at the induced oestrum. If the cow is not inseminated there is a possibility that she will relapse into anoestrum.

The treatment of dairy cows with GnRH causes the release of LH. This has been used successfully to treat anoestrous dairy cows with a single dose of 0.5 mg. The newer synthetic GnRH analogues such as buserelin at a dose rate of 0.02 mg. will stimulate oestrus in 1-3 weeks after treatment.

Progesterone treatment, often associated with estrogen has been used to induce ovarian activity postpartum. These are effective because they either simulate the short luteal phase that usually precedes the first normal oestrous cycle or else cause an accumulation of gonadotrophin by exerting a negative feedback effect on the anterior pituitary. The progesterone releasing intravaginal device (PRID) or controlled internal drug release (CIDR) is easily inserted and readily removed. When these devices are placed in anoestrous cows for 10-14 days, most show oestrus within a few days of their removal; although conception rates are sometimes poor at the first oestrous, there is a reduction in the calving conception interval. Injection of low doses of eCG (750 IU) at the time of PRID or CIDR withdrawal improves the response.

Oestrogens, both natural and synthetic have been used to treat anoestrus. They will readily induce behavioural oestrus without inducing ovarian activity and ovulation; however it is possible that in some cases they might disturb the hypothalamo-hypophyseal-gonadal axis so that cyclic activity is initiated.

Suboestrus/Silent heat: A genetic predisposition to silent heat has been identified with certain sire lines showing a statistically significant effect. Incidence of silent heat is more common in the hotter

months of the year. A number of nutritional deficiencies are also said to cause suboestrus; beta-carotene, phosphorus, cobalt, copper etc. Overweight may also have an effect. Eventhough attempts have been made to identify endocrinological reasons for suboestrus, till date none has been identified. Diagnosis of the condition is made on the clinical history and rectal palpation. If there is any doubt re-examination should be done in 10 days.

As far as treatment is concerned, if a mature corpus luteum is present and the cow is not pregnant, PGF2-α or an analogue followed by a fixed time insemination is indicated. If the corpus luteum is at a refractory stage, a double injection schedule at an interval of 11-13 days could be used. Alternatively a PRID or other progestogen implant could be used followed by fixed time insemination.

Persistent Corpus Luteum: Anything that interferes with the production or release of endogenous luteolysin will result in persistent corpus luteum. There is little firm evidence that persistence of corpus luteum (PCL) can occur in the absence of uterine lesion. Most cases of PCL in the absence of uterine lesion are incorrectly diagnosed and are due to silent heat or non-detected heat. The condition can be treated using PGF2-α or its synthetic analogue, provided that the clinician is confident that the cow is not pregnant.

Ovulatory defects: A number of defects associated with ovulation can occur. Ovulatory defects are due to endocrine deficiency or imbalance, failure of the development of hormone receptors at the target tissue and mechanical factors.

Delayed Ovulation: There is little information on the incidence of delayed ovulation as a cause of infertility. Certain cows have an apparently prolonged follicular phase of oestrous cycle. However there is no evidence that this is due to delayed ovulation; rather it is related to a delay in the corpus luteum assuming normal steroidogenesis. Diagnosis of the condition is difficult since it requires either sequential rectal palpation of the ovaries or sequential transrectal ultrasound imaging, both of which might interfere with the process of ovulation and may cause premature rupture. It has been recommended that a diagnosis can be made if the same follicle can be detected in the same ovary on two successive examinations, one at peak oestrus and the other 24-36 hours later. Delayed ovulation is generally assumed to be one of the causes of failure of conception in cyclic non breeders. Treatment consists of use of hormones which hasten timing of ovulation. Results of human chorionic gonadotrophin (hCG) have often been disappointing. Those for GnRH have been rather more encouraging especially by improving pregnancy rates for services other than the first. An alternative approach for treatment is to use do two inseminations, one at the normal time and one 24 hours later.

Anovulation: If cows are examined per rectum during the first few weeks after calving, a number of enlarged anovulatory follicles can often be detected. They are incorrectly described as cysts but are transient and do not persist even if no treatment is given. Some follicles fail to ovulate after reaching the maximum size. Instead the wall becomes leutinised. This structure i.e. leutinised follicle functions in the same way as a corpus luteum either regressing after 17 - 18 days or frequently much earlier so that the cow returns to oestrus at a shorter than normal interval. After the demise of the leutinised follicle, the subsequent oestrus will probably be followed by a normal ovulation.

Diagnosis of anovulation can only be made retrospectively by noting on rectal palpation that the follicle persists longer than one would have suspected. In the case of leutinised follicle it will remain for 17-18 days before regressing; the ovary containing it will be rounded, smooth and fluctuating rather than irregular and solid as it is with a solid corpus luteum. Treatment as described for delayed ovulation can be tried with GnRH and hCG.

Cystic Ovaries: Ovaries are said to be cystic when they contain one or more persistent fluid filled structures larger than a mature follicle in one or both ovaries resulting in aberrant reproductive function. Cows frequently develop large fluid filled structures in the ovaries in the immediate postpartum period. It has been reported that up to 60% of cows develop cysts which spontaneously regress before the first postpartum ovulation.

Treatment: Spontaneous recovery can occur quite frequently. Since the chances of development of ovaro-bursal adhesion are more, manual rupture should not be done. The choice of treatment and its success will depend to some extent upon the diagnosis of the type of the cyst. hCG at the dose rate of 3000-5000 IU has been successfully used for the treatment of follicular cyst. GnRH at the dose rate of 100-250 ug causes leutinisation of the cyst. Larger dose rate of 0.5-1 mg causes ovulation of follicle. Buserelin (GnRH analogue) can also be used at the dose rate of 10 µg. One of the most successful methods of therapy is the use of a PRID. Signs of nymphomania abate within 24 hours, the cyst gradually regress and following removal after 10-12 days there is oestrus with ovulation and corpus luteum formation. It is believed that the progesterone absorbed from the PRID suppresses the gonadotrophin support that is required for the maintenance of the cyst, resulting in its demise. Following its withdrawal, there is a surge of gonadotrophin with ovulation and corpus luteum formation.

Luteal cysts can be treated with hCG, GnRH and PGF2α. hCG and GnRH stimulate further luteinisation and the heavily luteinised cyst becomes susceptible to the action of the endogenous luteolysin. A suggestion for routine treatment is to inject GnRH when the cyst is first diagnosed followed by PGF2α 9 days later. Prophylactic use of GnRH at the dose rate of 100-200 µg, 12-14 days postpartum has shown success in reducing the prevalence of cysts in herds.

Luteal insufficiency

Progesterone is necessary for the maintenance of pregnancy. Until 150-200 days of pregnancy, and perhaps in some cases to full term, the main source of progesterone is the corpus luteum so that if this is not completely formed or it is not functioning adequately then insufficient progesterone is produced and the pregnancy fails. It is impossible on rectal palpation to differentiate between a normal and abnormal corpus luteum.

Since LH is luteotrophic in the cow, administration of hCG or GnRH after ovulation may stimulate the development and function of the corpus luteum or more likely induce accessory corpus luteum formation. This is one of the holding injections used in infertile cows. Alternatively hCG or GnRH might be given 11-13 days after insemination, since in the absence of pregnancy it would be several days before the corpus luteum would be starting to regress and if the stimulus for the maternal recognition of pregnancy is weak, it might prevent the corpus luteum regression and provide sufficient time for pregnancy to become established.

HORMONAL PREPARATIONS COMMONLY USED IN INFERTILITY CASES

Gonadotrophin releasing hormone and analogues

Fertirelin, synthetic GnRH peptide (Ovalyse)
Dose : 100 mg i/m

Gonadorelin, ,, (Fertagyl)
Dose : 0.5 mg i/m,i/v or s/c

Buserelin, GnRH analogue (Receptal) 4 mg/mg, 10ml vials, Dose : 10-12 mg i/m,i/v or s/c

Gonadotrophins

Equine chorionic gonadotrophin (eCG) (Previously known as PMSG)

eCG or serum gonadotrophin (Folligon)
Dose : 1500-3000 IU i/m or s/c

Human chorionic gonadotrophin - hCG

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