

Anestrus in Cattle and Buffalo

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Introduction

Anestrus is one of the most commonly occurring reproductive problems in cattle and buffalo in India, affecting livestock productivity and economics to a great extent. The problem is more severe in sub urban and rural areas of the country. It is a functional disorder of the reproductive cycle which is characterized by absence of overt signs of estrus manifested either due to lack of expression of estrus or failure of its detection. Anestrus is observed in post pubertal heifers, during pregnancy, lactation and in early postpartum period in adult animals. The condition may be associated with uterine pathology such as pyometra, fetal resorption, maceration and mummification. Anestrus is a multi-causative factor associated problem but its occurrence signals the inadequate nutrition, environmental stress, uterine pathology and improper managemental practices. Diagnosis of the condition is based on the exploration of the different causative factors responsible for it. Though many therapeutic agents (hormonal and non-hormonal) have been used but as such there is no single panacea to correct it.

Physiological Anestrus

Animals remain anestrus during certain physiological stages which does not related to infertility viz., before puberty, during pregnancy, lactation and early postpartum period. Accordingly, physiological anestrus has been classified into pre-pubertal, gestational, lactational and post-partum anestrus.

Prepubertal Anestrus

The follicular waves in pre-pubertal animals are similar to that of adult but follicles grow in response to FSH secretion only up to the stage where they have a theca interna and then regress. Such heifers remain in anestrus before the onset of puberty. The reasons of pre-pubertal anestrus includes low LH pulse frequency that results in insufficient growth of

follicles; inhibitory effect of opioids on LH secretion and high threshold for positive feedback effect of estradiol on LH surge.

Gestational Anestrus

The elevated level of progesterone during pregnancy exerts negative feedback effect on GnRH secretion from hypothalamus and reduces LH pulse frequency resulting into anestrus. However, some cattle and buffaloes exhibit estrus during early pregnancy (known as gestational estrus) which is seen most often during first four months of pregnancy. The incidence of gestational estrus has been recorded as 3.33 to 20.3% and 6.05 to 14.40% in Indian cattle and buffaloes, respectively. Usually cow or buffalo exhibits gestational heat only once during pregnancy, however, few animals show twice or thrice in same gestation.

Postpartum Anestrus

Following parturition, all the females undergo through anestrus for a variable but short period of time, known as postpartum anestrus. The period of postpartum anoestrus is usually longer in buffalo than the cattle under similar management conditions, probably due to low LH secretion during early postpartum period. Under normal conditions, buffaloes resume cyclicity by 30–90 days, however; only about 45% of Indian buffaloes resume cyclicity within 90 days postpartum and rest 55% remain in anestrus for about 150 days. Most of the dairy cows resume ovulatory estrus cycle within 15–45 days postpartum. The physiological postpartum anestrus cannot be avoided and is useful to allow uterine involution prior to first postpartum anestrus.

Lactational Anestrus

High lactation suppresses the fertility in almost all the. Higher level of prolactin in high yielding animals suppresses GnRH secretion and ultimately reduces production of gonadotrophins from pituitary, resulting into anestrus.

Pathological Causes of Anestrus

Certain pathological conditions i.e. ovarian agenesis, dysgenesis or derangement of follicular–luteal dynamics leads to anestrus causing infertility and pose a herd problem. Such conditions may be congenital or acquired.

Anestrus Due to Persistent Corpus Luteum (PCL)

In this type of anestrus, the follicular growth proceeds through all the developmental stages and undergo ovulation and CL formation which subsequently turn into anestrus due to failure of luteal regression. This is probably due to absence of estrogenic dominant follicle at

the time of luteal regression secreting adequate estradiol to induce the formation of uterine oxytocin receptors and consequently resulting in to pulsatile release of PGF₂ α for luteolysis. Persistent corpus luteum (PCL) is mostly associated with uterine pathology such as endometritis, pyometra, fetal resorption, maceration, mummification and uterine unicornis. Retained corpus luteum may also be associated with embryonic death when death of embryo occurs after maternal recognition of pregnancy where corpus luteum persists until resorption of embryo.

Sub-Estrus/Silent Estrus

Sub estrus or silent estrus or quite ovulation is clinically characterized by failure of overt symptoms of estrus, though the animal is surprisingly normal. Under these conditions, follicular development and ovulation occurs normally in animals without the manifestation of overt signs of estrus. Sub estrus is common during the post pubertal period in heifers and early post-partum (30 to 120 days) in high yielding dairy cows. Progesterone secreted from regressing CL of previous cycle potentiates the action of estrogen and seems to favours the manifestation of estrus in next cycle. Thus, lack of progesterone priming results in sub-estrus. Such conditions have been frequently reported in dairy buffaloes especially in summer months and may be the one of the reasons of prolonged calving interval in buffaloes. The concentration of estrogen determines intensity of behavioral signs of estrus which is low in high yielding dairy cow. Lower concentration of estrogen may be either due to higher metabolism and clearance with a high metabolic load or sub-optimal follicular growth. The probable cause of silent estrus is sub-optimal secretion of estradiol by mature follicles or higher threshold of estrogen in central nervous system to display the symptoms of estrus in that particular individual animal. Silent estrus also appears to be hereditary in predisposition in certain breeds. Other causes of sub estrus are heat stress, nutritional deficiencies, overweight, foot lesions, aging and ergotism (fescue toxicity) but most common cause considered for sub estrus is the failure of estrus detection.

Anestrus Due to Failure to Observe Estrus/Unobserved Estrus

Estrus detection is critical aspect of dairy herd management where artificial insemination is being practiced. The length of estrous cycle and estrus period varies among breeds and within a breed. It also varies with season, nutrition, lameness, presence of bull, housing, herd size and production status. Earlier, it was reported that intensity and duration of

standing estrus is shorter in *Bos indicus* cattle as compared to *Bos taurus* cattle, probably due to small follicular diameter. However, recent studies indicate that there is no difference in intensity and duration of estrus between *Bos taurus* and *Bos indicus* cows. In high yielding cows, many times the estrus cycles become irregular in terms of its intensity and duration of standing estrus, resulting in low estrus detection rates. The condition may be due to low estrogen concentration, insulin and IGF-I mediated deficiency of follicular growth or increase metabolism and clearance of estrogen with high metabolic load. The short period of estrus often fails to notice by the farmers.

Treatment

Anestrus can be treated according to their cause, however; there is no single panacea to correct it. Various therapeutic agents including hormonal and non-hormonal compounds have been used extensively for the restoration of cyclicity in anestrus cattle and buffalo by several workers with varying degree of success. In order to ensure effective treatment, the health and nutritional status of the animals must be in good conditions. Besides deworming, the supplementation of vitamins, minerals and antioxidants in feed are useful to improve health status of the animals.

Non-Hormonal Treatments

Plant Based Heat Inducers

Plants have been used for the treatment of animals since long back. Plants synthesize varieties of phytochemicals such as alkaloids, glycosides, terpenes and tannins (secondary metabolites) as a part of their normal metabolic activity and many of these have therapeutic actions when consumed by animals. Many plants are rich source of vitamins and minerals whereas some have estrogenic property which is useful in restoration of cyclicity in anestrus animals. Almost all the parts of plant such as seeds, berries, roots, leaves, bark and flowers have been used as therapeutic agents either directly (crude drugs) or their active principles, after separation through various chemical process. Many plants such as *Murraya koenigii* (curry leaves), *Nigella sativa* (kalonji), *Abroma augusta* (Ulatkambal), *Saraca asoca* (Ashoka), *Trigonella foenum-graecum* (Methi), *Bambusa aruninacea*, *Carica papaya*, *Asparagus recemosus*, *Leptadenia reticulate*, *Courupita guianensis*, *Pergulacia daemia*, *Semecarpus anacardium cucumber*, and *jute plants* either alone or in combinations have been fed to treat the anestrus animals with variable response on induction of estrus.

Indigenous herbal preparations such as Prajana HS (Indian Herbs), Janova (Dabur), Sajani (Sarabhai), Heat up (Century) Heat raj (Ranjan), Fertivet (Ar Ex Labs) and Aloes compounds (Alarsar) are commercially available and effective in restoration cyclicity with good success rates. These formulations are potent combinations of herbs, formulated to induce ovarian activity.

Lugol's Iodine

Lugol's iodine treatment is cheaper and effective means of management of anestrus but response has been variable (45 to 91.7%) among cattle and buffaloes. Lugol's iodine solution (5%) has traditionally been used as a cervical paint. It is presumed that painting of Lugol's iodine on posterior part of the cervix causes local irritation and brings about reflux stimulation at anterior pituitary for secretion of gonadotrophins and consequently cyclicity. Lugol's iodine is an irritating solution and intrauterine infusion of Lugol's solution (0.5 to 1.0%) causes hyperemia (enhanced circulation) of uterine mucosa resulting into degree of iodine absorption from uterus. The absorbed iodine probably increases the metabolic rate of body through stimulating the thyroid hormone secretion. Increased metabolic rate trigger the ovarian functions by enhancing the energy utilization. Injectable Lugol's iodine has also been used with the same assumption (Sarkar, 2005). Another probable mechanism of intrauterine use of Lugol's iodine is that it acts as chemical curator (due to its irritating nature) and replaces the uterine mucosa with new tissue. The newly formed tissues of endometrium release luteolytic factors (PGF₂ α) that reaches to the corpus luteum via utero-ovarian pathway and causes luteolysis (Gupta et al., 2011). Thus, it initiates the estrus cycle, if anestrus is due to PCL. Now-a-days, the use of Lugol's solution is not being recommended for treatment of anestrus due to its irritating nature and damaging effect on endometrium.

Hormonal Treatments

Estrogens Based Treatment

Exogenous administration of estrogen produces estrus signs in anestrus animals with or without concurrent ovulation. In presence of dominant follicle, estrogen administration results in expression of estrus and ovulation because of its positive feedback effect over pituitary for LH surge. For this reason, it has been used to induce ovulation and to reduce postpartum anestrus period. Conversely, estrogen induces anovulatory estrus in absence of dominant follicle. Estrogens have also been shown to cause luteolysis in ruminants probably through

stimulating the prostaglandin secretion from endometrium as well decreasing the level of circulating LH. One or two doses of intramuscular injections estradiol (3–10mg) or estrone (5–15mg) at three days interval can be used to regresses the retained corpus luteum associated with pyometra, mummification and mucometra.

Progesterone Based Treatment

Exogenous administration of progesterone mimics the luteal phase of the estrus cycle by exerting negative feedback effect over hypothalamus and pituitary for LH release. Upon withdrawal of progesterone, the normal follicular phase of the cycle is stimulated. However, for such treatment seem to be effective, abrupt decrease in progesterone level is required at the end of treatment. Intravaginal progesterone releasing devices such as PRID (progesterone–releasing intravaginal device), CIDR (controlled internal drug release) and CueMate are effective in restoration of cyclicity in anestrus animals. Ear implants (Crestar and Synchronate–B) also produce required abrupt decrease in progesterone concentration at the end of treatment. Progesterone therapy alone is not particularly effective for the treatment of anovulatory anestrus; hence other hormones have been incorporated in most of the progesterone-based therapy.

Gonadotropic Releasing Hormone (GnRH) Based Treatment

The single intramuscular injection of GnRH analogue (10 to 20 μ g Buserelin) has been used effective in induction of estrus and concurrent ovulation with variable response (45.5 to 87.5%) within 4–22 days. The variable response may be due to differential action of GnRH on different stages of follicular development. It induces ovulation, if mature follicle is present at the time of administration by inducing the LH surge. However, single injection of GnRH is not always effective in deep anestrus animals. On the contrary, it stimulates emergence of new follicular wave through enhanced secretion of FSH, thus effective in long term. Pulsatile/intermittent injections of small dose of GnRH (at every 2 hours, intravenously) has been tried in order to induce LH pulses, however, intermittent injection make this technique impractical.

To achieve better response, GnRH has been combined with other drugs such as phosphorus injection (Tonophosphan), prostaglandin, estradiol and progesterone. The Ovsynch protocol or GPG regimen (GnRH–PG–GnRH), used to synchronize ovulations in dairy cows has been widely used to treat anestrus cattle and buffaloes and results are also promising. Under

this protocol first injection of GnRH (at day 0) induces ovulation, if dominant follicle is present and if not luteinizes with emergence of new follicular wave 1 to 2 days later, PGF₂ α injection given on day 7 regress the CL formed in response to first injection of GnRH and second injection GnRH on day 9 induces ovulation of new dominant follicle subsequently, all the treated animals are inseminated within 16–20 hours of second injection of GnRH.

Prostaglandin Based Treatment

Prostaglandin (PGF₂ α) is the treatment of choice for persistent corpus luteum and sub estrus. Natural or synthetic analogue of PGF₂ α as a single dose has been used with a reasonable degree of success for management of silent estrus in cattle and buffaloes. It should be born in mind that PGF₂ α is only effective between days 6–16 of the cycle and in the presence of active corpus luteum. An intramuscular injection of 25mg (total dose) of natural PGF₂ α or 250 to 500 micrograms of synthetic ones is required to regress the CL in both cattle and buffaloes. However, a lower dose of PGF₂ α (5mg) are also effective to regress the CL through intra–vulvo–submucosal.