Review Article

Estrous Synchronization in Farm Animals - A Review

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Abstract

Estrous synchronization creates the opportunity to capture the economic benefits of artificial insemination (AI). Because AI involves a substantial investment of labor and time, most commercial farms or ranches will not utilize this technology unless this investment can be confined to a period of less than 5 to 7 days. To make the labor requirements of AI compatible with modern cattle breeding, the estrous cycle must be synchronized so that a high percentage of treated females show a fertile, closely synchronized estrus. Estrus synchronization based on different effective hormonal therapy can be planed considering its utility and economical implication by analysing its merits and demerits. But choosing one of the best suited therapies must be designed for its effectiveness.

Key words: Farm Animal, Hormone, Oestrus Cycle, Synchronization

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Introduction

The term "estrous" refers to the point of female sexual excitement in mammals which causes ovulation. At ovulation females are most receptive to mating. This period is commonly referred to as heat. This periodic pattern of sexual receptivity is the result of an organized and complex series of changes that occur in the reproductive system of cattle. Managing oestrus in appropriate and desirable ways to increase the efficiency of reproductive life is always in demand. The manipulation estrus cycle and induction of estrus to bring a large percentage of a group of females into estrus at a short, predetermined time is known as estrus synchronization (Odde, 1990).So the present review depicts different recent hormonal therapy for oestrus synchronization in farm animals. Out of which synchronisation based on GnRH hormones are most commonly practice therapy in dairy cattle.

Purpose of Estrus Synchronization

Estrus Synchronization involves in manipulating the estrous cycle within a herd to express estrus approximately at the same time. It is a managemental process through which the humane errors and managemental costs could be minimized. It is very useful in large herd size where individual animal monitoring is difficult and often subjective, or because small intensively managed herds are milked in robotic systems that minimize animal: staff interactions. Additional reasons arise from high producing cows having less obvious symptoms of estrus. Furthermore Estrus Synchronization is a labor saving breeding management tool effective in artificial insemination and embryo transfer program. Groups of females are benefited in perspective of parturition by decrease labor, decrease calving period; reduce calving season and more uniform weaning weights. Estrus synchronization not only reduces or eliminates estrus detection but also shorten the breeding season by creating a scope for artificial insemination. Cows or heifers are in estrus during a predictable interval that facilitates AI. It can be synchronized by a large group to ovulate at same time. It helps in scheduling the parturition time at most favourable season when the newborns can be reared in suitable environment with ample food for better survivability. for At the same time it also facilities short calving season, reduce labour required for AI breeding, marketing of uniform calf crop (same age) and improves management practices (cattle grouped-closer observation, better feeding practices, etc.). Estrus synchronization has a number of advantages but still possess few problems in its practical use like low conception rates, expensiveness, skilled labour etc. Cows all calving at once which especially bad if have many calving problems.

Manipulating the Estrous Cycle

The systems of estrous control that are used to synchronize or induce heat are designed to manipulate various components or functions of the estrous cycle. In order to manipulate various components or functions of the estrous cycle to synchronize or induce heat, it is necessary to understand the estrous cycle. The primary glands or tissues that control the estrous cycle are the hypothalamus, pituitary, ovary, and uterus. Each of these components of the reproductive system secretes chemical compounds called hormones, which regulate their own function, or the function of other components. Many hormones are involved in control of the estrous cycle, and their release into the bloodstream can be measured experimentally. Estrous synchronization is the process of targeting female mammals to come to heat within a short time frame (36 to 96 hours).

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One approach to synchronization is to prevent ovulation until all cows in the herd have regressed their CL. This is usually accomplished with natural or synthetic progesterone such as Norgestomet in Syncro-mate B. Once suppression of ovulation is removed, cows return to estrus and ovulate in a short period of time. Another way to manipulate estrus is by shortening the cycle so that a large number of cows come into estrus at the same time. This is accomplished by treating cows with prostaglandin, the same hormone that causes CL regression during the normal estrus cycle. Examples of prostaglandins used today include Lutalyse and Estrumate. It is important to note that prostaglandin is effective only after day 6 or 7 of estrus. The third concept employs both of the principles cited above. The aim with this system is to inhibit ovulation with a progesterone compound until most of the cows have regressed the CL with natural prostaglandin. Upon removal of the progestogen, animals will cycle within a few days but are not inseminated due to inherent low fertility of the herd. This system allows for more comprehensive management of the estrous cycle and even boosts fertilization over and above natural heat. Examples here include Syncro-mate B and the 14-day MGA-prostaglandin system.

While estrous synchronization traditionally focused on controlling the CL on the ovary, researchers in recent years have developed new programs aimed at synchronizing estrus by manipulating ovulation. As the cyclical wave continues, one follicle, the dominant follicle, grows to a much larger size than the others. Remember that ovulation occurs only when progesterone levels are low. If the correct physiological signals aren't present, the dominant follicle doesn't ovulate, regresses, dies and is replaced by a new dominant follicle from a subsequent wave. High levels of progesterone secreted by the CL during the middle of the estrous cycle (days 5 to 15) send signals that inhibit ovulation.

Synchronization of Estrus Utilizing Progestogens

For many years, progestogens have been known to suppress estrus in cattle and were the first products used in an attempt to control the estrous cycle. Zimbelman *et al.* (1970) reviewed 24 studies that addressed the effectiveness of the progestogen, melengestrol acetate (MGA) as an estrus synchronization agent. They showed a 14% reduced first service conception percentage in treated females compared to controls when MGA was fed for 10 to 18 days. Fertility has also been shown to be reduced after long term administration of other progestogens such as: 6-methyl-17 acetoxy-progesterone (MAP), 6-chloro-6-dehydro-17-acetoxyprogesterone (CAP), and dihydroxyprogesterone acetophenide (DHPA). Treatment of cattle with progestogens for less than 14 d was reported not to reduce conception percentage (Roche, 1976). In addition, short-term exposure to progestogens causes some anestrus (postpartum or prepubertal) cattle to begin cycling. However, for these short-term progestogen systems to be effective in synchronizing estrus, a luteolytic agent must be incorporated (Kamboj, 1993).

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Synchronizing Estrus Utilizing Progestogen Plus Prostaglandin $F_2\alpha$

Prostaglandin $F_2\alpha$ ($PGF_2\alpha$) and its analogs cause luteolysis and a return to estrus in cattle when given during the luteal phase (Days 5 to 17; Day 0=estrus) of the estrous cycle 14, 15 and the fertility of the induced estrus is normal. 12, 16, 17 Research has shown that a higher percentage of cattle treated with PGF during the late luteal phase (Days 10 to 17) exhibited estrus than those treated during the early luteal phase (Days 5 to 9)18, 19. It has also been shown that the closest synchrony of estrus occurs when cattle are at a similar stage of the estrous cycle when $PGF_2\alpha$ is administered. Based on the results of these research trials, a system that initially synchronizes heifers by feeding MGA and then administers $PGF_2\alpha$ during the late luteal phase of the subsequent cycle should produce a high percentage of heifers displaying closely synchronized estrus and with improved fertility (Brown *et al.*, 1988) (Fig. 1).

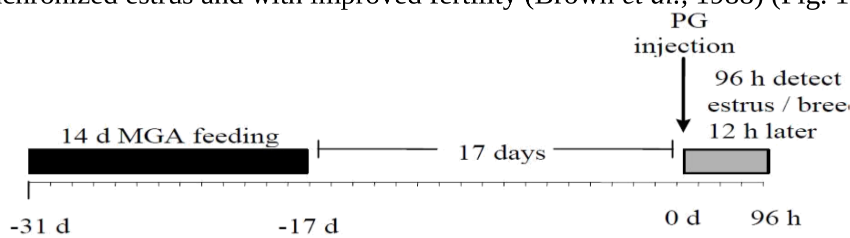

Fig 1: Melengestrol acetate (MGA) administered orally in the feed can be combined with prostaglandin $F_2\alpha$ (PG) with estrous behaviour for 96 hours after PGF treatment.

One impediment to the widespread use of estrus synchronization and AI among producers is the amount of time and expertise required to accurately detect heifers in estrus. Timed-insemination, where artificial insemination is scheduled for an appointed time after synchronization is designed to decrease this time, commitment and expertise. Breeding at an appointed time without regard to estrous behavior following the Colorado system of MGA/$PGF_2\alpha$ estrous synchronization, has been shown to give satisfactory pregnancy percentages in cycling heifers (serum progesterone > 1 ng/mL at time of PGFα administration) (Larson *et al.*, 1996). Cycling heifers time-inseminated at 72 h after $PGF_2\alpha$ administration had a conception percentage of 50.8% compared to a conception percentage of 66.7% for cycling heifers detected in estrus and bred 12 hours later. 21 However, because all heifers in the timed-insemination group were inseminated artificially versus only those heifers detected in estrus in the estrus-detected group, 50.8% of the heifers in the timed-inseminated group became pregnant to AI, compared to 42.7% of the estrus-detected group. This indicates that the timed- insemination was successful in causing conception in heifers that ovulated at a time consistent with the synchronization system but had not been detected in estrus. This was confirmed by the fact that 39.1% of the heifers that were considered cyclic, based on serum P4 above 1 ng/ml at the time of $PGF_2\alpha$ administration, but that were not detected in estrus, did become pregnant to the timed AI. 21 Others found that the percentage of puberal heifers, as determined by P4 analysis, that failed to exhibit estrus within 6 d of MGA/$PGF_2\alpha$ treatment and within

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21d for the non synchronized controls were 17.1 and 15.3%, respectively (Xu *et al.*, 1997) (Fig. 2).

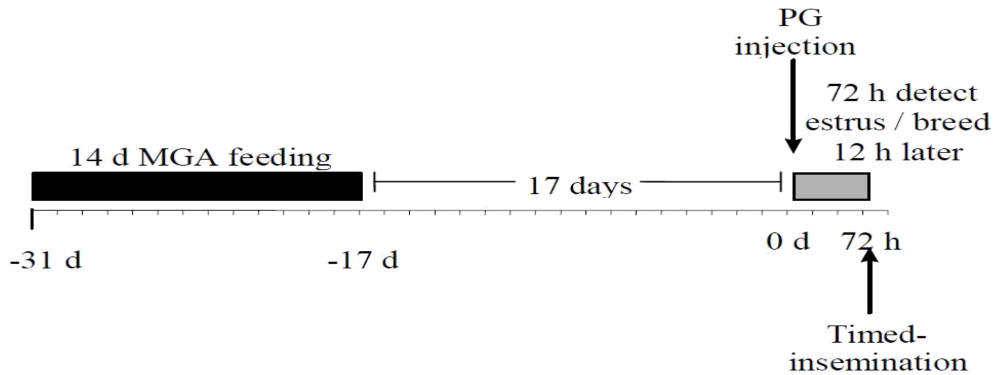

Fig 2: Melengestrol acetate (MGA) administered orally in feed can be combined with prostaglandin $F_2\alpha$ (PG) where estrous detection followed by insemination 12 hours later is combined with timed-insemination 72 hours after PG administration with estrous behavior for 72 hours after PG treatment.

Synchronizing Estrus Utilizing Prostaglandin $F_2\alpha$ Alone

The exact mechanism of action of $PGF_2\alpha$ on the corpus luteum (CL) is not known; however, it probably acts to disrupt delivery of LH to the CL, or by negatively affecting LH receptors in the CL. Injecting $PGF_2\alpha$ causes luteolysis and a corresponding decrease in progesterone levels in the circulation. Decreasing progesterone concentrations allow the final maturation of the ovulating follicle and then expression of estrus followed by ovulation. This series of events is indistinguishable from the normal events surrounding the endogenous release of $PGF_2\alpha$ that occurs around day 17 of the estrous cycle. Prostaglandin $F_2\alpha$ as well as an analogue are currently available and labeled for use in the bovine for estrous synchronization. Assuming that about the same number of heifers in a group exhibit estrous each day, 55% of cycling heifers should have a CL that would respond to an injection of $PGF_x\alpha$ (heifers in d 5-16 of the estrous cycle), 45% of heifers either have "young CLs" (less than the undergoing spontaneous CL regression (d 17-20). Commonly utilized involves two injections of $PGF_2\alpha$ administered 11 to 14 days apart (Cooper, 1974). No oestrous detection or breeding is done after the first injection and all heifers, regardless of whether or not they responded to the first treatment are given the second injection. The 75% of cycling heifers that should respond to the first injection within 96 hours are on days 6 to 14 of the estrous cycle at the time of the second injection. The 25% of cycling heifers that are not expected to respond to the first injection because they have "young CLs" ovulation) are on days 10 to 19 of the estrous cycle at the second injection. Therefore, by utilizing two injections, 100% of the heifers should be at a stage of the estrous cycle that will allow them to respond to the second PGF injection. Observation of heifers for indications of estrous behaviour followed by artificial insemination 12 hours after first detection follows the second $PGF_2\alpha$ treatment for at least 96 hours. The advantage of this system is that

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only 4 days are required for estrus detection and AI (Fig. 3).

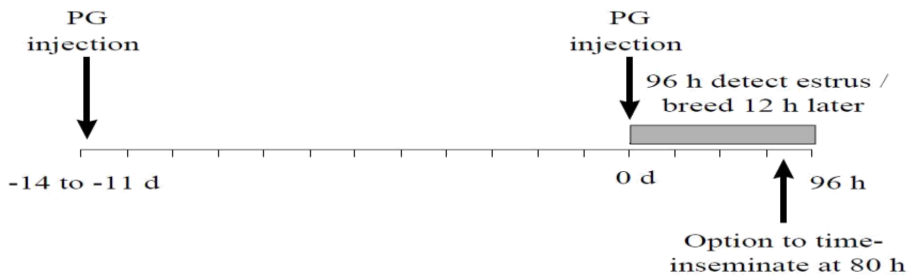

Fig 3: Prostaglandin F2α(PG) used alone in one method is to inject all heifers in group with PG twice at a 11- to 14-day interval. The second injection of PG, approximately 11-14 days after the first, should result in all cycling heifers responding to the PG treatment. Animals are observed for estrous behaviour for 96 hours after PG treatment.

The disadvantage is the increased cost, labor, and management that results from the fact that all the heifers are handled twice for $PGF_2\alpha$ treatments, as well as being handled once for insemination. And, although sound theoretically, the effectiveness of synchronization and pregnancy percentages are not always acceptable following this method (Stevenson *et al.*, 1987). However, synchronization and pregnancy percentages are improved when the injections are 14 days apart rather than on an 11 day interval (Folman *et al.*, 1900).

Synchronizing Estrus Utilizing Progestogen Plus Prostaglandin CIDR®

Recently, beef producers in the U.S. gained a new tool to be used in estrus synchronization programs. This tool is called a CIDR. It is a T-shaped devise that is about 5 inches long that is inserted into the vagina of breeding females. The CIDR releases progesterone, which is absorbed into the blood stream. CIDRs were developed in New Zealand and have been used there and in other countries for several years with good results. The wings of the CIDR are pulled in so that the entire device is shaped like a rod that can be inserted into the vagina with an applicator. On the end opposite the wings, a tail is attached that hangs outside the heifer and allows you to easily remove the insert seven days after administration. The backbone of the CIDR is a nylon spine covered by a progesterone impregnated silicone skin. Upon insertion, blood progesterone concentration rise rapidly. Maximal concentrations are reached within an hour. Progesterone concentrations are maintained at a relatively constant level during the seven days the insert is in the vagina. Upon removal of the insert, progesterone concentration in the bloodstream drops quickly. If a CIDR device is left in an animal longer than 7 days, fertility to subsequent breeding will start to decline. If a CIDR device is accidentally placed in a pregnant cow or heifer, no problems will occur due to the CIDR itself, but injection of Lutalyse will cause abortion in many animals. There is no slaughter withdrawal for either Lutalyse or CIDR (Fig. 4).

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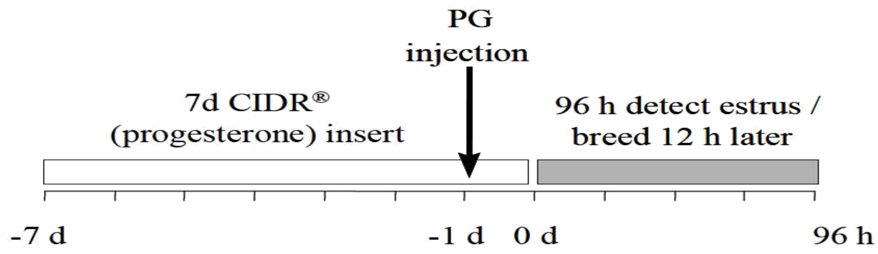

Fig 4: Progesterone can be combined with prostaglandin F2α (PG) and used as an estrous synchronization place for seven days before being removed. One day prior to the removal of the norgestomet implant, PG is administered system (CIDR®). An insert containing progesterone is placed intra vaginally. The CIDR device is left in.

GnRH-Based Systems of Estrous Synchronization

A series of GnRH-based systems of varying complexities has been developed. The simplest programs are designed for use primarily in cyclic females with insemination based on detection of estrus. Others have been developed in order to support the use of timed AI and/or to induce varying proportions of anestrous females to ovulate. Furthermore, it has been reported that GnRH is not always successful in producing a new follicular wave in cows was reported by Barros *et al.* (2000) (Fig. 5).

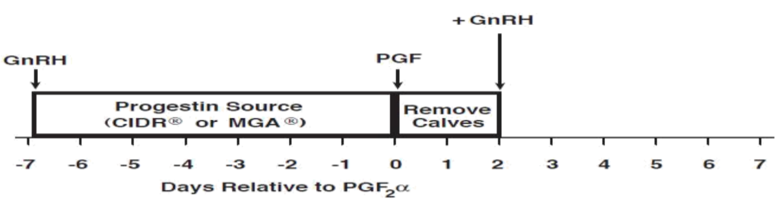

Fig 5: GnRH-based systems in postpartum cows (Ova synch protocol)

Synchronizing Estrus Utilizing GnRH Plus Prostaglandin F_2 α

Another method of synchronization is the combination of Gonadotropin releasing hormone (GnRH) and PGF_2 α. The protocol involves an injection of GnRH followed 7 days later by an injection of PGF_2 α. A second injection of GnRH follows the PGF_2 α injection by 30 to 48 hours. The method is designed to be used with timed insemination 8 to 24 hours after the last GnRH injection (Pursley *et al.*, 1997). This synchronization system results in a tight synchrony of estrus, allowing breeding at an appointed time without detection of estrus. The first injection of GnRH causes either ovulation or luteinization of all dominant or large growing follicles. As a result, a new follicular wave is initiated in all cows about 3 days after the injection. Therefore, all the females in the group have growing follicles of about the same stage of development. In addition, GnRH stimulates development of luteal tissue from the cells that were previously the dominant follicle. The PGF_2 α injection lyses the CL resulting from the GnRH injection that initiates the process that leads to ovulation. The final GnRH injection serves to increase the synchrony of ovulation within the group of females. The success of the first injection of GnRH to

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synchronize follicular growth is very good in cows, but less in heifers (Pursley *et al.*, 1997; 1995)

Co-Synch

One of the simplest modifications of the classical Ovsynch system used is so called Co-Synch protocol. The second injection of GnRH and AI are performed at the same time i.e. 48h after the treatment with prostaglandins. Although most research using the Cosynch protocol has focused on a 48h interval between prostaglandin injection and GnRH+AI, intervals to oestrus following the treatment indicates a 60-64h interval post PGF as used in Ovsynch, would more closely match appropriate insemination timing for beef dairy (DeJarnette *et al.*, 2001b) (Fig. 6).

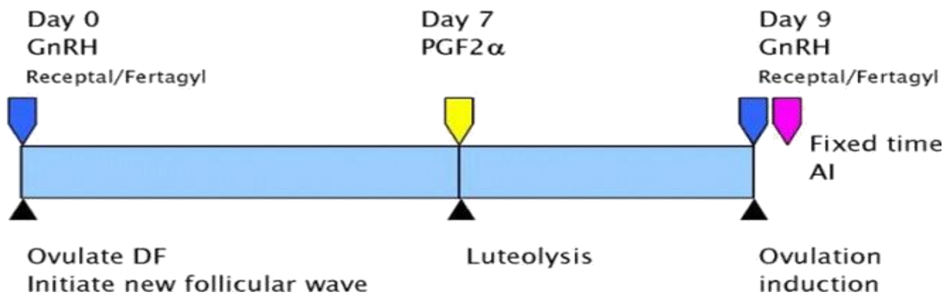

Fig 6: Co-Synch

Heat Synch

More recently, novel, hormone-based protocols have been developed to synchronize ovulation for timed insemination in dairy cows, the first of which was termed Ovsynch (Pursely *et al.*, 1997; Mohan *et al.*, 2009). Ovsynch consists of an injection of gonadotropin releasing hormone (GnRH; to terminate the dominant follicle and initiate a new follicular wave), then an injection of prostaglandin (PG)F_2, 7 days later (to induce luteolysis) and, finally, a second injection of GnRH 24–48 h later to induce ovulation. One variation of Ovsynch is termed Heat Synch and substitute's estradiol cypionate (ECP) for the second GnRH injection (Lopes *et al.*, 2000). ECP induces a surge-like release of (GnRH) from the hypothalamus to induce ovulation. Since ECP is less expensive than GnRH, a major advantage of Heat Synch is reduced hormone costs (Fig. 7).

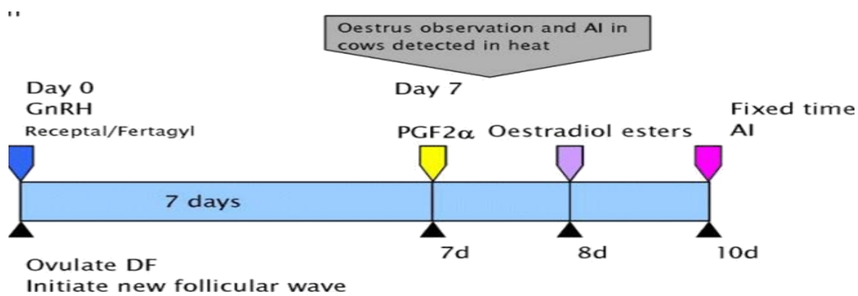

Fig. 7: Heat-Synch

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Pre-Synch

A presynchronisation protocol prior to implementation of Ovsynch protocol was developed by giving one or two injections of PGF 14 days apart, with the second injection given 12 days prior to the first GnRH of the Ovsynch protocol. The Presynch-Ovsynch protocol increased pregnancy rates by 18% (25% to 43%) in lactating cyclic cows as reported by Moreira *et al.* (2001). Post partum presynchronisation with GnRH can also be performed at 7 days before the actual Ovsynch protocol. This approach also has the advantage of being potentially effective in both cyclic and anoestrus cows (Stevenson *et al.*, 2000). Combination of prostaglandin and GnRH as a presynchronisation treatement proceeding the classical Ovsynch or Cosynch protocol were also tried with various success rates usually resulting however in some improvement of pregnancy rates to the final Ovsynch AI (DeJarnette *et al.*, 2003) (Fig. 8).

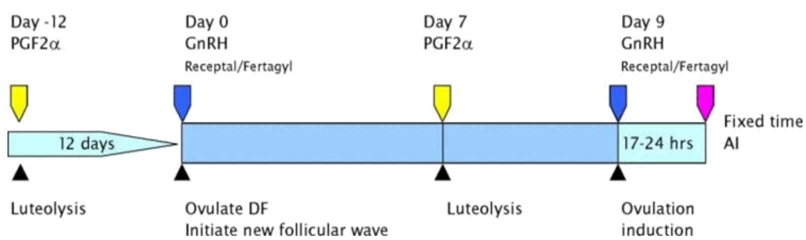

Fig 8: Pre-Synch

Double Synch Protocol

Mirmahmoudi and Prakash (2012) recently modified the ova synch protocol and named as Doublesynch protocol. This protocol comprised of PGF_2 treatment = day 0), followed by 10 lg of a GnRH analog on day 2, a second PGF_2a dose (25 mg) on day 9, and a second GnRH dose (10 lg) 48 h after the second PGF_2a dose (day 11). Doublesynch protocol produced efficient synchronization of ovulation twice i.e., after the first and second GnRH administrations, and resulted in satisfactory pregnancy rates in cycling buffaloes irrespective of the stage of estrous cycle during the low breeding season (Fig. 9).

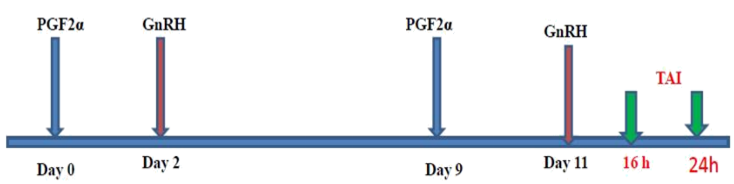

Fig. 9: Double-Synch

Modification of the GnRH-PG System

A modification of the GnRH-PG system designed to be used with timed insemination is a system whereby the second GnRH injection is not given and insemination follows estrous detection. Because 5 to

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15% of females treated with GnRH will exhibit estrus prior to the time of the PG injection 7 days later, estrus detection should begin about 4 days after the GnRH injection and should continue for 4 days past the PG injection. This system is easy to implement with only 3 trips through the squeeze chute and it captures the advantage of initiation cycling in some anestrous postpartum cows and prepuberal heifers as the result of GnRH administration. A modification of the method illustrated in Fig. 10 utilizes an initial dose of Gonadotropin-releasing hormone (GnRH) to synchronize ovulation in a group of heifers followed by a Prostaglandin $F_2\alpha$ (PG) injection given 7 days later to lyse the resulting CL.

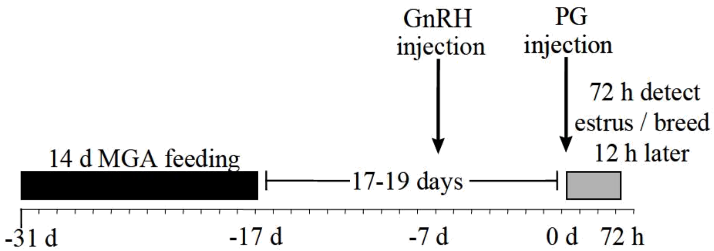

Fig 10: A modification of the MGA (progestogen)/PG (prostaglandin $F_2\alpha$) system utilizes an injection of Gonadotropin-releasing hormone (GnRH) 7 days prior to PG injection

The second GnRH injection given 30 to 48 hours after PG is omitted, and rather than utilizing timed-insemination, the females are observed for estrous behavior for beginning 4 days after GnRH treatment and continuing for 4 days past the PG injection. Any female displaying signs of estrus is identified and bred artificially 12 hours after first detection of estrous behavior. Synchronizing estrus utilizing progestogen and prostaglandin $F_2\alpha$ plus GnRH. Adding an injection of GnRH to synchronization systems that utilize feed-grade progestogen (MGA) and prostaglandin $F_2\alpha$ (PG) appears to slightly improve the percentage of females that exhibit estrus and causes the animals that exhibit estrus to do so in a shorter time span. With this modification, GnRH is injected 7 days prior to the PG injection. Randel *et al*. (1996) also proved that exogenous PGF enhanced GnRH-induced LH release in postpartum cows.

Managemental Intervention

Management has always significant role in animal production and animal Breeding program. Besides various protocol and hormonal therapy, appropriate nutritional management is essential for successful implementation of several synchronization programs both in heifer and cow**.**

Nutrition

The major factor which determine the success of any estrus synchronization protocol is the percentage of animals cycling at the initiation of treatment. The most important factor affecting cyclicity is nutrition. Feeding to cows to achieve a better at least a moderate body condition by the time of calving besides

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these increase energy levels in rations prevent loss in body condition after calving. Regular health check-up to animals and ensure the right nutrition program is necessary for optimum reproductive performance in herd.

Herd Health

It is necessary to maintain an intensive herd health and vaccination program for all the diseases which relevant to concern geographic region. All vaccinations and deworming programme should be completed least three weeks before the synchronization and breeding period to provide ample time for the immune system to respond and provide protection from the disease.

Teaser Bull Exposure

Exposure of females to vesectomised bulls in the early postpartum period has been shown to decrease the number of days to the first postpartum ovulation and to increase the percentage of cows cycling at the beginning of the breeding season. Bulls should be surgically altered to prevent insemination and disease transmission. In another way androgenized females have a biostimulatory effect like that of bulls and are inexpensive to produce.

Early Weaning of Calf

Frequency of suckling by calves causes a hormonal response that inhibits return to estrus (suckling inhibition). Therefore suckling stimulus of extends the duration of postpartum anestrus. Early weaning of calves provides an excellent means to improve the cycling status. Many studies have concluded that short-term calf removal (early weaning) combined with other forms of synchronization improves estrus synchrony and conception rate in cow. Even 48-hour calf removal alone has been shown to cause synchrony and cyclicity in some cows.

Miscellaneous Details

First-calf heifers, late calving cows, difficult births, and retained placentas are all associated with reduced fertility. Separate these “high risk” animals for maximum nutrition, better monitoring and effective veterinary care can be provided. Adequate labor must be available for heat detection and breeding. All handling facilities and equipments should be in proper working order and safe.

Conclusion

Synchronization of fertile estrus can be accomplished with progestogens, combinations of progestogens and prostaglandin $F_2\alpha$, prostaglandin $F_2\alpha$ alone and combinations of gonadotrophin-releasing hormone and prostaglandin $F_2\alpha$. Out of different protocol described presynch and ovsynch protocol are commonly

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used in dairy cattle whereas for sheep and goat production, therapies using intravaginal progesterone impregnated sponge rampantly practice with good results. Besides this advantages and disadvantages of each system as well as the management capabilities, farm economy and expectations of the producer should be considered when determining the most appropriate estrous synchronization product or protocol.

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