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Hormonal management of ovarian activity during early post-partum phase in dairy cows

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Abstract

The synchronization of estrus in post-partum dairy cows involves various methods such as prostaglandins, progesterone-releasing devices like CIDR and PRID, and GnRH analogues. Incorporating a period of progesterone administration enhances the proportion of cows exhibiting estrus within a specific timeframe while maintaining a normal luteal phase. However, the effectiveness of synchronization is influenced by factors related to ovarian activity, including body condition score, age, parity, and negative energy balance. To optimize synchronization outcomes, it is essential to address these variables that may impede post-partum ovarian activity. Managing factors like negative energy balance through appropriate nutrition and tailoring protocols based on age and parity could potentially improve the success of estrus synchronization in these cows.

Keywords: Management, ovarian, during early, dairy cows

Introduction

Reproductive efficiency is a measurement of the potential of a cow to become pregnant. It is a key limiting indicator to measure dairy cow productivity and profitability. The calving interval has an impact on a cow's productive life. Cows with shorter calving intervals produce more milk per day and have more progeny. By reducing the number of days open, the ideal calving interval may be attained. And to obtain the best conception rate and profitability, cows must have normal uterine involution, early resumption of ovarian periodicity, be observed in estrus, and be inseminated between 40 to 60 days post-partum. (Nayana 2019) ^[1]. Producers can improve the reproductive production of their herds and raise their profit levels by using reproductive technologies like estrus synchronization and artificial insemination (Bonacker 2019) ^[14]. Estrus synchronization reduces or eliminates the necessity for estrus detection, increasing cow fertility and productivity (Larson *et al.* 2006) ^[47]. Furthermore, it enhances AI planning, reduces the calving interval in post-partum dairy cows, and aids in the maintenance of uniform calf crops (Larson *et al.* 2006) ^[47]. According to current reports, the first AI conception rate in dairy cows is between 20 and 40 percent (Lucy 2001; Washburn *et al.* 2002) ^[52, 93]. Progesterone comes in two forms: natural (progesterone) and synthetic (progestin) (Demeterco 2017) ^[27]. Progesterone prevents spontaneous estrus and prolongs the estrous cycle by delaying the onset of estrus after natural or artificial luteolysis (Lucy *et al.* 2001) ^[52]. P4 products are available in a variety of forms for cow estrus synchronization. Melengestrol acetate powder, injectable solution, ear implant, and vaginal implants are all available. PRID and CIDR are the most widely utilized vaginal inserts/devices in cattle (Demeterco 2017) ^[27]. Exogenous progestin administration for short period mimics the post-partum cow short luteal phase, efficiently reprogramming the reproductive axis to commence or resume normal estrus cycling (Bonacker 2019) ^[14]. Following the cessation of progesterone therapy results in a quick decline in progesterone levels in the bloodstream and encourages the release of GnRH, which is followed by the release of FSH and LH and leads to the restoration of ovarian cyclicity (Zerbe *et al.* 1999) ^[97].

Post-partum period

The post-partum period is a transition phase meanwhile in which the reproductive axis recovers after parturition to successively come to the anatomical and functional status required to set up a new pregnancy (Murphy *et al.* 1990; Perea *et al.* 1998) ^[58, 69]. The post-partum period in cows is categorized into three phases, early puerperium, clinical puerperium, and whole puerperium. Duration of early puerperium lasts up to 9 days whereas clinical puerperium extends to 21 days during which the uterus returns to its standard size, but the

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histologically normal structure is not attained. The entire period of post-partum lasts about 42 days during which the uterus retrieves its normal histological structure. Based on endocrine status, the post-partum period is divided into the puerperal period, intermediate period or pre-ovulatory period, and post-ovulatory period. The intermediate or pre-ovulatory period extends from the initiation of pituitary sensitivity to GnRH up to first ovulation at 20-30 days post-partum whereas the post-ovulatory period starts with first ovulation and lasts until completion of uterine involution at 40-45 days post-partum. The physiological changes that occur during the puerperium, include uterine and cervical involution, ovarian rebound, and return to cyclicity as well as the elimination of bacterial infection that sets up during calving (Elmetwally 2018) [30].

Events occurring during the early post-partum period

Uterine and cervical involution

After parturition, the uterus returns to its normal non-pregnant size and function, which is termed uterine involution. The restoration of the uterus to its normal size depends on the rate of myometrial contractions, removal of bacterial infection, and revitalization of the endometrium (Elmetwally *et al.* 2016) [29]. Smooth muscles play a chief role in the ejection of the uterine contents and the shrinkage in uterine size (Bajcsy *et al.* 2005) [5]. The contraction of the uterus also leads to a reduction in uterine and cervical diameters. The cervix reduces its size from roughly 30 cm immediately after parturition to around 2 cm by day 7 post-partum (Wehrend *et al.* 2003) [94]. Kasimanickam *et al.* (2004) [44] reported that larger the diameter of the cervix after parturition, the longer the time required for involution to occur. The pattern of remodelling of the structures starts at the cranial end of the cervix and progresses caudally (Wehrend *et al.* 2003) [94]. Cervical diameter is a better indicator of reproductive problems than uterine size as there is less fluctuation in the size and accessibility of the cervix during involution (Dobson-Hill 2009) [28].

Regeneration of the endometrium

The endometrial epithelium is often abraded during parturition, the caruncular tissue sheds as a part of the physiological form of the puerperium, and there is marked tissue recasting during the post-partum period (Tian and Noakes 1991) [101]. It is thought that the tissue architecture of the endometrium requires 3 to 4 weeks to regenerate fully, which is equally important for fertility (Sheldon and Owens 2017) [83].

Post-partum ovarian activity (ovarian rebound)

To achieve normal fertility and an acceptable calving interval, early resumption of post-partum ovarian activity is mandatory (Hafez 2000) [37]. Ovarian rebound after parturition relies upon the recovery rate of the hypothalamic-pituitary interaction that appears to occur in three distinct phases (Williams 1990). The phase first starts 2-4 weeks after parturition and is described by satiation of the anterior pituitary store of LH. The depletion/repletion cycle of anterior pituitary LH is surely a prime limiting factor for early post-partum recovery (Nett *et al.* 1988) [62]. Phase second is allied to an upsurge in the activity of the hypothalamus to the positive feedback effect of estradiol (Short *et al.* 1974) [85]. The third phase of retrieval needs to flee from the outcome of suckling (Rexroad *et al.* 1975) [75]. The early onset of

follicular growth within 7 to 10 days post-partum has been observed in both dairy and beef cows. The fate of the dominant follicle within the first follicular wave is reliant on LH pulse pattern (Crowe *et al.* 2014) [22]. The first dominant follicle of the post-partum period ovulates normally from wave 3.2 ± 0.2 (~30 days) (Murphy *et al.* 1990) [58]. In the case of dairy cattle, ovulation of the first dominant follicle after parturition usually occurs in 30 to 80 percent of cows, whereas it encounters atresia in 15 to 60 percent of cows or 1 to 5 percent of cows observe the cystic conditions (Sartori *et al.* 2004; Sakaguchi *et al.* 2004) [81, 79]. First ovulation of dominant follicle in both dairy and beef cows is usually silent (Kyle *et al.* 1992) [46] and generally (>70 percent) accompanied by a short estrous cycle, typically involving just one follicular wave. The short time span of first luteal phase is mainly due to premature release of PGF_{2α} (Peter *et al.* 1989) [70]. This second ovulation is usually cognate with the expression of estrus behaviour and succeeded by a luteal phase of normal duration producing normal quantities of progesterone (Crowe *et al.* 1998) [23]. The growth rate of the antral follicles is ceased because of the persistence of the corpus luteum of pregnancy even after calving. This inhibitory action persists for about 20 days post-partum and the frequency of ovulation decreases from the ovary ipsilateral to the previously gravid uterine horn. Ovarian activity is affected by the post-partum sub-clinical and clinical uterine infection. The permanence of pathogenic bacteria often causes clinical disease or sub-clinical endometritis. Uterine disease curbs hypothalamic gonadotropin-releasing hormone (GnRH) and possibly pituitary luteinizing hormone (LH) secretion and has confined effects on ovarian function (Mateus *et al.* 2002) [54]. High circulating levels of PGF_{2α} during the first 3 weeks post-partum due to sub-clinical infection serve as a uterine signal, hampering premature onset of ovarian cyclicity once the puerperal infection has been largely removed (Sheldon *et al.* 2002) [84].

Development of ovarian follicles after calving

Around the fifth day after parturition, the emergence of the first ovarian follicle occurs in dairy cows. Follicular activity on the ovary ipsilateral to the previously gravid uterine horn was reported to be lesser than that of the contralateral ovary during the post-partum phase (Nation *et al.* 1999) [61]. Under physiological conditions, after day 12 post-partum, the first dominant follicle appears with a diameter of more than 9 mm (Schwarz and Zieba 1999; Huszzenicza *et al.* 2008) [82, 41]. Ovulation occurs after the second and more frequently after the third or fourth wave with the dominance of follicles (Adams *et al.* 2008) [2]. Based on the fate of the first dominant follicle- outlines three potential ways of post-parturition growth of ovarian follicles i.e., 1) the first follicle wave ended with the ovulation of dominant follicle; 2) development of the non-ovulating dominant follicle of the first wave taking place after various additional waves preceding the first ovulation; and 3) the development of the dominant follicle, being converted into a cyst. The fate of dominant follicles post-partum is closely linked to the metabolic status of animals - for instance, pre-partum diet (Cavestany *et al.* 2009) [18], energy balance post-partum (Beam and Butler 1997) [8], and parity (Zhang *et al.* 2010) [98].

Short estrous cycle

A large portion of cattle is generally sensitive to abnormal luteal function following first ovulation post-partum. In a

short estrous cycle, the lifespan of the corpus luteum (CL), known as the luteal phase, is normally less than 10 days. A typical luteal phase generally consists of 14-18 days of a normal 21-day estrous cycle. This phenomenon is referred to as a short estrous cycle and is usually observed in females overcoming post-partum anestrus (Bischoff *et al.* 2018) [10]. The first post-partum ovulation often takes place without visual signs of estrus and is followed by a short estrous cycle of 8 to 12 days in the major portion of cows (Stagg *et al.* 1995; Yavas *et al.* 1999) [86, 96]. Incidence of short estrous cycle commonly appears during the first 30 to 40 days post-partum in beef cows (Short *et al.* 1990). Premature secretion of PGF_{2α} from the uterus on day 5 of a short estrous cycle is possibly the mechanism involved in the subnormal luteal activity in sheep and cattle (Zollers *et al.* 1991) [100].

Days open (DO) and calving interval (CI)

Calving interval is the timespan between successive calving and is an outcome of days open (duration from calving to next conception) and gestation length. Meanwhile, gestation length is more or less constant for a given breed, the number of days open to conception set off the sole variable of calving interval. The ideal amalgamation of better management and good physiological condition of the cow, reasonably decrease calving intervals of 12-13 months. Days open is the common variable regulating portion of calving interval and is usually affected by the timespan taken by the uterus to completely involute, resumption of ovarian cyclicity, the incidence of silent ovulation, the correctness of heat detection, how soon to rebreed following parturition, fertility of a bull or semen and efficacy and/or skill of inseminator (Gebremichael 2015) [33].

Synchronization of estrus

Synchronization of estrus entails the manipulation of the estrous cycle or induction of estrus to bring a large portion of a group of females into estrus at a short, predetermined period. Estrus synchronization aid in fixing the breeding time within a short predefined interval. Synchronization of estrus and fixed-time artificial insemination (FTAI) is an effective technique in breeding management, particularly in dairy cattle as it enhances heat detection efficiency (Jayaganthan *et al.* 2016) [43]. The major constraint of estrus synchronization is their inadequacy to induce fertile estrus and ovulation in non-cyclic cattle i.e., pre-pubertal heifers and anestrus suckling cattle (Graves 2009) [35].

Methods of estrus synchronization

For the selection and successful execution of the synchronization of estrus, information on the hormonal profile and functional structures present on the ovaries during different phases of the estrous cycle is very much crucial (Patterson *et al.* 2002) [68]. The various ways for modulating cycle length are the administration of prostaglandin to regress the corpus luteum (CL) present on the ovary before the time of natural luteolysis, or progesterone administration, or more often synthetic progestin administration to halt the ovarian activity for a while, or a recent way of framing estrus synchrony by including use of Gonadotropin-releasing hormone (GnRH) or an analogue, which motivates ovulation of a large follicle (Ozill *et al.* 2011) [64]. Various estrus synchronization protocols can induce 75 to 90 percent of the cyclic cows to express estrus within a period of 5-days (Dejarnette *et al.* 2004) [25].

Prostaglandins based protocol approach

commercially available PGF_{2α} have the potential to concurrently eliminate the CL from all cyclic animals at a predefined period that is favourable for detection of estrus and breeding (Patterson *et al.* 2003) [67]. Throughout the normal estrous cycle of a non-pregnant animal, PGF_{2α} is secreted from the uterus at 16-18 days. The administration of PGF_{2α} once only amidst days 14 and 18 post-calving ensued in a decline in days open (Benmard and Stevenson 1986; Lopez-Gatius 2003) [9, 50]. Estrus synchrony and fertility with PGF_{2α} is more fit with cyclic females, such as virgin heifers, but not in non-cyclic cows (Bader 2003) [4].

1. One-shot prostaglandin: In this method, cyclic females are injected with a single dose of prostaglandin, and bred during estrus (Pal and Dar 2020) [65].
2. Two-shot prostaglandin: if the stage of the estrous cycle in the cows is not known, then, prostaglandin is administered twice at an interval of 10 to 14 days (Sahatpure and Patil 2008) and observation of estrus is not needed before or between administration of prostaglandins (Pal and Dar 2020) [65].

GnRH-based protocol

Manipulation of estrus by administration of GnRH during the bovine estrous cycle causes regression or ovulation after treatment (Pursley *et al.* 2005) [72]. Artesia or ovulation of the dominant follicle commences the emergence of a new follicular wave. Ovulation of a follicle relies upon the status (growing, static, or regressing) of the dominant follicle at the time of GnRH injection (Twagiramungu *et al.* 1994) [91]. Ovulation of a growing dominant follicle comes about 100 percent after GnRH administration, however, ovulation of dominant follicles in the static or regressing phase resulted in 33 and 0 percent, respectively (Helmer and Britt 2005) [38].

GnRH-PGF_{2α} system

The six systems for synchrony of estrus with GnRH-PGF_{2α} combinations are; ovulation synchronization (Ovsynch), combination synchronization (Cosynch), pre-synchronization (Presynch), select synchronization (Select synch), heat synchronization (Heat synch) and hybrid synchronization (Hybrid synch) (Patterson *et al.* 2003) [67].

Ovsynch protocol

Ovsynch protocol is one of the synchronization systems that help in minimizing the days open and successful insemination of a large portion of cows up to the 100th day post-partum (Opsomer *et al.* 2000; Mejia and Lacau-Mengido 2005) [63, 56]. The Ovsynch protocols composed of injection of GnRH on day 0 followed by administration of PGF_{2α} 7 days later, and the second injection of GnRH 48 to 56 h following PGF_{2α} treatment with fixed-time AI 16 h later (Bo *et al.* 2012) [12]. The first GnRH injection results in ovulation/luteinization of any viable dominant follicle present on the ovary and induces the subsequent emergence of a new follicular wave roughly around 1.5 to 2 days later (Pursley *et al.* 1995) [71]. During the following 7 days, there is the emergence of a new follicular wave which undergoes selection and dominance of follicle. On day 7, PGF_{2α} induces luteolysis, thus promotes further growth and maturation of the dominant follicle. In the end, the second injection of GnRH administered 48 hours following PGF_{2α} induces a pre-ovulatory LH surge that initiates ovulation within 8 hours (Pursley *et al.* 1995) [71].

Cows enlisted in the Ovsynch protocol between days 5 and 12 following ovulation have an appreciable pregnancy rate than cows enlisted in other stages of the estrous cycle (Vasconcelos *et al.* 1999; Moreira *et al.* 2000) [92, 57]. Similarly, it was reported that the pregnancy rate was better i.e. 45 percent when TAI has carried out 16 hrs after the second GnRH injection in comparison with the 41 percent rate which was reported on AI after 8 hours of GnRH administration (Pursley *et al.* 1998) [73]. A key modification in the Ovsynch protocol involves the insertion of a CIDR or PRID for the interval between the first GnRH injection and the PGF_{2α} injection (Stevenson 2011; Bisinotto *et al.* 2015) [89, 11]. However, the constraints of Ovsynch protocol application are often associated with selection of acyclic animals, implementation of the protocol at random the stage of the cycle, the season of the year, poor ovulatory response to the first GnRH, atresia of the dominant follicle before PGF_{2α} and premature luteolysis between the first GnRH and PGF_{2α} (Vasconcelos *et al.* 1999; Hoque *et al.* 2014) [92, 40].

Cosynch

In the Cosynch method, the second injection of GnRH i.e., 48 hours after PGF_{2α}, is given at the same time when fixed-time insemination is performed (Pursley *et al.* 1998; Geary *et al.* 2001) [73, 32]. Cosynch protocol can be carried out as a treatment for cows that are unable to show signs of estrus and it also permits the treatment of cows with subestrus or ovulation problems (Barolia *et al.* 2016) [6].

Presynch

In this program, two PGF_{2α} injections are administered 14 days apart and 12 days after the second injection of PGF_{2α}, the Ovsynch protocol starts. The aim is to have maximum animals between days 5 and 12 of the estrous cycle after the commencement of the Ovsynch program (Colazo and Ambrose 2013) [21]. This protocol has been successful in synchronization of the ovulation for first post-partum TAI; therefore, the Presynch + Ovsynch protocol has been widely accepted by the dairy industries (Caraviello *et al.* 2006) [17]. Higher conception rates were recorded in cows instigating the 12-day presynch-ovsynch protocol with serum progesterone values ≥ 1 ng/mL (Ribeiro *et al.* 2011) [17]. However, the protocol has moderate effects in anovulatory cows (those without CL), which narrows the effectiveness of pre-synchronization (Galvao *et al.* 2007a) [31]. Therefore, a combination of GnRH and PGF_{2α} for pre-synchronization might be helpful for anovulatory cows by inducing estrus cyclicity before starting the timed AI program (Ribeiro *et al.* 2011) [77].

Heat synch

Heat synch is a recent synchronization protocol (Dejarnette *et al.* 2001) [24] that uses the cost-effective hormone estradiol cypionate (ECP) in place of the second GnRH injection of the Ovsynch protocol. It is well known that GnRH has a direct and almost prompt effect on the secretion of LH, while ECP has an impeded effect (Dejarnette *et al.* 2004) [25]. A recent survey reported that cows administered with GnRH have an LH surge within an hour, while the LH surge was not detected for 41 h in ECP-treated cows (Stevenson *et al.* 2002) [88]. This variance in time to LH surge means the hormonal injection intervals must also be modified when ECP switches for GnRH. Both Ovsynch and heat synch entails a GnRH injection followed by an injection of PGF_{2α} seven days later

(Bartolome *et al.* 2002) [7]. Heat synch cows detected in estrus should be bred mostly at 72 h after PGF_{2α} injection (Dejarnette *et al.* 2004) [25].

Hybrid synch

Hybrid synch is a combination of select synch and co-synch systems (Stevenson *et al.* 2000) [87]. Estrus detection and AI are carried out until 72 hours after the PGF_{2α} injection (Dejarnette *et al.* 2004; Larson *et al.* 2004) [25, 49]. Pregnancy rates in cows administered the hybrid synch protocol was 34 (Stevenson *et al.* 2000) [87], 46 (Dejarnette *et al.* 2001) [24], 53 (Larson *et al.* 2004) [49], and 52 percent (Dejarnette *et al.* 2004) [25].

Progestogens in the hormonal manipulation of the estrous cycle

Hormonal manipulation of the estrous cycle using progestogens is done to imitate the luteal phase progesterone secretion. Progesterone has potent negative feedback on the hypothalamus, thus, lessening the pulsation of the basal episodic secretion of GnRH. However, the amplitude of LH pulses (together with FSH secretion), induced by the tonic GnRH release, is intense enough to allow the growth of follicles during the luteal phase. These follicles do not attain the pre-ovulatory position until the progesterone block is eliminated. Blood progesterone concentration higher than 1 ng/mL is needed to suppress the pre-ovulatory LH surge and estrus (Lucy 2004) [51]. Synchronization of estrus with progestogens regulates high levels of progesterone in the system of females, even after the regression of the corpus luteum. Synchrony of estrus attains 2 to 5 days following progestin withdrawal. Estrus was synchronized in only 48 percent of the cows at the start of treatment on day 3, but the synchronization was 100 percent when treatment commenced on day 9 of the estrous cycle. The longer the progestin was administered to cattle, the higher the rate of estrus synchronization with lesser fertility (Moreira *et al.* 2000) [57]. The poor fertility of cows bred at the synchronized estrus following long-term progestin administration is due to the premature resumption of meiosis of ova or abnormal development of embryos raised from ova of persistent follicles (Revah and Butler 2006) [74].

Melengestrol acetate (MGA) feeding

MGA is added to feed such that females pick up 0.5 mg per head per day for 14 days. Upon withdrawal of MGA from the feed, cyclic females begin to display signs of estrus but this is sub-fertile and breeding is not advised (Imwalle *et al.* 2002) [42]. MGA does not hinder the pulsatile secretion of LH and the presence of high-frequency LH pulses along with the absence of ovulation at the time of MGA treatment which is indicative of MGA led prevention of the pre-ovulatory surge of LH, causing the ovum to age to a no activity state (Kojima *et al.* 1995; Imwalle *et al.* 2002) [45, 42]. Research has revealed that an amount of 0.25mg of MGA fed daily is ample at hindering estrus but 0.5mg/hd/d in a single feeding is needed to impede both 100 percent estrus and ovulation (Zimbelman and Smith 1996a) [99]. Feeding melengestrol acetate (MGA) for 14 d followed by an injection of PGF_{2α} 17 days after MGA feeding (14/17 d MGA/PG protocol) is an efficacious method for regulation of estrous cycle (Brown *et al.* 1988) [16]. Short-term feeding of MGA (5 or 7 d) combined with an injection of PGF_{2α} is effective in synchronizing estrus in a high percentage of cattle (Chenault *et al.* 1990) [20].

Controlled internal drug release (CIDR) based treatment for synchronization of estrus

The CIDR was traded first in New Zealand in 1987 and contains 1.9 g of progesterone, whereas the CIDR sanctioned in the United States comprises only 1.38 g. The CIDR is a T-shaped vaginal insert impregnated with natural progesterone (1.38g/insert) which is placed intravaginally for seven days, imitating luteal phase progesterone secretion. One day before the removal of CIDR cows are treated with the PGF_{2α} for the elimination of the potential endogenous source of progesterone. The removal of progesterone (exogenous as well as endogenous) should create favourable conditions for the final stages of dominant follicle development and maturation (Gvozdic *et al.* 2013) [36]. The decrease in circulating concentrations of progesterone tended to increase LH pulse frequency and decrease the variance in follicle size at CIDR removal (Grant *et al.* 2011) [34]. The amount of P₄ liberated from the CIDR insert is ample to elevate and uphold the circulating level of P₄ in the blood >2.0 ng/ml in the absence of a CL (Chenault *et al.* 2003) [19]. The blood levels of P₄ speedily reach a peak within 1 h after CIDR insertion; similarly, P₄ levels quickly declined between 12 to 24 h following CIDR removal (Lamb *et al.* 2006) [47]. Most of the cows are likely to come in estrus over the next 3-5 days after CIDR removal (Gvozdic *et al.* 2013) [36].

Modified CIDR protocols

Protocols modified to more accurately line up with follicular waves and hamper over maturation have been promoted. Bridges *et al.* (2008) [15] assumed that lesser the duration between the initial GnRH and PGF_{2α} as well as the span of CIDR insertion within the Co-synch plus CIDR protocol would improve estrogen production and elevate TAI pregnancy rates. Bridges *et al.* (2008) [15] reported an increase in pregnancy rates in 5-day co-synch by arranging TAI from 60 to 72 h after PGF_{2α} and CIDR removal. Nash *et al.* (2012) [60] recorded that outcome of pregnancy rates from FTAI were

indistinguishable for cows allocated to long-term CIDR-based protocols correlated to short-term CIDR-based protocols. However, estrus response after PG and ahead of FTAI was turned down in cows assigned to the long-term (23 percent; 14-d CIDR-PGF_{2α}) collated with the short-term protocol (49 percent; Co-Synch + CIDR) (Nash *et al.* 2012) [60]. Ahmed *et al.* (2017) [3] reported the conception rate to be higher in CIDR-based protocols than in GPG-ovsynch protocol. In the GPG group, the acyclic cows displayed lower conception rates than those of cyclic (33.3 vs. 44.4 percent) but the response was inverted in the CIDR-treated Ovsynch groups where the acyclic cows exhibited higher conception rates in comparison to cyclic in the CIDR-GPG (70.0 vs. 68.8 percent) and G-CIDR-PG (55.6 vs. 50.0 percent). The 7 & 7 Synch method comprises of a simple, one-step approach to elevate the percentage of cows introducing with a physiologically mature, LH-responsive follicle at the time of administration of GnRH (Bonacker *et al.* 2020) [13]. It is supposed that the presynchronization mechanism of the 7 & 7 synch method (PGF_{2α} administration and progesterone treatment seven days prior to the administration of GnRH) would activate cyclicity among cows that were anestrus due to shorter days post-partum, lower body condition score, or younger age. In addition to this, the 7 & 7 Synch protocol would add to estrus expression and lessen variation in synchrony among recipient females. On day 0, cow allocated to the 7 & 7 Synch protocol received an Eazi-Breed intravaginal controlled internal drug release insert with the administration of PGF_{2α}. On day 7, cows were administered gonadotropin-releasing hormone whereas on day 14, all cows were administered PGF_{2α} and CIDR inserts were removed (Bonacker *et al.* 2019) [14]. The follicle diameter was greater at the time of GnRH administration for the cows receiving 7 & 7 Synch when compared to cows receiving the 7-day Co-synch + CIDR method, with CL status and estrus expression indicating a high ovulatory response to GnRH (Bonacker *et al.* 2020) [13].

Table 1: Pregnancy per artificial insemination (AI) in dairy cows subjected to timed AI for the first post-partum insemination of the breeding season

Timed AI protocol	Pregnancy /AI (%)	References
MGA-PG	76	Patterson <i>et al.</i> (2001) [66]
Ovsynch + CIDR	67.7	Sakase <i>et al.</i> (2005) [80]
EB + CIDR + GnRH	73.2	Sakase <i>et al.</i> (2005) [80]
Ovsynch	33.9	McDougall <i>et al.</i> (2010) [55]
Ovsynch with progesterone	45.7	McDougall <i>et al.</i> (2010) [55]
Cosynch	39.0	McDougall <i>et al.</i> (2010) [55]
Ovsynch	47.0	Herlihy <i>et al.</i> (2011) [39]
Ovsynch with progesterone	54.0	Herlihy <i>et al.</i> (2011) [39]
Presynch-5-day timed AI	49.1	Ribeiro <i>et al.</i> (2011) [77]
G6G-5-day timed AI	49.9	Ribeiro <i>et al.</i> (2011) [77]
5-day timed AI with progesterone	34.3	Ribeiro <i>et al.</i> (2012a) [76]
Double Ovsynch-5-day timed AI	56.8	Ribeiro <i>et al.</i> (2012b) [78]
14-to-19-d CIDR-PGF _{2α}	84.6	Martin <i>et al.</i> (2014) [53]
14-to-16-d CIDR-PGF _{2α}	83.9	Martin <i>et al.</i> (2014) [53]
7-day CIDR	50.0	Naikoo <i>et al.</i> (2016) [59]

Conclusion

To sum up, the synchronization of estrus in post-partum dairy cows relies on various effective methods but is intricately linked to factors like body condition score, age, parity, and negative energy balance that influence ovarian activity.

Addressing these variables is pivotal to optimizing synchronization outcomes. Tailoring protocols, managing nutrition, and considering individual cow characteristics are key steps toward improving the success of estrus synchronization in this population.

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