Review Article

Status of Estrus Synchronization in Nepal

Abhishek Pandit[1], Suman Poudel[2], Manish Gautam[3*] and Shambhu Shah[4]

[1]Department of Comparative Biomedical Sciences, Louisiana State University and Agriculture and Mechanical College, Baton Rouge-70808, Louisiana, USA; [2]Department of Veterinary Surgery and Pharmacology, Faculty of Animal Science, Veterinary Science and Fisheries, Agriculture and Forestry University, Chitwan, Nepal; [3]Department of Physiology, Paklihawa Campus, Institute of Agriculture and Animal Science, Tribhuvan University, Rupandehi-3290, Nepal; [4]Department of Theriogenology, Paklihawa Campus, Institute of Agriculture and Animal Science, Tribhuvan University, Rupandehi-3290, Nepal.

Abstract | Estrus synchronization refers to manipulating the estrous cycle or inducing heat in a vast number of females in a given time period. Ovulation can be controlled by interrupting or influencing the wave-like follicular growth pattern. Estrus synchronization is achieved by shortening or prolonging the luteal phase using prostaglandins or exogenous progestogens, respectively. The selection of protocol depends on the assessment of resources, including facilities, labor, experience, and budget. PGF2α induces luteal regression followed by estrus and ovulation in cows when administered during the luteal period. Progestin suppresses the activity of the ovary and inhibits the dominant follicle maturation due to the suppression of both FSH and LH. Gonadotropin-releasing hormone or an analog is administered with PGF2α to estrous- cyclic and noncyclic cattle disrupts the patterns of follicular growth, inducing ovulation on a large follicle. To select and successfully implement the estrus synchronization regime in animals' proper knowledge of the hormonal profile and functional structure prevalent in ovaries in stages of estrus. Various protocols are available based on the hormone used, route of administration, requirements for heat detection, number of hormone injections, number of cattle handled, and injection time. Increased labor and upfront cost of hormone treatment, standard degree of supervision, and decent handling facilities are some of the drawbacks of this technique. Successful estrus synchronization necessitates optimum nutrition, a good body condition score, the best semen quality, general health, and an efficient estrus detection technique.

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***Correspondence** | Manish Gautam, Department of Physiology, Paklihawa Campus, Institute of Agriculture and Animal Science, Tribhuvan University, Rupandehi-3290, Nepal; Email: mgautam305@gmail.com, manish.gautam@pakc.tu.edu.np
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Introduction

Estrus synchronization refers to manipulating the estrous cycle or inducing heat in a vast number of females in a given time period (Odde, 1990). Using estrus synchronization, we can circumvent the key problem of estrus detection. Proper estrus detection and timely insemination are crucial in cattle farming. Estrus synchronization optimizes labor and time, minimizes estrus detection errors, and enhances the usability of artificial insemination. Successful estrus synchronization necessitates optimum nutrition, a good body condition score, the best semen quality, general health, and an efficient estrus detection technique. Estrus in anestrous animals can be induced by a certain protocol for synchronization (Senger, 2004). Synchronized cattle display standing estrus at a predetermined time, conceive and calve early in their respective seasons, and wean heavier and older calves (Perry, 2004).

A successful approach can alter the usual 21-day estrous cycle in beef cattle with an additional opportunity (four chances) of conceiving during that same 66-day mating season (Salverson and Perry, 2005; Timothy, 2003; Wilson *et al*., 2010) and can reduce the time to breed to < 5 days, based on the protocol used (Stevenson *et al*., 2000). Ovulation can be controlled by interrupting or influencing the wave-like follicular growth pattern (Yizengaw, 2017). Estrus synchronization is achieved by shortening or prolonging the luteal phase using prostaglandins or exogenous progestogens, respectively (Xu, 2016). Prostaglandin and gonadotropin-releasing hormone (GnRH) therapy are strategically synchronized in almost all programs. Within a cattle herd, heifers are an easy draw to synchronize a group of females. Heifers have responded exceptionally well to the MGA/PGF2 system since they are not nursing calves and can be housed in settings where they can be fed (Hadgu and Fesseha, 2020; Wood *et al*., 2001). The review aims to determine methods of estrus synchronization, the economic importance and disadvantage of estrus synchronization together with the status of estrus synchronization in Nepal.

Bovine estrus cycle

A thorough understanding of the bovine estrus cycle, heat period, ovulation timing, hormonal profile, and functional structures is the utmost for the selection of the desired estrus synchronization protocols. The Estrus cycle in cattle is of 21 days (range 18 to 24 days). The cycle is divided into two phases: the follicular phase and luteal phase or four stages (proestrus, estrus, metestrus, and diestrus). Progesterone hormone dominates the luteal phase whereas estrogen dominates the follicular one. The luteal phase follows the follicular phase, from ovulation to regression of the corpus luteum. The follicular phase consists of relapse of the corpus luteum followed by ovulation. (Dorsey *et al*., 2011). Anestrous periods refer to times during which the animal is devoid of a regular cycle, as well as sexual quiescence, either due to physiological reasons (pregnancy, lactation, time of the year, failure to detect estrus) or pathological ones (Kumar *et al*., 2014).

The fundamentals of estrous synchronization

The basic process is to alter the duration of the estrous to influence the time of the beginning of estrus: initially regress the corpus luteum (CL) before the time of natural luteolysis, then start new follicular wave, and finally trigger estrus or ovulation (Chaudhari *et al*., 2018). Heat detection is one of the major limiting factors and base for the success of synchronization (Roelofs and Van Erp-van der Kooij, 2018; Sveberg *et al*., 2011). Animals should be examined for synchronization before choosing a required framework. Body condition scores of both heifers and cows and post-partum days for cows (at least 50 days) need to be addressed. Cows with a Body Condition Score (BCS) > 2.5 have a significantly higher reproductive potential than cows with a BCS of 2.5 (Michael, 2007). Assessment of resources, including facilities, labor, experience, and budget is required. Treatment administration and timing are critical to the program's success. The foundation for excellence is the selection of a technically adept and practically possible protocol (Gizaw *et al*., 2016).

Synchronization hormones

Prostaglandins (PG) or an analog, an effective luteolytic, can cause regress of the corpus luteum and are used in the estrus synchronization (Roche, 1977). This hormone is commercially used in both natural and synthetic forms to shorten the luteal phase, making it economically feasible for the estrous synchronization (Lucy *et al*., 2004; Oaxaca *et al*., 2009; Paul *et al*., 2015). After the intramuscular shots of PGF2α or one of its analogs in cattle, estrus occurs within 2 to 6 days. The prescription in the breeding management of bovine species is estrus synchronization by prostaglandin and its potent analog (Ahlawat *et al*., 2015). It was shown that PGF2α would induce luteal regression followed by estrus and ovulation in cows when administered during the luteal period (Hadgu and Fesseha, 2020; Ozill *et al*., 2011).

Progesterone or synthetic progestin suppresses the activity of the ovary. Its treatment inhibits the dominant follicle maturation due to suppression of both FSH and LH which promote atresia of all ovarian (Baruselli *et al*., 2010; Suadsong, 2011) follicles. Two types of products are in use: Controlled intravaginal release devices (CIDR®) and MGA® (Melengestrol acetate), a progestin feed additive. Long-term administration of progestin results in higher synchronization rates, while it lowers fertility (Moreira *et al*., 2000).

The follicular phase of the estrus cycle is controlled by GnRH. When Gonadotropin-releasing hormone or an analog is administered with PGF2α to estrous-cyclic and noncyclic cattle, the patterns of follicular growth are disrupted, inducing ovulation on a large follicle (Ozill *et al*., 2011). In 10 to 30% of anestrous females, this therapy may induce an estrus (Sprott and Carpenter, 2007). Prepubertal heifers are not recommended for GnRH since the fertile estrous cycle is not well established and they have no consistent response to this hormone injection (Wood *et al*., 2001).

Estrus synchronization protocols

To select and successfully implement the estrus synchronization regime in animals' proper knowledge of the hormonal profile and functional structure prevalent in ovaries in stages of estrus is essential (Patterson *et al*., 2002). Various protocols are available based on the hormone used, route of administration, requirements for heat detection, number of hormone injections, number of cattle handled, and injection time. Instead, if AI is not assessable, these protocols can be practiced with natural service as well.

Prostaglandin-based protocol approach

Prostaglandin-based systems improved estrus detection and shortened the time between artificial inseminations.

One shot prostaglandin

Cyclic females were given 1 shot of Prostaglandin and bred on estrus expression. Although the breeding season was 15 days shorter, a single dose of prostaglandin F2 ended in early birth in more cows (Larson and Funston, 2009). One-third of females do not respond to this injection which limits the efficiency of this program. A modified program can be started by detecting the estrus in the cows for five days before inseminating the cow showing estrus while administering a single shot of prostaglandin to the rest of the cows. Since only one injection is necessary and not all cows need it, this is the most cost-effective treatment option.

Two shot prostaglandin

Two prostaglandin injections to females 11 days afar, followed by heat detection and AI within 5 days, or group insemination after 76-80 hours of 2nd shot. All cyclic cows must respond to the second injection, regardless of what stage of their estrous cycle they were in when given the first injection. This results in the formation of two synchronized groups of cattle rather than one, and an elongated breeding season (Sahatpure and Patil, 2008).

Progesterone-based protocol approach

When cattle receive progastrin for a longer time, their estrous cycles are synchronized at an increased rate while their fertility is lowered.

Melengestrol acetate feeding

MGA inhibits the luteinizing hormone ovulatory surge, which decreases estrus. It is not a commonly used technique in estrus synchronization because of the decrease in the rate of pregnancy rate after artificial insemination at the estrus synchronized cattle's (Morrell, 2011). In heifers, adding MGA to nutritional blocks had higher pregnancy rates at the start of the breeding season (Mingoti *et al*., 2018).

The female cattle were administered MGA at a daily rate of 0.5 mg for 14 days and were bred on the second estrus following MGA removal. When taken at the daily recommended dose of 0.5 mg, MGA suppresses behavioral estrus, suppresses the preovulatory surge of LH, and prevents ovulation (Imwalle *et al*., 2002).

Prostaglandin injection on 15-19 days following the ejection of MGA from feed after 14 days is efficacious due to stage-dependent responsiveness of the corpus luteum (Lamb *et al*., 2000). Higher rate of synchronization than PGF2α alone.

Injecting prostaglandin, first on the day of removal of MGA from feed and the next 15 days later.

Syncro-mate-b (Ear implant)

Estrus response is maximum when treatment starts between days 8 to 12 of the estrus cycle (Ravikumar and Asokan, 2008). In cows and heifers, SBM treatment induces estrus independently of the ovaries (McGuire *et al*., 1990). It consists of an ear implant with 6 mg of norgestomet that is left in the ear for 9 days, followed by injections of 3 mg of norgestomet and 5 mg of estradiol valerate into the muscle after the implant. This ear implant prevents the cattle from coming into the heat by releasing progestin (Bendy, 2000; Peterson *et al*., 2000). This method of synchronization is proven effective only in beef females, except on met estrus, approximately 85% of heat at a given time (Lyimo *et al*., 2000; Tegegne *et al*., 2016).

Controlled intravaginal drug release (CIDR)

The device has 1.38-gram progesterone and maintains elevated blood concentrations of progesterone at least 2 ng/ml for up to 10 days. It is inserted in the vagina for 7 days and upon removal causes a sudden decrease in progesterone level leading to estrus synchronization. A new CIDR device provided sufficient progesterone to facilitate an estradiol-induced turnover of follicular waves (Burke *et al*., 1998).

GnRH-based protocol approach

It deals with regression of corpus luteum, or ovulation following administration of GnRH and starting a new follicular growth wave.

Combination systems

GnRH-$PGF_{2\alpha}$ system: It is also called select synch. GnRH is injected on the 1st day while injecting prostaglandin on the 8th day followed by Artificial insemination after 12 hours of heat.

GnRH-$PGF_{2\alpha}$ + GnRH system: Involves a second GnRH injection given between 48-72 hours after $PGF_{2\alpha}$. Ovsynch, Co-synch, and Hybrid synch are the variations of this system.

Ovulation synchronization (OVSYNCH)

With the administration of the initial shot of GnRH, the dominant follicle ovulates, thereby altering the follicular growth and forming additional or new corpus luteum. In the meantime, the PGF2a shot regresses the naturally formed CL and secondary CL derived from the first GnRH injection (Vasconcelos *et al*., 1999). Synchronization and conception rate was affected by the stage of estrus when ovsynch was initiated. It is demonstrated in Figure 1 as well.

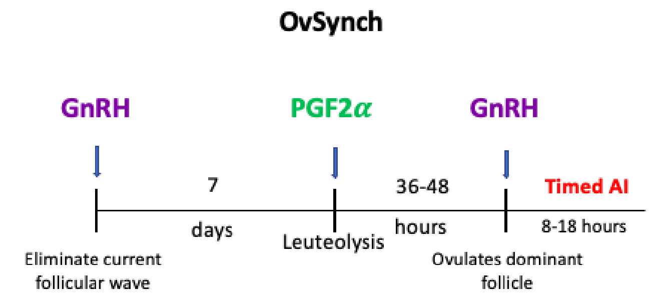

Figure 1: *Methods used to synchronize ovulation in cows Nepal: Ovsynch.*

Combination synchronization (CO-SYNCH)

Most of the females respond to this program and is effective for the non-cycling 30 days post-partum females (Harrison *et al*., 1990). On the first day of the program, a GnRH injection is administered, followed by a prostaglandin injection on the eighth day. After 2 days the second injection of GnRH is given. It is demonstrated in Figure 2 as well.

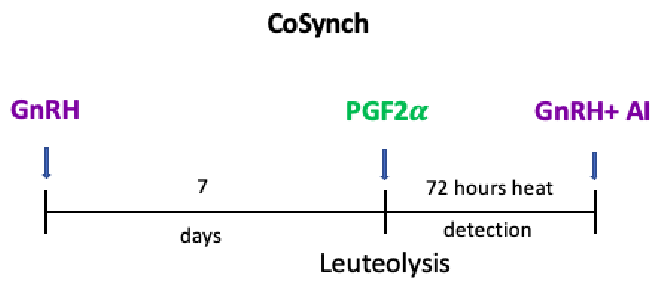

Figure 2: *Methods used to synchronize ovulation in cows in Nepal: Co-synch.*

Select synch

The first GnRH shot induces ovulation in cyclic females and the PGF2a leads to the regression of Cl to decrease progesterone. The second GnRH shot enables the dominant follicle to ovulate that was preprogrammed by the first GnRH injection (Savio *et al*., 2003). It is demonstrated in Figure 3 as well.

Hybrid synch

Of all the GnRH-PGF2a regimens, this one has the highest conception rates. GnRH is injected on day 1, PGF2a is injected on day 8, and AI from 7-10 days after estrus detection. The females not exhibiting the estrus signs are bred on day 10 along with 2nd shot of GnRH given.

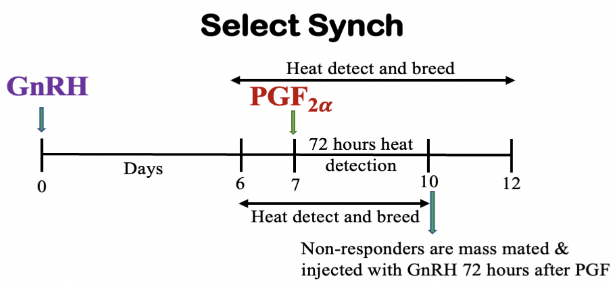

Figure 3: *Methods used to synchronize ovulation in cows Nepal: Select Synch.*

CIDR to GnRH-based protocol

CIDR is inserted for 7 days (day 1 to day 8). GnRH injection is also given on the first day. On the first day, a GnRH injection is also administered. On day 8, a prostaglandin injection is administered, followed by a second GnRH injection two days later. The CIDR assures that females are exposed to progesterone between days 1 and 8 in GnRH-based protocols.

Suggested approach for cattle: Both heifers and cows may be classified under heat detection, fixed time, and heat and time detection approach. Detection of heat entails the surveillance of estrus activity to determine the best time to reproduce. Fixed-time AI methods conclude with all cattle being mated at a predefined period, with GnRH injection provided during the mating period. Timed AI and heat detection protocols specify when heat detection and AI must take place. Animals who have never shown estrous signs are inseminated and given a GnRH injection at a preset period, usually 72–84 hours after receiving a PG injection. In heifers, long-term progestin regimes (MGA-PG or 14-day CIDR + PG) have achieved a higher reliable response to estrus and successful pregnancy in heifers. The CO-Synch + CIDR technique was more efficient in cattle and offered reproductive advantages relative to the Ovsynch treatment (Azevedo *et al*., 2014).

Disadvantage of estrous synchronization

Increased labor and upfront cost of hormone treatment, standard degree of supervision, and decent handling facilities required. Also, animals must be cycling with optimum body score conditions. Faults in estrus detection and timely insemination lead to failure in conception, eventually leading to reduced production and economic loss (Ball, 1982). In non-cycling cattle (like prepubertal heifers and anestrous suckling cattle), these programs are in the bale to stimulate viable estrous and ovulation (Fesseha and Degu, 2020).

Table 1: *Estrous Synchronization experiments conducted in cow and buffalo in Nepal.*

S.	Animal	Treatment protocol	Conception rate	References
1	Buffalo (n=35) good breeding season	Ovsynch	45.71%	(Shah *et al*., 2017)
2	Buffalo (n=14, 42) Transition and poor breeding season	CIDR Co-synch	50.00 %, 42.85%	(Shah *et al*., 2017)
3	Buffalo (n=5) Active season (September)	Ovosynch	(40%)	(Devkota and Bohara, 2009)
4	Buffalo (n=8) Low breeding season (May)	Double PGF2α+ EB protocol	0%	(Devkota and Bohara, 2009)
5	Cows (n=19)	CIDR-PG protocols	60%, 44.4%	(Gautam *et al*., 2019)
6	Cows (n=25)	CoSynch + CIDR (n=8) OvSynch + CIDR and CIDR + PGF2α	0% , 14.3 %, 12.5 %	(Gautam *et al*., 2019; Sah *et al*., 2019)
7	Cows (n=20)	Ovosynch protocol, Buserelin acetate and dinoprost tromethamine	55% positive on day 60	(Karki *et al*., 2018)
8	Cows (n=10) with inactive ovaries	One shot PGF2α	6/10 4 months after conception	(Devkota *et al*., 2013)
9	Cows (n=7)	Single shot GnRH	2/7	(Devkota *et al*., 2013)
10	Buffalo (n=14)	Ovsynch	(28.6%) on day 41 after FTAI	(Chapagain *et al*., 2019)
11	Murrah (n=15)	GnRH administration, after 8-18hrs estrus detection and inseminate	53.34% four months after conception	(Sah *et al*., 2012)
12	Murrah (n= 12)	GnRH + mineral mixture and AI on estrus	75.00% four months after conception	(Sah *et al*., 2012)

Status of estrous synchronization in Nepal

Current status and method of estrous synchronization conducted by various scientist in Nepal is summarized in the tabular form in the Table 1 along with references.

Conclusions and Recommendations

Estrus synchronization is the most essential and commonly used biotechnology in reproduction. It enables to sort out the hindrances in heat detection in large cattle herds, long calving intervals and allows timely insemination. Application of the standard protocol needs to be done based on the requirements and management capabilities of a framer or producer. Novel synchronization methods where progesterone treatment precede the GnRH-PG regime, offer effective estrus synchronization with high fertility. Good body condition score (> 5), days postpartum (at least 50), adequate nutrition and insemination time are factors to be considered to obtain optimal conception rates with any synchronization approach.

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Novelty Statement

This is a review paper describing about the latest techniques of estrus synchronization based on the different research article.

Author's Contribution

AP, SP, MG: Conceptualization of the study.
AP, SP: Literature review.
AP and SP: Writing the original paper.
AP, SP, MG: Review and editing.
MG and SS: Supervision
All authors have read and approved the manuscript.

Ethics approval and consent to participate

Not applicable

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Conflict of interest

The authors have declared no conflict of interest.

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