

## Controlled Internal Drug Release (CIDR) Based Hormonal Protocols Effect upon Estrus Response and Pregnancy Outcome in Anestrous Cows

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### ABSTRACT

*Controlled internal drug release (CIDR) based hormonal protocols CoSynch + CIDR, OvSynch + CIDR and CIDR + PGF2 $\alpha$  were applied to 25 crossbred anestrous Holstein and Jersey cows to improve the fertility at the farm of National Cattle Research Programme, Rampur, Chitwan. All three protocols were found equally effective ( $P > 0.05$ ) with 100% estrus expression rate, out of which, 80% (8/10), 85.7% (6/7) and 75% (6/8) had estrus expression with well cervix open at fixed time artificial insemination in CoSynch + CIDR, OvSynch + CIDR and CIDR + PGF2 $\alpha$  protocols respectively and rest had estrus expression with partial cervix open. Statistically non-significant ( $P > 0.05$ ) pregnancy outcome that is 14.3 % (1/7) in CIDR+PGF2 $\alpha$  group and 12.5 % (1/8) in OvSynch group while none in CoSynch + CIDR group were pregnant following fixed time artificial insemination. Poor pregnancy outcome of the anestrous cows in all protocols might not only have hormonal problem but also could have various other reasons which was beyond the objective of this research findings. Hence, study concludes anestrous cows respond well to the CIDR based hormonal protocols to revive the estrus.*

**Keywords:** Fixed time artificial insemination, Intra-vaginal insert device, Progesterone, Prostaglandin analogue and synchronization

### INTRODUCTION

Reproductive efficiency is dependent upon optimization of management, health, and physiology of cows (Lucy, 2001, Sartori *et.al.*, 2010). It is important that cows become pregnant at a biologically optimal time and produces offspring at defined calving interval (Sakaguchi M, 2011), otherwise leads to Infertility or Sub-fertility. Major physiological aspects that affect fertility in dairy cows are behavioral estrus or physiological anestrous, timely ovulation, quality semen, and oocytes, uterine environment, maternal recognition of pregnancy, release time and concentration of progesterone and negative energy balance (Lucy, M C, 2007; Walsh *et.al.*, 2011).

Anestrous condition is characterized by absence of estrus behavior (Peter, A T *et.al.*, 2009). During postpartum period negative energy balance may cause anovulation which leads to physiological anestrous (Kumar *et.al.*, 2014). It is obvious for the most of the cows to remain in anestrous during 10 to 12 weeks postpartum due to state of negative energy balance and thereafter animal may be cyclic but again due to incompetent oocytes, smaller dominant follicle,

abnormal progesterone profiles and poor embryo survival may affect the fertility (Peter, A T *et. al.*, 2009).

Cows having concentrations of progesterone <1.0 ng/ml in both of the first 2 blood samples at least 10 days apart were classified as anestrus (Chebel *et.al.*, 2006). Adams G P *et.al.*, 2008 reported that oocytes that developed under a prolonged-low-progesterone level (*i.e.*, mimicking persistent oversized follicles) failed to ovulate. Hence, it can be regarded as progesterone hormone has significant role in the estrus expression and ovulation in the dairy cows.

This research work focuses on the management of anestrus cows through application of hormonal approach. Increased progesterone hormone during the growth of follicular wave increases fertility more than 10% to the subsequent timed AI. Also, many manipulative studies have reported improvement in ~5-7% pregnancy using CIDR in OvSynch hormonal protocol prior to artificial insemination (Wiltbank *et.al.*, 2012) and similarly 10 % more pregnancy with co-synch protocol alone (Lamb *et.al.*, 2001).

A new reproductive tool—the CIDR (controlled internal drug release) was approved by Food and Drug Administration in 2002 for the synchronization of estrus. The CIDR, an intra-vaginal progesterone insert device can be used in conjunction with prostaglandin analogue (Darrel J K, 2002). Hence the objective of this experiment was to apply the CIDR as a source of progesterone hormone with various protocols upon prolonged anestrus cows for their effect on estrus expression and pregnancy outcome following fixed timed artificial insemination.

## METHODOLOGY

Twenty five crossbred dairy anestrus cows of Holstein and Jersey that had not expressed heat for at least last six months were selected from the farm of National Cattle Research Programme, Rampur, Chitwan during February 2017 to July 2018. Parity of selected cows was in between 1 to 4 and milk yield less than two liters a day per cow. Selected cows were applied to three different CIDR based hormonal estrus synchronization protocols. Hormones used in the protocols were progesterone (P4), gonadotropin releasing hormone (GnRH) and prostaglandin (PGF2 $\alpha$ ). Eazi-Breed CIDR<sup>®</sup> cattle devices each of 1.9 gram in each cow was used as a source of progesterone which was intra-vaginally inserted, Cloprochem 0.025% (Cloprostenol) as a prostaglandin analogue at the rate of 2 ml intramuscular injection and Gynarich (Busereline 4mcg/ml) as a source of GnRH at the rate of 2.5 ml intramuscular injection was used in protocol I: OvSynch+CIDR in 7 cows, protocol II: CoSynch+CIDR in 10 cows and protocol III: CIDR insert for 10 days + PGF2 $\alpha$  8 cows as shown in the Figures 1, 2 and 3.

Fixed time artificial insemination was done in cows of all groups as per the protocols where protocol III received double fixed time artificial insemination. Estrus expression signs like mucus discharge, swollen vulva, pinkish vaginal mucus membrane and status of cervix (well open or partial open) at the time of artificial insemination was observed and recorded accordingly. Estrus expression response in the cows due to the effect of various protocols were divided into two sub-groups namely estrus signs with well open cervix and estrus signs with partial open cervix.

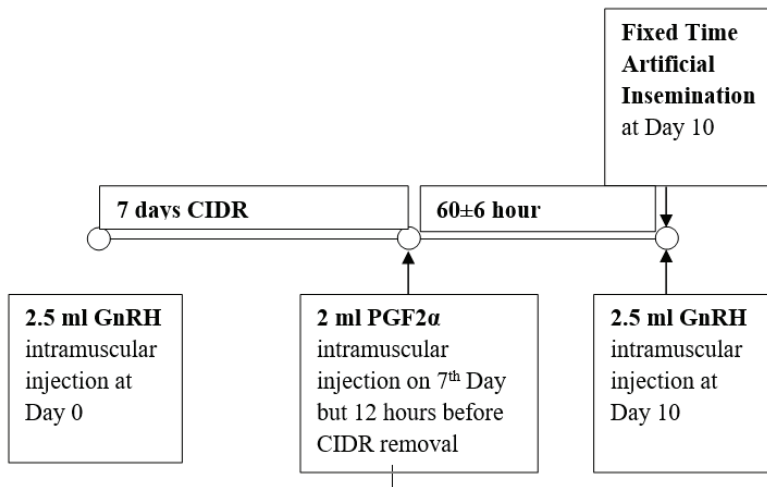


Figure 1. CoSynch + CIDR protocol

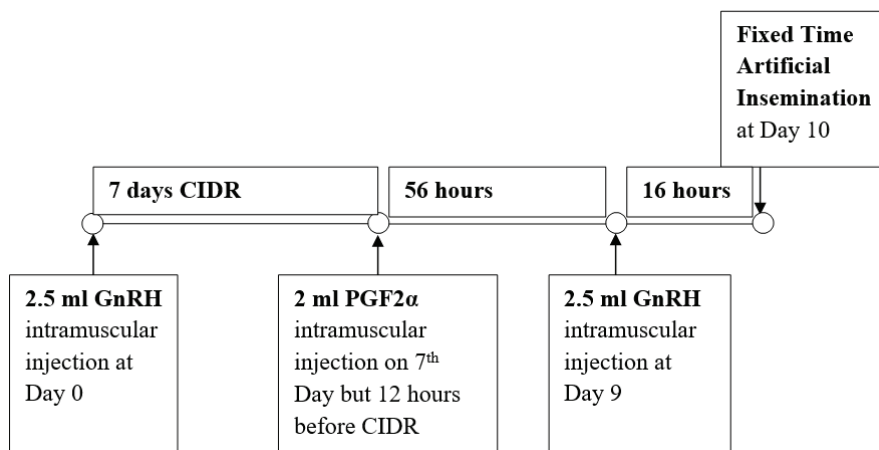


Figure 2. OvSynch + CIDR protocol

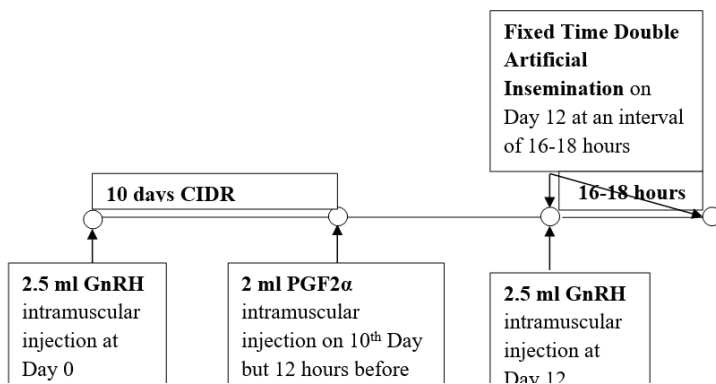


Figure 3. CIDR + PGF2 $\alpha$  protocol

Pregnancy diagnosis was done after 60 days post artificial insemination and recorded as positive and negative results for all the cows under experiment. Data on the pregnancy outcome and estrus response outcomes were entered in the IBM SPSS version 20 and applied Fisher’s exact test to find the association of pregnancy outcome and estrus response outcome with respect to various hormonal protocols at the confidence interval (CI) 95% and significance value  $P = 0.05$ .

## RESULTS

### Effect of Hormonal Protocols

100% estrus expression observed by the time of fixed time artificial insemination all protocols. However, there were only 80.0% (8/10), 85.71% (6/7) and 75.0% (6/8) estrus response with well open cervix and rest with estrus response with partial cervix open at the time of fixed time artificial insemination in CoSynch + CIDR, OvSynch + CIDR and CIDR + PGF $2\alpha$  protocols respectively as shown in Figure 4. Estrus expression were statistically non-significant ( $P=1.00$ ) among all the protocols applied.

CIDR based hormonal protocols effect upon estrus response in anoestrus crossbred cows

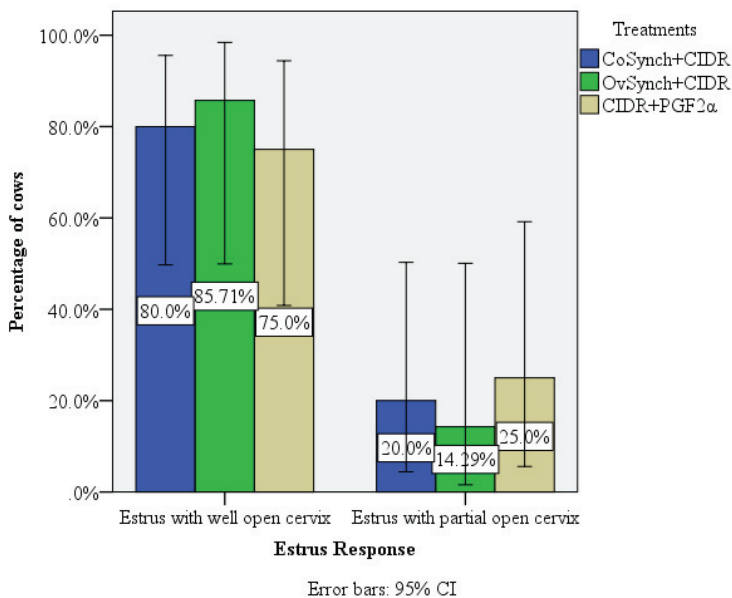


Figure 4. CIDR based hormonal protocols effect upon estrus response in anoestrus crossbred cows

### Pregnancy Outcomes Following Fixed Time Artificial Insemination

Statistically non-significant ( $P=0.50$ ) pregnancy outcome was found following the fixed time artificial insemination in all protocols with only 14.3 % (1/7) in OvSynch + CIDR protocol followed by 12.5 % (1/8) in CIDR + PGF $2\alpha$  and with no pregnancy outcome in CoSynch + CIDR as shown in Table 1. The results of pregnancy outcomes were found to be non-significant ( $P=0.50$ ) with respect to three protocols applied in the experiment.

Table 1: CIDR based hormonal protocols effect upon pregnancy outcome in crossbred anestrous cows

CIDR Based Hormonal Protocols	Pregnancy Outcome (%)
Protocol I: CoSynch + CIDR (N=10)	0
Protocol II: OvSynch +CIDR (N=7)	14.3 (1/7)
Protocol III: CIDR + PGF2 $\alpha$ (N=8)	12.5 (1/8)
	P=0.50 (Non-significant)

## DISCUSSION

Result of 100 % estrus expression is found to be consistent with the results reported by Dhami, *et.al.*, 2015; V Kumaravel and S Sendur Kumaran, 2017 but in contrast to other reports like Chebel *et.al.*, 2006, Kalwar Q *et.al.*, 2015 where 30 and 76.47 % estrus expressions were reported respectively. After progesterone withdrawal, anestrous cows experience increased pulse frequency and mean concentrations of lutenizing hormone (LH), increased numbers of LH receptors in the granulosa and theca cells of follicles (Inskeep *et.al.*, 1988) there by increased estradiol production by the follicles, and an estradiol-stimulated LH surge and ovulation (Rhodes *et.al.*, 2003; Gumen and Wiltbank, 2005).

Poor pregnancy outcome in this experiment is not in agreement with most of the studies where at least 26 % pregnancy rate by CIDR + PGF2 $\alpha$  protocol was reported by Lucy *et.al.*, 2001 to higher conception rates like 52.94% in OvSynch + CIDR (Kalwar Q *et.al.*, 2015), 53.33 % by Kumaravel and Kumaran, 2017, and conception has been reported up to 80 % in CoSynch + CIDR by A J Dhami, *et.al.*, 2015.

High progesterone near at the time of fixed time artificial insemination also leads to decreased fertility (Wiltbank *et.al.*, 2012) as high progesterone produces incompetence oocyte whereby poor fertilization or poor embryo quality production and finally reduced pregnancy which could have happen with this experiment work. Hence, in such researches hormonal assay of progesterone, follicle stimulating hormone, estradiol and lutenizing hormone is also required to correlate and interpret the results in a more precise way. Besides, conception is governed by many factors like semen quality, maternal recognition pregnancy, and early embryonic deaths etc. which were beyond the objective of this research findings.

## CONCLUSION

CIDR based protocols OvSynch + CIDR, CoSynch + CIDR and CIDR + PGF2 $\alpha$  are equally effective in estrus induction of anestrous dairy cows with poor pregnancy outcome where reason for poor conception rate need further research findings.

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