Alleviation of Reproductive Deficiency of Postpartum Holstein Dairy Cows Using Controlled Internal Drug Release Device in Conjunction with Equine Chorionic Gonadotropin or Prostaglandin F2α

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Abstract: This study was designed to determine the efficiency of two different protocols of estrus synchronization on reproductive performance of postpartum dairy cows. Forty-nine postpartum Holstein dairy cows (days in milk, DIM: 45 days) were randomly assigned to three groups. The first group (CIDR-eCG, n:16) received a controlled internal drug release (CIDR) device for 8 days in conjunction with 500 IU of equine chorionic gonadotropin (eCG) i.m. on the day of CIDR withdrawal. The second group (CIDR-$PGF_2\alpha$, n: 15) received CIDR combined with 500 µg prostaglandin $F_2\alpha$ ($PGF_2\alpha$) a day before CIDR withdrawal. The third group (n: 18) served as control. Using CIDR combined with eCG or $PGF_2\alpha$ protocols improved ovarian activity as indicated by increasing ($P<0.05$) total number of follicles and diameter of largest follicles compared to control. Nevertheless, CIDR-eCG protocol was superior in reducing ($P<0.05$) number of small follicles and increasing ($P<0.05$) number of large follicles compared to CIDR- $PGF_2\alpha$ protocol. The pronounced luteotrophic effect of CIDR-eCG protocol expressed as greater ($P<0.05$) progesterone (P_4) concentration compared with both of CIDR-$PGF_2\alpha$ and control groups, between which no significant difference was observed. Both CIDR-eCG and CIDR-$PGF_2\alpha$ groups increased ($P<0.05$) estradiol (E_2) concentration compared to that of control. These differences were reflected in estradiol: progesterone ratio (E_2: P_4) which was lowest ($P<0.05$) in the CIDR-eCG group and highest ($P<0.05$) in the control group while the CIDR-$PGF_2\alpha$ group was intermediate. Furthermore, the two estrus synchronization protocols successfully reduced ($P<0.05$) the days to first estrus (DFE) compared to control (56.33 and 61.25 vs. 84.6 days respectively). Nevertheless, the reproductive performance including estrus rate (ER), conception rate (CR), conception failure (CF) and number of services during 100 DIM (NS100) were not different between estrus synchronized and control groups. However, pregnancy rate (PR) achieved the highest ($P<0.05$) value in the CIDR-eCG protocol. In conclusion, usage of CIDR-eCG protocol alleviated the deterioration in reproductive traits of postpartum Holstein dairy cows through increasing the numbers of large follicles and P_4 concentration and reducing day to first estrus and E_2:P_4 ratio. The reduction in E_2:P_4 ratio in the CIDR-eCG protocol was reflected in increasing ($P<0.05$) pregnancy rate compared to the CIDR-$PGF_2\alpha$ and control groups.

Keywords: CIDR, Equine chorionic gonadotropin, Prostaglandin $F_2\alpha$, Postpartum, Dairy cow

INTRODUCTION

The profit of dairy enterprises is dependent on the high reproductive performance of dairy cows (Galvão *et al.,* 2013). However, in the last few decades, genetic selection for increasing milk production was a success but has negative effects on cow's fertility (Gilmore *et al.,* 2011). Hence, it was suggested that many of physiological pathways are negatively influenced by high milk production that reduces the likelihood of associated establishment of pregnancy. Thus, changes in management practices may play an important role to enhance the poor fertility in high milk producing cows. Estrus synchronization is a valuable management tool that has been successfully used to improve reproductive efficiency, particularly in dairy herds (Hashemi *et al.,* 2006). It refers to imply the manipulation of the estrous cycle or induction of estrus to bring a large percentage of cows into estrus at a short, predefined time (Odde, 1990). Many hormonal treatments were used to synchronize the estrous cycle and ovulation of dairy cows.

Progesterone is an important hormone that has a control of reproductive events whereas high plasma progesterone concentration prevents ovulation by negative feedback on the pituitary gland to reduce LH secretion (Ireland and Roche, 1982), but does not suppress FSH secretion (Adams *et al.,* 1993), and follicular waves continue to emerge in the presence of a functional corpus luteum (CL), which it is essential to the establishment and maintenance of pregnancy in cattle (Spencer *et al.,* 2006). Thus it was and still widely used in estrus synchronization programs. Estrus synchronization with progesterone preserves high plasma progesterone concentrations even after CL regression, and estrus occurs 2 to 5 days following progesterone removal (Nellor and Cole, 1956). Progesterone can be provided to cows in three common products as syncro-mate-B (ear implant), melengestrol acetate (oral feeding), and CIDR (intra-vaginal device). They are used in combination with prostaglandins F2 alpha ($PGF_2\alpha$), equine chorionic gonadotropin (eCG), estrogens or with GnRH (Bisinotto *et al.,* 2014; Wiltbank *et al.,* 2014).

A controlled internal drug release (CIDR, 1.38 g of progesterone) based estrus synchronization protocols have been widely studied (Williams *et al.,* 2011; Siregar *et al.,* 2015). It is becoming popular because of the short treatment period (7-10 day) and reduced incidence of persistent follicles (Ahmad *et al.,* 1995), They are more preferable than using prostaglandin ($PGF_2\alpha$) alone, due to ineffectiveness of $PGF_2\alpha$ to induce cyclicity/estrus in animals which do not have a CL, nor does it exert an effect on follicular wave (DeJarnette, 2013). Furthermore, the main function of $PGF_2\alpha$ is inducing

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luteolysis and has been implicated to enhance fertility (Weems *et al.,* 2006) by increasing uterine contractility thereby enhancing sperm transport and improving the uterine environment for early conception development (Garcia-Ispierto and Lopez-Gatius, 2014).

Administration of eCG in dairy cattle results in fewer atretic follicles, the recruitment of more small follicles showing an elevated growth rate, the sustained growth of medium and large follicles and improved development of the dominant and pre-ovulatory follicles. Also, it has been suggested that usage eCG at the time of progesterone removal increased the ovulation rate, especially in early postpartum cows (Garcia-Ispierto *et al.,* 2012). Recently, Mekonnin *et al.* (2016) demonstrated that a high estrus response, conception rate and calving rate in cows and heifers assigned to progesterone (10-day CIDR)-$PGF_2\alpha$-eCG based estrus synchronization protocol. Therefore, the objective of the present study was to evaluate the reproductive performance of postpartum Holstein dairy cows following treatment with CIDR in combination with eCG or $PGF_2\alpha$.

MATERIALS AND METHODS

All procedures and experimental protocols were conducted in accordance with the Guide for the Care and Use of Agricultural Animals in Research and Teaching (McGlone, 2010). This study was carried out using lactating Holstein cows during transitional period (early lactation) at a private dairy farm that belongs to the Universal Company for Agricultural Development and Soil Reclamation (Al-Alamiah) located 90 km on the Alexandria-Cairo desert road.

Animals and management

Lactating Holstein cows (n: 49) at their 3-4 parities with an average milk yield of 30 kg/head/day were machine-milked thrice daily at approximately 8-hrs intervals and were dried for 60 days before the next calving were used in this study. Cows were fed four times daily a total mixed ration (TMR) consisting of corn silage, artichoke and alfalfa hay as forage, and the concentrate mixture (18% crude protein) which consisted of yellow corn, soybean meal, wheat bran, cotton seed cake, molasses, rumen-protected fat (Bergafat@ F-100, Berg-Schmidt company, Germany), and minerals mixture (Premix) (Council, 2007). Cows were housed in open barns with shades and had access to fresh water ad libitum. The animals were healthy and free from any parasites and diseases.

Experimental design

Forty-nine multiparous dairy cows at their 45 days after calving were allocated to three groups. The first group (CIDR-eCG, n:16) was synchronized for estrus using controlled internal drug release CIDR device (1.38 g P_4; Eazi-BreedTM CIDR®, Pfizer Animal Health, Auckland, New Zealand) which inserted for 8 days, and 500 IU equine chorionic gonadotropin (eCG; Gonaser, Hipra, Spain) injected at day of CIDR withdrawal. The second group (CIDR- $PGF_2\alpha$, n: 15) was treated with CIDR for 8 days and were injected by 500 µg Cloprostenol ($PGF_2\alpha$: Synchromate Bremer Pharma GMBH, Germany) at a day before CIDR removal. In the first and second groups, estrus detection was observed throughout 24-72 hrs of CIDR removal. Cows that showed estrus were artificially inseminated and cows that returned back to estrus were inseminated accordingly. In the third group (control, n:18) cows received no treatment and estrus signs was observed after 45 days of parturition and cows that showed estrus were artificially inseminated. The experimental layout is showed in Fig. (1).

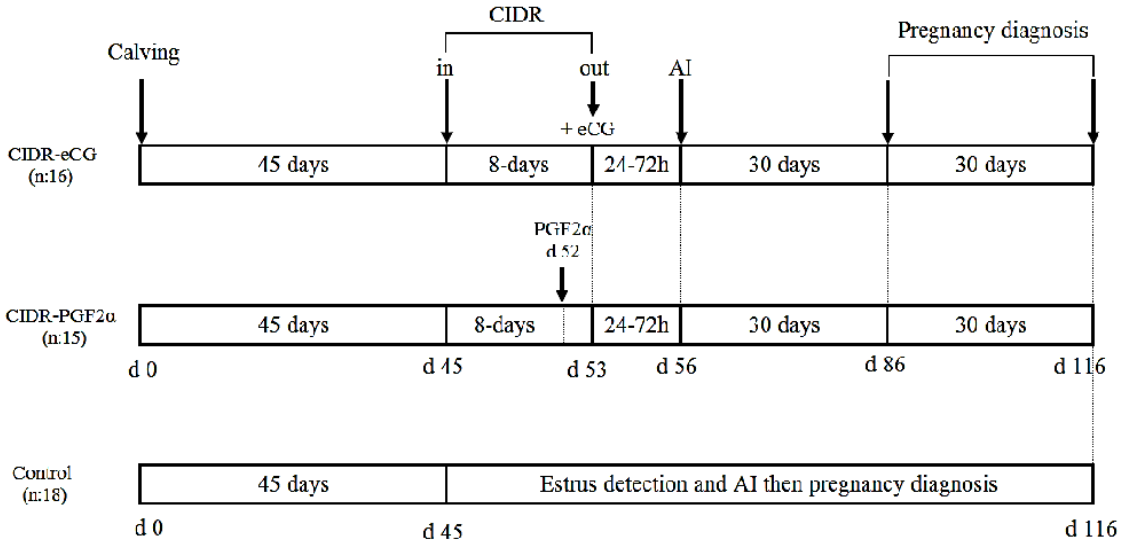

Fig. (1): Experimental design of controlled internal drug release (CIDR) device combined with equine chorionic gonadotropin (eCG) prostaglandin F2α ($PGF_2\alpha$) protocols in postpartum Holstein dairy cows

Ovarian activity and pregnancy diagnoses

Transrectal ultrasonography of the ovaries was performed six hours after CIDR removal in the two estrus synchronized groups and at the same time in the control group, using a real-time B-mode ultrasound scanner equipped with 5- and 7.5-MHz linear-array endorectal probes (Pie Medical Equipment B.V., Maastricht, the Netherlands) according to the method described by Ginther (Ginther, 1995). Briefly, after fecal material was evacuated from the rectum, the probe lubricated by a hydro-soluble gel and sheathed with polyvinyl chloride pipe was gently inserted through the rectum. Ovarian activity, including total number of follicles (3 mm or greater) and follicle population (*i.e.,* small follicles ≥ 3 to 6 mm; medium follicles > 6 to <9 mm; large ovulatory follicles > 9 mm), numbers and diameters of corpora lutea were recorded in each treated cow (Alvarez *et al.,* 2000). Pregnancy diagnosis was recorded by scanning the uterine content at days 30 and 60 post insemination.

Hormonal assays

Blood samples were collected in 10-ml silicon-coated evacuated tubes (Becton Dickinson, Franklin Lakes, NJ) from the coccygeal vein of each cow before access to feed on d 0, 14, 28 and 45 before CIDR insertion; day of CIDR removal (d 53); and d 15, 30 and 60 after insemination (representing days 71, 86 and 116 after calving) for pregnancy diagnosis. Sera samples were obtained by centrifugation of samples at 3,000 × g for 20 min at 4°C, and stored at −20°C until analyses. Blood serum concentration of progesterone (P_4) was measured using solid-phase enzyme immunoassay kits (Chemux BioScince, Inc. USA). The lower limit of detection was 0.11 ng/ml, and the intra- and inter-assay coefficients of variation were 9.3% and 9.9%, respectively. Blood serum concentration of estradiol (E2) was measured using solid-phase enzyme immunoassay kits (Chemux BioScince, Inc. USA). The lower limit of detection was 8.2 pg/ml, and the intra- and inter-assay coefficients of variation were 9.9% and 8.2%, respectively. In addition, E_2:P_4 ratio was calculated.

Reproductive indices

Reproductive performance including estrus rate (ER), day to first estrus (DFE), conception rate (CR), conception failure (CF) and number of services during 100 DIM (NS100) was calculated using the following formulas: estrus rate (ER): no. of cows showed estrus signs / no. of synchronized cows × 100; day to first estrus (DFE): no. of days from the parturition until the first time of estrus appearance; conception rate (CR): no. of cows diagnosed pregnant after insemination / no. of inseminated cows; pregnancy rate (PR): no. of cows diagnosed pregnant after insemination / no. of synchronized cows; conception failure (CF): no. of cows diagnosed non-pregnant after insemination / no. of inseminated cows; number of services during 100 days in milk (NS100) was calculated for each individual cow during the first 100 day postpartum.

Statistical analysis

All data were tested for normality with the Shapiro-Wilk test from the UNIVARIATE procedure of SAS (SAS Institute Inc., Cary, NC), and results indicated that all data were distributed normally (W ≥ 0.90). To avoid the heterogeneity of error if it existed, all percentage data records greater than 10% were transformed to their corresponding arcsine angles according to Steel *et al.* (1997). Data for the effect of treatments were analyzed using the MIXED procedure of SAS for repeated measures. Treatment and times were used as fixed effects, and individual cows were used as random effects. Data for the effect of treatments on reproductive performance, hormonal level and ovarian activity were analyzed by adapting the following model:

$$Y_{ijk} = \mu + T_i + D_j + (T \times D)_{ij} + e_{ijk},$$

where: Y_{ijk} is the observed value of the dependent variable determined from a sample taken from each animal; μ is the overall mean; T_i is the fixed effect of the i^{th} treatment; D_j is the fixed effect of the j^{th} day on ovarian activity and hormonal level only; $(T \times D)_{ij}$ is the first-order interaction between treatment and day; and e_{ijk} is the residual error. Significant differences among means within each classification were tested using least significant differences (LSD at $P<0.05$). The data of reproductive performance parameters were analyzed using the chi-squared test. A 95% confidence interval was used.

RESULTS AND DISCUSSION

To the best of our knowledge, no estrus synchronization protocol has yet proven effective in improving fertility over that observed after spontaneous estrus, especially during the postpartum period of high producing dairy cows. Different protocols used for estrus synchronization recorded pregnancy rate of 22.3 – 43.3 % during the postpartum period in dairy cows (De Rensis and López-Gatius, 2014). Therefore, this study was designed to evaluate the effect of two estrus synchronization protocols based on CIDR combined with eCG or $PGF_2\alpha$ on reproductive traits of early lactating Holstein dairy cows.

Effect of hormonal treatments on ovarian activity and hormonal levels

Ovarian activity and hormonal levels as affected by hormonal treatments are displayed in Table (1). The superiority of ovarian activities of CIDR-eCG and CIDR-$PGF_2\alpha$ groups compared to control group was expressed as increasing ($P<0.05$) total number of follicles and diameter of largest follicles which resulted in increasing ($P<0.05$) serum estradiol concentration. The superiority of CIDR-eCG in the total number of follicles represent a state of low atretic effect where low ($P<0.05$) number of small follicles was associated with highest ($P<0.05$) number of large follicles. These results are consistent with those reported in dairy cows (Păcală *et al.,* 2010), sheep (EL-Mokadem *et al.,* 2018), and goats (El-Mokadem *et al.,* 2017). The reduction of follicular atresia is attributed to the benefits of eCG with its long half-life and its dual FSH- and LH-like activity (Murphy and Martinuk, 1991). Usage of eCG was noted to promote the first wave follicle development and

reduced follicular atresia in dairy cows (Rostami *et al.,* 2011). Moreover, the present study showed that application of eCG in conjunction with CIDR withdrawal led to an increase the diameter of the largest follicle compared to the control group. Injection of eCG was used to enhance follicular growth and fertility at the end of estrus synchronization program in dairy (Souza *et al.,* 2009) and beef cows (Cutaia *et al.,* 2003). Also, it was found that administration of eCG at CIDR withdrawal enhanced the growth rate of follicles, thus leading to an increase in the diameter of the largest follicle at estrus in cows (Sá Filho *et al.,* 2010). The highest (P<0.05) number of small follicles observed in the CIDR-$PGF_2\alpha$ group compared to other groups seemed to reflect the increase in follicular atresia due to impaired oocyte maturation. Boone and Tsang (1998) reported that Luteal regression induced by $PGF_2\alpha$ was founded to cause apoptotic DNA degradation in the rat ovary.

Table (1): Effect of controlled internal drug release (CIDR) device combined with equine chorionic gonadotropin (eCG) or prostaglandin $F_2\alpha$ ($PGF_2\alpha$**)** on ovarian activity and hormonal levels of postpartum Holstein dairy cows

Items	Control	CIDR		SEM
		eCG	$PGF_2\alpha$	
Ovarian activity				
Follicles/cow, no.	3.77[b]	5.80[a]	5.08[a]	0.38
Follicular population, no				
Small follicles, ≥3 to 6 mm	0.59[b]	1.30[b]	2.08[a]	0.29
Medium follicles, >6 to <9 mm	0.77	0.70	0.67	0.21
Large follicles, >9 mm	2.50[b]	3.80[a]	2.42[b]	0.33
Diameter of largest follicles, mm	14.28[b]	17.26[a]	17.70[a]	0.66
Corpora lutea, no.	1.09	0.90	0.92	0.15
Diameter of corpus luteum, mm	15.51[a]	13.08[ab]	11.85[b]	0.93
Hormonal assay				
P_4 (ng/ml)	2.46[b]	5.10[a]	2.27[b]	0.51
E_2(pg/ ml)	13.32[b]	16.56[a]	17.76[a]	1.22
E_2:P_4	0.022[a]	0.014[c]	0.016[b]	0.004

[a-c] Means within a row with different superscripts differ (P < 0.05)

Furthermore, in the present study, CIDR-eCG and CIDR-$PGF_2\alpha$ protocols did not affect the number of medium follicles and corpora lutea compared to control group. Concerning the luteal activity, the CIDR-eCG group showed superior luteal activity expressed as highest progesterone concentration compared to both CIDR-$PGF_2\alpha$ and control groups, although the diameter of the corpus luteum was not affected. The improvement of luteal activity observed in the present study is in agreement with results of Rostami *et al.* (2011) who reported that administration of eCG could enhance CL formation with relatively optimal progesterone production in dairy cows. eCG has the capacity to bind to both LH and FSH receptors (Murphy and Martinuk, 1991), which may stimulate theca and granulosa cells of the dominant follicle (Kuran *et al.,* 1996) as well as progesterone secretion by the early corpus luteum (Peres *et al.,* 2009). The rise (P<0.05) in E_2 concentration of both CIDR-eCG and CIDR- $PGF_2\alpha$ groups was associated with the greatest (P<0.05) diameter of the largest follicles compared to control (Table 1). These differences resulted in decreased (P<0.05) E2: P_4 ratio in CIDR-eCG group compared to CIDR- $PGF_2\alpha$ group which in turn was lower (P<0.05) than control group. The reduction in E_2:P_4 ratio using CIDR-eCG protocols has been reported previously in sheep (EL-Mokadem *et al.,* 2018), and goats (El-Mokadem *et al.,* 2017). Serum progesterone concentration tended to increase (P<0.05) with advancement of day of treatment (days 71, 86 and 116 representing days 15, 30 and 60 after AI) in the CIDR-eCG group compared to both CIDR- $PGF_2\alpha$ and control groups (Fig. 2), and agree with results of (Rostami *et al.,* 2011). Utilization of eCG in a synchronization protocols showed also a positive effect on progesterone plasma levels in the ensuing estrous cycle in dairy cows (Souza *et al.,* 2009).

Effect of hormonal treatments on reproductive performance

The present results indicated that usage of CIDR combined with eCG or $PGF_2\alpha$ decreased (P < 0.05) the days to first estrus compared to control group (56.33 and 61.25 vs. 84.61 days respectively; Table 2). This results seemed to be due to the effect of high concentration of progesterone which induced the

ovarian activity after CIDR removal, hence a rapid drop in concentration of systemic progesterone occurs and the negative feedback influence in pituitary stopped, thus promoting a new follicular phase beginning and estradiol concentration increase thereby the animal will come into estrus and ovulate (Bo *et al.,* 1995a; Bo *et al.,* 1995b; Martinez *et al.,* 2000). An injection of eCG at CIDR withdrawal stimulates follicular development and final maturation of the dominant follicle, thus increasing estradiol production which introduces the animal into estrus (Sá Filho *et al.,* 2009; Small *et al.,* 2009). Also, usage of $PGF_2\alpha$ a day before CIDR removal induced luteolysis and promoted a new follicular phase thus elevating estradiol level and animals displayed estrus 1 to 3 days after CIDR removal (Bo *et al.,* 1995a; Bo *etal.,* 1995b; Martinez *et al.,* 2000).

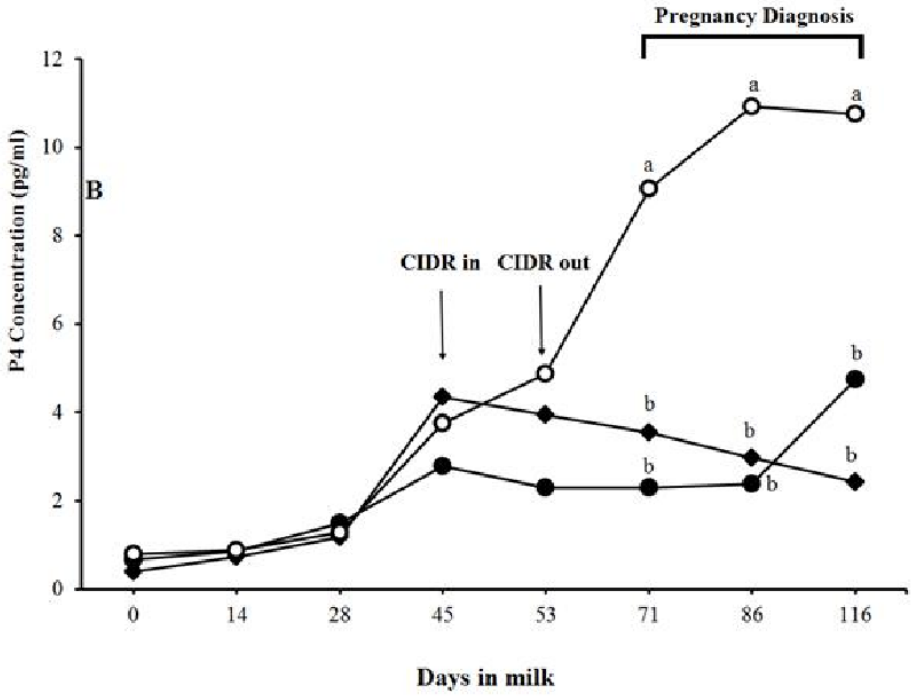

Fig. (2): Changs in progesterone concentration of control (♦), controlled internel druge release (CIDR) deviece combined with equine chorionic gonadotropin, eCG (○) or prostaglandin $F_2\alpha$, $PGF_2\alpha$ (●) of postpartum Holstein dairy cows

Table (2): Effect of controlled internal drug release (CIDR) device conjunction with equine chorionic gonadotropin (eCG) or prostaglandin $F_2\alpha$ ($PGF_2\alpha$) on reproductive performance of postpartum Holstein dairy cows

Items	Control	CIDR		SEM
		eCG	$PGF_2\alpha$	
Days to first estrus, DFE (d)	84.61[a]	56.33[b]	61.25[b]	2.19
Estrus rate, ER (%)	72.22(13/18)	100.00(16/16)	66.67(8/15)	8.36
Conception rate[1], CR (%)	0.00(0/13)	43.75(7/16)	12.50(1/8)	10.02
Conception failure, CF (%)	100.00(13/13)	56.25(9/16)	87.50(7/8)	10.02
Number of service[2], NS100	1.46	1.78	1.80	0.29
Pregnancy rate[3], PR (%)	0.00(0/18)[b]	43.75(7/16)[a]	6.67 (1/15)[b]	9.20

[a,b,] Means within a row with different superscripts differ ($P < 0.05$).
[1] Percentage of cows pregnant exposed to AI.
[2] NS100: number of services during 100 days in milk.
[3] Percentage of cows pregnant of all cows treated.

The insignificant effects of hormonal treatments on reproductive indices (ER, CR, CF, and NS100) compared to control are presented in Table (2). However, the greatest ($P<0.05$) pregnancy rate was achieved using CIDR-eCG protocol. This result agree with those of Souza *et al.* (2009) who reported that eCG treatment at CIDR removal increased pregnancy rate in dairy cows. The superiority of CIDR-eCG protocol in pregnancy rate seemed to be due to the positive correlation reported between pregnancy rate and circulating progesterone concentration (Binelli *et al.,* 2009), which confirmed the association of the highest ($P<0.05$) progesterone concentration (Fig. 2 and Table 1) with greatest ($P<0.05$) pregnancy rate achieved using CIDR-eCG protocol in the present study (Table 2). Furthermore, eCG seems to hasten follicle maturation, resulting in a superior oocyte and a more steroidogenic CL culminating in increased pregnancy rates (Baruselli *et al.,* 2003; Bó *et al.,* 2003). In addition, eCG treatment during the anestrus period aids CL development and helps to increase the secretion of progesterone (Fukui *et al.,* 2001). Moreover, administration of progesterone prior to ovulation inhibits oxytocin receptors in the endometrium, thus reducing the uterine response to oxytocin for the secretion of $PGF_2\alpha$ (Leyva *et al.,* 1998). On the other hand, the lowest ($P < 0.05$) value of E_2:P_4 ratio was associated with the highest ($P < 0.05$) value of serum progesterone concentration (Table 2) in the CIDR-eCG group. This low value of E_2:P_4 ratio indicated the success of maternal recognition of pregnancy as high E_2:P_4 ratio in early pregnancy may generate large $PGF_2\alpha$ episodes which increase the risk of failure of maternal recognition of pregnancy (Abecia *et al.,* 2003). This finding could explain the association of increased ($P<0.05$) E_2:P_4 ratio (Table 1) with reduced ($P<0.05$) pregnancy rate in both CIDR-$PGF_2\alpha$ and control groups (Table 2). Interestingly, usage of CIDR-$PGF_2\alpha$ protocol in the present study did not enhance reproductive performance that may be due to the extra day of progesterone treatment after $PGF_2\alpha$ injection that allowed some dominant follicles to be maintained for a longer than optimal period, resulting in the ovulation of "aged" oocytes with reduced developmental capacity (Mihm *et al.,* 1994; Revah and Butler, 1996).

CONCLUSION

In conclusion, using CIDR combined with eCG represents a promising protocol to attenuate the reproductive dysfunction of postpartum Holstein dairy cows. CIDR-eCG protocol achieved superiority in reducing days to first estrus and E_2:P_4 ratio and increasing pregnancy rate. Further investigations are needed to enhance the effectiveness of this protocol in improving conception rate during postpartum period in dairy cows.

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تخفيف نقص الأداء التناسلي لأبقار الهولشتاين الحلابة حديثة الولادة بإستخدام التحاميل المهبلية مقترنة بالهرمون المشيمي الخيلى المنبه للغدد التناسلية أو هرمون البروستاجلاندين

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صممت هذه التجربة لتقييم كفاءة المعاملات الهرمونية على الأداء التناسلي للأبقار الحلابة حديثة الولادة. حيث خصصت تسع وأربعون بقرة هولشتاين حلابة حديثة الولادة (DIM: أيام الحليب حوالي 45 يوم) وتم تقسيمهم عشوائياً إلى ثلاث مجموعات. المجموعة الأولى (CIDR-eCG، n:16) تم غرس التحاميل المهبلية (السيدر, CIDR) لمدة ٨ أيام وحقنتٌ في العضل بـ ٥٠٠ وحدة دولية من الهرمون المشيمي الخيلى المنبه للغد التناسلية (eCG) في يوم إزالة السيدر. المجموعة الثانية (CIDR-PGF2α، n:15) تم غرس السيدر وحقنتٌ بـ ٥٠٠ ميكروجرام من الكربستينول (PGF2α) قبل إزالة السيدر بيوم واحد. المجموعة الثالثة (الضابطة ، n:18) فلم تتلقى أي معاملات هرمونية. وأوضحت النتائج أن إستخدام السيدر مقترناً بـ eCG أو PGF2α أدى إلى تحسين النشاط المبيضي من خلال زيادة ($P <0.05$) العدد الكلى للحويصلات المبيضية وقطر أكبر الحويصلات مقارنةً بالمجموعة الضابطة. بالرغم من ذلك فإن النتائج أظهرت أن برنامج الـ CIDR-eCGكان متفوقًا في تقليل ($P <0.05$) عدد الحويصلات الصغيرة وزيادة ($P <0.05$) عدد الحويصلات الكبيرة مقارنة ببرنامج الـ CIDR-PGF2α. كذلك أوضحت النتائج أن تطبيق برنامج الـ CIDR-eCG أدى إلى زيادة ($P<0.05$) تركيز هرمون البروجسترون في الدم مقارنةً بكلاً من الـ CIDR-PGF2α والمجموعة الضابطة واللتان لم يلاحظ وجود اختلاف بينهما. بالإضافة إلى ذلك فإن النتائج أوضحت أن إستخدام كلاً من برنامج الـ CIDR-eCG و برنامج الـ CIDR-PGF2α أديا إلى زيادة تركيز هرمون الإستراديول في الدم مقارنةً بالمجموعة الضابطة، وقد إنعكس هذا الاختلاف في تركيز تلك الهرمونات على النسبة بين الإستراديول والبروجسترون (E2: P4) والتي كانت منخفضة ($P <0.05$) في مجموعة الـ CIDR-eCG مقارنةً بالمجاميع الأخرى. علاوة على ذلك فقد وجد أن برنامجي تزامن الشياع نجحت في تقليل ($P <0.05$) عدد الأيام اللازمة لظهور أول شياع مقارنةً بالمجموعة الضابطة ،و بالرغم من ذلك فإن الأداء التناسلي بما في ذلك معدل الشياع والإخصاب وفشل الإخصاب وعدد التلقيحات خلال ١٠٠ يوم الأولى من الحليب لم تختلف معنوياً بين المعاملات. ومع ذلك فإن المجموعة المعاملة ببرنامج الـ CIDR-eCG أظهرت أعلى ($P <0.05$) معدل الحمل مقارنةً بالمجاميع الأخرى. الخلاصة: أشارت النتائج إلى أن إستخدلم برنامج الـCIDR eCG خفض من التدهور في الصفات التناسلية لأبقار الهولشتاين الحلابة حديثة الولادة وذلك من خلال زيادة أعداد الحويصلات الكبيرة و زيادة تركيز هرمون البروجسترون بالدم وتقليل عدد الأيام اللازمة لظهور أول شياع وكذلك E2: P4 وإنعكست نقص نسبة E2: P4 على زيادة معدل الحمل في برنامج CIDR-eCG مقارنةً بالمجاميع الأخرى.