Research Article

Efficiency of Previously used CIDR Stored for a Prolonged Period

Hany Abdallah*, Ali Abd El Rahim

Faculty of Veterinary Medicine, Zagazig University, Zagazig, Sharkia, Egypt.

Abstract | This study investigated the efficiency of the previously used controlled internal drug release (CIDR) stored for 30 days before reusing. In the first experiment, twenty seven Holstein cows at the day of estrus (day 0) received either no treatment (control), new or reused CIDR and blood samples were collected at day 0, 1, 3 and 7. At day 1 and 3, serum progesterone concentration in cows received new CIDR (1.417 and 1.616 ng/ml) was significantly higher than in cows received a reused one (0.545 and 0.954 ng/ml) which in turn was higher than the control group. In the second experiment, estrous cycle was synchronized using Ovsynch, New-CIDRsynch or Reused-CIDRsynch. Cows in Ovsynch (n=119) received GnRH on day 0 then PGF2α on day 7. Fifty six hours after the PGF2α cows received another dose from GnRH and inseminated 18 h latter. Cows in new-CIDRsynch (n=870) and reused-CIDRsynch (n=220) were treated in the same way with exception of inserting a new or reused CIDR between day 0 and day 7. Non returned cows were examined for pregnancy diagnosis at 30 and 70 days post-insemination. Pregnancy-30 and 70 rates after New-CIDRsynch (36.1% and 30.5%) and Reused-CIDRsynch (36.4% and 31.8%) tended to be higher than after Ovsynch (27.7% and 25.2%) (P= 0.07: 0.08). In conclusion, the previously used CIDR -stored for 30 days- have residual progesterone and incorporating new or reused CIDR into Ovsynch improved the efficiency of the protocol in a similar way.

Keywords | Estrus Synchronization, Ovsynch, CIDR, Progesterone residual

Editor | Kuldeep Dhama, Indian Veterinary Research Institute, Uttar Pradesh, India.
Received | September 24, 2014; **Revised** | October 06, 2014; **Accepted** | October 07, 2014; **Published** | October 12, 2014
***Correspondence** | Hany Abdalla, Zagazig University, Sharkia, Egypt; **Email:** hlabdallah@zu.edu.eg
Citation | Abdallah H, Abd El Rahim A (2014). Efficiency of previously used CIDR stored for a prolonged period. Adv. Anim. Vet. Sci. 2 (9): 508-515.
DOI | http://dx.doi.org/10.14737/journal.aavs/2014/2.9.508.515
ISSN (Online) | 2307-8316; **ISSN (Print)** | 2309-3331

INTRODUCTION

The aim of ovulation synchronization accompanied with fixed-time insemination (FTAI) is to achieve the best reproductive performance without estrus detection. The concept of ovulation synchronization protocols is to terminate the current follicular wave and subsequently induce a new synchronized follicular wave. After an appropriate time, the luteal phase is terminated to allow maturation and ovulation of the synchronized dominant follicle. Termination of the follicular wave can be achieved by treating the animal with GnRH or estradiol. In the GnRH based protocols, the GnRH induces ovulation or regression of the dominant follicle according to its developmental stage. In estradiol based protocols, a specific progesterone concentration is necessary to induce regression of the dominant follicle. Therefore, all estradiol based protocols include progestin treatment coincided with estradiol administration (Mapletoft et al., 2003; Wiltbank et al., 2011).

The most widely applied GnRH based ovulation synchronization protocols is the Ovsynch (Pursley et al., 1995). Several studies had investigated the effect of inserting a controlled internal drug-release (CIDR) or a progesterone-releasing intravaginal device (PRID) between the day 0 and 7of the Ovsynch (Stevenson et al., 2003; Galvão et al., 2004; El-Zarkouny et al., 2004; Rivera et al., 2005; Melendez et al., 2006; Stevenson et al., 2006; Stevenson et al., 2008; Chebel et al., 2010; Mendonçaa et al., 2012; Colazo et al., 2013). Based on conception rate, some studies reported no improvement either in heifers or cows (Galvão et al., 2004; Rivera et al., 2005; Mendonçaa et al., 2012). Other studies reported higher conception rate in cows that not previously observed in heat or without CL at the beginning of the protocol (Melendez et al., 2006; Stevenson et al., 2008; Chebel et al., 2010). Others showed controversial results (El-Zarkouny et al., 2004; Stevenson et al., 2006). However, incorporating the CIDR into the Ovsynch imposes an additional cost. Since insertion of the CIDR elevated the serum progesterone level to 1-2ng/ml up to 15 days (Uehlinger et al., 1995) and the 1.9 g and 1.38 g containing CIDR were found to have 1.3 and 0.7 g residual progesterone after 7 days using (Rathbone et al., 2002). It was suggested that CIDR used for a short period (5-7 days) can be reused to minimize the cost.

Several reports compared the progesterone concentration achieved after insertion of new or once or more reused CIDR (Zuluaga and Williams, 2008; Long et al., 2009; Carvalho et al., 2014). Additionally, the efficiency of the estradiol-progestin based synchronization protocols after incorporating once or more reused CIDR had been investigated in bovine (Colazo et al., 2004; Colazo et al., 2006; Meneghetti et al., 2009; Carvalho et al., 2014) or small ruminant (Vilariño et al., 2011; Souza et al., 2011; Vilariño et al., 2013). To our knowledge the efficiency of GnRH based protocols after incorporating the previously used CIDR never been investigated.

Reused CIDR can be a source of microbial transmission among cows; therefore intensive sterilization process is indicated (Zuluaga and Williams, 2008). Reusing the CIDR in the same animal will eliminate the possibility of microbial transmission. However, this requires a prolonged storage period up to 30 days. The residual progesterone amount in the previously used CIDR is affected by several factors including the initial progesterone concentration 1.38 Vs 1.9 g (Rathbone et al., 2002), the method of sterilization between the cycles (Zuluaga and Williams, 2008), the duration of the insertion period 7 Vs 9 days (Long et al., 2009; Carvalho et al., 2014), the number of the reusing cycles once Vs more cycles (Vilariño et al., 2011; Carvalho et al., 2014) and/or the conditions and the duration of the storage between the cycles. Except for Souza et al. (2011), all previous studies reused the CIDR without storage (Nogueira et al., 2011), after storage for 48 h (Zuluaga and Williams, 2008), 7 days (Long et al. 2009) or unrecorded period (Colazo et al., 2004; Carvalho et al., 2014). To our knowledge, no previous reports investigated the efficiency of the previously used CIDR after a prolonged storage. Therefore, the current study was designed to investigate the residual progesterone and the effect of incorporating the reused CIDR stored for 30 days into Ovsynch protocol.

MATERIALS AND METHODS

Animals

This study was carried out on AL-Qasem farm, Ismailia road, Cairo at the period between December 2012 and February 2014. A total number of 700 Holstein cows were used. The body condition score was ranged from 2.5 to 4 and the days in milk ranged from 90 to 250. The cows were housed in a free stall, had a free access to water and feed a total mixed ration. The ration was adjusted according to the NRC to meet the nutritional requirement of a lactating cow weighting 650kg and producing 40kg. The cows were supplied with pedometers. All the events include schedules for estrus synchronization, insemination and pregnancy diagnosis were generated, tracked, and recorded using a commercial on-farm computer software programs (AfiFarm version 4.1).

Progesterone Profile after Insertion of a new or a Previously used CIDR

The reused CIDR (Eazi-Breed CIDR Cattle Insert; Pfizer Animal Health. containing 1.38g P4) was previously used for 7 days. After withdrawal, the CIDR was washed in a povidone–iodine-based disinfectant solution to remove all genital discharge, dried on air and packaged in a clean plastic bag labelled with the number of the cow. The bags are stored in room temperature for 30 days.

Twenty seven cows at the day of estrus were classified into three groups. The first group (n=9) received a new CIDR. The second group (n=9) received a previously used CIDR. The third group (control, n=9) did not receive any treatment. Cows in the first and second group did not receive any additional treatment rather than CIDR. The CIDR was maintained for seven days. Blood samples were collected from all animals in all groups at day 0, 1, 3 and 7 were day 0 is the day of estrus and day of CIDR insertion.

Blood samples were collected from jugular vein and kept in an ice box. The serum was separated and stored at -20 °C until used for progesterone analysis. The progesterone concentration was measured by an electrochemiluminescence immunoassay kit for *in vitro* quantitative determination of progesterone (Elecsys progesterone II, Roche diagnostic Gmbh, Mannheim, Germany). The lower detection limit and the maximum of the master curve is 0.03 and 60 ng/ml; respectively and the functional sensitivity is 0.15 ng/ml.

Reproductive Efficiency after Ovysynch, New-CIDRsynch or Reused-CIDRsynch

Cows at different stage of estrus cycle were randomly allocated to one of the following treatments. The cows in the Ovsynch group (n=119) received 10µg GnRH (Buserelin; Receptal; Intervet) on day 0 followed by 25mg PGF2α (dinoprost; Lutylase; pfizer) on day 7. Fifty six hours after the PGF2α cows received another dose from the GnRH and 18h later all cows were subjected to fixed time insemination (FTAI). The cows in the new-CIDRsynch group (n=870) and cows in the reused-CIDRsynch (n=220) treated in the same way with exception of insertion of a new or a previously used CIDR between the day 0 and the day 7. The reused CIDR was reused in the same cow in which it had been used in the first time.

In all protocols, cows suspected in heat after the PGF2α and before the FTAI based on the activity recorded by the pedometer were examined for findings of the estrous and were inseminated and received 10µg GnRH at the time of insemination. Non returned cows in all protocols were examined by transrectal ultrasonography for pregnancy diagnosis at 26-29 days post-insemination. Pregnant cows were re-examined to confirm pregnancy by rectal palpation at 70 days post-insemination.

Pregnancy-30 and 70 rates were calculated as the number of cows diagnosed as pregnant at day 30 and 70 post-insemination, respectively divided by the number of inseminated cows. The embryonic loss rate was calculated as the number cows diagnosed non pregnant at day 70 divided by the number of cows diagnosed pregnant at day 30.

Statistical Analysis

The differences between pregnancy-30 and 70 and embryonic loss after different protocols were analysed using the chi-square test. The concentration of the serum progesterone after different treatment was compared using the one-way ANOVA using the SPSS program. A value of $P<0.05$ was considered statistically significant.

RESULTS

Serum Progesterone Profile after Insertion of a new or a Previously used CIDR

The serum progesterone concentration was similar in all groups at day 0 and 7. Cows received a new CIDR had a significantly higher progesterone level at day 1 and day 3 (1.417 and 1.616 ng/ml; respectively) than those received a reused one (0.545 and 0.954 ng/ml; respectively). However, the reused CIDR achieved a significantly higher serum progesterone level than that recorded in the control group at day 1 and 3 (Table 1).

In the control group most of the cows had a comparatively low progesterone level up to the day 3. In cows received a new CIDR, the serum progesterone level rapidly increased to reach a level higher than or around 1 ng/ml at the day 1. In cows received a reused CIDR, the serum progesterone level at day 1 was lower than 1 ng/ml in all cows. At day 3, five cows had a serum progesterone level higher than or around 1 ng/ml and 3 showed a serum progesterone level slightly lower than 1 ng/ml and the last one had a considerable low serum progesterone concentration (Figure 1).

Reproductive Efficiency after Ovsynch, New-CIDRsynch or Reused-CIDRsynch Protocols

The pregnancy-30 and 70 rates after the Ovsynch protocol (27.7% and 25.2%; respectively) tended to be lower than after the New-CIDRsynch (36.1% and 30.5%; respectively) or the Reused-CIDRsynch (36.4% and 31.8%; respectively) (P=0.07: 0.08). The pregnancy-30 and 70 rates after the Reused-CI

Table 1: Serum progesterone level ng/ml (mean ± SD) at day 0, 1, 3 and 7 after insertion of a new or a previously used CIDR.

	day 0*	day1	day 3	day7
Control	0.137± 0.131	0.150±0.108[c]	0.227±0.167[c]	2.057±0.599
New CIDR	0.282±0.212	1.417±0.543[a]	1.616±0.867[a]	2.022±0.627
Reused CIDR	0.082±0.60.	0.545±0.173[b]	0.954±0.437[b]	2.077±0.483

*Day 0 is the day of estrus and day of CIDR insertion
Values in the same column which have a different superscript are significantly different (p <0.05)

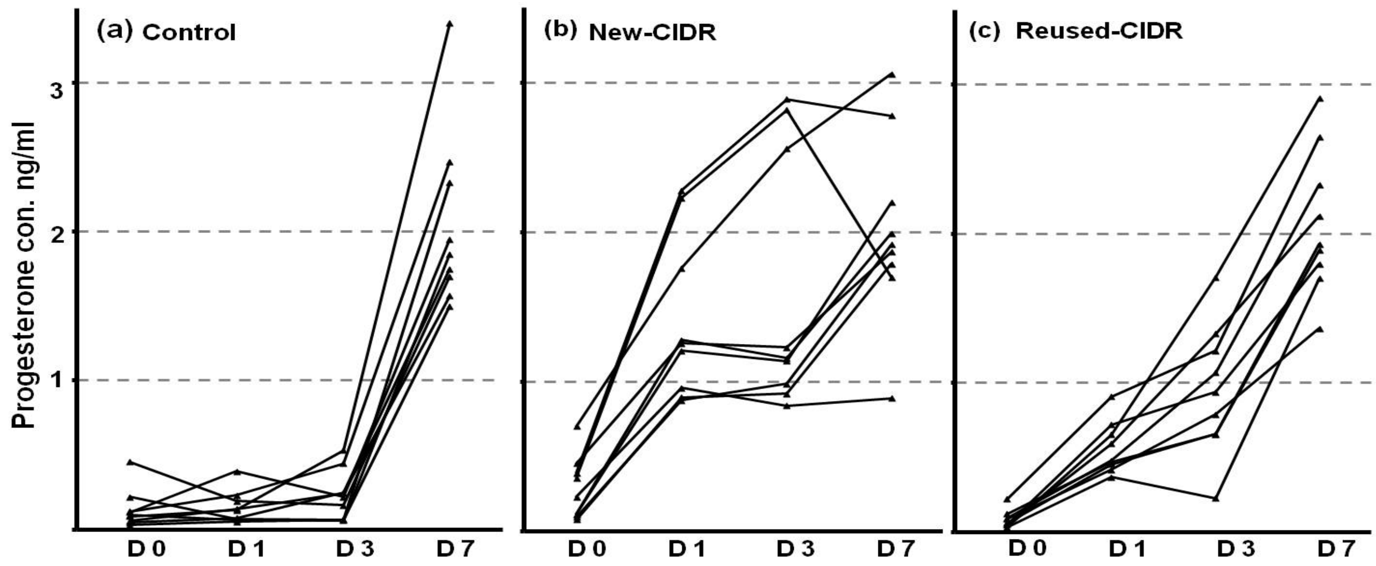

Figure 1: Serum progesterone concentration in individual cows in control group (a), cows received a new CIDR (b) or cows received previously used CIDR (c). The CIDR was inserted at day of estrus (day 0) and serum progesterone level was measured at day 0, 1, 3 and 7.

DRsynch were similar to those recoded after the New-CIDRsynch. The embryonic loss rate was similar in all protocols and ranged from 9.1% to 12.5 % (Table 2).

The proportions of the cows that inseminated before the FTAI were ranged from 5.5 to 9.3%. In the Ovsynch, the pregnancy-30 and 70 rates were non-significantly higher in cows inseminated before the FTAI (45.5% and 45.5%; respectively) than in cows inseminated at the FTAI (25.9% and 23.1%; respectively). In the New-CIDRsynch, the pregnancy-30 and 70 rates in cows inseminated before FTAI were about 6 % higher than in cows inseminated at FTAI. In the Reused-CIDRsynch protocol no clear difference was observed. In all protocols, the embryonic loss ratio tended to be higher in cows inseminated at the FTAI than those inseminated before the FTAI (Table 3).

DISCUSSION

If the previously used CIDR that stored for a prolonged period can function as a new one, reusing the CIDR in the same animal will greatly reduce the cost of the GnRH-progestin based protocols and will eliminate the possibility of the microbial transmission by the reused CIDR.

The common method to investigate the extent of the residual progesterone in the previously used CIDR is to compare the progesterone level achieved after insertion of a reused or a new CIDR into ovariectomized cows. Unfortunately, that type of cows is not available to us. Therefore we decided to use intact cows at the day of estrus to utilize the physiological period characterized by a limited internal progesterone source to compare between the new and the reused CIDR. The inability of the reused CIDR

Table 2: Reproductive performance after Ovsynch, CIDRsynch or Reused-CIDRsynch.

Protocol	Pregnancy-30*	Pregnancy-70*	Embryonic loss**
Ovsynch	33/119 (27.7)	30/119 (25.2)	3/33 (9.1)
New-CIDRsynch	314/870 (36.1)	265/870 (30.5)	49/314 (15.6)
Reused-CIDRsynch	80/220 (36.4)	70/220 (31.8)	10/80 (12.5)

*Pregnancy-30 and 70 rates were calculated as the number of cows diagnosed as pregnant at day 30 and 70 post-insemination, respectively divided by the number of inseminated cows.

**The embryonic loss rate was calculated as the number cows diagnosed non pregnant at day 70 divided by the number of cows diagnosed pregnant at day 30 post-insemination

Table 3: Reproductive performance in cows inseminated before or at the FTAI after Ovsynch, New-CIDRsynch or Reused-CIDRsynch.

Protocol	Complete protocol		Pregnancy-30*	Pregnancy-70*	Embryonic loss**
Ovsynch	No[a]	11/119 (9.3)	45.5	45.5	0
	Yes[b]	108/119 (90.7)	25.9	23.1	10.7
New-CIDRsynch	No[a]	63/870 (7.2)	41.3	36.5	11.5
	Yes[b]	807/870 (92.8)	35.7	30	16
Reused-CIDRsynch	No[a]	12/220 (5.5)	33.3	33.3	0
	Yes[b]	208/220 (94.5)	36.5	30	13.2

*Pregnancy-30 and 70 rates were calculated as the number of cows diagnosed as pregnant at day 30 and 70 post-insemination, respectively divided by the number of inseminated cows.

**The embryonic loss rate was calculated as the number cows diagnosed non pregnant at day 70 divided by the number of cows diagnosed pregnant at day 30 post-insemination

[a]No: Cows showed estrus sings after the PGF2α and before the time of the fixed time insemination.

[b]Yes: Cows inseminated at the fixed time insemination.

to achieve a serum progesterone level similar to that achieved by the new one is in agreement with previous studies used ovarectomized cows (Savio et al., 1993; Zuluaga and Williams, 2008; Long et al., 2009; Carvalho et al., 2014) or cyclic cows received a luteolytic dose of prostaglandin at the time or before CIDR insertion (Savio et al., 1993; Cerri et al., 2009). The mean serum progesterone concentration in cows received a new or a reused CIDR -recorded in the present study- is considerably lower than that reported in previous studies (Van Cleeff et al., 1992; Savio et al., 1993; Zuluaga and Williams, 2008; Long et al., 2009; Carvalho et al., 2014) but higher than that recorded by Cerri et al. (2009). This may be due to the fact that, with exception of Cerri et al. (2009) and Carvalho et al. (2014) the other studies had used a CIDR contains 1.9g progesterone but in the current study the initial progesterone concentration was 1.38g. The other possible reason is the variation in progesterone metabolism among animals in different studies due to variation in species, breed, production rate, dry matter intake, lactation season and/or climatic conditions (Rabiee et al., 2001; Vasconcelos et al., 2003). Higher progesterone concentration at day three in comparison to the day one after insertion of new or reused CIDR indicates a slow increase in the serum progesterone concentration. This is in agreement with Van Cleef et al. (1992) who recorded maximum progesterone concentration at the day 2 after CIDR insertion. Otherwise, it is in disagreement with others who reported maximum progesterone concentration after few minutes, hours or during the day CIDR insertion (Rathbone et al., 2002; Zuluaga and Williams, 2008; Long et al., 2009; Carvalho et al., 2014). The stage of cycle at which CIDR was inserted found to influence the changes in the progesterone concentration (Macmillan et al., 1991) may be due to variable progesterone absorption ability of the vaginal membrane at different stage of estrus. Slow increase in the serum progesterone level after CIDR may be due to insertion of CIDR at day of estrus. Variable progesterone absorption ability phenomena may be the actual cause of variable progesterone levels recorded in cows received the same treatment.

The improvement in the pregnancy-30 and 70 rates (around 10% and 5%; respectively) after incorporating a new CIDR into the Ovsnch protocol (New-CIDRsynch) is in agreement with previous studies incorporated the CIDR into the Ovsynch (Stevenson et al., 2006; Stevenson et al., 2008; Colazo et al., 2013) Presynch (Melendez et al., 2006; Chebel at al., 2010) or Cosynch (Stevenson et al., 2003) but in disagreement with other reports incorporated the CIDR into Presynch (Bartolome et al., 2009; Colazo et al., 2013) or Ovsynch (Rivera et al., 2005; Mendonçaa et al., 2012). The improvement occurred after incorporating the CIDR in to Ovsynch was explained by higher ability to induce estrous in non-cyclic cows (Stevenson et al., 2003; Cerri et al., 2009) or improving the fertility of cows which did not have a CL at the beginning of the protocol (Stevenson et al., 2008) or cows showed an early luteolysis before administration of PGF2α (Stevenson et al., 2006). In present study, cows were divided randomly among treatments. Therefore it is suspected that the proportions of cyclic and noncyclic cows are same in each treatment group. Better reproductive performance in cows received FTAI in New-CIDRsynch than in Ovsynch may be due to the previous hypothesis that, including the CIDR in the GnRH protocols improves the conception in the noncyclic cows.

The pregnancy-30 and 70 rates after Reused-CIDRsynch were similar to the New-CIDRsynch but they were numerically higher than the Ovsynch. This indicate that lower progesterone concentration achieved by the reused-CIDR have the same biological effect as that achieved by the new CIDR. The previously used CIDR had the same efficiency as the new CIDR when used to synchronize or resynchronize cows or heifers (Colazo et al., 2004; Colazo et al., 2006; Meneghetti et al., 2009) or treat seasonal anestrum buffalo cows with estradiol-progestin based protocols (Carvalho et al., 2014). In the GnRH based protocol, the progestin prevents early estrus expression in animals those have no CL at the beginning of the protocol or begin the protocol at the late diestrus. Additionally it assures presence of circulating progesterone concentration during follicular growth and maturation which have a great substantial impact on the quality of the released oocytes (Mapletoft et al., 2003; Inskeep et al., 2004; Wiltbank et al., 2011). Higher difference in the pregnancy rate between cows inseminated before or at FTAI in the Ovsynch (20%) in comparison to New-CIDRsynch (6%) or the reused-CIDRsynch (3%) may indicate that incorporation of new or reused CIDR improved the conception rate in the cows inseminated at FTAI.

Incorporating the CIDR either new or previously used one had no effect on the embryonic loss. In the other hand embryonic loss in New-CIDRsynch or Reused-CIDRsynch is numerically higher than Ovsynch. These results are in agreement with previous results in cows with unknown cyclicity status (Galvão et al., 2004; Stevenson et al., 2006), cows with no CL at the beginning of the protocol (Stevenson et al., 2006; Stevenson et al., 2008), cyclic or anovulatory cows (Galvão et al., 2004). Otherwise they are in disagreement with other reports on cows with different cyclicity status (Bartolome et al., 2009), cows with no CL or anovulatroy cows (Stevenson et al., 2006; Chebel et al., 2010). The cyclicity status of the cow greatly affected the embryonic loss after the GnRH-based synchronization protocol and the embryonic loss in noncycling cows was twice that in cycling cows (Galvão et al., 2004; Stevenson et al., 2006). The embryonic loss in cows inseminated before the FTAI was lower than in cows inseminated at FTAI in all groups. It seems that although incorporating the CIDR into the GnRH based protocol improved the ability of the protocol to induce ovulation and subsequently increase the conception rate in noncyclic cows. These cows may have a limited ability to maintain pregnancy. Cows inseminated before FTAI suspected to have a mature follicle that reach the size and the activity to induce estrus sings but some cows introduced to FTAI are suspected to have a small follicle. Embryos originated from oocytes ovulated form a small size follicle had a lower survivability (Perry et al., 2005).

In conclusion, the previously used CIDR stored for 30 days had the ability to induce an increase in the serum progesterone level and incorporating the new or the reused CIDR in to Ovsynch protocol improved the conception rate in a similar way. Thus the Reused CIDR functioned as the new one.

CONFLICT OF INTEREST

None of the authors have any conflict of interest to declare.

AUTHOR CONTRIBUTIONS

Both of the authors have been involved in designing the study, analysing the data and drafting the manuscript.

ACKNOWLEDGEMENT

The authors wish to thank the owner of AL-Qasem farm, Ismailia road, Cairo for allowing us to use his cattle and facilities. We greatly appreciated the great help of veterinary doctor Mohamed Hussein the head manger of the farm in collecting and managing the data by the AfiFarm.

REFERENCES

- Bartolome JA, Van Leeuwen JJ, Thieme M, Sa'filho OG, Melendez P, Archbald LF, Thatcher WW (2009). Synchronization and resynchronization of inseminations in lactating dairy cows with the CIDR insert and the Ovsynch protocol. Theriogenology 72: 869- 878.
- Carvalho NA, Soares JG, Souza DC, Vannucci FS, Amaral R, Maio JR, Sales JN, Sá Filho MF, Baruselli PS (2014). Different circulating progesterone concentrations during synchronization of ovulation protocol did not affect ovarian follicular and pregnancy responses in seasonal anestrous buffalo cows. Theriogenology 81: 490- 495.
- Cerri RLA, Rutigliano HM, Bruno RGS, Santos JEP (2009). Progesterone concentration, follicular development and induction of cyclicity in dairy cows receiving intravaginal progesterone inserts. Anim. Reprod. Sci. 110: 56 –70.
- Chebel RC, Al-Hassan MJ, Fricke PM, Santos JEP, Lima JR, Martel CA, Stevenson JS, Garcia R, Ax RL (2010). Supplementation of progesterone via controlled internal drug release inserts during ovulation synchronization protocols in lactating dairy cows. J. Dairy Sci. 93: 922- 931.
- Colazo MG, Dourey A, Rajamahendran R, Ambrose DJ (2013). Progesterone supplementation before timed AI increased ovulation synchrony and pregnancy per AI, and supplementation after timed AI reduced pregnancy losses in lactating dairy cows. Theriogenology 79: 833-841.
- Colazo MG, Kastelic JP, Mainar-Jaime RC, Gavaga QA, Whittaker PR, Small JA, Martinez MF, Wilde RE, Veira DM, Mapletoft RJ (2006). Resynchronization of previously timed-inseminated beef heifers with progestins. Theriogenology 65: 557- 572.
- Colazo MG, Kastelic JP, Whittaker PR, Gavaga QA, Wilde R, Mapletoft RJ (2004). Fertility in beef cattle given a new or previously used CIDR insert and estradiol, with or without progesterone. Anim. Reprod. Sci. 81: 25-34.
- El-Zarkouny SZ, Cartmill JA, Hensley BA, Stevenson JS (2004). Pregnancy in dairy cows after synchronized ovulation regimens with or without presynchronization and progesterone. J. Dairy Sci. 87: 1024-1037.
- Galvão KN, Santos JE, Juchem SO, Cerri RL, Coscioni AC, Villaseñor M (2004). Effect of addition of a progesterone intravaginal insert to a timed insemination protocol using estradiol cypionate on ovulation rate, pregnancy rate, and late embryonic loss in lactating dairy cows. J. Anim. Sci. 82: 3508-3517.
- Inskeep EK (2004). Preovulatory, postovulatory and postmaternal recognition effects of concentrations of progesterone on embryonic survival in the cow. J. Anim. Sci. 82(E. Suppl.): E24–E39.
- Long ST, Yoshida C, Nakao T (2009). Plasma progesterone profile in ovariectomized beef cows after intra-vaginal insertion of new, once-used or twice-used CIDR. Reprod. Domest. Anim. 44: 80- 82.
- Macmillan KL, Taufa VK, Barnes DR, Day AM (1991). Plasma progesterone concentrations in heifers and cows treated with a new intravaginal device. Anim. Reprod. Sci. 26: 25–40.
- Mapletoft RJ, Martinez MF, Colazo MG, Kastelic JP (2003). The use of controlled internal drug release devices for the regulation of bovine reproduction. J. Anim. Sci. 81(E. Suppl. 2): E28–E36.
- Melendez P, Gonzalez G, Aguilar E, Loera O, Risco C, Archbald LF (2006). Comparison of two estrus-synchronization protocols and timed artificial insemination in dairy cattle. J. Dairy Sci. 89: 4567-4572.
- Mendonçaa LGD, Deweyc ST, Lopes Jr, Riverab FV, Guagninib FS, Fetrowa JP, Bilby TR, Chebel RC (2012). Effects of resynchronization strategies for lactating Holstein cows on pattern of reinsemination, fertility, and economic outcome. Theriogenology 77: 1151-1158.
- Meneghetti M, Sa´ Filho OG, Peres RFG, Lamb GC, Vasconcelos JLM (2009). Fixed-time artificial insemination with estradiol and progesterone for Bos

indicus cows I: Basis for development of protocols. Theriogenology 72: 179-189.
- Nogueira DM, Lopes Júnior ES, De Peixoto RM, Christilis M, Martins SR, Do Monte APO (2011). Using the same CIDR up to three times for estrus synchronization and artificial insemination in dairy goats. Acta Scientiarum. Animal Sciences 33: 321-325.
- Perry GA, Smith MF, Lucy MC, Green JA, Parks TE, MacNeil MD, Roberts AJ, Geary TW (2005). Relationship between follicle size at insemination and pregnancy success. PNAS 102: 5268-5273.
- Pursley JR, Mee MO, Wiltbank MC (1995). Synchronization of ovulation in dairy cows using PGF2α and GnRH. Theriogenology 44: 915-923.
- Rabiee AR, Macmillan KL, Schwarzenberger F (2001). Excretion rate of progesterone in milk and faeces in lactating dairy cows with two levels of milk yield. Reprod. Nutr. Dev. 41: 309-319.
- Rathbone MJ, Bunt CR, Ogle CR, Burggraaf S, Macmillan KL, Burke R, Pickering KL (2002). Reengineering of a commercially available bovine intravaginal insert (CIDR insert) containing progesterone. J. Control Release 85: 105-115.
- Rivera H, Lopez H, Fricke PM (2005). Use of intravaginal progesterone-releasing inserts in a synchronization protocol before timed AI and for synchronizing return to estrus in Holstein heifers. J. Dairy Sci. 88: 957-968.
- Savio JD, Thatcher WW, Morris GR, Entwistle K, Drost M, Mattiacci MR (1993). Effects of induction of low plasma progesterone concentrations with a progesterone-releasing intravaginal device on follicular turnover and fertility in cattle. J. Reprod. Fertil. 98: 77-84.
- Souza JM, Torres CA, Maia AL, Brandão FZ, Bruschi JH, Viana JH, Oba E, Fonseca JF (2011). Autoclaved, previously used intravaginal progesterone devices induces estrus and ovulation in anestrous Toggenburg goats. Anim. Reprod. Sci. 129: 50-55.
- Stevenson JS, Lamb GC, Johnson SK, Medina-Britos MA, Grieger DM, Harmoney KR, Cartmill JA, EL-Zarkouny SZ, Dahlen CR, Marple TJ (2003). Supplemental norgestomet, progesterone, or melengestrol acetate increases pregnancy rates in suckled beef cows after timed inseminations. J. Anim. Sci. 81: 571-586.
- Stevenson JS, Pursley JR, Garverick HA, Fricke PM, Kesler DJ, Ottobre JS, Wiltbank MC (2006). Treatment of cycling and noncycling lactating dairy cows with progesterone during ovsynch. J. Dairy Sci. 89: 2567-2578.
- Stevenson JS, Tenhouse DE, Krisher RL, Lamb GC, Larson JE, Dahlen CR, Pursley JR, Bello NM, Fricke PM, Wiltbank MC, Brusveen DJ, Burkhart M, Youngquist RS, Garverick HA (2008). Detection of anovulation by heatmount detectors and transrectal ultrasonography before treatment with progesterone in a timed insemination protocol. J. Dairy Sci. 91: 2901-2915.
- Uehlinger H, Binder H, Hauser B, Rüsch P, Zerobin K (1995). Comparison of vaginal devices CIDR and PRID in ovariectomized cows using hormone analysis. Schweiz. Arch. Tierheilkd. 137: 81-86.
- Van Cleeff J, Lucy MC, Wilcox CJ, Thatcher WW (1992). Plasma and milk progesterone and plasma LH in ovariectomized lactating cows treated with new or used controlled internal drug release devices. Anim. Reprod. Sci. 27: 91-106.
- Vasconcelos JLM, Sangsritavong S, Tsai SJ, Wiltbank MC (2003). Acute reduction in serum progesterone concentrations after feed intake in dairy cows. Theriogenology 60: 795-807.
- Vilariño M, Rubianes E, Menchaca A (2011). Re-use of intravaginal progesterone devices associated with the Short-term Protocol for timed artificial insemination in goats. Theriogenology 75: 1195-1200.
- Vilariño M, Rubianes E, Menchaca A (2013). Ovarian responses and pregnancy rate with previously used intravaginal progesterone releasing devices for fixed-time artificial insemination in sheep. Theriogenology 79: 206-210.
- Wiltbank MC, Sartori R, Herlihy MM, Vasconcelos JL, Nascimento AB, Souza AH, Ayers H, Cunha AP, Keskin A, Guenther JN, Gumen A (2011). Managing the dominant follicle in lactating dairy cows. Theriogenology 76: 1568-1582.
- Zuluaga JF, Williams GL (2008). High-pressure steam sterilization of previously used CIDR inserts enhances the magnitude of the acute increase in circulating progesterone after insertion in cows. Anim. Reprod. Sci. 107: 30-35.