MANAGMENT STRATEGIES TO OPTIMIZE REPRODUCTIVE PERFORMANCE OF THE DAIRY HERDS: Focus on FTAI

Lucas Cutaia
Technical Manager - Syntex SA
Luis Guillon, Buenos Aires, Argentina
lcutaia@syntexar.com

Introduction

Dairy cows are handled differently in different part of the world. Pastoral systems (usually in New Zealand, Australia, some countries of the European Union and South America) usually maintain a seasonal calving pattern. Cows that do not maintain an annual calving interval are usually discarded as non-pregnant or induced to calving before term. Another alternative is to serve those cows in the next breeding period, in herds with two breeding seasons, common in Australia and also used in Argentina. Cows that are in stable systems (some countries of the European Union, North America, Mexico, Chile and Brazil) and in mixed systems (such as those of Argentina), do not need a seasonal calving pattern and it is about maintaining an interval between deliveries close to 12-13 months.

Theoretically, maintaining a calving interval of 1 year for high producing cows can be detrimental because cows would have to be dried when milk production is still profitable. However, maintaining an interval between calving of 12-13 months has been transformed into a utopia, due to the fact that in recent years there has been a constant decline in reproductive rates in dairy cows (Lucy, 2001; Wiltbank et al., 2006). This is related to a decline in the fertility of dairy cows in dairy farms around the world and the low efficiency in detecting jealousy (Thatcher et al., 2002).

An immediate solution to the decrease in fertility in dairy herds includes the use of hormonal intervention. A series of hormonal treatments has been developed to control the timing of the first AI and subsequent inseminations in non-pregnant cows and for the treatment of anestrus cows. One of the hormones that has had much discussion in recent years is Equine Chorionic Gonadotrophin (eCG). The eCG is a high molecular weight glycoprotein produced by the endometrial cups in the mare between 35 and 100 days of gestation (Murphy and Martinuk, 1991). If administered to cows, eCG produces stimulation of follicular development, because it has the ability to bind to FSH and LH receptors of follicles. It has been shown that treatment with eCG increases the development of the dominant follicle and ovulation of a larger follicle resulting in a larger and more functional CL, which is believed to result in embryo survival. With the conception and pregnancy rates in continuous decline, this review aims to present data and explore strategies to use the potential benefits of eCG in improving pregnancy rates in dairy cows.

Control of luteal activity through the use of luteolytic agents

Since its commercial use as a hormone involved in the lysis of the corpus luteum, prostaglandin F2α (PGF) remains the hormone most used in the world to synchronize estrus in beef and dairy cows. The response to the administration of PGF will be different in the different stages of the estrous cycle (Momont and Seguin, 1983). From day 1 to 5 no response is observed since ovulation has occurred and the corpus luteum is developing. On days 6 and 7, the response is partial, it is reaching the end of the development of the corpus luteum. Between days 8 and 17, the corpus luteum is developed and is sensitive to the luteolytic effect of PGF and, finally, between days 18 to 21, the corpus luteum is already in regression and the animal will go into heat even though we do not inject the PGF.

Based on the knowledge of the luteal response to PGF, different protocols were designed to group or synchronize jealousy. In this way a protocol of synchronization of jealousy (Target Breeding or Controlled Reproduction) was developed based on an interval of 14 days between the injections of PGF (Ferguson and Galligan, 1983). This protocol is based on three administrations of PGF, applying the first of them 14 days before the start of the service (initial dose). The second PGF (first service dose) determines the beginning of heat detection and AI. After the last administration, estrus and AI are detected for 3 days and at 80 hours an FTAI is performed on all female not detected in estrus (Nebel and Jobst, 1998). Currently it has been decided to slightly alter this protocol, obviating the use of FTAI due to the low fertility that is obtained and recommended, as an alternative for cows that were not seen in heat using the IATF protocols that are described later in this document. article (reviewed in Bó et al., 2007).

Control of follicular dynamics and ovulation through the use of GnRH in combination with PGF

Different hormones can be used to control follicular dynamics, so that the ovulatory follicle obtained after implementing a treatment to control the estrous cycle comes from a young follicle, that is, originated in a recent wave of follicular growth. As mentioned, the different schemes that use PGF to synchronize jealousy do not control follicular dynamics. Consequently, the use of GnRH associated with PGF was used to control follicular dynamics, luteal activity and generate new protocols to control the estrous cycle.

The use of GnRH to manipulate follicular development was originally reported by Macmillan and Thatcher (1991) and is based on the induction of a LH peak and consequently on the ovulation of a dominant follicle. If GnRH results in ovulation, an accessory CL will be formed and in turn a new follicular growth wave will begin 2 or 3 days later. This then led to the development of the protocol called Ovsynch (Pursley et al., 1995). The treatment consists in the administration of a GnRH analogue (to synchronize the follicular development), followed by an injection of PGF 7 days later (to induce luteolysis), an injection of GnRH 48 at 56 h after the PGF (for synchronize ovulation) and IATF at 15 h of the second GnRH.

The pregnancy rates obtained with the Ovsynch protocol in dairy cows vary between 30% to 55%. The results of pregnancy have been similar to those obtained with inseminations performed at 12 h of estrus observed (Burke et al., 1996, De la Sota et al., 1998, Pursley et al., 1995, 1997, Stevenson et al. ., 1999; Thatcher et al., 2001, 2006) and for this reason is the protocol most used in the USA for the insemination of lactating cows (Caravielo et al., 2006).

Although Ovsynch treatment in dairy cows resulted in rates comparable to those obtained at detected estrus, it was observed that the response to treatment was mainly linked to the effectiveness of the first GnRH in inducing ovulation of the dominant follicle (Vasconcelos et al., 1999). To avoid variability in the response, a protocol called Presynch was developed in which the animals received an injection of PGF 12 days before initiating the Ovsynch protocol or two injections every 14 days, the second of which was administered 12 days before the start of the protocol (Moreira et al., 2001). In general, an improvement in the fertility of lactating cows has been found from 12% to 14% with this protocol (Moreira et al., 2001; Thatcher et al., 2006). The interval between the PGF and the second GnRH has also been altered and it is currently suggested to administer the GnRH at 56 h of the PGF and to perform the IATF 12 at 15 h afterwards.

Treatments using intravaginal devices with progesterone

Currently, there are several intravaginal devices with progesterone in the international market. Since these devices were created, 7 or 8 days protocols have been developed. The treatment will vary in different regions of the world according to the availability of drugs. For example, the most used treatment in South America and New Zealand (NZ until 2007) is to administer 2 mg of EB at the time of device insertion (Day 0), remove the device on Day 7 or 8 and administer PGF. Twenty-four hours later, 1 mg of EB is administered to synchronize ovulation and the FTAI is performed at 54-56 hours post-removal. These protocols have been used by dairy producers in different parts of the world with pregnancy rates ranging between 35 and 55%, being very influenced by body condition, days of lactation and cow production.

In regions of the world where estrogens are not licensed such as North America and Europe (since August 2007, New Zealand) progesterone devices are used in association with the Ovsynch protocol to improve the fertility of cows that have not yet started cycling. Beginning of the mating period (called cows in anovulatory anoestrus). Anestrus is a common problem in dairy production systems. Approximately 20 to 40% of cows in pastoral production systems are in anoestrus at the beginning of the service season (Rhodes et al., 2003). In a study of cows in the United States, it was found that 28% of the primiparous cows and 15% of the multiparous cows had not ovulated at 60 days postpartum (Gumen et al., 2003). In the United Kingdom, 11% of cows had not ovulated 44 days postpartum (Lamming and Darwash, 1998).

In a work done by Pursley et al. (2001) conception rates in cows treated with Ovsynch + a device with progesterone were higher than those treated with Ovsynch (41% vs. 51%, n = 634). Interestingly, there were no differences in conception rates between Ovsynch and Ovsynch + progesterone in cows that were cycling. However, progesterone devices markedly increased pregnancy rates in cows that were not cycling (34.7% vs. 55.2%, n = 182). Therefore, the inclusion of a device with progesterone can increase fertility in lactating milk cows that are not cycling.

A study was carried out with the objective of evaluating the treatment with progesterone devices in combination with GnRH to synchronize lactating cows (Veneranda et al., 2006). We used 400 Holstein cows belonging to Los Lazos SA, in the localities of Totoras, Sta. Fe and El Fortín, Córdoba. The animals used had an average BCS of 3.0 ± 0.25 (Scale 1-5), with 58.0 ± 11.6 days in milk (DIM) and an average production of 31.1 ± 6.6 liters per day. The cows were distributed randomly and according to the data previously described in 4 treatment groups in a 2x2 factorial design. Half of the cows received a device with progesterone (DIB, 1 g of progesterone, Syntex SA) for 7 days, together with the application of a dose of GnRH at the time of placing the device and a second dose at 48 h removed the device. A dose of PGF was applied when the device was removed and the cows were FTAI 60 h after the device was removed. The other half of the animals received a DIB for 8 days combined with 2 mg of EB at the time of insertion. A dose of PGF was applied at the time of removal of the device and 1 mg of EB 24 h later. All the animals were IATF at 60 h after the DIB was removed. Each group (P4 + EB or P4 + GnRH) was subdivided to receive or not 400 IU of eCG (Novormón, Syntex, Argentina) at the time of withdrawal of the device. The diagnosis of pregnancy was made by rectal palpation between 45 and 50 days post-FTAI. The pregnancy percentages were compared by logistic regression. A higher percentage of pregnancy was obtained in cows treated with eCG and EB than in those not treated with EB (44.9 vs 30.0%, respectively) and the treatments with GnRH did not differ significantly (GnRH 37.0% and GnRH + eCG 30.0%).

From the obtaining of these results, we carried out a second experiment with the objective of determining if the numerical difference found in the treatments P4 + EB + eCG and P4 + GnRH (without eCG) was maintained. As a secondary objective of this second experiment, the pregnancy rates obtained were compared with a DIB intravaginal device and a CIDR (Pfizer, Animal Health, 1.9 g of progesterone). In this experiment, 200 Holstein cows were used in lactation, with characteristics similar to those of the previous experiment. A 2x2 factorial design was used. Initially the cows were divided at random in two treatment groups (EB + eCG or GnRH) and the cows were FTAI 60 h after the device was removed and the pregnancy diagnosis was made 50 days after the IATF by rectal palpation. No significant differences were found in the pregnancy rates (P = 0.4) between the cows in which a DIB (51%) or CIDR (42%) was used, in turn the pregnancy rates did not differ (P = 0.18) among cows treated with EB + eCG (52.0%) or GnRH. (41.0%). However, if we add the data from the two experiments, the pregnancy rates in the cows of the treatment using EB + eCG is significantly higher.

Because the pre-synchronization treatment has shown an increase in the pregnancy rate of the Ovsynch protocols (Moreira et al., 2001), an experiment was designed to compare the pregnancy rates in cows treated with a modified pre-synch program. With the treatments evaluated in the previous works (P4 + EB + eCG and P4-synch) (Veneranda et al., 2008). 500 cows were used from the same establishment as the previous studies. The animals used were between 30 and 51 d postpartum (when the PGF treatment was applied to the pre-synch group), with an average milk production of 29.5 ± 7.0 Kg daily (range of 13.0 to 46.0 Kg) and a CC between 2.5 and 3 of scale 1-5. The cows were grouped by postpartum days and randomized into 5 treatment groups. The Pre-synch group received PGF 28 and 14 days before the insertion of the DIB device and 50 µg of Lecireline (GnRH) im (Day 0). On Day 7 the device was removed and PGF was applied. On day 9, all cows received a second treatment with GnRH and were IATF 16 h later (60 days after the device was removed). The animals of the pre-synch + P4 group were treated in a similar manner except that they received the device for 7 days prior to the second injection of PGF, and did not have the device when the first GnRH was injected. The cows in the P4-Synch group were treated as those in the pre-synch group but did not receive the two doses of PGF 28 and 14 days before. The cows of the last two groups received a DIB and 2 mg of EB on Day 0. On Day 8, the device was removed and PGF and 400 IU eCG IM were injected. The cows of group P4 + EB + eCG + EB received 1 mg of EB on day 9, while those of group P4 + EB + eCG +

GnRH received GnRH on day 10. All cows were FTAI 60 h after the device was removed. The diagnosis of pregnancy was made 50 days after the FTAI by rectal palpation and the data were analyzed by logistic regression.

As shown in Figure 1, the two groups treated with P4, EB and eCG had the highest pregnancy rates and the group in which the device was inserted before the second PGF (Pre-synch + P4) had the lowest pregnancy rate. The pregnancy rates of the other groups were intermediate and did not differ with the extremes.

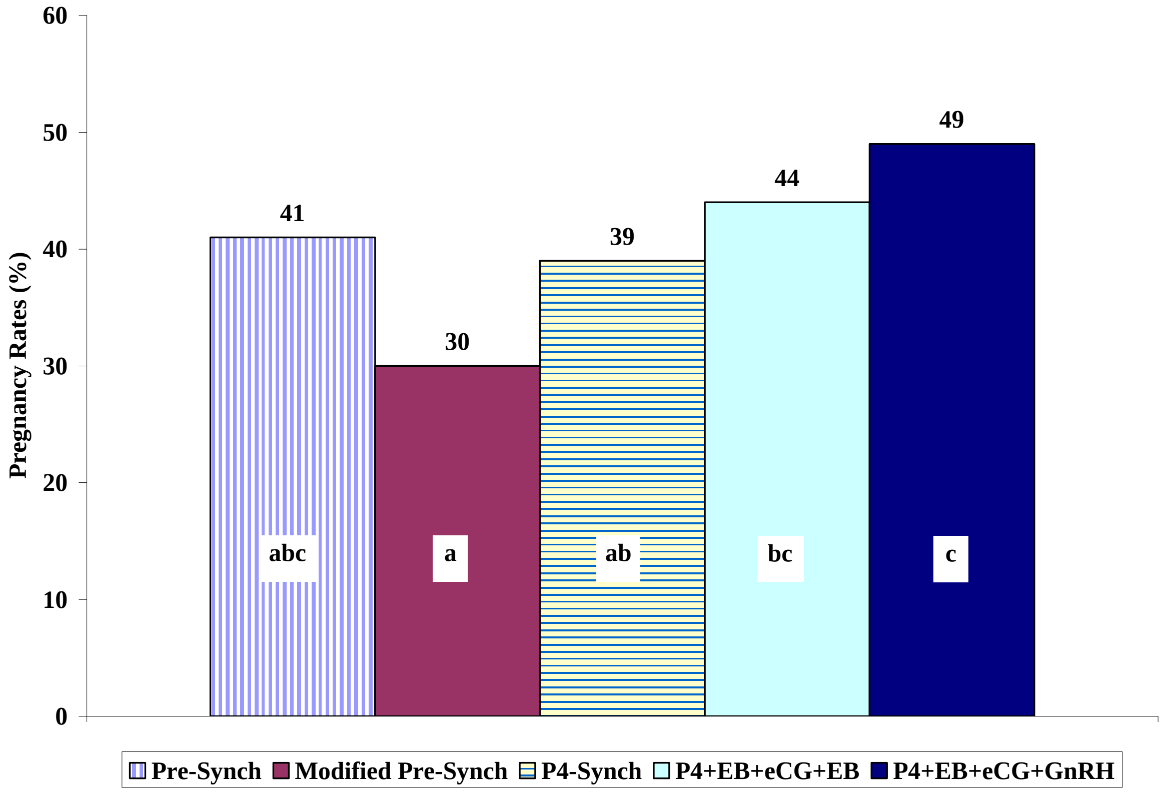

Figure 1. Pregnancy rates of lactating cows treated with different FTAI protocols. The percentages with different letters have a significant difference (abc; P <0.05)

The results of these experiments suggest (Figure 2) that the addition of eCG would increase pregnancy rates with FTAI in milking dairy cows in mixed systems. When the three experiments are taken together, the pregnancy rates are significantly higher (P <0.008) in the P4 + EB + eCG treatment (145/298, 48.7%) than in the Pre-synch treatment (117/298, 39.3%)). Conversely, eCG did not increase pregnancy rates in cows that received GnRH at the time of insertion of the device with progesterone, this is probably due to the different follicular dynamics between cows treated with EB and those treated with GnRH. It is necessary to conduct studies to investigate the most appropriate interval between the administration of GnRH and the treatment with eCG in dairy cows in lactation.

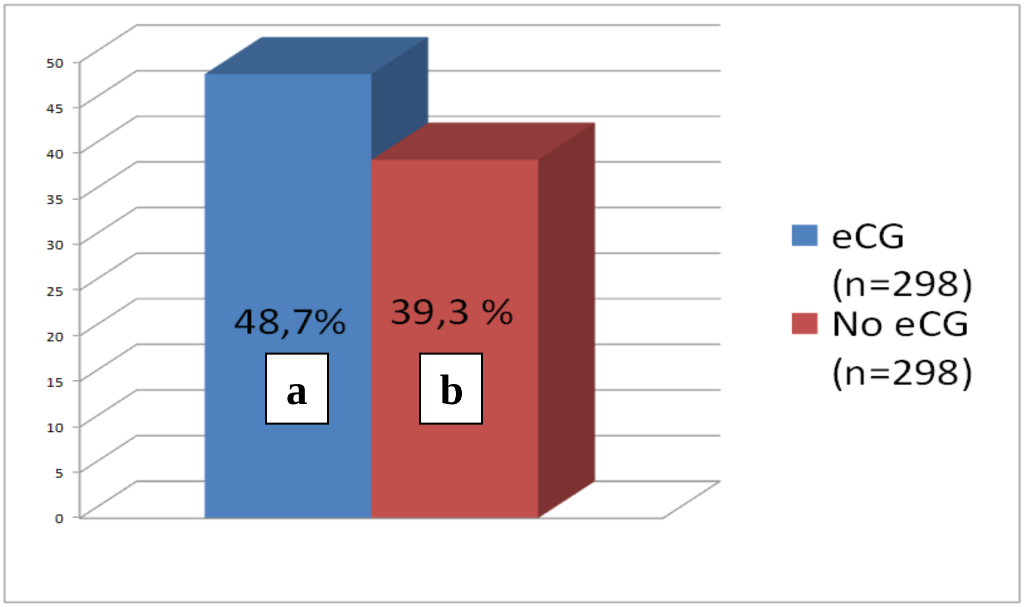

Figure 2. ***Pregnancy Rates in Lactating Dairy Cows in Argentina (all first service at 76±7 DIM) (ab; P<0,01)***

In addition to the results observed in the mixed systems of Argentina, the treatment of dairy cows with eCG together with devices with progesterone and EB has also been studied in an intensive production system in Brazil and in seasonal systems in Argentina and New Zealand. The objective of the Brazilian study was to evaluate the effects of eCG and estradiol cypionate (ECP) on the peak of LH and the conception rate in high production Holstein cows synchronized with protocols for FTAI (Souza et al., 2009). The cows were producing 36.2 ± 0.4 Kg / day with 151.6 ± 3.5 days in lactation. The same hormonal treatment was used in 22 dairy farms (intensive). On Day 0, all cows received 2 mg of EB (Estrogin, Farmavet, Brazil) and a progesterone device (CIDR, Pfizer Animal Health, Brazil). On Day 8, the CIDRs were removed and PGF was injected (Lutalyse, Pfizer Animal Health, Brazil). The cows were randomly assigned to 1 of the 4 treatment groups. Group 1: eCG (400 IU, Folligon, Intervet, Brazil) + ECP (1 mg) on Day 8; Group 2: eCG on day 8 + GnRH (Fertagyl, Intervet, Brazil) at 48 h; Group 3: ECP (1 mg) on Day 8 and Group 4: GnRH at 48 h. In phase I (n = 31), ultrasonography was performed every 12 hours and blood samples were taken every 4 hours from 30 h to 60 h after removal of the CIDR. In phase II, a field study (n = 782) was performed with the same hormonal treatments. All cows were inseminated 56 to 58 after removing the CIDR. The diagnosis of pregnancy was made 30 to 40 days after FTAI by ultrasonography. Despite the use of different drugs to induce ovulation at the end of the hormonal treatments (EPC vs GnRH), there were no differences in the characteristics of the preovulatory peak of LH between the experimental groups (mean 43.5 ± 1.5 h of the CIDR removed). Pregnancy rates in Group 1 (29.1%), Group 3 (30.9%) and Group 4 (28.9%) did not differ. In contrast, the cows of Group 2 had a higher pregnancy rate (33.8%) than those of Group 4 (P = 0.02). In addition, differences in pregnancy rates were more evident among cows with the lowest CC (<2.75); these were higher in cows treated with eCG (44.4%) than in those not treated with eCG (6.1%, P <0.05). In contrast, the pregnancy rates did not differ in cows with CC> 2.75 and treated (32.1%) or untreated (33.5%) with eCG. These results suggest that the eCG increases the pregnancy rate in high production cows, especially in those with low CC.

Another experiment was carried out in a dairy farm, with fix breed season in Argentina (Mian, 2007). We used cows (n = 81) Holstein and Holstein x Jersey with a CC of 2.7 ± 0.3 (scale 1 to 5), producing 21.8 ± 5.1 kg of milk and 132.8 ± 86.2 days in lactation. Groups were formed according to days in lactation and were randomly assigned to 1 of the 2 treatment groups. On Day 0, the cows received a DIB and 2 mg of EB i.m. On day 8, the DIBs were removed; PGF was injected and the groups were subdivided to receive 400 IU eCG or not treated at that time. On Day 9, all cows received 1 mg of EB and were FTAI 54 to 56 h after the device was removed. In order to make the diagnosis of pregnancy, the cows were examined 35 d after the IATF with ultrasonography. The pregnancy rate was significantly higher in cows treated with eCG (21/46, 45.6%) than in those not treated with eCG (8/35, 22.8%, $P < 0.05$).

Another experiment was designed in New Zealand to compare the reproductive response of dairy cows in a pastoral system with breeding season (Bryan et al., 2010). The cows were in anestrus, diagnosed by rectal palpation. Two treatments were assigned. The experiment was carried out in 6 commercial dairy farms. The tail was painted to all cows for 3 weeks and those that did not manifest heat behavior with absence of LC determined by rectal palpation 7 days before the one stipulated to begin with the application (PSM) were selected. All cows received an intravaginal device with 1.56 g of progesterone (Cue-Mate, Bioniche Animal Health) for 8 d, and 2 mg of EB at that time (Day 0) and 1 mg of EB 24 h after removing the device (Day 9). Approximately half of the cows were randomly assigned to receive 400 IU of eCG (Pregnecol, Bioniche Animal Health) on the day of removal of the device (Day 8). All cows were observed and AI were 12 h after heat, those that did not show estrus were IATF at 36 h of the EB dose (60 hs after the device was removed). The results considered were conception rate in the first 48 h, and pregnancy rate at 7 and 28 days. The cows treated with eCG were those that best conceived in the first 48 h (eCG: 48.9%, n = 432 vs No eCG: 43.1%, n = 420, P = 0.059); and had a higher pregnancy rate at 7 days after the end of treatment (eCG: 47.3%, n = 488 vs No eCG: 41.7%, n = 503, P = 0.073). The effect of eCG was greater in cows over 5 years of age, given that they were significantly more likely to conceive within 48 h (P = 0.003, RR 1.52, 95% CI: 1.15 to 2.01) or within 7 days (P = 0.002, RR 1.44, 95% CI: 1.42 to 1.82). In addition, cows older than 5 years treated with eCG were significantly more likely to be pregnant at 4 weeks (P = 0.02, RR 1.21, 95% CI: 1.03 to 1.43). It was concluded that adding 400 IU of eCG on day 8 to the standard regimen of progesterone and EB, increases the probability of pregnancy within 48 h and 7 days, especially in cows over 5 years of age. This experiment is particularly important in staged service farms, where it is essential that cows conceive within the first 90 days postpartum, to achieve the goal of an annual calf. Anestrus rates in some rodeos can be high and an increase of 5% in the conception rate, adding eCG, is very important.

Finally an experiment (Shephard et al., 2013) was made in New Zealand to compare the performance of intravaginal devices containing 1.0 g (DIB) or 1.38 g (CIDR) progesterone and to determine the efficacy of inclusion of eCG into progesterone-based anoestrous cow treatment protocols for New Zealand dairy cows. Anoestrous cows (n=1,906) from 12 herds were randomly assigned to four treatments: 100 µg gonadorelin (GnRH) at Day -10; 500 µg cloprostenol at Day -3; 100 µg GnRH at Day -1 and FTAI on Day 0 (gonadotrophin-prostaglandin-gonadotrophin [GPG] group, n=475); GPG with CIDR device (1.38 g progesterone) inserted between Day -10 and Day -3 (CIDR group, n=477); GPG with DIB device (1.0 g progesterone) inserted between Day -10 and Day -3 (DIB group, n=477); and DIB with 400 IU eCG at Day -3 (DIB + eCG group, n = 477).

Conception rates to FTAI and pregnancy at Day 28 were analyzed using generalized estimating equations (GEE). Time to conception and time to return to oestrus were analysed using Kaplan-Meier survival analysis and Cox's proportional hazards regression. The proportion of cows conceiving to FTAI was 0.34 (95%CI = 0.29–0.37), 0.38 (95%CI = 0.34–0.43), 0.38 (95%CI = 0.33–0.42) and 0.41 (95%CI = 0.37–0.46) for GPG, CIDR, DIB and DIB + eCG groups, respectively. The proportion of cows pregnant by Day 28 was 0.55 (95%CI = 0.51–0.60), 0.57 (95%CI=0.52–0.61), 0.56 (95%CI = 0.52– 0.60) and 0.63 (95%CI = 0.59–0.67) for GPG, CIDR, DIB and DIB + eCG groups, respectively. There was an interaction between treatment and number of days calved ($p < 0.05$). Cows more than 60 days calved and treated with DIB + eCG had higher FTAI conception and 28-day pregnancy rates than cows treated with GPG ($p < 0.001$). Median interval to conception did not differ between treatments ($p > 0.05$). There were no differences between DIB and CIDR groups for any parameter ($p > 0.05$). The range of the relative risk distribution among herds comparing DIB + eCG to DIB groups was greater than that comparing CIDR to DIB groups for conception to FTAI and pregnancy at Day 28.(Figure 3)

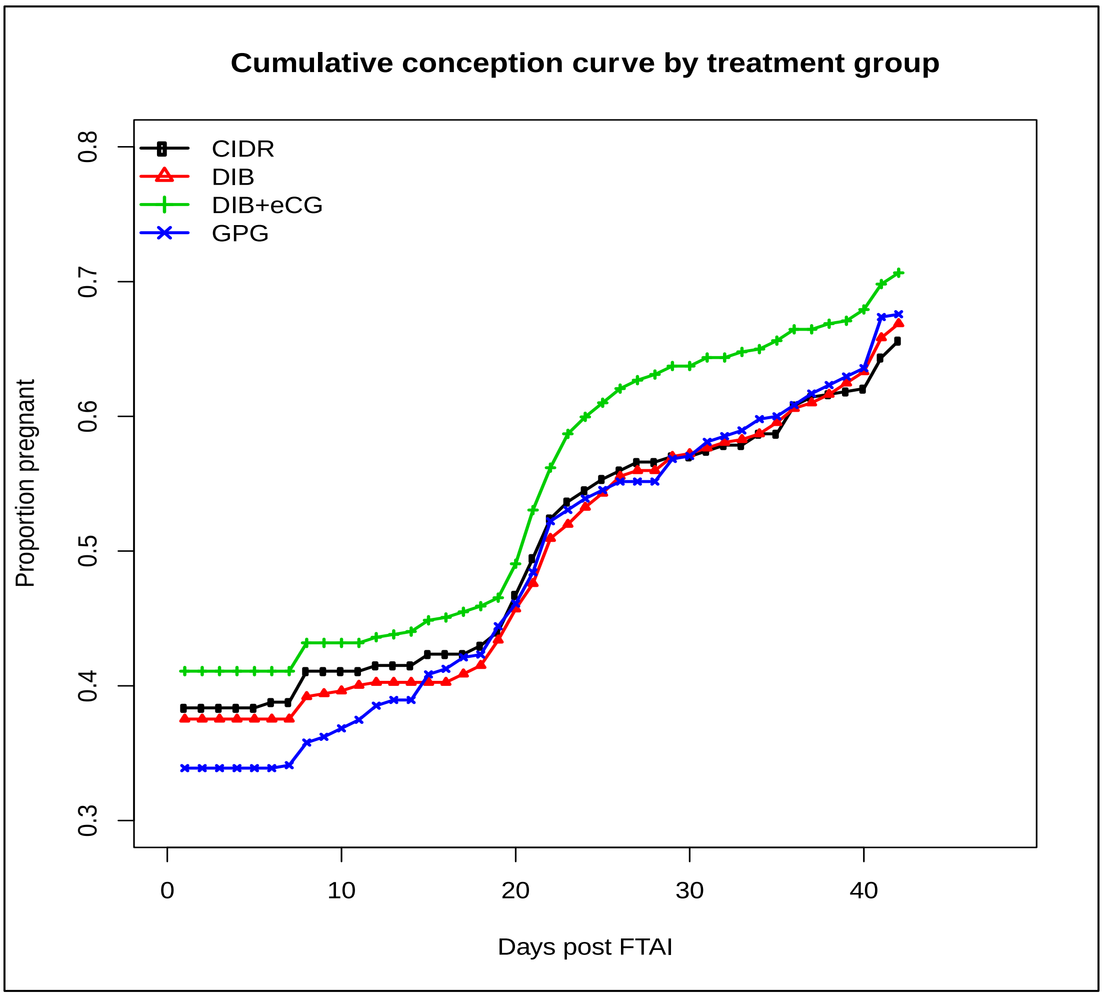

Figure 3. Cumulative proportion of 1,906 anestrous cows conceiving to FTAI from Day 0 to Day 42 following treatment commencing on Day -10 . Cows were treated with either: gonadotrophin-releasing hormone (GnRH) on Day -10, cloprostenol on Day -3 and GnRH on Day -1 (GPG:); GPG with a CIDR device (CIDR:); GPG with a

DIB device (DIB:); or DIB with 400IU of equine chorionic gonadotrophin on Day -3 (DIB + eCG:).

Conclusions

Increased milk production in modern cows has led to reduced conception rates and a greater demand for new tools for the management of reproduction. In the future, reproductive management programs should be adapted to each establishment. The tendency is that the herds are getting bigger, the workforce less trained and the profit margins smaller. Therefore the need for training and technology will be critical to succeed. The investigation of hormonal control of the estrous cycle and, specifically, the follicular wave patterns has improved the knowledge base for the development of synchronization programs and made possible a close synchrony between estrus and ovulation. Probably, the evolution of recommended programs will continue as basic knowledge increases and new approaches are envisioned. Undoubtedly staying informed and well advised is the key to success.

Reference

Bó GA, Cutaia LE, Souza AH, Baruselli PS. 2007. Systematic Reproductive Management in Dairy Herds. New Zealand Veterinary Association (NZVA) Conference 2007, Dairy Cattle Conference, Christchurch, New Zealand (disponible on line en SciQuest), 155-168.

Bryan MA, Bo GA, Emslie R, Mapletoft RJ. 2009. Efecto del tratamiento con eCG en vacas lecheras en anestro tratadas con protocolos con GnRH y dispositivos con progesterona por 6 o 7 días. En: VIII Simposio Internacional de Reproduccion Animal, Cordoba, Argentina (Ed. D. Moreno and G.A. Bo) Instituto de Reproduccion Animal Cordoba, CD.

Bryan MA, Bo GA, Heuer C, Emslie FR. 2010. Use of equine chorionic gonadotrophin in synchronized AI of seasonal-breeding, pasture-based, anoestrous dairy cattle. Reprod. Fertil. Dev. 22: 126–131.

Burke JM, de la Sota RL, Risco CA, Staples CR, Schmitt EJ-P, Thatcher WW. 1996. Evaluation of timed insemination using a gonadotropin-releasing hormone agonist in lactating dairy cows. J Dairy Sci 8: 1385-1394.

Caraviellllo DZ, Weigel KA, Fricke PM, Wiltbank MC, Florent MJ, Cook NB. 2006. Survey of management practices related to the reproductive performance of dairy cattle on large commercial farms in the United States. J. Dairy Sci 89: 4723-4735.

De la Sota RL, Risco C, Moreira F, Thatcher WW. 1998. Efficacy of a timed insemination program in lactating dairy cows during summer heat stress. Theriogenology 49: 761-770.

Ferguson JD, Galligan DR. 1983. Prostaglandin synchronization programs in Dairy Herds. Part I, Compendium on Continuing Education for the Practicing Veterinarian 15: 646-655.

Gumen AJ, Guenther M, Wiltbank MC. 2003. Follicular size and response to Ovsynch versus detection of estrus in anovular and ovular lactating dairy cows. J Dairy Sci 86: 3184-3194.

Lamming GE, Darwash AO. 1998. The use of milk progesterone profiles to characterise components of subfertility in milked dairy cows. Anim Reprod Sci 52: 175–190.

Lucy MC. 2001. Reproductive Loss in High-Producing Dairy Cattle: Where Will it End? J Dairy Sci 84: 1277-1293.

Lucy MC, McDougall S, Nation DP. 2004. The use of treatments to improve the reproductive performance of lactating dairy cows in feedlot or pasture based management systems. Anim Reprod Sci 82-83: 495-512.

Macmillan KL, Henderson HV. 1984. Analyses of the variation in the interval from an injection of prostaglandin $F_{2}\alpha$ to estrus as a method of studying patterns of follicle development during diestrous in dairy cows. Anim Reprod Sci 6: 245-254.

Macmillan KL, Peterson AJ. 1993. A new intravaginal progesterone releasing device for cattle (CIDR-B) for estrus synchronization, increasing pregnancy rates and the treatment of post-partum anestrus. Anim Reprod Sci 33: 1-25.

Macmillan KL, Burke CR. 1996. Effects of oestrus cycle control on reproductive efficiency. Anim Reprod Sci 42: 307-320.

Macmillan KL, Taufa VK, Day AM. 1997. Manipulating ovaries follicle wave patterns can partially synchronise returns to service and increases the pregnancy rate to second insemination. Proc NZ Soc Anim Prod 57:237.

Macmillan, K.L., Colson, D.D., Eagles, V.M. 1999. Modifications to improve whole herd synchrony programs in seasonal dairy herds. Proc Australian Assoc of Cattle Vets, 121-129.

Momont HW, Seguin BE. 1984. Influence of the day of estrous cycle on response to $PGF_{2}\alpha$ products: Implications for AI programs for dairy cattle. 10th International Congress on Animal Reproduction 3: 336.

Moreira F, Orlandi C, Risco CA, Mattos R, Lopes F, Thatcher WW. 2001. Effects of presynchronization and bovine somatotropin on pregnancy rates to a timed artificial insemination protocol in lactating dairy cows. J Dairy Sci 84: 1646-1659.

Murphy, B.D., Martinuk, S.D. 1991. Equine chorionic gonadotropin. Endocr Rev;12:27–44.

Nebel RL, Jobst SM 1998. Evaluation of Systematic Breeding Programs for Lactating Dairy Cows: A Review. J Dairy Sci 81: 1169-1174.

Pursley JR, Mee MO, Wiltbank MC. 1995. Synchronization of ovulation in dairy cows using PGF2α and GnRH. Theriogenology 44: 915-923.

Pursley JR, Kosorok MR, Wiltbank MC. 1997. Reproductive management of lactating dairy cows using synchronized ovulation. J Dairy Sci. 80: 301-306.

Pursley JR, Witbank MC, Stevenson JS, Ottobre JS, Garverich HA, Anderson LL. 1997. Pregnancy rates per artificial insemination for cows and heifers inseminated at a synchronized ovulation or synchronized estrus. J Dairy Sci 80: 295-300.

Pursley JR, Fricke PM, Garverick HA, Kesler DJ, Ottobre JS, Stevenson JS, Wiltbank MC. 2001. NC-113 Regional Research Project. Improved fertility in noncycling lactating dairy cows treated with exogenous progesterone during Ovsynch. Midwest Branch ADSA 2001 Meeting, Des Moines, IA; 63.

Rhodes FM, McDougall S, Burke CR, Verkerk GA, Macmillan KL. 2003. Invited review: treatment of cows with an extended postpartum anestrous interval. J Dairy Sci 86: 1876–1894.

Shephard RW. Efficacy of inclusion of equine chorionic gonadotrophin into a treatment protocol for anoestrous dairy cows. New Zealand Veterinary Journal Vol. 61, Iss. 6, 2013

Souza AH, Viechnieski S, Lima FA, Silva FF, Araujo R, Bó GA, Wiltbank MC, Baruselli PS. 2009. Effects of equine chorionic gonadotropin and type of ovulatory stimulus in a timed-AI protocol on reproductive responses in dairy cows. Theriogenology 72: 10-21.

Stevenson JS, Kobayashi Y, Thompson KE. 1999. Reproductive performance of dairy cows in various programmed breeding systems including Ovsynch and combinations of gonadotropin-releasing hormone and prostaglandin $F_2\alpha$. J Dairy Sci 82: 506-515.

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.

Thatcher WW, Moreira F, Santos JEP, Mattos RC, Lopez FL, Pancarci SM, Risco CA. 2001. Effects of hormonal treatments on reproductive performance and embryo production. Theriogenology 55: 75-90.

Thatcher, W.W., Staples, C.R., Danet-Desnoyers, G., Oldick, B., Schmitt, E.P. 1994. Embryo health and mortality in sheep and cattle. J Anim Sci; 72 (Suppl. 3): 16-30.

Thatcher, W.W., Binelli, M., Arnold, D., Mattos, R., Badinga, L., Moreira, F., Staples, C.R., Guzeloglu, A. 2001. Endocrine and physiological events from ovulation to establishment of pregnancy in cattle. In: Fertility in the high producing dairy cow. 26 Occ Publ Br Soc Anim Sci; 81-91.

Thatcher WW, Guzeloglu A, Meikle A, Kamimura S, Bilby T, Kowalski AA, Badinga L, Pershing R,Bartolome J, Santos JEP. Regulation of embryo survival in cattle. Reproduction 2003, Suppl 61:253-266.

Thatcher, W.W., Bilby, T.R., Bartolome, J.A,, Santos, J.E. 2002. Strategies for improving fertility in modern dairy cow. Theriogenology; 65:30-44.

Vasconcelos JLM, Silcox RW, Rosa GJ, Pursley JR, Wiltbank MC. 1999. Synchronization rate, size of the ovulatory follicle, and pregnancy rate after synchronization of ovulation beginning on different days of the estrous cycle in lactating dairy cows. Theriogenology 52: 1067-1078.

Vasconcelos JL, Sartori R, Oliveira HN, Guenther JG, Wiltbank MC. 2001 Reduction in size of the ovulatory follicle reduces subsequent luteal size and pregnancy rate. Theriogenology 56:307-314.

Veneranda G, Filippi L, Racca D, Romero G, Balla E, Cutaia L, Bo GA. 2006. Pregnancy rates in dairy cows treated with intravaginal progesterone devices and different fixed-time AI protocols. Reprod. Fertil Dev 18:118.

Veneranda G, Filippi L, Racca D, Cutaia L, Bó GA. 2008. Pregnancy rates in dairy cows treated with intravaginal progesterone devices and GnRH or estradiol benzoate and eCG. Reprod. Fertil. Dev. 20: 91.

Wiltbank M, Lopez H, Sartori R, Sangsritavong S, Gumen A. 2006. Changes in reproductive physiology of lactating dairy cows due to elevated steroid metabolism. Theriogenology 65: 17-29.

Wiltbank MC, Gumen A, Sartori R. 2002. Physiological classification of anovulatory conditions in cattle. Theriogenology 57: 21-52.