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Control of Ovarian Function for Fixed-timed AI and Embryo Transfer without Estrus Detection

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Introduction

Elective abbreviation or prolongation of the luteal phase can result in estrus and ovulation within a range of 4 days, which obviates fixed-time AI (FTAI), but is generally acceptable for embryo transfer recipients. The variation in the interval to estrus and ovulation has been attributed to variations in follicular wave status at the time of treatment. Recent protocols designed to control both luteal and follicular status provide new possibilities for synchronization that is precise enough to permit FTAI or transfer of embryos without the need for estrus detection (FTET).

Synchronization of estrus and ovulation

Prostaglandin F2α (PGF) has been most commonly used for synchronization of estrus in cattle (1). Early studies showed that PGF did not effectively induce luteolysis during the first 5 d following estrus, and when luteolysis was induced, the ensuing estrus occurred over a 6-day period. The interval from PGF treatment to estrus and ovulation is determined by the stage of development of the dominant follicle at the time of treatment. These responses emphasize that both luteal and follicular phases must be controlled to precisely control the timing of ovulation. There are several possible ways to control follicular development in cattle. Although follicle ablation is easily mastered, it requires more sophisticated equipment and skill than a hormone injection and consequently, it has been used mainly in superstimulation protocols (1); hormone treatments are commonly used in estrus synchronization protocols.

GnRH and pLH

An injection of GnRH or pLH can induce ovulation of a dominant follicle (10), which will result in synchronous emergence of a new follicular wave, on average, 2 d later. Therefore, protocols that utilize GnRH and PGF have been developed for fixed-time AI in beef and dairy cattle. The protocol known as Ovsynch (13), involves an injection of GnRH followed in 7 d by PGF, an injection of GnRH 48 h later, and FTAI in 0-24 h; Cosynch involves AI at the second GnRH. The Ovsynch protocol has been less efficacious in heifers than in cows primarily because the first injection of GnRH induces ovulation in only about 50% of heifers and more than 80% of cows (11,13). The addition of a CIDR to a 7-day GnRH-based protocol improved pregnancy rates after FTAI in heifers (11), and improved pregnancy rates in non-cycling, lactating dairy cows (15), but not in cycling beef (11) or dairy (15) cows.

Ovsynch protocols have been used to synchronize ovulation in recipients that received in-vivo- or in vitro-derived embryos (reviewed in 1). In two studies, the overall pregnancy rate (recipients pregnant over recipients treated) was higher (P<0.05) following treatment with the Ovsynch protocol (39.1%) than treatment with only PGF (31.3%), because it was not dependent on estrus detection. In another study, pregnancy rates did not differ between recipients treated with an Ovsynch protocol (44.0%) or an Ovsynch protocol plus a progestin for 7 days (Ovsynch+SMB; 49.7%) or recipients transferred 6 to 8 days after detected estrus (39.6%), but more (P<0.01) recipients were selected for embryo transfer in the Ovsynch and Ovsynch+SMB groups. In a field trial involving 1637 recipients treated with an Ovsynch protocol plus progestin for 7 days, without estrus detection, overall pregnancy rate was 59.9%.

Progesterone and estradiol

Poor fertility following prolonged progestin treatment has been attributed to spontaneous maturation of oocytes within persistent dominant follicles. Treatments that induce regression of the persistent follicle have resulted in emergence of a new follicular wave and improved pregnancy rates (1). Although estradiol has been used to induce luteolysis in progestin-based protocols, it also has been shown to suppress antral follicle growth by suppressing circulating concentrations of FSH (1). Following metabolism of estradiol, FSH surges and a new follicular wave emerges. The administration of 5 mg estradiol-17β (E-17β) in progestin-implanted cattle was followed by the emergence of a new follicular wave, on average, 4.3±0.2 d later (1). Intramuscular injections of 5 mg of estradiol benzoate (EB) or estradiol valerate (EV), or 1 mg estradiol cypionate resulted in less synchronous wave emergence (1); administration of 2 mg EB (1) or 2 mg EV (9) resulted in synchronous wave emergence in 3 to 5 d.

Estradiol and progestin treatments have been increasingly used in estrus synchronization programs in beef and dairy cattle (1,2,8). Treatments consist of insertion of a progestin device and concurrent administration of estradiol and progesterone (to synchronize wave emergence) on Day 0, PGF (to ensure luteolysis) at device removal (Days 7-9), and the administration of either a low dose of estradiol 24 h later, or GnRH/pLH at 48-54 h, to synchronize ovulation. Conception rates to a single FTAI were similar to those after detection of spontaneous estrus. In a recent analysis of 10,602 FTAI in beef cattle, pregnancy rate was 53.9% (6). Although pregnancy rates did not differ between suckled cows (55.9%) and heifers (54.9%), nutrition and management critically affected results. Cows with a body condition score (BCS) of 2 or less (1 to 5 scale) had significantly lower (P<0.01) pregnancy rates (27.8% and 46.5% in cows with BCS of 1.5 and 2, respectively) than those with BCS ≥2.5 (52.3 to 57.7%). Furthermore, pregnancy rates were higher (P<0.01) in cycling (56.3%) than in anestrous (47.0%) cows.

A series of experiments evaluated estradiol/progestin protocols to synchronize recipients without estrus detection (1). Treatments evaluated were similar to those used of FTAI (progestin device insertion and an injection of 2 mg EB + 50 mg progesterone on Day 0, PGF at device removal (Days 7 or 8) and 1 mg EB 24 h later. Pregnancy rates to FTET (8 d after the second EB) were comparable to that of recipients synchronized with two doses of PGF 14 d apart and embryo transfer 7 d after an observed estrus. Clearly, acceptable pregnancy rates can be achieved following protocols which synchronize ovulation, without the necessity of estrus detection.

Although the use of estradiol and progestins has eliminated the need for estrus detection, overall pregnancy rates (recipients pregnant over recipients treated) have remained 20 to 35%, requiring improvement (1). Therefore, a series of experiments were designed to determine if the time of PGF treatment in estradiol/progestin protocols would affect the number of recipients selected for embryo transfer. Initiating luteolysis at the time of wave emergence (Day 4) resulted in synchronous ovulation of a larger follicle and higher plasma progesterone concentrations at the time of embryo transfer as compared to treatment at the time of device removal (1). This resulted in more recipients selected for embryo transfer (70.5 vs 52.7%; P<0.02) and higher overall pregnancy rates (41.1 vs 21.5%; P<0.004) following embryo transfer.

Treatments to increase circulating progesterone concentrations and pregnancy rates

Several studies over the years have been aimed at increasing pregnancy rates in cattle by increasing plasma progesterone concentrations. However, supplementary progesterone has inconsistently affected pregnancy rates in recipients (1), and alternative strategies such as hCG, pLH or GnRH on Day 5 (14) or Day 7 (7) of the estrous cycle to induce ovulation and an accessory CL have also produced inconsistent results. The beneficial effects of higher progesterone seem to be evident only when pregnancy rates in controls (not treated) were lower than expected, suggesting that BCS and/or embryo quality may have been contributing factors.

Another approach to increasing circulating progesterone concentrations in recipients is to induce multiple ovulations by injecting eCG during the synchronization protocol (1). Treatment with 1000 or 800 IU of eCG 2.5 d prior to progestin device removal resulted in more recipients selected for embryo transfer and a higher overall pregnancy rate than when animals were treated similarly, but without eCG. It is also noteworthy that plasma progesterone concentrations tended to be higher in heifers treated with eCG (but with 1 CL; n=8), than in those not treated with eCG (n=17). In a follow up-study (1), 400 IU of eCG resulted in only 3/156 cows with 2 CL, but plasma progesterone concentrations and pregnancy rates (48.7% vs 33.9%) were higher than in untreated controls. The current treatment protocol consists of insertion of a progestin device and injection of 2 mg EB on Day 0, PGF and 400 IU eCG on Day 5 (1 day after wave emergence), device removal on Day 8, 1 mg EB on Day 9 and FTET on Day 17. In a recently study (12), administration of eCG on Day 5 increased (P<0.05) plasma progesterone concentrations and tended (P<0.1) to increase pregnancy rates (47.0%) compared to administration of eCG on Day 8 (40.7%); injection of progesterone at the time of progestin device insertion did not affect pregnancy rates. This treatment protocol is currently used to synchronize large groups of recipients in South America; 85 to 90% of treated recipients are selected for embryo transfer, and overall pregnancy rates (recipients pregnant over recipients treated) range from 40 to 50%.

Treatment with eCG has also been shown to increase pregnancy rates to FTAI in suckled beef cows with high incidence of anestrus (3). In three recent studies involving 526 suckled beef cows, the overall pregnancy rate was higher in cows treated with eCG (51.9%) than in untreated controls (38.8%; P<0.05), and this was mainly due to an increased pregnancy rate in cows without a CL (i.e. not cycling) at the beginning of the treatment (3,4).

Resynchronization of non pregnant recipients

Progestin devices have also been used to resynchronize cattle that previously received an embryo or were FTAI (2). Animals receive a new or used device at the time of transfer, or on Days 12 or 13 after estrus. When devices are removed on Day 21, 50 to 60% of the non pregnant animals were detected in estrus on Days 22-25 (2). Cows not detected in estrus were presumed pregnant, whereas those in estrus were AI or examined by ultrasonography 7 d later and if found not to be pregnant were reused for embryo transfer. In another protocol, cows that had been FTAI received a used device and 1 mg EB on Day 13, devices were removed on Days 20 or 21, and 1 d later, 0.5 mg EB was injected (2,8). Although non pregnant (80 to 90%) cows were in estrus within a 5-day period, one must be cautious regarding the choice of dose and estradiol ester, as there is the potential to induce luteolysis, as has been reported in yearling heifers (5). In any case, AI and embryo transfer programs can be designed, utilizing these approaches, to minimize the interval between a diagnosis of non pregnancy and a reinsemination, or transfer of another embryo.

Résumé

Les programmes de synchronisation basés sur le contrôle des phases lutéales et folliculaires du cycle oestral permettent l'élimination de la détection de l'œstrus pour l'insémination et aussi dans les programmes de transfert embryonnaire. Ce sont de plus des opportunités pour améliorer le taux de gestation. Un protocole qui donnerait un taux de gestation de 50% par traitement de synchronisation semblerait rentable, considérant qu'il éliminerait le temps utilisé pour la détection de l'œstrus et, réduirait l'intervalle entre le traitement et la gestation.

References

1. Bó GA, Baruselli PS, Moreno D, Cutaia L, Caccia M, Tríbulo R, Tríbulo H, Mapletoft RJ. The control of follicular wave development for self-appointed embryo transfer programs in cattle. Theriogenology 2002; 57:53-72.
2. Bó GA, Cutaia L, Tribulo R. Tratamientos hormonales para inseminación artificial a tiempo fijo en bovinos para carne: algunas experiencias realizadas en Argentina. Segunda Parte. Taurus 2002; 15:17-32.
3. Bó GA, Baruselli PS, Martinez MF. Pattern and manipulation of follicular development in *Bos indicus* cattle. Anim Reprod Sci 2003; 78:307-326.
4. Bó GA, Cutaia L, Chesta P, Moreno D. The use of eCG to increase pregnancy rates in postpartum beef cows following treatment with progesterone vaginal devices and estradiol benzoate and fixed-time AI. Reprod Fert Dev 2004; 16:127 abstr.
5. Cutaia L, Tríbulo R, Tegli J, Moreno D, Bó GA. The use of estradiol and progesterone devices during mid-diestrus to synchronize return to estrus in beef cows and heifers. Theriogenology 2002; 57:373 abstr.
6. Cutaia L, Veneranda G, Tribulo R, Baruselli PS, Bó GA. Programas de inseminación artificial a tiempo fijo en rodeos de cría: factores que lo afectan y resultados productivos. Proceedings V Simp Internac Reprod Anim, June 27-29, Córdoba, Argentina, 2003; 119-132.

7. Marques MO, Nasser LF, Silva RCP, Bó GA, Baruselli PS. Increased pregnancy rates in *bos taurus x bos indicus* embryo recipients with treatments that increase plasma P4 concentrations. Theriogenology 2003; 59:369 abstr.
8. Macmillan KL, Colson DD, Eagles CM. Modifications to improve whole herd synchrony programs in seasonal dairy herds. Proceedings Aust Assoc Cattle Vets, Hobart, 1999; 121-129.
9. Mapletoft RJ, Colazo MG, Small JA, Ward DR, Kastelic J P. Effect of dose of estradiol valerate on ovarian follicular dynamics in CIDR-treated beef cows. Reprod Fert Dev 2004; 16:130 abstr.
10. Martinez MF, Adams GP, Bergfelt D, Kastelic JP, Mapletoft RJ. Effect of LH or GnRH on the dominant follicle of the first follicular wave in heifers. Anim Reprod Sci 1999; 57:23-33.
11. Martinez MF, Kastelic JP, Adams GP, Cook RB, Olson WO, Mapletoft RJ. The use of progestins in regimens for fixed-time artificial insemination in beef cattle. Theriogenology 2002; 57:1049-1059.
12. Nasser LF, Reis EL, Oliveira AM, Bó GA, Baruselli PS. Effect of time of eCG treatment on pregnancy rates in *bos indicus x bos taurus* recipients synchronized with P4 vaginal devices and transferred without estrus detection. Reprod Fert Dev 2004; 16:212 abstr.
13. Pursley JR, Kosorok MR, Wiltbank MC. Reproductive management of lactating dairy cows using synchronization of ovulation. J Dairy Sci 1997; 80:301-306.
14. Small J, Colazo M, Ambrose D, Mapletoft R, Reeb J, Kastelic J. Pregnancy rate following transfer of in vitro- and in vivo-produced bovine embryos to LH-treated recipients. Reprod Fert Dev 2004; 16:213 abstr.
15. Wiltbank MC, Gumen A, Sartori R. Physiological classification of anovulatory conditions in cattle. Theriogenology 2002; 57:21-52.