Strategies to Improve Reproductive Performance in Cattle

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Introduction

The decline in fertility reported from 1960 to early 2000's (Lucy, 2001) was the motive for prolific research in dairy cows, which in instance lead to identification of multiple culprit factors for this impaired reproductive performance in dairy cattle. (Norman et al., 2009; Santos et al., 2004). Reduced fertilization, embryonic survival, and high prevalence of anovulation in dairy cows compromising detection of estrus, pregnancy per AI and maintenance of pregnancy were defined as the major factors responsible for impaired reproductive performance in dairy cattle (Santos et al., 2004; Santos et al., 2010a). Extensive use of timed AI started with the development of OvSynch program (Pursley et al., 1995), the implementation of daughter pregnancy rate (DPR), the phenotypic measure used by the USDA for daughter fertility (Norman et al., 2009), and use of production life in selection program halted the decline in reproductive performance of dairy cows reported for the previous 40 years. However, DPR is influenced by voluntary waiting period and breeding policy at the farm level, thus it is unclear how much of this improvement is a true function of better fertility, or just implementation of better reproductive management. Herein, reproductive management strategies that empower veterinarians with tools to help dairy producers improve fertility will be discussed with emphasis on its implementation. Although data presented on this manuscript is from dairy cattle, there are many physiological responses and strategies that can be applied to beef cows. I will present some examples to illustrate scenarios for beef cattle during my seminar at the fall conference.

Implications of Estrous Detection Rate on Reproductive Performance

A critical factor determining the success of a reproductive program in dairy operations is the submission rate after voluntary waiting period (VWP). Thus, identification of cows in estrus at each 21 days' interval after VWP is prerequisite to obtain high pregnancy per AI. However, the modernization of dairy cows leading to an increased herd size, use free-stall barns with concrete flooring and to some extent selection of cows focused primarily on milk production made estrous detection a challenging task for dairy operations. Estrus expression is a direct response determined by threshold concentrations of estradiol that reach the hypothalamus of the cow (Allrich, 1994). However, environmental factors such as: treatment of dairy cows with bovine somatotropin, floor surface, lameness, crowding, rain, mud and heat stress are all known to negatively affect expression of estrus in dairy cows (Vailes and Britt, 1990; Allrich, 1994) that might not be necessarily related to concentrations of estradiol can also compromise estrus behavior and should be considered when a investigation on poor reproductive performance is needed. Another issue is that high-producing cows have shorter and less-intense estrus events, which has been associated with increased milk production (Lopez et al., 2004; Yániz et al., 2006). The decline in pregnancy rate is caused by the delayed first postpartum insemination and extended interval between re-insemination in non-pregnant cows that are not estrous detected. Routine monitoring of estrous detection rates and awareness of factors that might jeopardize estrous expression are integral components that needs be addressed by veterinarians in order to help producers overcome fertility issues in dairy operations.

Implications of Anovulation on Reproductive Performance

Another critical factor limiting submission rates of cows directly related to estrus behavior

is the prevalence of anovulation at the end of the voluntary waiting period. Studies conducted in North America revealed that postpartum anovulation after the VWP ranging from 5% to 41.2% at approximately 60 days postpartum (Walsh et al., 2007; Santos et al., 2009). Anovular cows have delayed breeding, reduced P/AI and increased pregnancy loss (Santos et al., 2004; Santos et al., 2009; Chebel and Santos, 2010). If left untreated, anovular cows will have extended interval to first insemination, thereby delaying pregnancy and increasing the likelihood of culling. Herds relying primarily on the detection of estrus for insemination typically do not have routine diagnosis to handle anovular cows and an extended interval to first AI is often perceived only retrospectively when issues with fertility are detected or reproductive performance is evaluated. A clear understand of the importance of anovulation and the use of strategies to proactively prevent its negative impact on fertility are essential for veterinarians assisting producers with implementation of successful reproductive programs.

Strategies to Overcome Issues with Estrous Detection and Anovulation

Throughout the year a plethora of evidence accumulated showing that estrous detection alone usually suffers when compared with management programs that allow for a systematic control of AI (Pursley et al., 1997; Tenhagen et al., 2004; Lima et al., 2009). Foundational work comparing AI after estrous detection demonstrated that even when cows were subjected only to timed AI, with no insemination between pregnancy diagnoses, time to pregnancy was reduced by almost an entire estrous cycle (19 days) compared with insemination based solely on detected estrus (Pursley et al., 1997). Tenhagen et al. (2004) compared insemination rates in two farms in which a portion of the cows were subjected to either AI following detected estrus or after timed AI. When cows were inseminated only after detected estrus, then insemination rates averaged 28.6% and 55.6%; whereas when timed AI was incorporated into the breeding program, insemination rates increased to 65.4% and 69.6%, respectively. A head to head comparison of well-managed natural service breeding program and exclusive timed AI breeding program resulted in similar reproductive performance (Lima et al., 2009), but a reduced cost for pregnancy in cows subjected for timed AI was reported (Lima et al., 2010). It is clear that incorporation of timed AI programs that allow synchronization of follicle growth, luteolysis, timing from ovulation to insemination are an essential tool that veterinarians can utilize to overcome issues with estrous detection and anovulation.

Key Factors to Optimize Fertility of Dairy Cattle

The OvSynch® program comprised of GnRH on day 0, followed by prostaglandin (PG)F2α on day 7, GnRH on day 9, and timed AI on day 10 (Pursley et al., 1995) was the groundbreaking work that served as platform to optimize reproductive physiology aspects needed to optimize fertility in cattle. The biological concepts that support the of timed AI program to improve fertility or at least match reproductive performance of cows inseminated at estrous detected ideal time is based on 3 major premises that are: I. synchronization of follicle emergence and growth; II. synchronization of luteolysis; and III. synchronization timing from ovulation to insemination. Currently, utilization of pre-synchronization program to improve response of actual synchronization protocol; alteration of period of follicle dominance, and manipulation of proestrus length are strategies can be used to optimize timed AI outcomes and fertility of dairy cows.

Implications of Pre-synchronization to Improve Reproductive Performance in Dairy Cattle

A fundamental study by Vasconcelos et al., (2009) investigated timing responsiveness of

the first GnRH of the OvSynch identifying that cows treated between days 5 and 9 of the estrous cycle had higher ovulatory response, a corpus luteum more responsive to $PGF_{2\alpha,}$ and a more synchronous ovulation in response to the final GnRH (Vasconcelos et al., 1999). The findings of the Vasconcelos' study were the motives for development of pre-synchronization programs. Moreira et al., (2001) developed the pre-synchronization program named "Presynch" that aimed to optimize first postpartum AI outcome to cows inseminated after the use of the OvSynch program. The Presynch program is constituted of two treatments of $PGF_{2\alpha}$ administered 14 days apart, followed up the the OvSynch protocol 12 days later improving pregnancy rates when compared with the OvSynch alone (Moreira et al., 2001). Throughout the years this program became the widely used by dairy producers. The reason for the popularity of this program is that beyond improving P/AI in the Ovsynch protocol the Presynch offers flexibility to inseminate cows on estrus after the second treatment with $PGF_{2\alpha}$ reducing the need of timed AI for every cow (Chebel and Santos, 2010). Although the Presynch program was originally designed for a 12-day interval between the pre-synchronization and the first GnRH of the Ovsynch protocol (Moreira et al., 2001), many farms for convenience use 14-day interval to allow giving all the $PGF_{2\alpha}$ injections on the same day of the week. Nonetheless, this alteration compromises response to the first GnRH of OvSynch or similar programs because ovulatory rates are optimum when cows are in early diestrus, between days 5 and 9 of the estrus cycle (Bisinotto and Santos, 2012).

Despite all the benefits of the classic Presynch program the use of $PGF_{2\alpha}$ has a major limitation that is the inability to synchronize estrous cycle and enhance fertility in anovular cows, which might represent up to 41% of dairy cows at the end of the VWP (Walsh et al., 2007; Santos et al., 2009). A potential alternative to overcome this limitation of $PGF_{2\alpha}$ in anovular cows is the incorporation of GnRH during pre-synchronization. Indeed, a pre-synchronization program evaluated at Michigan State University combined $PGF_{2\alpha}$ and GnRH in a program named G6G (Bello et al., 2006). The G6G is comprised of an injection of $PGF_{2\alpha}$ followed 2 days later by a treatment of with GnRH and the initiation of OvSynch 6 days later. The G6G improved fertility compared with cows subjected to the timed AI protocol (Bello et al., 2006).

A more precise comprehensive method to pre-synchronize the estrus cycle of dairy cows and to induce cyclicity in anovular cows is called Double-OvSynch (Ayres et al., 2013). The Double-OvSynch combines the use OvSynch program before the actual OvSynch protocol aimed to have cows inseminated. Recently, couple studies compared the Double-OvSynch with the classic Presynch-OvSynch revealing that the Double-OvSynch outperformed the Presynch in high-producing cows with special advantage for primiparous cows in most of the studies (Souza et al., 2008; Herlihy et al., 2012; Ribeiro et al., 2012a). Therefore, veterinarians have to keep in mind that for herds bearing a high prevalence of anovular cows the use of the Double-OvSynch protocol for the first postpartum insemination is the best choice. However, in herds in which the prevalence of anovulation is low and producers want flexibility to also inseminate cows in estrus, then the Presynch–OvSynch should be considered.

Implications of Follicle Dominance Period on Fertility

Townson et al., (2002) reported that lactating dairy cows with three waves of follicle growth during the estrous cycle have better fertility than cows with two-wave cycles. It has been suggested that the extended follicle dominance in cows with two follicular waves leads to reduced fertility because premature resumption of meiosis by the oocyte originated from follicles having an extended period of dominance (Mihm et al., 1999). A timed AI program was designed to limit the period of follicle dominance (Santos et al., 2010b). This program reduced the interval between

the first GnRH and induced luteolysis from 7 to 5 days showing improvements in P/AI when compared with the 7-day Cosynch 72 program (Santos et al., 2010b). For other animal categories including dairy and beef cattle, reducing the interval between the first GnRH to induction of luteolysis with $PGF_{2\alpha}$ from 7 to 5 days decreased the period of development of the antral follicle by 2 days, resulting in increased P/AI (Bridges et al., 2008; Santos et al., 2010b). Moreover, the reduced period of follicle dominance in the 5-day protocol resulted in the ovulation of follicles that were smaller in diameter (17.1 vs. 18.5 mm; Santos et al., 2010b). These findings are in agreement with the concept of neither too small nor too large needed to optimize P/AI in the OvSynch protocol as revealed by Wiltbank et al., (2011). The 5-d timed AI is certainly an alternative that seems appealing for lactating dairy with two follicular waves and large dominant follicles. Further research comparing the 5-d timed AI with the OvSynch program in lactating dairy cows are required to define the best option for lactating dairy cows.

On the other hand, several experiments in dairy were conducted to improve or simplify the 5-d timed AI program (Rabaglino et al., 2010; Lima et al., 2011; Lima et al., 2013). Based on the potential low ovulation to first GnRH of 5-d timed AI program, Lima et al. (2011) designed a study to investigate the effect of removing the first GnRH of the 5-d timed AI protocol on ovarian responses and P/AI in dairy heifers aiming to simplify the program without compromising fertility. The results of that study revealed no differences in P/AI (No GnRH = 52.1% vs. GnRH = 54.5%); however, ovulation at onset of the synchronization protocol and the proportion of heifers with progesterone concentrations above 0.5 ng/mL at AI was increased for heifers receiving GnRH (Lima et al. 2011). These results suggested that the possible benefits associated with follicle turnover might have been offset by a less effective CL demise in heifers due increased presence of new CL (fewer than 5 days of age) that are refractory to luteolysis after $PGF_{2\alpha}$ treatment (Miyamoto et al., 2009). A followed up study exploited the hypothesis that a combination of GnRH at the initiation of the 5-d timed AI and two injections of $PGF_{2\alpha}$, d 5 and 6 of the protocol, could improve the synchrony of the estrous cycle and fertility responses in dairy heifers (Lima et al., 2013). Indeed, the combination of GnRH with two treatments of $PGF_{2\alpha}$ increased the ovulation at initiation of the program (26.3% vs. 18.8%), the proportion of heifers with progesterone concentrations below 0.5 ng/mL at AI (87.1% vs. 83.0), and the P/AI (61.7% vs. 52.9%), therefore, optimizing fertility of in dairy heifers subjected to timed AI. Therefore, veterinarians should keep in mind that for dairy heifers the 5-day timed AI program is the most appropriate strategy to improve fertility.

Manipulating the Length of the Proestrus and Timing of Insemination

The success of timed AI program is dependent on adequate length of proestrus and proper timing of insemination relative to ovulation. When the classic OvSynch program is used, with 7 days interval between the initial GnRH and $PGF_{2\alpha}$, administering the final GnRH 56 h after $PGF_{2\alpha}$ and performing AI 16 h later lead to the highest P/AI in dairy cows supposedly due to improved synchrony between sufficient numbers of spermatozoa capable of fertilization in the oviduct and the presence of a viable oocyte (Pursley et al., 1998; Brusveen et al., 2008). Contrariwise, for cows subjected to the 5-day timed AI program, which results in smaller ovulatory follicles and reduced concentrations of estradiol in the plasma around the time of insemination compared with the OvSynch protocol (Santos et al., 2010a), the length of proestrus should be extended to 72 h (Bisinotto et al., 2010; Ribeiro et al., 2012b). Therefore, a refined balance involving follicle/oocyte maturation and timing between sperm and oocyte availability must be considered so that optimal fertility can be achieved. Extending the duration of the proestrus during the 5-day timed AI

program compensated for a less optimal interval between induced ovulation and insemination, which allowed for the administration of the final GnRH concurrently with AI at 72 h after $PGF_{2\alpha}$ without rendering P/AI (Bisinotto et al., 2010). Indeed, to extend the length of proestrus in the 5-day timed AI program for dairy heifers and beef cattle consistently improved P/AI (Bridges et al., 2008; Lima et al., 2011). Therefore, strategies to manipulate the proestrus length are a critical factor that veterinarians needed to consider when tailoring a reproductive form different animal categories.

Management Considerations For Implementation of Timed AI in Cattle

The high P/AI achieved for programs such as the Presynch-OvSynch or Double-OvSynch for lactating dairy cows of the 5-d timed AI for dairy heifers and beef cattle, when GnRH and two doses of $PGF_{2\alpha}$ are used, and the potential economic advantages achieved with the implementation of such programs can make timed AI a valuable tool for profitability of dairy farms and in many situations can even facilitate management. Implementation of timed AI can increase submission rates, treat anovular cows and even increase pregnancy per AI in lactating dairy cows and for dairy heifers provide 60% of all heifers pregnant at the first day of eligibility eliminating or at least mitigating the hassle with daily heat detection. Additionally, timed AI can facilitate early submission and re-synchronization of all eligible cows and the creation of homogeneous group of pregnant heifers that can be housed and moved to different groups simultaneously according to farm need. Although implementation of timed AI programs seems a simple task, some managerial aspects needs to be considered before the implementation of successful program can occur. First, each farm needs to evaluate if there is personnel and mindset in the farm to manage the program and mostly inseminate a large group of animals at once without compromising the quality of the service. For large dairy farms, it is important to consider if there is enough personnel and physical room in the maternity pen to handle a relatively large group of animals calving in short period of time. Just as occur for any successful program in dairy farm, a successful program is depending on compliance. The appropriate handling of all lists, injections, CIDR insert and removal is critical component that will separate a program that works from those programs that failed to present satisfactory results.

Conclusions

Implementation of strategies to manipulate the estrous cycle improving insemination rates is an important tool by which veterinarians can help producers to optimize fertility in their herds. Incorporation of timed AI protocols alone or combined with estrous detected insemination has become essential to optimize reproductive management helping to overcome challenges with the detection of estrus either because of poor expression of estrus or the inability of systems in place to identify cows in estrus. Use of pre-synchronization programs that consider nuances such as prevalence of anovulation and tailored strategies that optimize period follicle dominance and length of proestrus have to be considered when designing a program for different scenarios within the farm setting. Besides considering feasibility of a timed AI program to obtain pregnant cows veterinarians also need to consider managerial conditions prior to recommend a specific strategy.

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