Accessory Corpus Luteum in Cattle Reproduction - A Mini-Review

Silviu-Ionuț Borș[1*], Adina-Mirela Ariton[1], Ioana Poroșnicu[1], Alina Borș[2], Amalia-Ioana Hârbu[2], Vasile Vintilă[1*]

[1]*Research and Development Station for Cattle Breeding Dancu, 707252, Iasi, Iasi - Ungheni Alley No. 9, Romania*
[2]*"Ion Ionescu de la Brad" Iași University of Life Sciences, Faculty of Veterinary Medicine, 700489, Iaşi, Mihail Sadoveanu Alley, Romania*

Abstract
In dairy cows, current methods for managing reproduction still need improvement. Future advancements will require new strategies to minimize additional interventions and maintain acceptance among veterinarians. As a result, the development of new therapies in dairy cows' reproduction poses a significant challenge for improving reproductive performances. In recent years, there has been an increasing interest in inducing accessory corpus luteum in dairy cows, but the results have been controversial. It is still uncertain whether this strategy, injecting gonadotropin-releasing hormone (GnRH) or human chorionic gonadotropin (hCG) early in the luteal phase following artificial insemination, can be utilized as a herd management tool to enhance reproduction. Our work suggests that implementing this strategy on the farm is feasible only for repeat-breeder dairy cows with low genetic merit for fertility. In the assisted reproductive technologies this strategy seems to improve reproduction in recipient heifers.

Keywords: dairy cow, embryos, reproduction, repeat-breeding.

Introduction

New technologies and approaches addressing reproductive performance issues in high-yielding dairy farms have been developed in recent decades, resulting from a deeper understanding of the contemporary reproductive physiology of high-yielding dairy cows [1, 2].
Progesterone deficiency significantly contributes to embryo loss, a major cause of low reproductive performance in dairy cows. High-yielding cows undergo increased metabolism, leading to a higher rate of progesterone degradation and lower progesterone concentrations in peripheral blood [3, 4].

*Corresponding author: Borș Silviu-Ionuț, Email: bors.ionut@yahoo.com and Vintilă Vasile, Email: vasilevintilais@gmail.com

The timing of progesterone (P4) increase after ovulation is essential for establishing and maintaining pregnancy [5, 6], as it promotes a suitable uterine environment for embryo elongation [7]. Circulating progesterone (P4) concentrations greater than 1 ng/mL after the first 5 days after artificial insemination (AI), as well as an increase in P4 levels after day 7 in recipient cows, have been linked to a higher likelihood of achieving pregnancy [8, 9].
In contrast, low levels of circulating P4 are associated with reduced fertility [10]. To improve progesterone concentrations after AI, current fertility programs typically rely on a GnRH-induced LH surge to initiate a new follicular wave, trigger ovulation and promote the formation of an accessory corpus luteum (aCL). This process enhances the circulating concentrations of progesterone (P4) during the growth of the pre-ovulatory [11-13]. However, some studies have found that supplementing P4 during embryo

development does not consistently lead to improved fertility outcomes [14-16].
While many promising results have been observed, there is no standard protocol for enhancing aCL formation to improve fertility in high-yielding dairy cows.

Induction of accessory corpus luteum formation using GnRH or hCG in high-yielding dairy cows

The study conducted by Schmitt et al. [17] investigated the induction of an aCL using a GnRH agonist (Buserelin, 8 mg) or hCG (3,000 IU) to boost plasma progesterone levels and enhance conception rates in heifers and lactating cows. The findings revealed that both hormones produced similar effects on the formation of aCL and led to increased progesterone concentrations. However, neither hormone resulted in improved pregnancy rates in heifers and dairy cows during the summer season.
Other research indicates that administering GnRH between days 5 and 15 post-AI can enhance conception rates during the warm season by about 15 % [18, 19]. Our previous study [20] showed that administering GnRH 7 to 14 days after artificial insemination (AI) enhanced reproductive activity in repeat breeder cows. This finding suggests that administering gonadorelin later in the luteal phase may enhance the embryo survival in infertile repeat breeder dairy cows [20]. In contrast, administering GnRH on day 5 after AI in natural estrus or the OvSynch protocol did not improve reproduction in high-yielding dairy cows [21].
Similar findings have been observed with exogenous progesterone administered through the CIDR intravaginal delivery device [22].
According to the study of Doležel et al. [23], administering gonadorelin to induce aCL formation was more effective in cows treated on day 5 after AI, compared to those treated on days 6 or 7. Yan et al. [24] found that administering progesterone to dairy cows between 3 and 7 days after AI was beneficial, whereas treatment given earlier or later did not yield any advantages. Additionally, another study, such as Besbaci et al. [25], has shown that administering GnRH 10 days after AI can also lead to pregnancy following AI.
A large study conducted on six farms found that administering hCG on day 5 after timed artificial insemination (TAI) increased the pregnancy rate (P/AI) by 10% in treated primiparous cows compared to the no treatment control group. However, this treatment did not have any effect on multiparous cows [26].
A recent study revealed that administering ≥2,000 IU of hCG results in higher ovulatory efficiency compared to GnRH (86 μg of gonadorelin) when applied on day 7 after AI in lactating dairy cows [27]. Additionally, Cabrera et al. [27] found that cows treated with 2,500 IU of hCG exhibited a more significant increase in serum P4 concentrations from days 7 to 14 after AI, as well as a greater total luteal size on day 14 [27]. These results may be attributed to the formation of a new aCL combined with the luteotropic effect of hCG on the original CL, since hCG binds to LH receptors in the corpus luteum and may increase the P4 secretion capacity of luteal cells [28].
Furthermore, hCG reduced the number of multiparous cows returning to estrus [29], suggesting that the aCL induced by hCG may influence luteal and luteolytic dynamics.

Accessory corpus luteum regression

Treatment with GnRH or hCG administered on days 5 to 7 after AI produced aCL in 70 to 90% of the cows [30, 31] and increased circulating P4 levels [31]. Several studies have found that the induction of aCL results in higher progesterone concentrations and improved conception rates in dairy cows [32-36].
When aCL is induced via hCG or GnRH treatment early in the luteal phase, CL regression occurs in lactating dairy cows during pregnancy [30, 37]. Regression of the aCL primarily occurs in the aCL that is contralateral to the original CL. However, no clear explanation has been provided for this phenomenon [30, 37, 38].
Accessory corpus luteum regression during either early (days 19–23) or late (>45 days) pregnancy resulted in a ~40% reduction in circulating P4 [37].
Consistent with the findings of Baez et al. [30] and the study by Monteiro et al. [37], there are two crucial periods during which the contralateral accessory aCL underwent regression. The first occurred during the first month of pregnancy, with 30.8% of cows experiencing earlier aCL regression. The second period was noted in the second month of pregnancy, where 69.2% of cows

exhibited later aCL regression. The timing of aCL regression not only influenced circulating P4 concentrations but also affected the incidence of pregnancy loss [37].

Some studies show that pregnancy loss is higher when aCL regression occurs early in pregnancy [37]. This indicates that administering hCG to enhance conception rates may pose a risk of pregnancy loss. However, in the previous study, pregnancy diagnosis was conducted on Day 26 after AI, solely using the measurement of pregnancy specific protein B assay (PSPB), without confirming the presence of a living embryo. It remains uncertain whether the regression of the aCL contributes to pregnancy loss. However, the study by Bui et al. [39], found that pregnancy loss might not occur even if the aCL regresses after fetal detection. When hCG administration is used to promote conception rates, it can be suggested that although regression of aCL occurs during pregnancy, this regression does not increase the risk of pregnancy loss Bui et al. [39].

During pregnancy, the ipsilateral accessory corpus luteum (CL) did not regress, while most of the contralateral CLs had regressed by 63 days. This provides evidence for local mechanisms that contribute to the regression of the aCL and the protection of the CL during pregnancy [37].

Understanding the mechanism behind the regression of the aCL during pregnancy is important, as it may illuminate the processes that lead to luteal regression before pregnancy loss occurs. Gaining insight into how CL regression occurs during pregnancy could help reduce the risk of pregnancy loss.

Accessory corpus luteum in embryo transfere procedures

There have been few studies examining the effects of giving either GnRH or hCG on the day of embryo transfer (ET). Furthermore, most of these studies have small sample sizes and their results are inconsistent, with some revealing no change and others demonstrating beneficial impacts on pregnancy per embryo transfer (P/ET) [16, 40, 41]. A recent study by El Azzi et al. [42], with a large sample sizes, investigates the impact of administering GnRH or hCG immediately before ET on pregnancy rates per embryo transfer (P/ET), pregnancy loss and calving outcomes in a significant number of recipient dairy heifers and cows receiving *in vitro* produced (IVP) embryos.

Vasconcelos et al. [40] studied the effects of GnRH or hCG administered either 7 days after TAI or on the day of ET in lactating synchronized Holstein cows. In this study, the overall P/ET were 45.2% on day 28 and 37.4% on day 60. They found that administering GnRH or hCG 7 days post-ovulation improved conception rates in lactating dairy cows undergoing ET, but not in those subjected to TAI.

García-Guerra et al. [16] found that administering GnRH on day 5 of the estrous cycle had no effect on pregnancy rates in heifers that received fresh IVP. However, they noted that GnRH treatment on day 5 reduced pregnancy losses between days 33 and 60 of gestation in heifers receiving expanded blastocysts, with loss rates of 15.2% for treated heifers, compared to 27.1% for untreated heifers. Similarly, Niles et al. [41] reported that recipient heifers treated with hCG experienced lower pregnancy losses than controls, with rates of 10% and 22%, respectively.

In the study conducted by El Azzi et al. [42], the overall pregnancy rate per embryo transfer at 37 ± 3 days of gestation was found to be 56.5%. The treatment for the formation of an aCL did not have an impact on the overall P/ET or calving rate per embryo transfer [42]. This overall P/ET was considered high compared to studies that induced aCLs in recipient dairy heifers or cows using GnRH or hCG [40, 41].

Overall, the treatments for aCL formation did not significantly impact the P/ET or calving per embryo transfer, nor did they affect pregnancy loss. However, the high P/ET results observed in this study may have diminished any potential benefits of GnRH or hCG on the day of embryo transfer [42].

Conclusions

In conclusion, repeat-breeder or infertile cows can be treated with GnRH during the luteal phase after AI. This is because an aCL can compensate for low progesterone levels, reducing the risk of embryo loss and pre-term labor. Therefore, implementing this strategy on the farm is feasible only for cows with low genetic merit for fertility. In ET programs, this strategy does not appear to improve the overall P/ET or calving rate/ET in cows, but there seems to be a tendency for

improvement in P/ET for heifers. However, the success of these interventions is highly dependent on the timing of administration and the category of the cow (primiparous vs. multiparous).

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