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Pharmacological methods to improve embryo production and pregnancy in sheep and goats

Jeferson Ferreira da Fonseca[1]; Juliana Nascimento Duarte Rodrigues[2]

[1] *Embrapa Caprinos e Ovinos, Estrada Sobral/Groaíras, km 04, CP 145, CEP 62010-970, Sobral, CE, Brazil.*

[2] *Universidade Federal Rural da Amazônia, Campus Paragominas, Rodovia PA-256, s/n, CEP 68627-451, Paragominas, PA, Brazil.*

Abstract

Reproductive efficiency in sheep and goats is significantly affected by early luteal regression and insufficient circulating progesterone ([P4]) levels, particularly under conditions of induced or seasonal estrus and superovulation. This review explores the physiological basis and the effects of pharmacological interventions, especially the administration of human chorionic gonadotropin (hCG), to induce accessory corpora lutea (aCL) with the goal of improving progesterone profiles and supporting embryo production and pregnancy maintenance. Recent studies in Brazil have demonstrated the potential of hCG and other hormonal treatments to enhance luteal function, pregnancy rates, and in vivo embryo production in both cyclic and acyclic females. In addition, potential pharmacological intervention to overcome precocious regression of corpora lutea in superovulated sheep and goats are reported.

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One of the major reproductive challenges in small ruminants is the occurrence of short estrous cycles and early luteal regression, which are often associated with insufficient concentrations of progesterone (P4) required for the establishment and maintenance of pregnancy. This issue is particularly pronounced in seasonally polyestrous species such as sheep and goats . It has been reported that concentrations of P4 levels in ewes during the natural breeding season are higher than in those subjected to estrus induction , suggesting a physiological disadvantage in out-of-season breeding protocols.

To address low concentrations of P4 concentrations, two main strategies have been explored: administration of exogenous progesterone or stimulation of endogenous production via gonadotropins. The latter approach can promote the formation of corpora lutea from either the ovulatory follicle (CLo, during the follicular phase) or accessory ovulations (CLa, during the luteal phase). Accessory ovulations during diestrus have been documented in cattle , and similar findings have been reported in Brazilian studies on cattle, goats , and sheep .

A comprehensive understanding of the endocrine events during the early luteal phase, along with pharmacological modulation of ovarian and luteal function, may offer effective strategies to overcome challenges related to seasonal breeding and suboptimal progesterone levels, thereby improving the outcomes of assisted reproductive technologies in small ruminants. Thus, the aim of this review was to discuss the physiological mechanisms and potential outcomes of hormonal therapies administered early in the estrous cycle, with the goal of enhancing reproductive efficiency and optimizing in vivo embryo production in sheep and goats.

The dynamics of ovarian follicular development in sheep and goats follow a wave-like pattern, usually with three to four waves per estrous cycle, each lasting four to five days . Follicular recruitment and deviation are regulated by follicle-stimulating hormone and luteinizing hormone, and dominant follicles eventually develop luteinizing hormone receptors in gran-

ulosa cells to continue their growth . Seasonal fluctuations in follicular activity, largely influenced by photoperiod, affect the cyclicity of females, particularly in breeds raised at higher latitudes . During the luteal phase, the combined action of progesterone and estradiol reduces luteinizing hormone pulse frequency, restricting the final growth of non-dominant follicles . This suppression, when excessive, may lead to the persistence of follicles and premature luteal regression, a scenario detrimental to reproductive success.

Accessory corpora lutea can be induced through gonadotropin-based interventions administered during the early luteal phase. This approach promotes ovulation of follicles that did not dominate during the follicular phase, especially in the context of diestrus. The administration of human chorionic gonadotropin, due to its luteinizing hormone-like activity, has been the most widely studied method for inducing accessory corpora lutea in small ruminants . Fonseca et al. (2018) demonstrated that ewes treated with 300 IU of human chorionic gonadotropin on day 7 of the estrous cycle exhibited significantly increased luteal area, elevated progesterone levels, and a higher frequency of accessory corpus luteum formation. These findings were supported by Vergani et al. (2020), who reported a pregnancy rate of 81.6% in ewes that developed accessory corpora lutea.

In goats, the administration of hCG has shown equally promising results. reported that goats treated with 300 IU of hCG on day 7 exhibited significant increases in progesterone concentration and achieved a 100% pregnancy rate in animals that formed accessory corpora lutea. Rodrigues et al. (2022; 2023a) confirmed these results, noting improved luteal characteristics assessed by ultrasonography and robust pregnancy outcomes in hCG-treated goats.

In addition to improving pregnancy outcomes, these strategies have been associated with enhanced in vivo embryo production. Premature regression of the corpus luteum (PRCL) is one of the main limiting factors in embryo donor protocols. demonstrated that superovulated goats treated with hCG or GnRH 84 hours after estrus onset had reduced rates of PRCL and improved embryo viability. Recent studies have explored complementary strategies to further control this condition. found that a single injection of hCG on day 4 after device removal increased progesterone levels and embryo yield. demonstrated that reinsertion of a progesterone device similarly increased progesterone and embryo recovery at no additional cost. evaluated flunixin-meglumine injections on days 4 to 6 and observed significant increases in embryo viability with low additional cost, supporting its potential use as an anti-luteolytic agent.

The success of these hormonal strategies depends on several factors, including the physiological status of the animal, its reproductive cyclicity, the breed, and environmental influences such as seasonality. While hCG is widely accessible and cost-effective, its efficacy is largely dependent on appropriate timing of administration, particularly between days 5 and 7 of the estrous cycle, when accessory luteal structures are more likely to form. Combining hCG with other strategies, such as exogenous progesterone devices or flunixin-meglumine, may enhance the therapeutic outcome, especially in the context of embryo donor programs where maximizing recovery is critical.

The current evidence highlights the efficacy of pharmacological strategies to enhance corpus luteum function and increase reproductive success in small ruminants. The formation of accessory corpora lutea via hCG has been repeatedly shown to improve progesterone profiles and pregnancy rates, and more recently, to contribute to the yield of viable embryos. The integration of hormonal protocols such as hCG administration, progesterone supplementation, and luteolysis blockers into reproductive management systems represents a promising advancement for small ruminant production. However, the choice of strategy should be guided by reproductive objectives, economic feasibility, and the physiological status of the herd.

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