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Review Article

New Insights in Uterine Involution and Ovarian Resumption in Domestic Animals

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Abstract

One of the most crucial objectives of livestock husbandry is ensuring that the animals can reproduce without any interference. Each year, one live calf is the ultimate objective of breeding, which increases the milk supply through healthy pregnancies and reduces the time of uterus, spends in the involuted state. There is a long, varying period of sexual quiescence after giving birth. This phase with no cycles is commonly known as postpartum anestrus. The postpartum phase is an essential portion of reproductive life because of its enormous impact on future fertility. From the time of conception until the time when genital organs revert to their pre-pregnancy physiological status, a female is said to be in the postpartum period which is also known as the puerperium. This period is also referred to as the entire postpartum period. Postpartum injections of PGF2α, GnRH, and Oxytocin have been shown to enhance myometrium activity, which helps in clearing lochia after calving. As a result, such postpartum injections decrease uterine involution time and improve reproductive performance, all of which are attempts to reduce the rate of uterine infection, shorten the time it takes for the uterus to go through its natural process of involution, and resume ovarian function earlier. The reason for conducting this research was to summarize the impacts of uterine involution and ovarian resumption as they are influenced by various hormones, including PGF2α, GnRH, and Oxytocin, as well as other factors, including nutrition, season, and minerals.

Keywords: New Insights; Uterine; Ovarian; Resumption; Domestic Animals

Introduction

Postpartum females undergo various physiological and anatomical changes in their uterus and ovaries before regaining their ability to reproduce after giving birth. These changes allow the uterus and ovaries to return to their normal state. During the puerperium, several physiological changes occur, including the involution of the uterus, restoring normal function to the ovaries, resuming regular estrus cycles, and cleansing of the uterine lumen from any bacterial contamination that the birthing process may have caused. The term "involution of the uterus" describes how the uterus returns to its pre-pregnancy size and function following birth. The postpartum ovarian activity must be promptly restored for normal fertility. In postpartum females, the sequence of processes that lead to estrus and ovulation are similar to a regular cyclic pattern, and it is substantially depends on functional connection between the hypothalamus and the pituitary gland [1]. The involution process is complete when the uterine horns have retracted to their pre-pregnancy size and position on the pelvic floor and recovered to their pre-pregnancy tone and uniformity [2]. The size of the uterus shrinks exponentially during pregnancy, which goes from highest to lowest, with the most significant reduction happening in the first few days after calving [3]. The action of the uterine muscles is necessary for the involution process. Having a contractile uterus in the early stages of the postpartum period is beneficial for removing excess fluid and debris from the uterine lumen [4]. The three overlapping processes-contraction, tissue loss, and tissue repair—lead to uterine involution. There are two options for assessing involution: rectal palpation (subjective) or ultrasonography (objective). However, just because the uterus has stabilized in size or weight does not mean that all of its functions have returned. The speed of uterine involution as well as subsequent reproductive performances are dependent on several factors, including parity, season, climate where animals are kept, nutritional value, breed, and health issues both before and after parturition [5].

Uterine involution and ovarian resumption Influenced by Follows

Nutrition

In Cattle and Buffalo when looking at how nutrition affects the uterus, it was found that animals that were over-conditioned during the dry season gained weight and had a body condition score (BCS) of >4, both of which are associated with complications during parturition and, in the end, a delay in uterine involution and placenta retention [2]. The high protein consumption in the diet led to increased amounts of urea throughout the body, most noticeably in the uterus, and a reduction in PH. When urea is induced, production of prostaglandin PGF2α occurs; unfortunately, this reduces the embryo's viability [6]. Silent estrus, delayed postpartum estrus, a reduced ovulation rate and fetal mortality are all outcomes of inadequate prenatal nutrition that persist into the postpartum period [7]. Primiparous cows have exceptionally high nutrient requirements since they must meet their growing demands and nursing requirements in the postpartum phase [8].

In Sheep and Goats, due to the rapid development of the fetus, females have increased dietary requirements during the latter trimester of pregnancy. After delivery, the need for protein and energy peaks during nursing, creating a negative energy balance (NEB). The recovery of ovarian cycles will be postponed for physiological and nutritional anestrus if these demands are not met. NEB has an impact on fertility because it alters follicular development through metabolic and endocrine changes. Both excessive and insufficient dietary intake can impair the ovary's ability to produce luteinizing and follicle-stimulating hormones (LH and FSH, respectively). Changes in hormone levels (metabolic) such as growth hormone, insulin, insulin-like growth factor 1, leptin, and neuropeptide Y may influence the development of ovarian follicles, which are influenced by the animal's internal environment. Gonadotropins and steroids, among other hormones, are crucial in controlling follicle development and are anticipated to act as regulators of how nutrition affects ovulation [9].

Providing Mares with a variety of nutrients (Dietary Algae derived Omega-3 Fatty Acids, L-Arginine supplementation) can speed up the involution of uterine horns, shorten the time it takes for the placenta to expel, enhance blood flow in the uterus and ovaries, and increase the conception rates. L-arginine supplementation in mares enhanced vascular perfusion to the dominant follicle without affecting follicular growth and development. L-arginine supplementation reduced uterine size and fluid buildup in mares. The ability to reduce uterine fluid accumulation without affecting follicular development suggests that L-arginine supplementation could be used as a breeding control technique during the postpartum period to boost reproductive success [10]. The supplementation of 100 g/d L-arginine to mares enhanced ovulatory follicle perfusion and also helps in decreasing uterine diameter and postpartum fluid accumulation [11].

In Camels, postpartum follicular activity resumes within five days following birth, and by two to three weeks after delivery, excellent conception rates are attained under the effect of good nutrition [12]. Clinical and experimental findings show that diet has an evident influence on ovarian activity. Female follicular suppression occurs when fed with dietary limitation (BCS 2.5), results in decreased CL development, and reduces progesterone levels following ovulation, compared to females with an average BCS of 3.9 [13].

Season

In Cattle and Buffalo, it was observed that uterine involution probably occurs more quickly in the spring and summer [3]. The length of puerperium may also be influenced by the time of year when a female gives birth since uterine involution takes longer in the summer and fall than it does in the winter and spring [14].

In Sheep and Goats, it has been determined that daily photoperiod is the critical factor in seasonal reproduction, with moderating effects from other factors, including temperature, food, behavior, lambing date, and lactation duration [15]. In sheep and goats, the hormone melatonin, released by the pineal gland, modulates the reaction to variations in photoperiod [16]. Night time is the only time when considerable amount of melatonin is released since light acts as a suppressor. Melatonin production has a circadian cycle. As a result, melatonin secretion lasts for the least time on long days and rises on short days [15].

In She Camel, in some circumstances, female camels could exhibit seasonal fluctuations in follicular activity, which might be partly controlled by photoperiod. Since all camelids species are induced ovulators, follicular waves develop in an overlapping pattern in the absence of an ovulatory stimulus (mating or hormonal induction) [17].

In Mares, environment (photoperiod) influences postpartum ovarian activity, raising the possibility that breed variations are caused by environmental conditions. The typical assumption in temperate climates is that they will exhibit foal heat in 10 days and ovulate approximately 12 days after giving birth. However, the actual time from parturition to ovulation was 13.64 days [18].

Minerals

In Cattle and Buffalo, it was discovered that when there was a significant lack of calcium, poor production was linked to it. Infertility can be decreased by an irregular estrous cycle, endometritis, and follicular cysts caused by a sodium deficiency and an associated potassium excess [19]. It was discovered that when significantly lacking calcium, poor productivity has been attributed to it. Cows with a diet substantial in calcium and vitamin D experienced quicker uterine involution, shorter service waiting times, and fewer days open [20]. Postponed ovulation, ovarian cysts, and embryonic mortality are all possible side effects of vitamin A deficiency [1].

Sheep and Goats, when overfed, have higher protein and calorie intake, which positively impacts the most oversized follicle diameter during an ovulatory wave [21]. Increases in folliculogenesis are brought on by high-energy meals that augment nutrition, enhance folliculogenesis, and dampen adverse reactions [22].

Mares that were given nutritional supplements with algae-derived omega-3 fatty acids the day of impact showed a gradual decrease in size of uterus beginning on day three and continuing until day 15 postpartum, as well as between days 4 and 7 post-partum. The ALG group displayed a smaller uterine circumference during the first 15 days after delivery [23].

In She Camel, iodine supplements at a level of 1 mg/kg significantly improved the reproductive performance of lactating camels, as measured by the shortest time of the first heat onset; days open (DO), the number of services per conception (NSC), time of placental drop, uterine involution, and the calving interval. Iodine treatment also yielded the highest conception rate [24].

Prostaglandin $PGF_2\alpha$

In Cattle and Buffalo Prostaglandin treatment within 6-12 hours of calving to stimulate involution significantly influenced the duration of uterine involution and improved Friesian cow reproductive performance regarding conception rate [25]. The buffaloes treated with PGF2α required a short period of almost 22.75 ± 0.91 days. Uterine involution and first service conception rates were highest: 41.66%, indicating that PGF2α therapy is beneficial for improving postpartum fertility in buffaloes [26]. The following advantages came about as a result of PGF2α therapy and the puerperal phase follow-up protocol.

- Spontaneous placenta elimination occurred in 78.34% of the cows under study.
- 75.00% of the cows in the study had estrus and were inseminated within less than two months following calving [27].

PGF2α has a crucial role in ovarian and uterine development. Increased PGF2α production in the postpartum is inversely related to the time it takes for the uterus to finish contracting and for regular ovulation to resume [28]. Ovarian activity was promoted during the early postpartum interval and played a crucial role in ovarian and uterine development. Ovarian activity was elevated in the early postpartum PGF2α injection. Utilizing PGF2α between days 14 and 28 postpartum has been shown to hasten the return of regular estrus cycles in postpartum females [29]. When administered between days 14 and 18 following calving, PGF2α decreased the number of open periods [28]. The relatively short postpartum period and fewer days open were seen in PGF2α treated pluriparous dairy cows on day eight following calving [30].

In Sheep and Goats, by having a direct ecbolic impact on the uterus and raising the uterine muscle's tone, PGF2α accelerates uterine involution. The lack of a luteal structure also activates the uterine smooth muscle, aggravating uterine involution and postpartum estrus. Early in the post-partum phase, the exogenous PGF2α administration drastically reduced kidding intervals [31]. After injecting prostaglandin, uterine involution happens on a decreasing logarithmic scale. The uterus shrinks and contracts rapidly from day 3 to day 10 post-partum, as measured by uterine weight and length measurements, uterine body diameter, and the previously gravid horn [32]. Sheep treated with PGF2α, the diameter of the uterine horn reduced dramatically from (6.50 0.45) cm at the first week post-partum to (1.12 0.12) cm at the fourth week post-partum (28 -30) days after birth thus, uterine involution will complete around day 22 [33].

In Mares, uterine contractility is required for the elimination of intrauterine fluid following bacterial infusion in cyclic mares, as well as for the quick reduction of the enlarged post parturient uterus to its pre-gravid form. Various techniques have been studied in an attempt to change mare involution. The most common are PGF2α analogues [34]. For 40-60 min after injection, PGF2α or its analogs enhance uterine contractile activity and pressure. Following the bacterial infusion, uterine contractility is required for the removal of intrauterine fluid. In cyclic mares, persistent mating-induced endometritis is mediated by decreased uterine contractility [35].

In She Camel, uterine involution is thought to occur quickly in camels as micro-cotyledonary; thus in these species, the diffuse nature of the placentation does not result in a significant loss of uterine tissue [36]. Under the effect of PG, the mean intervals for complete involution of the previously-gravid horn into the non-gravid horn were 34.33 ± 3.9, 42 29.01 ± 0.81 days. The decrease in the previously gravid horn's mean diameter was faster between days 3 and 24 postpartum [37].

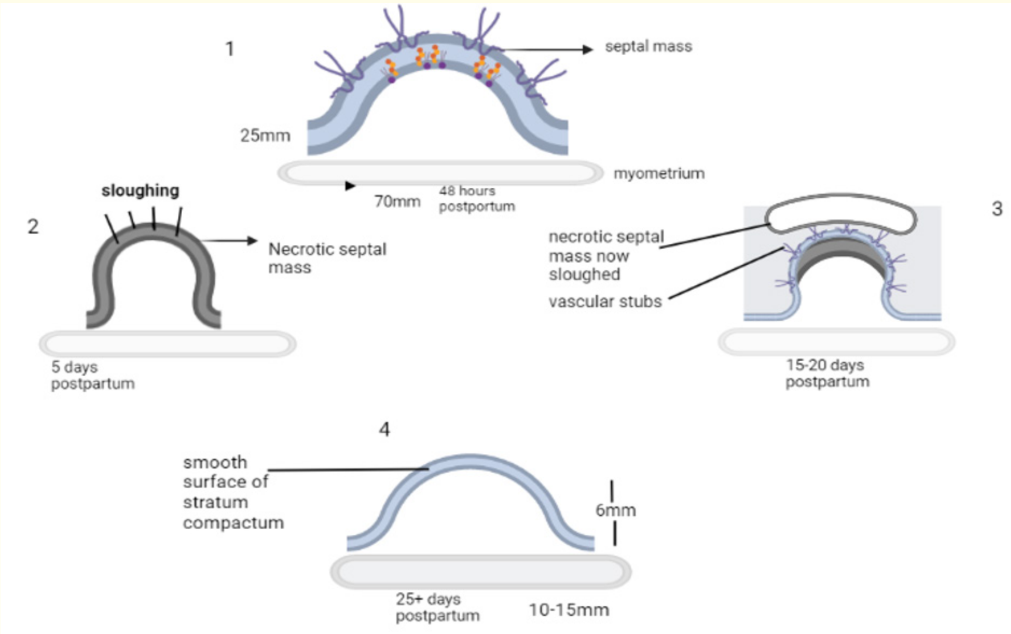

Figure a: Mechanism of Uterine Involution

GnRH

In Cattle and Buffalo, therapy with GnRH was anticipated to accomplish the following reproductive goals: 1-to begin cycling by the third week after giving birth; 2-to have their uterus involuted and be free of infection by the fourth week after giving birth and 3-to exhibit estrus behavior during their second cycle.in six cows with a plasma progesterone level of less than one ng/ml treated with 1.5 mg GnRH during the postpartum period (days 12-18), follicular development was observed in their ovaries on the same day of the GnRH injection, with ovulation one day later [38]. Postpartum dominant follicles fail to mature due to insufficient LH pulse frequency, which results in low androgen production in the follicle and insufficient estradiol positive feedback to induce an LH surge, which is required for follicular terminal maturation prior to ovulation. The absence of LH pulses between days 15 and 30 postpartum is owing to the hypothalamic GnRH pulse generator's persistent sensitivity to the negative feedback impact of estradiol-17, which results in the absence of GnRH pulses. The administration of GnRH will overcome the insufficient secretion of pituitary LH in the early postpartum period and restore ovarian function earlier in the postpartum period, as well as aid in cleansing the uterus, bringing about faster uterine involution, terminal maturation, and ovulation of the dominant follicle [26]. GnRH injection two weeks post-partum triggers ovulation and the release of LH [39]. A single GnRH injection was also shown to trigger ovulation and an LH surge in dairy cows between days 10 and 18 postpartum [40]. It has been documented that LH bursts and complete dominant follicle development are induced by intermittent intravenous injections of a low dose of GnRH in postpartum cows. As compared to the control cows given saline, cows given GnRH (200ug) between days 10 and 14 postpartum experienced a decrease in the time between the first ovulation and the first detected estrus, as well as an increase from 57% to 83% in the percentage of cows that ovulated three or more times prior to the first service [40].

In Sheep and Goats, postpartum ovarian cyclicity is induced when GnRH is administered, and these animals experience either direct or indirect effects on their ovaries [31]. Several studies have found that GnRH therapy improves fertility by increasing the frequency of estrus and ovulation.

Sheep's administered with GnRH between days 10 and 14 have higher fertility. After GnRH treatment, both the number of days open and the number of services per conception were reduced. Fertility improvement was linked with a higher frequency and occurrence of ovulation and estrus before first services and the re-establishment of normal-duration estrous cycles before six weeks postpartum. Early postpartum treatment of sheep and goats with GnRH can boost their fertility, suggesting the prospect of increasing kidding frequency (3 kiddings in 2 years) as a significant goal for improving production [41].

In She camel, when a huge follicle of about 0.9 cm in diameter was observed in either of the ovaries, she was given 20 g of buserelin acetate. The dominant follicle (DF) was found to be affected by GnRH agonist treatment. The lack of the dominant follicle, followed by the identification of the corpus luteum, was regarded as a sign of ovulation [37]. If GnRH treatment is given after parturition in the interval of 26.16 ± 3.24 days (17-34 days postpartum) then she camel will ovulate as a result of the GnRH agonist. Ovulation will occur between 57.64 ± 12.46 hours after treatment. At the time of the GnRH administration, the ovulatory follicle's average size was in the range of 0.9-1.5cm. Then corpus luteum was initially reported by day 4.2 ± 1.64 after GnRH treatments. The majority of the females experienced ovulation-inducing GnRH therapy. When the developing follicle measures around 0.9–1.9 cm in diameter, ovulation induction is most effective [42]. Conversely, when the DF is between 2.0 and 2.9 cm, the ovulation rate is drastically decreased to 20%, and no therapy will cause follicles larger than 3.0 cm to ovulate. Giving camels either 3000 IU hcG or a 20 g GnRH analogue could induce ovulation in them [43].

In Mares, during recent years, pharmacological techniques for inducing ovulation in anovulatory mares have primarily focused on the utilization of natural GnRH and several synthetic agonists. Continuous subcutaneous infusion of native GnRH at relatively low levels (2.5-5 mg/h) can successfully promote follicular development and ovulation in more than 80% of mares with persistent anovulation during the breeding season. Larger doses of continuously administered GnRH successfully induced earlier ovarian activity when initiated after the winter solstice, when normal processes associated with spring transition were underway or imminent, and in mares exhibiting persistent an ovulatory state during the breeding season. Mares that were given native GnRH had higher LH concentrations on the day of ovulation [44].

Oxytocin

In Cattle and Buffalo, it was found that the oxytocin treatment given at 0 hours after calving with the intention of stimulating involution had a noticeable impact on the conception rate and on the length of days open but had little impact on the diameter of the uterine horns [25]. It is indicated that administering either 50 IU of oxytocin or 0.35 mg of carbetocin, an oxytocin analogue, intramuscularly will elicit a similar uterotonic effect in healthy early postpartum cows between 14 and 16 hours after parturition [45].

Sheep and Goats treated with oxytocin at day 7 post-mating showed that the average number of distinct follicles, CL, and their sizes were larger [46]. After injecting oxytocin, uterine involution happens on a decreasing logarithmic scale. The uterus shrinks and contracts rapidly from day 3 to day ten postpartum, as measured by uterine weight and length measurements, uterine body diameter, and the previously gravid horn [32]. Uterine horn diameter decreased in ewes treated with oxytocin from (6.45 ± 0.25) cm at the first week post-partum to (1.70 ± 0.12) cm at the fourth week post-partum, so that uterine involution will complete around 24 to 28 days [33].

In Camels on the basis of trans-rectal examination uterine involution was recorded to be completed by the interval of 40 ± 2 days. The mean intervals for complete involution of the previously gravid horn, non-gravid horns, and cervix, according to ultrasonographic examination, were 34.33 ± 3.9, 42 .29 ± 0.81, and 28.71 ± 1.51 days, respectively. The reduction in the mean diameter of the previously gravid horn was significant between days 3 and 24 postpartum and non-significant after day 17 [37]. A prior study in camels found similar results, with uterine involution finished by days 25-30 [47].

In Mares, Oxytocin doses of 20 to 50 IU/mare can be administered to promote uterine involution. The uterine response is larger after 10 IU oxytocin than after 25 IU oxytocin [48] demonstrated that contractile activity and length of response for 20 and 40 IU oxytocin were greater than for 5 and 10 IU indicated the administration of 20 IU oxytocin for uterine clearance. In this trial, 30 IU/mare oxytocin was given [49]. It is possible that the following factors contributed to the inadequacy of oxytocin medication to promote fluid evacuation from the uterus or reduce uterine size.

- The inability of forced contractions to either reduce the size of the uterus or eliminate fluid.
- The inability to put on uterine contractions that endure for an extended period of time [50].

Conclusion

In conclusion, postpartum therapy with PGF2α, GnRH, and Oxytocin in dairy cattle, buffalo, sheep, goats, and mares with the goal of stimulating involution resulted in a substantial influence on the duration of involution while also enhancing reproductive performance in terms of conception rate.

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