



The Role of Certain Specific Hormonal Treatments in Estrus Synchronization of Ewes: A mini Review

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Abstract

Reproductive function is the cornerstone in achieving better profitability for sheep; researchers have developed several ways to guide the reproduction of ewes and develop their reproductive efficiency by its needs. This contributed to reducing the vaccination season and the timing of births in ewes during a limited year to provide optimal care conditions. The optimal use of these techniques in the reproductive function enables us to enter estrus, increase the ovulation rate, and the appropriate timing of artificial insemination, which in turn increases the reproductive efficiency of ewes. Therefore, it has become necessary to use modern biotechnologies such as estrus synchronization technology, which is one of the technologies that help reduce the time and effort required to detect estrus by collecting estrus cases in treated animals. By applying reproductive care programs such as synchronizing estrus and increasing fertility using compounds such as injections of human chorionic gonadotropin, gonadotropin-releasing hormone or progesterone after mating and prostaglandin F2alpha, prostaglandin E and melatonin hormone, it may help to be performed at a specific time if combined with ovulation induction programs and continue pregnancy and increase fertility rates. **Keywords: Estrus**

Synchronization, hormones, sheep

Aim of article

This review was aimed to determine the comparative effect of using various estrus synchronization programs to improve the fertility and the sustainability of reproduction and thus pregnancy insurance. Moreover, to review of various hormonal programs were aimed to synchronizing estrus and, as a result, modifying the reproductive path and improving the qualities of reproductive performance in ewes.

Introduction

Reproduction is important to preserve the species and continue production [1]. Due to the seasonality of production in sheep and increase demand for them in certain seasons, it is necessary to follow applied systems to improve reproductive and productive performance throughout the year under

conditions of intensive production. It can be applied by regulating erogenous compatibility in ewes and increasing the rate of twins at times that may be outside the pollination season, which is defined as the period when animal fertility is at its highest [2]. Sheep are seasonal animals with multiple estrus cycles [3]. Estrus synchronization has many benefits, including introducing the largest possible group of ewes in the estrus stage, thus facilitating their pollination and synchronizing their births in the reproductive season [4]. The onset of estrus can be controlled and made in the first week of the season, its off-season events, and the process of ovulation events [5]. There are several widespread ways to synchronize estrus in ewes, including natural methods (Ram effect) or pharmacological methods such as Progesterone hormone, which

is used in the form of vaginal sponges or injection or implantation under the skin at the base of the ears. Also, the hormone prostaglandin or melatonin can be used with variety of successful rate in or out season [6].

The reproductive season of ewes

Sheep are generally classified as seasonal polyestrous breeding animals; the breeding season begins as early as April and lasts until September. The natural breeding season for ewes is concentrated between late June and early September, which allows ewes to give birth between late November and early February [7]. Sheep are animals that depend on the photoperiod through the secretion of the melatonin hormone and other environmental factors such as temperature and nutrition [8]. The reproductive performance of ewes during the year shows a period of sexual dormancy followed by a period of sexual activity during the reproductive season. Several estrus cycles appear until the end of the season, or the female becomes pregnant [9]. The reproductive season of females is regulated by the presence of photosensitizers in the retina of the eye; impulses are sent by the optic nerve and other nerve impulses to the sheep's pineal gland to detect changes in daylight by the biological clock in the hypothalamus, which in turn sends signals by the axons of the gonads through the pineal gland [10]. Ewes' reproductive season appears when the day's length is shortened [11].

Asadi-Fozi et al. [12] pointed out that most species of animals that live in areas confined between 35 north and 35 south latitudes have different animals showing reproductive activity depending on the seasons. The reason is due to the different hours of light and the intensity of illumination, and there is no doubt that light plays an important role in the reproductive season in animals that are active in certain seasons and are sexually inactive in the rest of the seasons [13]. The melatonin hormone is secreted from the pineal gland which plays an important role in the occurrence of these significant changes in the functions of the gonads of animals that are affected by the season. The evidence indicates that the action of the melatonin hormone and

its effect on the gonads occurs at the level of the brain [14], hypothalamus, pituitary and epithelial tissues as the pineal gland plays a pivotal role in for the hormone GnRH from the hypothalamus [15]. Thus, the melatonin hormone indirectly regulates the reproductive season by controlling the secretion of gonads hormones from the anterior lobe of the pituitary gland and their activity is regulated in the reproductive season [16].

The estrus cycle in ewes and related hormones

The length of the estrus cycle in ewes ranges from 14-19 days and an average of 17 days, and usually, the first estrus cycle is at the beginning of the reproductive season for non-adult ewes in which ovulation occurs without signs of estrus, and this is called silent estrus [17]. Cunningham et al. [18] pointed out that ewes have 9-15 cycles per year and an average of 12 cycles per year. The ewes of the tropical and subtropical zone breed all year round, and many researchers have described that ewes have multiple seasonal estrus cycles (Seasonal Polyestrous) [19, 20]. The estrus cycle is divided into two phases, the first of which is the follicular phase and its duration is 3-4 days, and the second phase is the luteal phase (the phase of the corpus luteum), which lasts about 14-15 days, which is characterized by the formation of the corpus luteum and a rise in the level of progesterone as a result of its excretion from the corpus luteum [21]. The day before estrus occurs, one or more follicles grow rapidly, and there is a rise in the concentration of the estrogen hormone in the blood [22]. Estrogen works to show signs of estrus from the sexual acceptance, as well as works to increase the vascularity of the vagina and increase the secretion of watery mucus (a light watery nature) [23]. The LH hormone acts on the occurrence of ovulation, which occurs approximately 14 hours after the LH hormone concentration reaches the peak or 24 hours after the occurrence of estrus [24], and the LH hormone concentration remains low at other times of the estrus cycle [25]. The length of the estrus phase varies depending on the age, breed, presence of the male, the season and ranges from 18-72 hours with an average of 36

hours. The estrus phase in wool sheep is longer than in meat sheep. The duration of estrus is short at the beginning and end of the reproductive season when the male is present and in the first reproductive cycle of early ewes [26]. In the absence of pregnancy, luteinization will occur starting from the 15th day of the estrus cycle as a result of an increase in the concentration of the prostaglandin PGF₂ reaches its highest level on the 15th day of the estrus cycle, and on the 16th the level of progesterone begins to decrease, which stimulates the increased secretion of ovary nutrient hormones FSH, which works on the growth and development of new follicles [27]. The secretion of progesterone is mainly in sheep from the corpus luteum in the first trimester, but after the 50th day of pregnancy, the production of progesterone is from the placenta, and if the dissolution of the corpus luteum occurs, it does not affect the duration of pregnancy (maternal recognition of pregnancy) [28].

Hormonal regulation of the oestrous cycle of the ewes

The Hypothalamus -Pituitary -Ovaries Axis is the main axis that controls the regulation of the reproductive cycle in sheep [29]. The regulation of the estrus cycle requires mutual interference of the endocrine and neuroendocrine mechanism represented by reproductive hormones of the hypothalamus and anterior lobe of the pituitary gland and steroid hormones of the ovaries, as well as interference between the uterus and ovaries [30]. During the period of the end of estrus, progesterone concentrations are at high levels, as it leads to blocking the release of the hormones GnRH, FSH, and LH through the negative feedback mechanism of the hypothalamus and the anterior lobe of the pituitary gland and in case pregnancy does not occur [31]. The prostaglandin hormone (PGF₂ α) is released from the uterus and is released to the ovaries through the uterine-ovarian vein to the ovarian artery, as it leads to luteolytic of the corpus luteum and a decrease in the level of progesterone concentration [32]. As the decrease in the concentration of progesterone works to remove the negative

feedback of the hypothalamus and the anterior lobe of the pituitary gland, and then the impulses of GnRH, FSH and LH begin to be released and then stimulate the growth of ovarian follicles and increase the secretion of estrogen [33], and after 2 or 3 days of a decrease in the level of progesterone concentration, the level of estrogen concentration will reach the concentrations that stimulate the secretion of sufficient levels of gonadal inducers GnRH, FSH and LH before ovulation by positive feedback mechanism for the hypothalamus [34]. The FSH hormone works on the growth and development of the ovarian follicles until they reach maturity, and then it is called the mature follicle; the inhibin hormone is secreted from the mature follicle, as it regulates the release of the FSH hormone during estrus and then prevents excessive stimulation of the follicles [35]. The secretion of the LH hormone before ovulation occurs in the form of waves. The wave that occurs before ovulation is responsible for stimulating the final maturation of the ovum and breaking the wall of the mature follicle and ovulation events [36]. The secretion of the LH hormone occurs before ovulation at the beginning of estrus and lasts for 6-10 hours in most animal species, and the ovulation process occurs after the secretion of the LH hormone for about 24-30 hours in cows and ewes and goats 30-36 hours, and after ovulation, a corpus luteum is formed at the site of ovulation and begins to secrete progesterone 2-4 days after ovulation [37]. FSH, in synergy with estrogen, helps regulate the receptors of the hormone LH on granulosa cells; the secretion of the prolactin hormone Prolactin at the end of estrus also helps to perpetuate the LH hormone receptors on Granulosa cells, and when ovulation begins, the interaction of the LH hormone receptors with granulosa cells, which leads to their conversion into a corpus luteum [38]. The LH hormone works in perpetuating the function of the corpus luteum by increasing the rate of blood flow to the corpus luteum [39].

Estrus Synchronization

It is a technology that enables the ewes within the herd to accept mating and

pregnancy during the same time or close times of the year [40]. The Optimal Use of these technologies in reproductive function enables us to tune in to estrus, increase the rate of ovulation, and the appropriate timing of IVF, which, in turn, increases the reproductive efficiency of agricultural animals [41]. The uniformity of estrus depends mainly on the luteal phase. This phase can be performed by prolonging the presence of progesterone in the blood serum using progesterone. Its derivatives and estrus are controlled and induced in females using techniques that artificially control the balance of hormones through external hormones or other methods that lead to a change in the hormonal balance of the ewe [42]. The technique of estrus synchronization has many benefits; it unifies the time of feeding and childbirth and thus reduces the efforts and expenses spent on caring for newborns, and is useful in raising productive efficiency by obtaining additional births during productive life and is also useful in embryo transfer programs, and determining the date of pregnancy and childbirth, and then facilitates the process of feeding animals in homogeneous groups [43].

Several methods have been used in the process of unifying estrus, including administrative methods such as male influence and artificial control of light, including the use of hormonal treatment, and these hormones include progesterone, which is the best for ease of use and low cost, prostaglandin PGF2 α and melatonin, and treatment with these hormones is usually followed by injections of gonadotropins such as equine gonad stimulating hormone (eCG), human chorionic hormone (hCG) or follicle-stimulating hormone (FSH), the most common is eCG hormone [44].

Treatments of Estrus Synchronization

To synchronize estrus in sheep, several treatments are used, including:

1. Treatment with male pheromones (male effect)

The male effect is meant when the ewes are stimulated outside the cycle (estrus) for ovulation by the sudden presentation of females to the male after isolation, as it leads to stimulation and

synchronization of estrus outside the reproductive season and without additional treatment [44]. Estrus Synchronization using male isolation is one of the cheap and easy techniques by which lambs can be obtained outside the reproductive season [45]. The physiological mechanism of this response depends on the fact that males produce a chemical called pheromone, whose smell stimulates the onset of estrus; exposure to these pheromones stimulates the secretion of LH and is followed by the occurrence of ovulation and the return of active ovarian periodicity [46]. Males are isolated from females for 3-4 weeks. After this period, males are introduced to females, and the response is by increasing the proportion of the hormones LH and FSH, which the sudden introduction of a male induces their secretion through the effect of pheromones and ovulation is 2-3 days after the introduction of males and may be delayed to 4-7 days [47]. Ungerfeld and Silva [48] stated that the process of unifying estrus using male isolation is effective and does not differ in its results from hormonal treatment through a study in which he compared the use of vaginal sponges for 12 days with male isolation for 34 days after which Rams were introduced at the same time as sponges were removed and added that there were no significant differences between the two parameters in the concentration of the LH, FSH, estrogen hormones, follicular growth, time of entry into estrus, ovulation rate, and percentage of pregnancy.

2. Simulation of corpus luteum by exogenous progesterone

In this method, the function of the corpus luteum is simulated by the administration of progesterone. Progesterone suppresses the secretion of gonadotropins and thus prevents ovulation until the source of progesterone is removed [49]. If progesterone is given to a group of females and then withdrawn simultaneously, this will synchronize estrus and ovulation in this group. Initially, progesterone for a period equal to the normal luteal phase length (i.e., 18 - 21 days) [50]. This is a long period for corpus

luteum to undergo a simultaneous decomposition in all animals regardless of the phase of the estrus cycle in which they are at the beginning [51]. Treatment with progesterone for a period of 18 - 21 days resulted in low fertility rates, and this has been attributed to the ovulation of permanent follicles containing ova of inferior quality. The decrease in fertility can also be attributed to the adverse effects of progesterone within the internal uterine environment that affect sperm transfer and life [52].

3. The Use of two doses of prostaglandins

The secretion of $\text{PGF}_{2\alpha}$ by the internal endometrium in a non-pregnant female ends the luteal phase, which causes lysis of the corpus luteum and initiates a new estrus cycle. $\text{PGF}_{2\alpha}$ or one of its analogues can be successfully used for the timing of estrus in periodic ewes during the breeding season [53]. Studies have shown that injections of $\text{PGF}_{2\alpha}$ or one of its analogues during the middle of the luteal phase of the estrus cycle can induce lysis of the corpus luteum in the female, so we can expect to show signs of estrus after about 50 hours. The decomposition of the corpus luteum is followed by an increase in the secretion of estradiol 17 — beta-amino acid and culminates in the secretion of luteinizing hormone wave and then ovulation [54]. The decrease in progesterone concentrations occurs rapidly and steadily, reaching its minimum levels within 30 hours after the injection. The occurrence of ovulation after the injection of $\text{PGF}_{2\alpha}$ can be very variable [55]. The $\text{PGF}_{2\alpha}$ was used in various ways in the synchronization of estrus to reach high synchronization rates after proving the presence of an active corpus luteum by measuring the concentration of the Progesterone hormone and trans rectal examination and after detection of estrus [56]. The possibility of treatment with prostaglandins is limited only to periodic females during the reproductive season. As for the outside of the reproductive season, it is preferable to use progesterone or one of its synthetic analogues like progestagens [57].

4. GnRH in combination with prostaglandins $\text{PGF}_{2\alpha}$

Due to the development of estrus synchronization parameters and ovulation and fertilization control parameters, other alternatives based on the use of treatment with GnRH followed by a dose of $\text{PGF}_{2\alpha}$ have appeared; the use of a program based on treatment with GnRH followed by a dose of $\text{PGF}_{2\alpha}$, gave good pregnancy rates, this led to improved pregnancy rates when using the GnRH- $\text{PGF}_{2\alpha}$ program [58]. This method, called (Ovsynch) Ovulation synchronization or ovulation timing synchronization, is designed in order to reduce the differences in ovulation time, allowing for In vitro fertilization (IVF) to be performed at a specific time, usually using either the GnRH or hCG. Both hormones are effectively time luteinizing hormone waves and ovulation [59]. GnRH is injected at a random phase of the estrus cycle (Day 0), followed by a dose of Prostaglandin $\text{PGF}_{2\alpha}$ on Day 7 and then another injection of GnRH 48 hours later [60].

5. Control of Intravaginal Drug- Release (CIDR)

CIDR is placed in the vagina for 6, 7 or 12 days and sometimes stays 14 days after it is withdrawn, preferably injecting equine gonad stimulating hormone ECG after withdrawal to increase efficiency, after which rams enter at the time of CIDR removal and females reach the climax of estrus 24-48 hours after withdrawal [61]. One of the advantages of CIDR is that it can be used with young ewes (weaning) without causing problems, it is easy to give it, its low cost, as well as the lack of accumulation of vaginal fluids and bacteria because it is made of rubber, which reduces the incidence of vaginal infections while giving it good results in the technique of unifying estrus [62]. Many studies have been conducted to compare the effect of CIDR and vaginal sponges on reproductive performance and find out the best, as reported [63] in a study conducted on a flock of ewes to find out the efficiency of CIDR and compare with vaginal sponges, the results showed that the CIDR group was superior in terms of estrus rate, as it reached 100% compared to vaginal sponges 85.7%, but the pregnancy rate was for the CIDR group 87.4% and the vaginal sponge group 71.7%. As Martinez-Ros et al. [64]

noted that using vaginal sponges and CIDR gave similar results in the percentage of estrus, progesterone concentration, length of pregnancy and reproductive rate in Lacaune multiparous ewes.

6. The Use of the melatonin hormone

The pineal gland secretes the hormone melatonin, and its concentration level rises during the dark period; increased secretion of the hormone melatonin is responsible for inducing ovarian cycles in ewes [65], and continuous administration of the hormone leads to inducing the reproductive season by affecting the hypothalamus gland to secrete the release GnRH hormone and thus the secretion of the hormones LH and FSH from the anterior lobe of the pituitary gland [66]. Treatment of ewes with melatonin improved the reproductive performance of domestic ewes by increasing the fertility rate and the number of additional pregnancies [67]. As Kassim et al. [68] noted, Melatonin treatment at doses 12 and 15 mg/ head showed an increase in the percentage of fertility and twinning in ewes.

Conclusion

By extrapolating the article's topic, it highlights what modern international research has included in the extent of the response of the ewes synchronization methods and indicates the best of them in terms of the vital effect on various reproductive traits of ewes.

Conflict of interest:

The author declare that there is no conflict of interest of this work.

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