DOI: https://doi.org/10.54393/mjz.v4i02.67

MARKHOR
THE JOURNAL OF ZOOLOGY
https://www.markhorjournal.com/index.php/mjz
Volume 4, Issue 2 (July-Dec 2023)

Review Article

Effects of Reproductive Hormones in Dairy Farm Animals

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ARTICLE INFO

Key Words:
Reproductive Hormones, Oxytocin, Progesterone, Prostaglandin, Cattle, Sheep

How to cite:
Javed, M. ., Mazhar, M. ., Hayat, S. ., & Abbas Tahir, M. A. . (2023). Effects of Reproductive Hormones in Dairy Farm Animals: Reproductive Hormones in Dairy Farm Animals. MARKHOR (The Journal of Zoology), 4(02). https://doi.org/10.54393/mjz.v4i02.67

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Received Date: 18th July, 2023
Acceptance Date: 6th September, 2023
Published Date: 31st December, 2023

ABSTRACT

Reproductive hormones are utilized in the dairy industry all over the world to improve reproductive effectiveness and, as a result, dairy cow lifespan. The management system of a farm, especially the sort of calving pattern adopted, appears to be a major determinant of variation between countries. The use of pharmaceutical goods like reproductive hormones and antibiotics in animal husbandry, notably dairy production, has been investigated in the recent decade. Consumer concern about food safety, as well as examples of pharmaceutical product misuse, has led to widespread suspicion about using antimicrobials and hormones in industrial agriculture. Hormones aren't involved in the development of resistant bacteria, yet customers are concerned about hormone residues in animal products. One of the most significant aspects of public perception in dairy farming is food safety. Despite their lack of fundamental understanding of the dairy sector, the public is concerned about using reproductive hormones in modern farming, despite the dearth of information regarding their detrimental consequences. On dairy farmed animals, we looked at the effects of oxytocin, progesterone, and prostaglandin. These reproductive hormones are used in milking animals such as cattle, sheep, and goats to boost milk production, reproductive rate, and developmental processes.

INTRODUCTION

Oxytocin is a nine-amino-acid peptide hormone with a twenty-member ring that is furthermore called as a-hypophamine. It's made by neurons in the hypoxytocinhalamus's par ventricular nuclei and supraoptic nucleus, and it store in the posterior pituitary for blood secretion [1]. Oxytocin is a natural birth hormone with uteroxytocinonic and galactogenic action that is released by the ovaries and testes in animals. Oxytocin is released into the bloodstream in minute amounts (from 15 to 90pg mL1) during the lactation phase of cattle, especially cows and buffaloes. Oxytocin induces constriction of the myoepithelial cells covering the milk alveoli in the mammary gland for milk release down in natural settings [2, 3]. Buffalo are known for their delayed milk ejection responses and stiff teat sphincter muscles, making them slow and hard milkers. Exogenous oxytocin supplementation is absorbed in the circulation, raising the levels, and is retained for at least 2 hours after injection into animals. It is thought that because of oxytocin's tiny size (1 kda), it has the potential to traverse the blood–milk barrier and enter the milk, producing alterations in the susceptibility of mammary gland tight junctions. Long-term oxytocin supplementation in dairy animals, on the other hand, may cause addiction and diminished voluntary milk ejection after oxytocin withdrawal [2, 4]. Oxytocin affects milk production by lowering intra-alveolar pressure as well as the availability of a lactation feedback inhibitor around the alveoli, as well as restoring normal mammary

DOI: https://doi.org/10.54393/mjz.v4i02.67

blood flow. Furthermore, oxytocin is required for the formation of the moxytocinher-offspring link [5]. Milk from milk-producing mammals does not normally include oxytocin, however when administered with hormones such as oxytocin at doses ranging from 0.1 to 20 IU, there is an excess of milk produced with traces of oxytocin. When there is an overabundance of oxytocin in edibles, the consumer may experience headaches, nausea, stomach discomfort, sleepiness, and other symptoms. Farmers in Pakistan are increasingly using exogenous oxytocin to boost milk output [6]. They are uninformed on how to take oxytocin in terms of dose and circumstances. Farmers provide oxytocin injections often due to their ignorance and lack of knowledge, which may affect the content of milk and, as a result, interfere with the purity of dairy products. Animal's oxytocin productive and reproductive efficiency is being lost due to indiscriminate usage of oxytocin without veterinary consultation [5]. Pakistan is predominantly a farming country, and animals take part in the financial system by producing key human food items such as milk, meat, eggs, and other dairy products. Livestock contributes around 55.9% of agricultural production value added and 11.8 percent of national GDP in Pakistan. The population of buffaloes in Pakistan was estimated to be 34.6 million tons in the 2013-14 economic survey. Buffaloes produce roughly 31 252 million tons of milk per year. During 2013-14, milk output was climbed by 3.2 percent, while meat production increased by 4.5 percent [5]. Raw milk is used mostly by the Pakistani population, with the dairy industry processing just 3% of total milk output [7].

Oxytocin

Oxytocin is a nine-amino-acid peptide hormone with a twenty-member ring that is referred as a-hypophamine (Figure 1). It's made by neurons in the hypoxytocinhalamus's par ventricular nuclei and supraoptic nucleus, and its stock in the posterior pituitary for blood secretion [1].

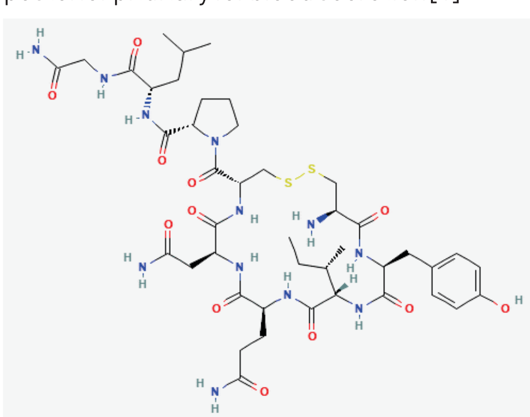

Figure 1: Structure of oxytocin

Effects of Oxytocin Injections on Buffaloes

Buffalo contributes significantly to the national economy by generating milk, meat, and draught energy. Buffalo milk accounts for roughly 68 percent of total milk production in the world, followed by cow (27 percent), sheep/goat/camel milk, and so on (5 percent). In Pakistan, buffalo milk is the most favored species due to its high fat content. For dairy farmers, manufacturers, and consumers, milk quality and functional qualities are critical. In water solution containing lactose, minerals, and oxytocin slight ingredients, considered to be a compound colloidal scattering of fat and protein [8]. 8-12 percent fat, 8.5-10.5 percent SNF and 74 percent entire solids make up milk. These components are crucial since they are standardized in the manufacturing of diverse items [9]. Exogenous oxytocin is commonly used in dairy practices to treat mastitis and to treat disrupted milk ejection. Exogenous oxytocin injection over a long time lowers internal oxytocin release and susceptibility to oxytocin in the mammary [10], presumably owing to oxytocin receptor down-regulation, which results in less impulsive milk ejection following oxytocin removal [11]. Exogenous oxytocin injection is regrettably becoming routine procedure in Pakistan, irrespective of physiological consequences or dose based on circumstances, with the sole purpose of increasing milk production. As a result of their ignorance and lack of information, the farmers provide oxytocin injections before to each milking. It provides short term advantages, but it is exceedingly detrimental to animals in the long run and may change milk composition, lowering the purity of milk goods. The impact of oxytocin on milk yield is a contentious topic. Several experts feel that oxytocin disrupts or modifies milk composition in many aspects [12, 13] while some are of the view that it does oxytocin have any issue with milk composition [14]. The goal of this study was to see how exogenous oxytocin affected the total milk content and mineral content of Nili Ravi Buffalo milk at 3 distinct lactation phases. Oxytocin affects milk production by lowering intra-alveolar pressure and the availability of a lactation feedback inhibitor around the alveoli, as well as restoring normal mammary blood flow. Oxytocin is also important for the establishment of the mother-child bond [5]. Milk from animals does not normally include oxytocin, however when administered with hormones such as oxytocin at doses ranging from 0.1 to 20 IU, there is an increase in milk production and small amount of Oxytocin IN can be identified in the milk. When there is an overload of oxytocin in edibles, the user may experience headaches, nausea, stomach discomfort, sleepiness, and other symptoms [15]. Farmers in Pakistan are increasingly using exogenous oxytocin to boost milk output [6]. They are uninformed regarding the usage of oxytocin, both in terms of dose and in terms of situations. Farmers provide oxytocin injections often due to their ignorance and lack of knowledge, which may affect the content of milk and, as a

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result, mess with the purity of dairy products.

Effects of Oxytocin on Milk Production in Cow

The milk-ejection reflex must actively transfer alveolar milk (80 percent of the overall milk stored in the cow's udder) into the cisternal cavity in order until it becomes available for removal. The myoepithelial cells around the alveoli flex in reaction to haptic stimulation, discharging milk accumulated in the alveoli through into mammary ducts and gland cistern. However, not all of the milk in the udder can be extracted. Through the activity of endogenous oxytocin, up to 90 percent of total of stocked milk is eliminated from cows throughout routine instrument milking. After administering oxytocin at a supraphysiological dosage (10 IU), the leftover residual milk can be eliminated. The myoepithelial cells around the alveoli flex in reaction to haptic stimulation, discharging milk accumulated in the alveoli through into mammary ducts and gland cistern. However, not all of the milk in the udder can be extracted. Through the activity of endogenous oxytocin, up to 90 percent of total of stocked milk is eliminated from cows throughout routine instrument milking. After administering oxytocin at a supraphysiological dosage (10 IU), the leftover residual milk can be eliminated. Exogenous oxytocin is commonly given to cows prior milking to treat disrupted milk ejection caused by a lack of or diminished oxytocin production, or to treat mastitis. The impact of intramuscular oxytocin administration on oxytocin blood pattern and milk ejection efficiency, on the other hand, remains unknown. Furthermore, long-term oxytocin administration in cows lowers spontaneous milk ejection following oxytocin cessation (Figure 2) [11].

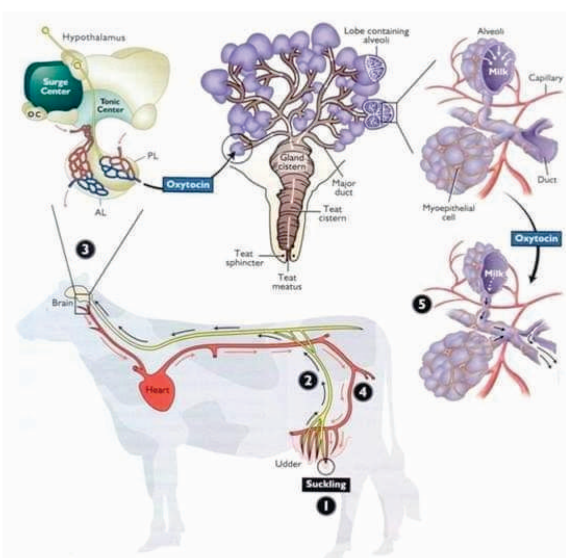

Figure 2: Role of Oxytocin in milk production [16]

Effects of Oxytocin on Behavior of Cows

Animal welfare has been a hot concern in the cattle industry in recent years [17, 18]. A number of studies have shown that providing appropriate animal wellbeing increases productivity [19]. Farmers with understanding and a favorable approach toward animals, according to [20], have a decreased occurrence of skin infections over the carpus in their dairy cows. However, in certain parts of the globe, animal rights are not a significant concern for farmers. Diverse production practices and a lack of controls in developing nations in tropical climates contribute to a variety of issues, including poor animal care [21]. The characteristics of milk production in these regions are influenced by confined typical weather and finances: for example, livestock with Bos indicus hereditary persuade proliferate stronger and more resistant to environmental conditions [22]; automatic milking has increased rapidly, as has exogenous implementation of oxytocin to stimulate milk ejection at milk production [22, 23]. In the tropical districts of México, the carry out of consistently injecting synthesized oxytocin to stimulate milk ejection has expanded [24]. The administration of oxytocin can promote milk ejection, particularly in cow farms deficient in optimal milk production procedures, where milk output might be boosted by up to 12 percent. Injecting 50 IU of oxytocin boosted milk gathering by 58 percent, according to [25]. While most farmers feel that injecting oxytocin on a regular basis is safe. Garcez *et al.,* found that when these cows were injected, their blood cortisol levels rose, suggesting an animal's reaction to stressful situations [23]. The assessment of animal behavior can be utilized as a stress indicator. Munksgaard *et al.,* studied the regularity of kicking leg, and tail actions, as well as excrement and urination, throughout milking sessions in order to assess whether or not cows were afraid of people (Figure 3) [26].

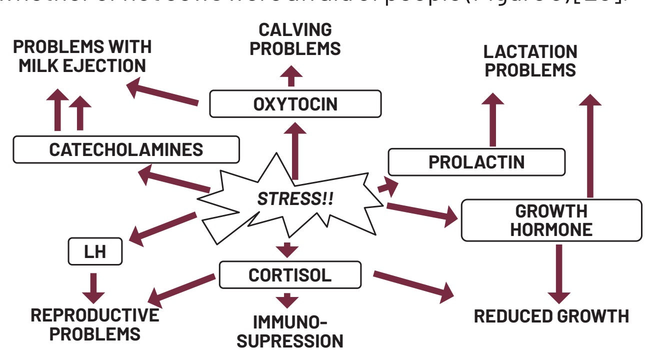

Figure 3: Effects of Oxytocin [16]

Effects of Oxytocin Injection on Sheep and Goat

Sheep and goats might generate enough milk to feed and give sustenance for the majority of the world's population since their milk is heavy in protein, lipids, lactose, minerals,

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and vitamins [27]. Milk is critical for premature growth and survival of lambs, particularly after delivery. The Arabi breed and local black goats are the most common household farm animals in Iraq's south, both of which have low milk production, with maximum milk production of (550, 827) g/day for Arabi sheep and (550, 827) g/day for local black goats, respectively. However, due of their strong capacity to survive tough environmental circumstances and illnesses, such breeds might be kept in semi-condition [28]. Some nuclei would be active in the manufacturing of oxytocin hormone, which is subsequently transported to the mammary tract through blood arteries and induces an increase in smooth muscle activity in mammary vesicles. Oxytocin is a nonpeptide hormone (it has nine amino acids in its structure) that is synthesized in hypothalamic nerve cells, particularly in the paraventricular and possess high nuclei [29], and secreted from the posterior lobe of the pituitary glands after transfer through the axons of the hypothalamus. When the posterior lobe is influenced, oxytocin is absorbed into the circulation. After and during mating, oxytocin rise the contraction of the smooth muscles of the uterine or ovary duct to deliver the sperm from the vagina to the fertile area in the 3rd top of the ovary duct, while also transporting the ovum from the top of the ovary duct to the fertility location to ensure fertilization [28]. The influence of oxytocin treatment on milk output was reported in Arabi sheep and local black goats. In the day before injection, no significant (p0.05) differences in milk yield were noticed in both kinds of animals in the morning or evening durations, whereas on the day of injection, milk yield significantly increased (p0.05) in goats after 4 hours of injection or in the evening duration, compared to sheep, possibly because oxytocin stimulates milk withdrawal from the lumen of alveoli to the secondary ducts, and then to the main duct and cistern. When oxytocin reaches the mammary alveoli, it binds to particular receptors just on myoepithelial cells, causing the wall of the alveoli to contract, allowing milk to be ejected from the top of the mammary duct to the udders [30]. Furthermore, production of milk was greater in goats either the day before or the day after injection as compared to goats. This can be explained as follows: The amount of milk that can be kept in the udder is limited by its morphology, and [31] found a positive link between milk output and both size and shape of the udder, as well as the quantity of the cisterns. In comparison to sheep, most goats have a big cistern that aids in the collecting and preservation of milk. As a result, the amount of milk produced by goats is naturally more than that produced by sheep, since goats retain 75 percent of their milk output in their cisterns, whilst sheep store less than half of their milk production in their cisterns [28].

Progesterone

Progesterone (P4) is an endogenous steroid as well as progestogen reproductive hormone that plays a role in the human menstrual cycle, pregnancy, including embryogenesis [32, 33]. Structure of Progesterone is given in Figure 4. It is the body's main progestogen and relates to a category of steroid hormones known as progestogens [33]. Progesterone serves a number of vital activities in the human body. It is also an essential metabolic intermediary in the manufacture of oxytocin endogenous steroids, such as sex hormones and corticosteroids, and as a neuro steroid, it plays a significant role in brain activity [34]. Progesterone is a natural hormone that is often used as a pharmaceutical for contraception, to minimize the danger of uterine or cervical cancer, hormone replacement treatment, and feminizing hormone therapy, among other things [35]. The first time it was prescribed in 1934 [36].

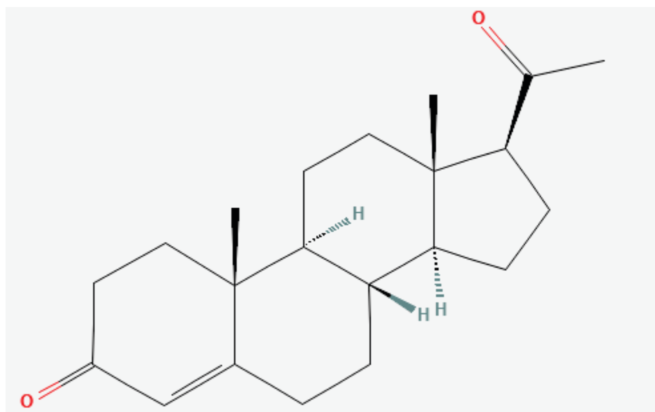

Figure 4: Progesterone structure

Effect of Progesterone on the Oocyte in Cow

High progesterone levels throughout the ovulatory follicle's development are linked to better oocyte integrity and pregnancy rates. The follicular fluid changes from an environment dominated by estradiol to one dominated by progesterone during in the final period of follicle development, between both the preovulatory LH surge and ovulation, even as granulosa cells luteinize in order to prepare for the formation of the CL after ovulation [37]. Although it is unknown whether such alterations in the follicle have such a direct impact on the oocyte, given that they occur at the same time as the beginning of meiosis and maturing of the oocyte, they are likely to have a role in deciding oocyte viability. Injection of trilostane, an inhibitor of 3-hydroxysteroid dehydrogenase, an enzyme that catalysis the production of progesterone from pregnenolone (to block the preovulatory rise in intrafollicular progesterone), into bovine preovulatory follicles led to a significant decrease in progesterone yield in the follicle but had no effect on ovulation rate or CL

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feature as measured [38]. Unfortunately, the integrity of the oocytes was not evaluated in that research. Termination of progesterone production by cumulus cells in vitro, on the other hand, led in a reduction in bovine embryogenesis, demonstrating that progesterone intracellular signaling is critical for oocyte growth performance[39].

Effects of Progesterone on the Endometrium in Dairy Farm Animals

Loss of PGR expression from uterine LE and subsequently GE is a need for developing uterine susceptibility to fertilization in all species investigated thus far [40]. Surprisingly, as the luteal phase of the estrous cycle develops, it is persistent administration of the endometrium to circulating progesterone concentrations that causes this downregulation of PGR. The amount of progesterone in the blood influences PGR expression in the endometrium, so that in animals with high levels of progesterone, early loss of the PGR occurs, indicating that uterine receptivity to implantation is developed sooner [41]. Low or inadequate progesterone concentrations, on the other hand, delay the loss of the PGR and consequently the formation of uterine susceptibility to fertilization [42]. Several publications have characterized the transcriptome of the cyclic and pregnant bovine endometrium under a variety of experimental circumstances [43, 44]. It is obvious that changes in endometrial gene expression occur regardless of where the cow is pregnant, and large differences in gene expression between pregnant and cyclic animals are just observable around d 16 when the cow's mother recognizes her pregnancy [42, 43]. These typical temporal alterations in the endometrial transcriptome of cattle are driven by a sufficient surge in progesterone following ovulation, which are required for the development of uterine susceptibility and the stimulation of conceptus formation. Forde *et al.*, characterized the endometrium's global transcriptome from days 5 to 16 in pregnant and cyclic cattle under normal and increased progesterone levels, revealing how circulating progesterone regulates endometrial genes [42]. Progesterone supplementation accelerates the typical temporal alterations in endometrial gene expression, especially for genes related with energy sources or histotroph contributors, which may lead to enhanced conceptus growth on days 13 and 16. The correct control of the maternal immune system to provide a receptive and embryotrophic conditions for the growth of the semi-allogenic conceptus is critical for successful pregnancy formation and management [45, 46].

Prostaglandin

Ulf Von Euler of Sweden was the first to identify and extract prostaglandins from human sperm in the 1930s. He called them Prostaglandins because he assumed, they came from the prostate gland. Prostaglandins, like hormones, operate as signaling molecules, but they don't go to other locations; instead, they work just inside the cells where they're made. Physiologically active lipids in human seminal plasma were first discovered and named Prostaglandins. Prostaglandins, despite their name, are generated and stored in the seminal vesicle before to ejaculation, with testosterone acting as a stimulant. Prostaglandins are a key lipid mediator generated from arachidonic acid via the enzymatic activity of cyclooxygenase (cox), and noted that there are several forms of Prostaglandins, including PGE, PGF, PGI2, PDG2, and PGH2. Primary prostaglandins are PGEs and PGFs, which each include three members: E1, E2, E3 and F1, F2, and F3 (Figure 5). Other Prostaglandins are secondary Prostaglandins that arise as a result of PGEs [47]. The lungs, liver, kidney, and placenta are the principal organs of metabolism, and these biologically active chemicals are claimed to exist in all mammalian tissues in the body. Although it is clear that Prostaglandins play an important role in a variety of reproductive processes. Prostaglandins produced in the female are required for several reproductive processes and are concerned from the earliest events to the final event. Prostaglandins are a kind of hormone that is used in animal reproduction, particularly in oestrus synchronisation and parturition [47].

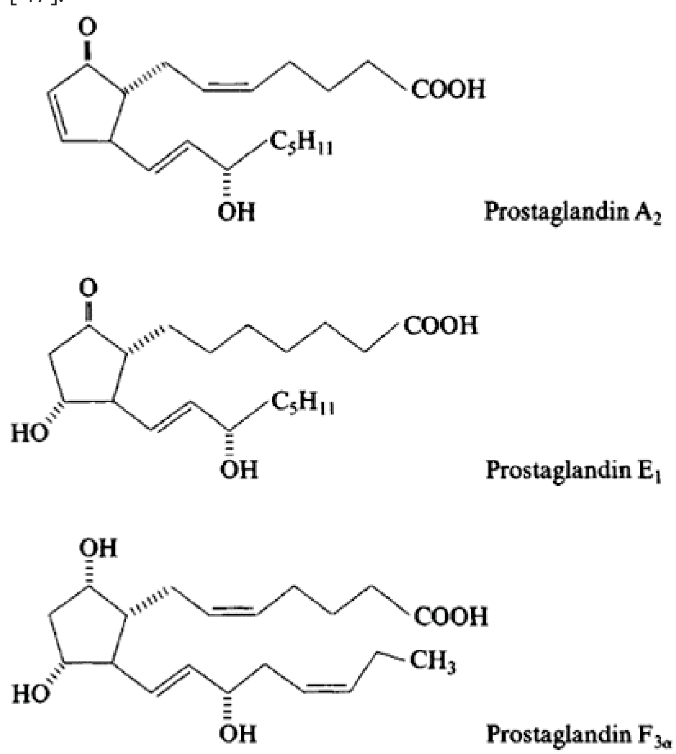

Figure 5: Structure of prostaglandin

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Effects of Prostaglandin in Reproduction of Cattle

Throughout pregnancy, prostaglandins, especially PGF2, increase uterine activity. The induction or evacuation of the conceptus's products, namely the foetus and placenta, has found practical use. Furthermore, both in vitro and in vivo PGF2 causes leutolysis of a functioning Corpus luteum, which can aid in the termination of pregnancy by lowering progesterone levels in the blood[47].

Role of Prostaglandin in Stimulation of Progesterone in Cattle

PGE2 and PGI2 promote progesterone production by the Corpus luteum in the ovary in numerous species. Cyclic AMP is involved in the activities of certain PGs. As a result, these PGs behave as LH mimics in this regard. The intra-follicular injection of indomethacin suppresses ovulation but not luteinization of the follicle into a structure that secretes normal quantities of progesterone, according to a comprehensive research on sheep[47]. Whereas PGs have a role in LH-induced ovulation, they are not engaged in luteinization or progesterone secretion. This emphasises the fact that a rise in plasma progesterone concentrations does not always imply ovulation(Figure 6)[48].

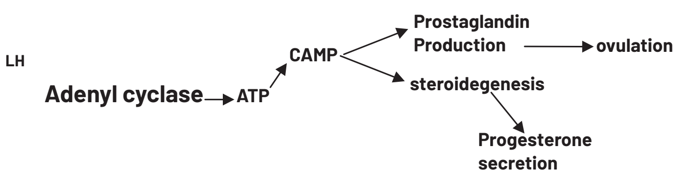

Figure 6: Pathway in ovulating and progesterone secretions induced by LH[47]

Effect of a Prostaglandin F2α on the Cyclic Corpus Luteum During its Refractory Period in Cows

When provided during the luteal phase of the oestrous cycle, prostaglandin F2 (PGF2) and prostaglandin analogues (PGF) are luteolytic in cows and other domestic species, and typically cause oestrus. The time between hormone injection and the beginning of oestrus varies between 2 and 6 days. Follicular activities at the time of prostaglandin administration, in addition to the dosage and mode of administration, have a major impact on this interval. When taken within the first several days following ovulation, prostaglandin does not cause luteolysis. The reason for this is that for the first 5 to 7 days after ovulation, the cyclic bovine corpus luteum is resistant to prostaglandin. PGF2 instillation in the uterine horn ipsilateral to the corpus luteum 1 to 4 days after ovulation did not cause luteolysis, whereas instillation on day 5 caused oestrus within 3 days [49]. Whenever cows with a corpus luteum reaching at least 17 mm in diameter and a blood progesterone level of at least 0.8 mg/ml were administered PGF2, the luteal cross-sectional area on ultrasonograms and the blood progesterone level both decreased continuously and significantly within 24 hours. Within 24 hours of PGF treatment on day 10 of the cycle, the volume of the corpus luteum and blood progesterone concentration of cyclic cows reduced dramatically, but the hormone had no impact on the corpus luteum and blood progesterone concentration when administered on day 4 of the cycle. Degranulation of big and small bovine luteal cells, which contain cytoplasmic electron-dense granules, might be regarded an early indicator of luteolysis. The number of granules in big luteal cells falls after PGF injection, but not in tiny luteal cell[50]. PGF administration to cows around day 4 of the oestrus cycle causes neither cell type to degranulate. In contrast to cattle, mares administered PGF on day 3 post-ovulation experienced a 2 day drop in ultrasonographically visible luteal tissue and a transitory fall in blood progesterone levels. On day 9 or 10 following PGF, all of the mares went into oestrus and ovulated. Signs of oestrus were found within 4 days in administered PGF2 on day 3 post ovulation, and ovulation happened 9 days following the hormone injection. The purpose of this study was to look at ultrasonographic alterations in the corpus luteum and alterations in plasma progesterone levels in cows after they were given PGF 3 and 5 days after fertilization[51].

CONCLUSIONS

In present review, we studied the effects of oxytocin, progesterone, and prostaglandin on dairy farmed animals such as cow, buffalo, sheep and goat. Oxytocin affects milk yield by reducing intra-alveolar pressure, restoring normal breast blood flow, and reducing the presence of a lactation feedback inhibitor surrounding the alveoli. Despite the fact that most studies showed that oxytocin levels rose in response to social contact, only a handful included a nonsocial control condition. Oxytocin levels did not differ between sheep housed in groups and those kept alone in a new environment. Furthermore, baseline plasma oxytocin in dairy cows shows a negative relationship with interest and general activity, but a positive relationship with uneasiness. Progesterone also has an influence on the growth of the dominant follicle, which can influence oocyte viability. Prostaglandins play an important role in a variety of reproductive processes. Study concluded that these hormones used to enhancing milk production, reproduction rate and developmental processes but they have many serious effects on dairy farm animals. In future research may be performed on this review topic. We will check the effects of reproductive hormones on dairy farm animals at large level.

Authors Contribution

Conceptualization: MJ, MM

Writing-review and editing: MJ, MM, SH, MAAT

DOI: https://doi.org/10.54393/mjz.v4i02.67

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

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