# EXAMINING THE UNREGULATED USE OF HORMONAL PREPARATIONS IN ANIMAL REPRODUCTION

**Akhter Rasool1\*, T.Sarath2, K.Porteen3 and Keerthana Joshy B1**

# 1MVSc Scholar, Department of Veterinary Gynaecology and Obstetrics, Tamil Nadu Veterinary and Animal Sciences University, Chennai, India

# 2Associate Professor, Department of Veterinary Gynaecology and Obstetrics, Tamil Nadu Veterinary and Animal Sciences University, Chennai, India

3Assistant Professor, Department of Veterinary Public Health and Epidemiology, Tamil Nadu Veterinary and Animal Sciences University, Chennai

# \* Corresponding Author: mirakhter1312@gmail.com

# ABSTRACT

# Hormones play a pivotal role in addressing diverse reproductive disorders in domestic animals, with their prevalence surpassing that of antibiotics in daily veterinary practice. Hormonal preparations are frequently administered to restore animals' reproductive capabilities, contingent upon precise diagnostic procedures. It is imperative to eschew the indiscriminate utilization of hormones, which may serve as a facade for managerial issues or purportedly enhance production performance. To ensure optimal breeding outcomes, meticulous records of diagnoses and treatments must be maintained. Inappropriate use of pharmaceutical preparations for manipulating breeding cycles, especially when not administered in accordance with veterinary guidelines, should be discouraged due to its potential to significantly reduce the overall fertility of breeding stock. Rather than relying on hormones for the treatment of reproductive ailments, the adoption of sound management practices is advocated to enhance animal health and fertility. Furthermore, consumer interest in animal health and welfare is on the rise, coinciding with ethical concerns regarding the utilization of hormones in animal reproduction. This review comprehensively addresses the indiscriminate use of hormonal preparations in animal reproduction.

# *Key words*: Animal reproduction, Endocrine disruptors, Hormones, Infertility

# INTRODUCTION

# Traditionally, the foremost objective of farmers in many countries has been to ensure that each cow gives birth to a calf approximately every 12 months. One beneficial approach is to voluntarily extend the interval between calving and the first service, subsequently elongating the calving interval (Holroyd and McGowan, 2014). This strategy can enhance the fertility of high-yield cows, affording them more time for post-calving recovery. As a result, the reliance on hormonal treatments to address anoestrus is reduced, along with the number of inseminations required per cow (Larsson and Berglund, 1999).

# Hormonal Preparations in Animal Reproduction

# Reproductive hormones, originating from both the anterior pituitary gland and the gonads, play a pivotal role in regulating reproductive function and are equally indispensable for diagnosing associated disorders. Estrogen, a primary female sex hormone primarily produced by the ovarian follicles and corpus luteum, as well as the placenta (Weil *et* al., 2015), plays a crucial role in the development of female sex organs, regulation of gonadotropin secretions, stimulation of uterine epithelial cells, growth of blood vessels, and development of endometrial glands (Gulati *et al*., 2013). Progesterone, released by the ovaries and the adrenal glands, serves as the precursor for estrogens and androgens, aiding in the regulation of the estrous cycle and the maintenance of pregnancy (Sangsritavong *et al*., [2002](https://www.tandfonline.com/doi/full/10.1080/09712119.2022.2089149)). Gonadotropin-Releasing Hormone (GnRH), secreted from the hypothalamus, stimulates the pituitary gland to secrete Follicle-Stimulating Hormone (FSH) and Luteinizing Hormone (LH). FSH plays a vital role in ovulation by stimulating follicular growth and estrogen secretion in synchrony with LH. LH, on the other hand, plays a crucial role in follicular maturation, rupture, and ovulation. Estimating LH and FSH levels is of prime importance in diagnosing disorders related to the normal reproductive cycle and fertility (Hafiz, 2013; Manocha *et al*., 2018).

# When diseases impact the reproductive performance of individual animals or groups, it is widely acknowledged that effective treatments, if available, should be employed. In pursuit of farmers' objectives, hormones serve as vital remedies for treating reproductive diseases. Hormones, in particular, are crucial tools for managing breeding. A prevailing trend in most countries is the expansion of herd sizes. In large herds, artificial insemination (AI) necessitates rigorous estrus detection, demanding substantial labor. To streamline this process, synchronization of estrus and ovulation is advocated, achieved through the use of various hormones such as progesterone, oestrogen, prostaglandins, gonadotrophin-releasing hormones (GnRH), and human chorionic gonadotrophin (HCG), either individually or in combination (Roche, 1979; Macmillan and Peterson, 1993). Exogenous luteinizing hormone (HCG) and gonadotrophin-releasing hormone (GnRH) are administered to induce ovulation in cases of delayed ovulation relative to estrus and insemination (Jaswal and Singh, 2013). GnRH has also been employed during the luteal phase of cows to stimulate the corpus luteum (Sheldon and Dobson, 1993). Additionally, progesterone administration has been utilized in repeat breeder cows to support progesterone levels during early pregnancy (Sreenan and Diskin, 1983). These treatments are employed to expedite the onset of puberty or reduce the interval between calving and conception. In cases of retained placenta, prostaglandins are sometimes used and have been demonstrated to reduce the incidence of the condition in cows induced to calve with corticosteroids (Gross *et al*., 1986). Uterine motility-boosting drugs like oxytocin are also employed. Prostaglandins are commonly administered in cases of pyometra and endometritis to induce regression of the corpus luteum, followed by follicle maturation and estrus, ultimately leading to uterine contractility (Douglas and Ginther, 1973). Corticosteroids, either alone or in conjunction with prostaglandins, are used for parturition induction (Adams and Wagner, 1970). Furthermore, the embryo transfer program relies on the extensive use of hormones to synchronize estrus and superovulation.

# Unregulated use of hormones and its consequences

# Exogenous substances or hormonal preparations that disrupt normal endocrine function are classified as endocrine disruptors (Zoeller *et al*., 2012). These substances are known to interfere with various hormonal and metabolic processes, affecting the activation, secretion, synthesis, release, and binding of normal hormones (Arsenescu *et al*., 2008). The administration of exogenous hormonal preparations can disrupt normal hormone-receptor interactions through various mechanisms. These preparations may mimic hormones, triggering inappropriate responses at inappropriate times, or block hormone action, resulting in alterations in both hormonal and homeostatic systems (Gore *et al*., 2015). Chronic exposure to these agents has been associated with detrimental effects on the development of endocrine tissues and reproductive systems (Martyniuk *et al*., 2020; Segner, 2009). The documented adverse effects of endocrine disruptors encompass infertility, cancer, irregular reproductive cycles, disturbances in folliculogenesis and ovulation (Gibson and Saunders, 2014; Van den Belt *et al*., 2002). Imbalances in Follicle-Stimulating Hormone (FSH) and Luteinizing Hormone (LH) levels can lead to various reproductive disorders, including cystic ovaries, ovulation failure, delayed ovulation, and infertility (Manocha *et al*., 2018). Specific hormonal alterations, often induced by the unnecessary administration of exogenous progesterone, Gonadotropin-Releasing Hormone (GnRH) analogs like Buserelin or Gonadorelin, as well as prostaglandins such as Cloprostenol, Dinoprost, Tiaprost and Luprostiol can significantly impact fertility. These hormonal shifts can lead to irregular estrous cycles and an elevated risk of reproductive tract infections, often characterized by increased progesterone concentration and reduced estradiol levels (Miller and Hunt, 1996; Bosu, 1980). It's crucial to note that the administration of progesterone has been linked to an increased incidence of mammary, ovarian, and uterine tumors in experimental animals (Galbraith, 2002). Melengestrol acetate (MGA), an orally administered progestogen, is a synthetic steroid used as a feed additive and for estrus synchronization (Schiffer *et al*., 2001; Patterson *et al*., 2005). Classified as a xenobiotic anabolic agent, MGA is associated with the potential for endocrine-disrupting activity (Lange *et al*., 2002).

# Regulatory Framework and Challenges

# Comprehensive record-keeping of treatments is essential on every farm, serving multiple critical purposes. Firstly, it enables continuous herd monitoring, allowing for the early identification of disease trends, potential outbreaks, and health issues. Secondly, it provides valuable data for informed breeding decisions, aiding in the selection of animals with improved genetic traits related to health. Thirdly, it contributes to disease population statistics, enhancing our understanding of prevalence, transmission patterns, and risk factors within the herd, including environmental influences. Accurate and thorough recording of inseminations and treatments is of utmost importance, facilitating the incorporation of fertility and health traits into a comprehensive breeding program (Refsdal, 2000). To promote animal health and welfare, the use of synthetic substances or hormones should be minimized and reserved for genuine necessity. Routine treatments of reproductive disorders with synthetic hormonal preparations should be discouraged. Each animal should possess a health card, meticulously documenting diagnosed diseases (Refsdal, 1998). Local veterinarians must rigorously oversee the use of hormonal preparations in animal production, educating farmers about potential adverse effects and ethical concerns associated with unnecessary hormone usage. Promoting awareness and responsible practices are fundamental to maintaining animal well-being, ensuring sustainable farming, and safeguarding food product safety for consumers.

# Regulating unnecessary hormone use in animal reproduction is a complex challenge involving various stakeholders—farmers, veterinarians, regulators, and consumers. Challenges include regulatory non-uniformity, difficulty in educating farmers, reluctance to disclose information, and limited affordability and effectiveness of alternatives. Addressing these challenges demands a collaborative effort among governments, researchers, and farmers to develop and implement consistent regulations, promote alternatives, and ensure the responsible use of hormones in animal reproduction.

# CONCLUSIONS

# To comprehensively grasp the impact of exogenous hormonal preparations on animal reproduction, extensive research into their mechanisms is imperative. Furthermore, there is a critical need for an extensive array of studies. Promoting awareness and educating farmers and local veterinarians on the advantages and potential risks associated with hormone use in animal reproduction is essential. Effective communication is the key to enabling informed decision-making and instigating meaningful change.

# CONFLICT OF INTEREST

None.

# REFERENCES

# Adams, W.M., Wagner, W.C., (1970). The role of corticoids in parturition. *Biol. Reprod*. 3: 223–228.

# Arsenescu, V., Arsenescu, R.I., King, V., Swanson, H., Cassis, L.A., (2008). Polychlorinated biphenyl-77 induces adipocyte differentiation and proinflammatory adipokines and promotes obesity and atherosclerosis. *Environ. Health Perspect*. 116: 761–768.

# Bosu, W. T. K. (1980). Practical Uses of GnRH and Prostaglandins in Bovine Reproduction. In American Association of Bovine Practitioners Conference Proceedings., p. 137-150.

# Douglas, R.H., Ginther, O.J., (1973). Luteolysis following a single injection of PGF2in sheep. *J. Anim. Sci.* 37: 990–993.

# Holroyd, R. G., & McGowan, M. R. (2014). Reproductive management of beef cattle. Beef cattle production and trade. 14: 291.

# Galbraith H. (2002). Hormones in international meat production: biological, sociological and consumer issues. *Nutr Res Rev.* 15:293–314.

# Gibson, D.A., Saunders, P.T.K., (2014). Endocrine disruption of oestrogen action and female reproductive tract cancers. *Endocr. Relat. Cancer* 21: 13–31.

# Gore AC, Chappell VA, Fenton SE, Flaws JA, Nadal A, Prins GS, Toppari J, Zoeller RT. (2015). The Endocrine Society's second scientific statement on endocrine-disrupting chemicals. *Endocr Rev* ; 36(6): 1–150.

# Gulati M, Meikle AW, *et* al., (2013). Chap 22: gonadal function. In: Bishop, ed. Clinical chemistry: techniques, principles and correlations. 7th ed India: Wolters Kluwer; p. 472–488.

# Gross, T.S., Williams, W.F., Moreland, T.W., (1986). Prevention of the retained fetal membrane syndrome retained placenta during induced calving in dairy cattle. *Theriogenology* 26: 365–370.

# Jaswal, R.S. and Singh, M. (2013). The effect of administration of gonadotropin releasing hormone analogue at estrus or during luteal phase on reproductive performance of dairy cows maintained under sub-temperate climate. *Iranian J. Vet. Res.* 14(1): 57-60.

# Refsdal, A. O. (2000). To treat or not to treat: a proper use of hormones and antibiotics. *Ani. Repro. Sci.*, 60, 109-119.

# Refsdal, A.O., (1998). Animal health service and reproductive problems in Norwegian cattle. *Reprod. Domest. Anim.* 33: 223–226.

# Larsson, B., Berglund, B., (1999). Reproductive performance in cows with extended calving interval. *Reprod. Domest. Anim*. 35(5): 277-279.

# Lange IG, Daxenberger A, Schiffer B, Witters H, Ibarreta D, Meyer HH. (2002). Sex hormones originating from different livestock production systems: fate and potential disrupting activity in the environment. *Anal Chim Acta.* 473:27–37.

# Macmillan, K.L., Peterson, A.J., (1993). A new intravaginal progesterone releasing device for cattle CIDR-B for oestrus synchronisation, increasing pregnancy rates and the treatment of post-partum anoestrus. *Anim. Reprod. Sci.* 33: 1–25.

# Manocha, A., Kankra, M., Singla, P., Sharma, A., Ahirwar, A. K., & Bhargava, S. (2018). Clinical significance of reproductive hormones. *Current Med. Res. and Prac.*, 8(3), 100-108.

# Martyniuk, C.J., Mehinto, A.C., Denslow, N.D., (2020). Organochlorine pesticides: agrochemicals with potent endocrine-disrupting properties in fish*. Mol. Cell. Endocrinol*. 507: 110764.

# Miller L, Hunt JS. (1996). Sex Steroid Hormones and Macrophage Function. *Life Sci* 59:1–14.

# Patterson, D. J., Schafer, D. J., & Smith, M. F. (2005). Review of estrus synchronization systems: MGA. Proceedings, App. Repro. Strat. in Beef Cattle, 12: 60-150.

# Roche, J.F., (1979). Control of oestrus in cattle. *World Rev. Anim. Prod*. 15: 49–76.

# Hafez, E. S. E., & Hafez, B. (Eds.). (2013). Reproduction in farm animals. John Wiley & Sons. p. 33-53

# Sangsritavong S, Combs D, Sartori R, Armentano L, Wiltbank M. (2002). High feed intake increases liver blood flow and metabolism of progesterone and estradiol-17β in dairy cattle. *J Dairy Sci.* 85: 2831–2842.

# Segner, H., (2009). Zebrafish (Danio rerio) as a model organism for investigating endocrine disruption. Compar. Biochem. Physiol. Pt. C Toxicol. Pharmacol. 149: 187–195.

# Schiffer B, Daxenberger A, Meyer K, Meyer H. (2001). The fate of trenbolone acetate and melengestrol acetate after application as growth promoters in cattle: environmental studies. *Environ Health Perspect*. 109: 1145–1151.

# Sheldon, I.M., Dobson, H., (1993). Effects of gonadotrophin releasing hormone administered 11 days after insemination on the pregnancy rates of cattle to first and later services. *Vet. Rec*. 133: 160–163.

# Sreenan, J.M., Diskin, M.G., (1983). Early embryonic mortality in the cow: its relationship with progesterone concentration. *Vet. Rec*. 112: 517–521.

# Van den Belt, K., Wester, P.W., van der Ven, L.T.M., Verheyen, R., Witters, H., (2002). Effects of ethynylestradiol on the reproductive physiology in zebrafish (Danio rerio): time dependency and reversibility*. Environ. Toxicol. Chem*. 21: 767–775

# Weil PA, *et al*., (2015). The diversity of the endocrine system. In: Rodwell, ed. Harper’s illustrated biochemistry. 30th ed. McGraw Hill Education; p. 498–517.

# Zoeller, R.T., Brown, T.R., Doan, L.L., Gore, A.C., Skakkebaek, N.E., Soto, A.M., Woodruff, T.J., Vom Saal, F.S., (2012). Endocrine-disrupting chemicals and public health protection: a statement of principles from the Endocrine Society. *Endocrinology*. 153: 4097–4110.