

THE ROLE OF PROSTAGLANDINS IN LIVESTOCK PRODUCTION

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ABSTRACT

Prostaglandins belong to the family of lipid. Soluble unsaturated hydroxyl acid containing twenty carbon (c) atoms and based on the prostanic acid skeleton. There are two main types of Prostaglandins (PGs), the E and F series each having 3 members E_1, E_2, E_3 and F_1, F_2, F_3 . The other PGs are known as secondary PGs and are products of enzymic or chemical dehydrations of PGEs e.g PG_{+2}, PGA_2, PGD_2 and PGB. Prostaglandins are probably the most important regulators of female productive functions (ovulation, uterine receptivity, Implantation and parturition) and associated with pathologies (pain, fever, and inflammation), apart from sex steroids. Prostaglandins are not stored in tissues but are synthesized and released in response to a given stimulus. Prostaglandins are produced by all nucleated cells of the body and act locally in a paracrine (locally active) or autocrine (acting on the same cell from which it is synthesized) fashion. Prostaglandins are therefore regarded as essential mediators of female reproductive processes, hence, this paper seeks to review the role of Prostaglandins which is exploited in livestock production especially oestrus synchronization and induced parturition.

KEYWORDS: Prostaglandins, Production, Role, Livestock

INTRODUCTION

Prostaglandins were first discovered and isolated from human semen in the 1930s by Ulf Von Euler of Sweden. Thinking they had come from the prostate gland, he named them Prostaglandins. Prostaglandins are like hormones in that they act as chemical messengers, but do not move to other sites, but work right within the cells where they are synthesized (Ophardt, 2003). Von Euler (1937) also stated that biologically active lipids in human seminal plasma were first detected and called Prostaglandins. Despite their name, Prostaglandins are synthesized and stored in the seminal vesicle prior to ejaculation with testosterone being the stimulus for Prostaglandins synthesis.

Prostaglandins is a major lipid mediator synthesized from arachidonic acid via the catalytic activities of cyclooxygenase (cox) and Karim (1976) with Olson (2003) pointed out that, there are different types of Prostaglandins ranging from PGE, PGF, PGI_2, PDG_2, PGH_2 . The PGEs and PGFs are known as primary Prostaglandins with each having three members E_1, E_2, E_3 and F_1, F_2 and F_3 . Others are secondary Prostaglandins formed as a result of PGEs. These biologically active substances are said to occur in all mammalian tissues in the body with lungs, liver, kidney and placenta being the major organs of metabolism.

Although it is clear that Prostaglandins play an important role in a number of reproductive processes; Clark and Myatt (2008) also added that Prostaglandins produced in the female are necessary for several

reproductive processes and are involved from the earliest events (i.e Luteinizing hormone release) through ovulation and up to the final event which leads to successful parturition.

This review work is to outline the role of Prostaglandins which is exploited in livestock reproduction especially in oestrus synchronization and indeed parturition.

Reproductive Effects

Prostaglandins specifically PGF_2 stimulate activity of the uterus during pregnancy. This has found practical application in the induction or expulsion of the products of conceptus viz the fetus and placenta. According to Karim (1976), only small quantities of the PGs are required, either intravenously or by introduction directly into the uterine cavity, to produce abortion. In addition, both the *in-vitro* and *in-vivo* PGF_2 produce luteolysis of a functional Corpus luteum and can facilitate interruption of pregnancy by the reduction in blood level progesterone.

Oestrus cycle

Blatchley *et al.*, (1975) pointed out that a significant increase in the output of oestrodial from the ovary at oestrus stimulates the secretion of the luteinizing hormone from the anterior pituitary gland. The luteinizing hormone (LH) which causes ovulation and the transformation of the ovulated follicle into a Corpus luteum, is also involved in the secretion of progesterone

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in-vivo. An exception occurs in rats where a fully functional release of prolactin occurs as a result of coitus. Regression of the Corpus luteum terminates progesterone production and a new cycle begins.

Luteinizing Hormone (LH) Release

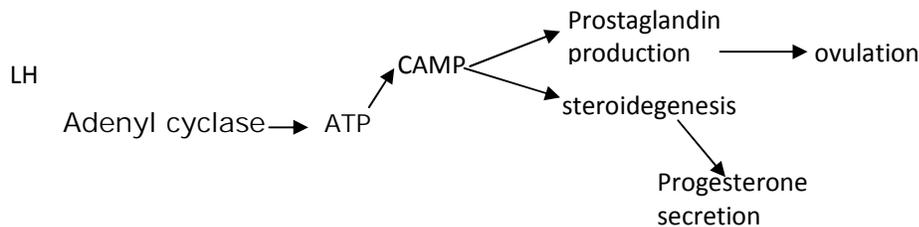
Carlson *et al.*, (1977), administering PGF_2 to sheep during the luteal phase of the cycle obtained an increase in the plasma concentrations of LH. The release of LH caused by oestradiol in anoestrus sheep is prevented by indomethacin (an inhibitor of PG synthesis). In sheep also, an increase in PGF_2 output from the brain is associated with induced oestradiol increase in LH release. This output is pulsatile like the outputs of luteinizing hormone releasing hormone (LHRH) and LH.

Conversely, Hams *et al.*, (1974) noted that PGE_2 stimulates the release of LH when injected into the third ventricle of the brain at the anterior pituitary gland in pre-ovestrous and ovariectomised rats treated with oestradiol. PGE_2 actually stimulates LH release by causing the release of LHRH and not by acting directly on the pituitary gland.

Ovulation

Ovulation has three major phases in which Prostaglandins may be involved.

- (1) Follicular maturation
- (2) Rupture of the follicle
- (3) Formation of the Corpus luteum



Source: Poyser (1992).

Fig. 1: Pathway in ovulating and progesterone secretions induced by LH.

Luteolysis

Progesterone which initially is produced in the Corpus luteum is necessary to prepare the uterus for implantation of a fertilized ovum and to monitor the pregnancy until the placenta can begin progesterone production. Interruption of progesterone production by the Corpus luteum then leads to termination of pregnancy. In 1969, it was shown that PGF_2 caused luteolysis in rats and in guinea pigs. The uterus was shown to be the source of luteolysin identified as PGF_2 (Blatchley, 1969). The luteolytic action of PGF_2 may be

La Maire and associates showed that isolated follicles could be stimulated with human chorionic gonadotropin (HCG) to increase their PGE and PGF_2 levels (Le Marie *et al.*, 1973). This increase only occurred in those follicles destined to be ovulated. Pre-treatment of animals with Prostaglandin synthesis inhibitors blocks ovulation (Zanagno *et al.*, 1999).

Apparently, PGs cause ovulation by increasing collagenolysis through activating collagenase. This increase in collagenolysis causes "thinning" of the follicular wall at the apex of the follicle resulting in eventual rupture of the follicle and release of ovum (Downs and Longe, 1983).

Stimulation of Progesterone secretion

Progesterone secretion by Corpus luteum in the ovary in many species is stimulated by PGE_2 and PGI_2 . The actions of these PGs is mediated by cyclic AMP. Consequently in this respect, these PGs act as LH mimics.

A detailed study carried out in sheep has shown that the intra-follicular injection of indomethacin prevents ovulation but does not prevent luteinization of the follicle into a structure which secretes normal amounts of progesterone (Merdock and Dunn, 1983).

Although PGs mediate ovulation induced by LH, they are not involved in luteinization and progesterone secretion which are also induced by LH (see figure 1 below). This points out that an increase in plasma progesterone concentrations does not necessarily mean that ovulation has taken place (Poyser, 1992).

directly through blood flow away from the Corpus luteum (Clark and Myatt, 2008).

Early pregnancy

It is evident that if an animal becomes pregnant, the luteolytic effect of the uterus has to be prevented, since continued progesterone output from the ovary is necessary for the whole gestation in some species e.g in cattle, pig, and goat or the first third of the gestation e.g sheep and guinea pig.

In species like sheep and goat, the embryo

secretes a protein called ovine trophoblast protein-1 (OTP-1) and caprine trophoblast protein-1 respectively and they are synthesized by the embryo from the 12th and 22nd day of pregnancy for the sheep and goat on the 15th and 21st day of pregnancy. These proteins inhibit endometrial PGF₂ synthesis (Imakawa *et al.*, 1988 and Gnatek *et al.*, 1989).

However in pigs the conceptus does not inhibit uterine PGF₂ secretion *in-vivo* (Harney and Bazer, 1989) and also Leckie and Poyser (1990) detected in guinea pig that interferon- does not inhibit endometrial PGF₂ synthesis.

Interestingly, in those species whose embryos secrete a trophoblast protein-1 are the species in which ovarian oxytocin form part of the physiological stimulus in increasing endometrial PGF₂ synthesis at the end of the oestrus cycle. While in pigs, endometrial PGF₂ synthesis is not inhibited during early pregnancy. The direction of secretion of PGF₂ produced by the uterus is changed from the uterine venous drainage into the uterine lumen, where the PGF₂ is secreted (Bazer and Thatcher, 1977). This means that the Corpora lutea in the early pregnant pig is protected from the luteolytic influence of PGF₂.

Parturition

Parturition occurs not only through withdrawal of inhibitory factors but also activation of stimulatory signals or hormones. Glucocorticoids not only stimulate fetal tissue differentiation and maturation, but in many species they also initiate parturition by acting in a series of positive feed toward loops to alter placental steroidogenesis (Jenkin and Young, 2004). Glucocorticoids also activate immune and inflammatory pathways, unregulated PGHS-2, attenuate PGDH leading to prostaglandin synthesis and stimulate further glucocorticoid production (Whittle *et al.*, 2006). It is clearly recognized in pregnant animals and women that labour, is associated with an inflammatory response that culminates in release of prostaglandin (Christiaens *et al.*, 2008).

Placental Delivery

Once delivery is completed and the allantochorion begins to detach from the uterus, maternal prostaglandin concentrations decline (Haluska and Currie, 1998). Generally, prostaglandin concentrations are low within one hour of spontaneous foaling associated with placental delivery (Vivrette *et al.*, 1995). In other species, reduced maternal prostaglandin concentrations at birth are associated with retained fetal membranes (Olson, 2003). This relationship was not observed in one study of heavy draught mares (Ishii *et al.*, 2008) but when prostaglandins were blocked by administration of the PGHS-2 inhibitor, flunixin meglumine, prior to labour, placental delivery was delayed (Vivrette *et al.*, 1995).

Prostaglandins and Oestrus synchronization

Three products, lutalyse, estrumate and bovilene, have been approved for use in beef cows and

heifers for oestrus synchronization. All are prostaglandins and work similar, but differ slightly in their chemical makeup with different half lives and dosage levels.

When injected at the recommended dosage, these products act by rapidly regressing the Corpus luteum (CL) on the ovaries of cycling females that are in days 6-16 of their oestrus cycles. In other words, the injection decreases the function of the CL; which allows these females to return to estrus within 2-5 days and synchronizing their oestrus cycles. Females in days 17-20 will be oestrus normally within 1-4 days and will also be synchronized. Females in days 1-5 of the cycle and non-cycling females that do not have a mature CL will not respond to the injection. Therefore with one injection, only about 75 percent of the cows cycling in a herd can be synchronized. If all cycling females are to be synchronized, two injections are needed (Deutscher, 1999).

Myometrial activity

It is well documented that PGF₂ and PGE₂ contract smooth muscles but PGF₂ infused into rats near their tail to induce uterine contractions and parturition (Liggus *et al.*, 1972). However, PGF₂ administration to sheep during parturition does not have a stimulant effect on the uterus, so PGs may aid but not initiate expulsion of the fetus (Mitchell *et al.*, 1976b).

CONCLUSION

In conclusion, prostaglandins are involved in several reproductive processes, namely: LH release, ovulation, luteolysis and parturition. Due to their luteolytic action, PGF₂ or lutalyse can be useful for oestrus synchronization and induced parturition in animals.

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