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Prolactin in Female Domestic Dogs: A Mini-Review

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ABSTRACT

Prolactin is a luteotrophic agent, acting from mid-luteal phase in both pregnant and non-pregnant animals. Its role in stimulating and maintaing the corpus luteum, allowing the gestation period to be maintained, as well as the role in preparing and maintaining lactation (in concert with estrogens, progesterone, corticosteroids, somatropin and insulin) in the bitch has been recognized. Prolactin seems to be also involved in ensuring maternal behaviour, including the preparations for delivery and the care of the litter thereafter.

KEYWORDS

Bitch; Dog; Estrus; Pregnancy; Prolactin.

INTRODUCTION

Among domestic animals, the dog (Canis familiaris) is a monoestric species, with a long oestrous cycle (12 months in most non-domesticated species; 7 ± 1.5 months in the dog) and with a period of about 4 months of anestrus, in which there is no ovarian activity [1]. Reproduction and pregnancy in dogs are regulated by many hormones, among which prolactin.

Prolactin (PRL) is a single-chain peptide hormone, composed of almost 200 amino acids, produced by the lactotrotropic cells of the anterior pituitary [2]. Prolactin secretion is pulsatile and this pulse rate is probably a result of the combined effect of different hypothalamic factors. Dopamine activates prolactin synthesis. Also thyrotropin-releasing factor (TRH), serotonin, vasoactive intestinal peptide (VIP), and estrogen substances activate prolactin synthesis, but about 100 times less than dopamine does. Gamma-aminobutyric acid (GABA) inhibits the synthesis of prolactin with an inhibitory effect 100-fold lower than the activating effect of prolactin.

In dogs, prolactin is secreted in a pulsatile fashion [3] and most prolactin is released during the second half of the luteal phase. Prolactin is an essential luteotropin in the dog from mid-luteal phase in both pregnant and non-pregnant animals. It appears to act by sustaining corpus luteum lifespan and function rather than by direct stimulatory effects on progesterone secretion [4]. Indeed, prolactin stimulates and maintains the corpus luteum of the ovary, which is the source of progesterone, allowing the gestation period to be maintained from the second half of the pregnancy. However, prolactin does not act alone; during pregnancy, prolactin, estrogen and progesterone stimulate the development of the mammary gland.

Originally, the observation in the bitch that PRL blood values rise during the second half of pregnancy, while progesterone values were simultaneously declining, led to the conclusion that PRL might have an anti-luteotropic effect [5]. The use of PRL inhibiting drugs, i.e. dopamine agonists like bromocriptine and cabergoline during the second half of pregnancy have shown that PRL must have a luteotrophic effect as their use results in an immediate sharp drop in the blood PRL concentrations followed by a drop in levels of blood progesterone [1]. In addition, using the same PRL-inhibitors in the treatment of dogs with clinical anoestrus (abnormally prolonged anoestrous period) reliably induces a fertile oestrus [6].

In pregnant bitches, the plasma prolactin concentration starts to rise about 1 month after ovulation, which is when the plasma progesterone concentration begins to decline. Also in healthy cyclic bitches, most prolactin is released during the second half of the luteal phase. The changes in growth hormone (GH) and prolactin release during the luteal phase may promote the physiological proliferation and differentiation of mammary gland tissue in the bitch. In the early part of the luteal phase progesterone-induced mammary GH initiates proliferation of the mammary epithelium, whereas in the late luteal phase, when progesterone concentrations decrease, prolactin release increases and promotes lobulo-alveolar differentiation [7]. Hence, the declining plasma progesterone concentrations during the second half of the luteal phase appear to influence prolactin secretion.

In monogastric animals, such as dogs, cats, primates and women, prolactin is also fundamental during the preparation and maintenance of lactation after birth. As a matter of fact, after delivery and during lactation, prolactin levels continue to be elevated [8].

Prolactin allows the growth and differentiation of the mammary gland, maintains segregation of breast milk, reduces fertility during the lactation period, facilitates immunological regulation in the female, as well as an exchange of water and electrolytes during pregnancy. The tactile stimulation of the nipple or breast in the mother after birth inhibits the release of dopamine into the hypothalamus, increasing the concentration of prolactin in blood. On the other hand, high concentrations of prolactin inhibit the secretion of gonadotropin-releasing hormone (LH, luteinizing hormone and FSH, follicle-stimulating hormone), which prevents gonadotropins to act on the gonads. Thanks to this mechanism, fertility levels are reduced during lactation, preventing females to become pregnant while feeding their offspring [9].

In pregnant bitches, plasma prolactin levels exceed 100 ng/ml [4]. Weaning, which can be defined as the phase of maternal care during which lactation decreases most rapidly [10], causes a decrease in prolactin blood values.

The use of potent prolactin inhibitors, mostly dopamine agonists like bromocriptine, metergoline and cabergoline, has confirmed that prolactin is the luteotropic hormone from day 30 of pregnancy onward and that prolactin is essential for the preparation, commencement and maintenance lactation, as well as for the activation maternal of maternal and sexual behavior [1]. Prolactin seems to be involved in ensuring maternal behaviour, including the preparations for delivery and the care of the litter thereafter, although it is not yet clear how it shares these effects with oxytocin [11].

Prolactin secretion is under the tonic inhibitory control of hypothalamic dopaminergic neurons and the stimulatory action of estrogens, with a number of other hypothalamic hormones playing a modulatory role in the control of prolactin secretion [12]. In most vertebrates, neuroendocrine functions are organized in regular cycles of different periodicity. Hormone secretion patterns are mainly regulated endogenously, although they are also under environmental influence [13]. For instance, seasonal variations in temperature and photoperiod have an influence on circannual rhythms of reproductive seasonal species [14]. Also dogs show a circannual rhythmicity of prolactin [15], whose function is unknown; it may be inherited from wolves functionally altered through domestication. Male and female dogs and wolves show almost identical seasonal changes in prolactin blood concentrations, with peak levels before mid-year and the nadir just before the year's end [1].

The rise in prolactin production during spring and towards the summer peak causes social tensions to subside and assures care for the offspring by females and males alike. This seasonality in canine prolactin production is maintained following pinealectomy [16]. This indicates the existence of a strong genetic base for prolactin's annual rhythm which might be influenced by melatonin but is neither triggered nor controlled by pineal hormones. This explains the persistence of the physiological pseudopregnancy in the bitch, although her reproductive cycle has shortened and no longer coincides with the seasons [1].

Information regarding the presence of a circadian rhythm of prolactin secretion in bitches is scarce, but Gobello et al. [17] have reported that in most anoestrous bitches there appears to be no circadian rhythm of prolactin secretion. Furthermore, Corrada et al. [15] concluded that there are ultradian differences between male and female dogs.

In certain cases, it is possible to find hyperprolactinemia, which is the presence of high levels of prolactin in blood. Increased prolactin secretion may be caused by damage to the hypophysial stem that disrupts the flow of dopamine from the hypothalamus or even triggers tumours. There may also be increased prolactin due to physiological disorders, high blood pressure or aches [9]. In some species which require prolactin in their reproductive processes, like dogs, as well as in humans, where the need for prolactin as a hormone for reproduction is not established, hyperprolactinemia inhibits male and female reproduction [1].

In conclusion, the role of prolactin as a luteotrophic agent, as well as an essential hormone for preparing and maintaining lactation (in concert with estrogens, progesterone, corticosteroids, somatropin and insulin) in the bitch has been recognized. Prolactin seems to be involved in ensuring maternal behaviour, including the preparations for delivery and the care of the litter thereafter, although it is not yet clear how it shares these effects with oxytocin.

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