Control of Follicle Development and Ovulation in Mare: Principal and Clinical Aspects

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Abstract

This review emphasizes the fundamental aspects of follicle development and also the usefulness of reproductive hormones and some clinical applications for manipulation of oestrous cycle, oestrus behavior and the ovulation rate in mares.

Keywords: hormone, mare, oestrous cycle

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During fetal development, a pool of primordial follicles forms as ovarian tissue, and each follicle consists of prophase I oocytes surrounded with a single layer of flattened granulosa cells. Several signals have been found to involve in the growth of these follicles but the entire pathway is largely unknown (Fortune et al., 1993). In fact, most of the follicles become atresia during folliculogenesis, while only a small number of them escape the atresia and reach a final stage prior to ovulation. Until recently, exactly how only one follicle per wave becomes dominant while the remaining follicles undergo atresia is not entirely clear, but the deviation in growth between the two largest follicles occurs soon after FSH levels decrease (Gastal et al., 1997). Equid has a unique pattern of follicle development in particular the mechanism that actively controls the follicular growth. Equine ovaries are anatomically ‘inside-out’, with the follicles developing within a central ovarian cortex surrounded by a vascularised, soft tissue medulla. As a result, ovulation can only occur at one specific area, as referred to ‘ovulation fossa’. These anatomical peculiarities have been proposed to limit multiple follicle development. Despite of the difference in ovarian structure, pattern of follicle development in the mare is comparable to that in cattle and women but equine follicles are about 2.2-2.5 times larger (Ginther et al., 2004). Follicle development in mare occurs in a wave-like fashion, with 1-2 follicular waves per 21-22 day estrous cycle (Ginther, 2000); the major follicle wave give rise to the ovulatory follicle (approximately 30 to 40 mm) while the dominant follicle will not develop during the minor wave as they are destined to be subordinate follicles and usually undergone atresia (Ginther, 1993). Until recently, little has been still unknown regarding the mechanism that controls the dominance and subordination. However, it has been suggested that the follicle destined to be a dominant follicle is the first to reach a critical follicle size of 21-23 mm prior to other follicles and thus creating a condition that inhibit the further growth of the subordinate follicle (Gastal et al., 1997). Several hormones have been demonstrated as potential factors that control the follicle growth and subordination. During a 21-22 day of oestrous cycle, the gonadotropin releasing hormone (GnRH) releases substantially from the hypothalamus and subsequently stimulates the production of the two important gonadotropins (follicle stimulating hormone (FSH) and luteinizing hormone (LH)). FSH plays a key role in the emergence of the ovulatory wave, but the plasma circulating FSH declines when the size of the largest follicle reaches approximately 13 mm (Gastal et al., 1997; Donadeu et al., 2001). It seems likely that the largest follicle have ability to utilize the low level of FSH, while other factors such as LH, inhibin, insulin-like growth factor 1 (IGF-1) and estradiol also play a role during follicle deviation (Bergfelt et al., 2001). Although the follicle selection ensures the growth of a dominant follicle, double/triple ovulations can naturally occur.

Recently, manipulation of the follicular growth in mare has become increasingly important since lacking an efficient superovulatory protocol to produce multiple ovulation/embryo per mare obscures the utilization of embryo transfer in equine industry. While a number of gonadotropin preparations including porcine FSH successfully induce multiple follicle development and ovulation in cattle, most fail to induce multiple follicle development in the mare, even when large amounts are used (McCue, 1996). Ironically, one of the most widely and successfully used inducers of superovulation in many domestic species is equine chorionic gonadotropin (eCG), produced by the trophoblast-derived endometrial cups during days 35-120 of pregnancy in the mare. However, eCG is wholly ineffective for inducing multiple ovulation in the horse, almost certainly because although it has high FSH activity in non-equine species, it exhibits only extremely low FSH receptor (FSHR) binding capacity in the horse, in which its activity is almost exclusively LH-like (Stewart and Allen, 1979). To date, equine pituitary extracted gonadotropins (crude equine pituitary extract [EPE] and equine FSH) are the only gonadotropins shown to stimulate commercially useful rates of follicle development in the mare, with early studies highlighting their promise as equine superovulatory agents by the stimulation of means of 1.7-3.8 ovulations per oestrous cycle (reviewed by McCue, 1996). More recently, Alvarenga et al. (2001) achieved mean ovulation and embryo recovery rates of 7.1 and 3.5 per oestrous cycle, respectively, after treating mares twice daily with 25mg of EPE starting in early diestrus (days 6-8 post ovulation); this is favorably comparable to the 1 ovulation and 0.7 embryo/cycles expected in unstimulated mares. Furthermore, the high ovulation rates obtained using EPE and following passive immunisation against inhibin (4.5 ovulations per cycle; Nambo et al., 1998) have proven conclusively that there is no insurmountable anatomical obstacle to superovulation in the mare.

In contrast to promote the follicle development, it is also demanding to temporarily inhibit the follicle growth of mare during competition or for disease control. Several techniques has been employed during the past decade such as prostaglandin (synthetic progesterone, Altenogest), GnRH antagonist and GnRH vaccine (Squires et al., 1979; Stout and Colenbrander, 2004). In horse, progesterone (either natural or synthetic progesterone) is commonly used for estrous synchronization, principally by suppressing estrus and allowing spontaneous regression of the corpus luteum. Unfortunately, follicle development remains during elevated progesterone levels. GnRH agonist and antagonist have also been used to suppress the oestrus and also to increase the inter-ovulatory interval (Guillaume et al., 2002; Johnson et al., 2002). However, these GnRH preparations require multiple administrations and generally result only a short-term effect with highly individual variation. More recently, temporary neutralization of natural GnRH via production of anti-GnRH antibodies using GnRH vaccine has become an attractive approach. This vaccine has been reported to suppress the oestrus cycle for approximately 3-5 months (Imboden et al., 2006). This technique, however, requires multiple
‘anti-GnRH’ boosters with sporadically local inflammation following injections.

References


