REVIEW

REFEREED

Dynamics of the Equine Preovulatory Follicle and Periovulatory Hormones: What's New?

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ABSTRACT

Recent studies (2005–2008) on the interrelationships among the preovulatory follicle and periovulatory circulating hormones are reviewed. Close temporal and mechanistic relationships occur between estradiol/inhibin and follicle-stimulating hormone (FSH), between estradiol and luteinizing hormone (LH), and between progesterone and LH. Estradiol from the dominant follicle forms a surge that reaches a peak 2 days before ovulation. Estradiol, as well as inhibin, has a negative effect on FSH, and estradiol has a negative effect on LH. When estradiol decreases, the negative effect diminishes and accounts for the beginning of an FSH increase and a transition from a slow to rapid increase in LH on the day of the estradiol peak. The decrease in estradiol and the reduction or cessation in the growth of the preovulatory follicle beginning 2 days before ovulation are attributable to the development of a reciprocal negative effect of LH on follicle estradiol production when LH reaches a critical concentration. The LH decrease after the peak of the LH surge on the day after ovulation is related to a negative effect of a postovulatory increase in progesterone. Measurable repeatability within mares between consecutive estrous cycles occurs during the preovulatory period in diameter of the ovulatory follicle and concentrations of LH and FSH. Hormone-laden follicular fluid passes into the peritoneal cavity at ovulation and transiently alters the circulating concentrations of LH and FSH. Double ovulations are associated with greater estradiol concentrations and reduced concentrations of FSH.

Keywords: Preovulatory follicle; Estradiol; LH; FSH; Ovulation; Mares

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INTRODUCTION

Characterization of the changes in concentrations of circulating hormones during the equine estrous cycle began in the early 1970s (progesterone,[1] luteinizing hormone [LH],[2] estradiol,[3] and follicle-stimulating hormone [FSH][4]); inhibin characterizations followed after a hiatus of 2 decades.[5] These classical descriptions were progressively honed and embellished over the ensuing approximately 34 years[6,7]). A flurry of temporal and mechanistic studies in 2005 to 2008 elucidated an intriguing interplay among the preovulatory follicle and circulating hormones. This review of the recent findings is directed to equine theriogenologists who are involved in monitoring, managing, and manipulating the mare reproductive system during the periovulatory period. Literature sources after 2004 are cited. Earlier reports may not be cited but can be found in reviews.[6-8]

FOLLICLE AND HORMONE INTERRELATIONSHIPS

Growth rates of the future ovulatory and nonovulatory follicles of the ovulatory follicular wave begin to deviate when the diameter of the future ovulatory follicle reaches an average of 22.5 mm. The ovulatory follicle grows at a rate of 3 mm/day, reaching 35 mm at day −4 (ovulation = day 0) or at the beginning of the preovulatory period. The growth rate continues until day −2 when it reaches a mean preovulatory plateau of approximately 41 mm (Fig. 1).

Mean circulating concentrations of estradiol, LH, FSH, and progesterone and the interrelationships among them[9,10] from day −4 to day 4 are depicted in Figure 1. Both the estradiol and LH periovulatory surges begin approximately 10 days before the periovulatory period or near the end of luteolysis and a day or two before follicle deviation. Estradiol from the dominant follicle forms a surge in the plasma that reaches a peak on day −2 and then recedes. The LH concentrations in the ovulatory surge increase slowly and then more rapidly, with the transition between the slow and rapid increases occurring at the peak of the estradiol surge. The enhanced output of LH reaches maximum on day 1. The prolonged ascending arm of the LH surge (10 days) with a peak occurring after ovulation contrasts with the short ascending arm (about 4 hours) with the peak before ovulation in cattle.[11] The

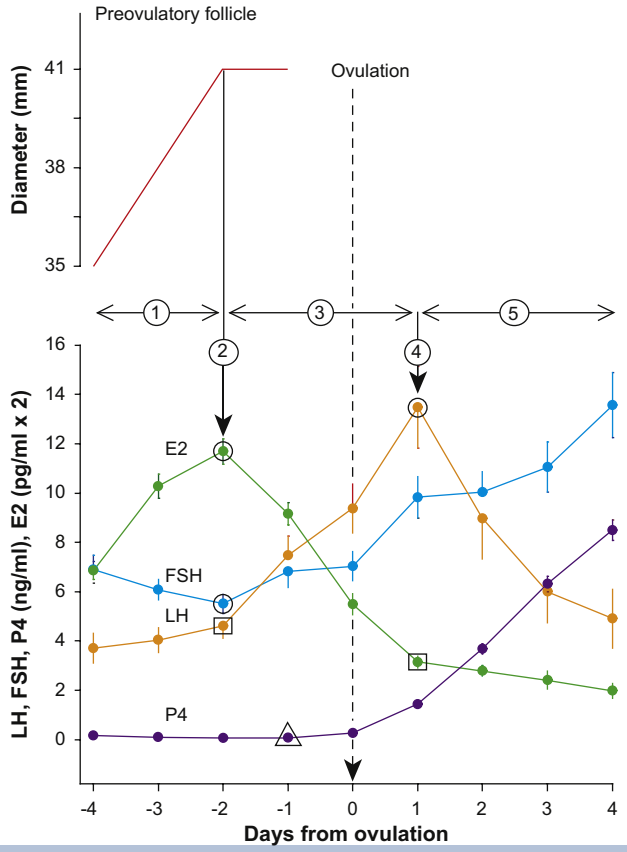

Figure 1. Schematic depiction of the growth of the preovulatory follicle and the mean ± SEM for periovulatory concentrations of estradiol (E2), LH, FSH, and progesterone (P4). Estradiol is shown at twice the actual concentrations. A circle around a mean indicates the day of a transition from a significant increase to a significant decrease (LH, E2) or from a decrease to an increase (FSH). A square indicates the day of change in the rate of a significant increase (LH) or rate of decrease (E2). A triangle indicates the beginning of a significant increase (P4). The circled numbers refer to the following: (1) days of continuous growth of the preovulatory follicle, decreasing FSH concentrations, and reduced rate of increase in LH, owing to a negative effect of the increasing E2; (2) day of acquisition of a negative effect of LH on E2 and apparently on cessation of follicle growth at the peak of E2; (3) days of rapidly decreasing E2 from the increasing negative effect of the rapidly increasing LH, resulting in turn in a lessening of the negative effect of E2 on LH and FSH and therefore a greater rate of production of LH and an increase in FSH; (4) day of transition between increasing and decreasing LH when P4 reaches a critical concentration; and (5) days of reduction in LH from increasing P4, with a lessening of the negative effect of LH on E2 and therefore a slower decrease in E2. Data were adapted from Jacob et al.[10]

change in rate of LH output during the surge in mares is attributable to a negative effect of estradiol on LH throughout the LH surge.[12] That is, the LH surge represents the positive influence of environmental factors, especially through changes in day length,[6] and a counteracting negative effect of estradiol[13]; the extent of the negative effect varies according to the changing concentrations of estradiol. A negative effect of the follicles[13] and specifically estradiol[12] on LH has been demonstrated by follicle ablations and treatments with estradiol.

The decrease in estradiol and the reduction or cessation in growth of the preovulatory follicle beginning on day −2 are attributable to the development of a reciprocal negative effect of LH on follicular estradiol production when LH reaches a critical concentration. This conclusion is based on temporal relationships and on the estradiol decrease and reduction in follicle expansion beginning immediately after human chorionic gonadotropin treatment.[14] The initial rapid decrease in estradiol on days −2 to 1 is attributable to the negative effect of the rapidly increasing LH on estradiol, and the slower decrease after day 1 is attributable to the diminishing negative effect of the decreasing LH, as depicted in Figure 1. The apparent molecular mechanisms in the granulosa cells that account for the intrafollicular preovulatory development of a negative effect of LH on estradiol have been discussed.[14]

One to three surges in FSH concentrations occur during the luteal phase. The first surge begins just before ovulation when estradiol is decreasing (Fig. 1), and the peak of the last surge occurs when the largest follicle of the resulting ovulatory follicular wave is approximately 13 mm. Concentrations of FSH reach a nadir between the last surge of the estrous cycle and the first surge that will peak during the next cycle. The nadir occurs concomitantly with the preovulatory estradiol peak, as shown in Figure 1. The occurrences of surges at different times and variation in the number of surges among mares account for the plateau in the mean FSH profile.[10] A negative effect of estradiol on FSH accounts for the periovulatory estradiol/FSH temporal relationships; the negative effect has been demonstrated by administration of estradiol.[15] Another player of follicle origin in the control of FSH surges is inhibin. The temporal relationships between FSH and inhibin during the estrous cycle are approximately inverse. The primary role of inhibin, however, appears to be early in the follicular wave before circulating estradiol begins to increase.[16] Thereafter, the two FSH suppressors work in concert, and the two hormones have a greater FSH-suppressing effect than either hormone alone.[17]

A slight but significant increase in circulating progesterone occurs with consistency among mares on the day of detection of ovulation or a collapsed follicle (Fig. 1). The LH decrease after the peak of the LH surge on day 1 is related to a negative effect of the postovulatory increase in