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Follicle suppression of circulating follicle-stimulating hormone and luteinizing hormone before versus after emergence of the ovulatory wave in mares

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Abstract

The effect of the ovarian follicles on plasma concentrations of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) before versus after the expected emergence of the ovulatory follicular wave was studied on Days 0 to 18 (Day 0 = ovulation) in four groups of mares (n = 6/group). In addition to a control group, all follicles ≥6 mm in diameter were ablated on Days 0.5, 6.5, or 12.5 in a herd of mares with reported emergence at 6 mm of the future ovulatory follicle on mean Day 10.5. Concentrations of FSH were not different between the Day-0.5 or Day-6.5 ablation groups and the corresponding controls. However, ablation on Day 12.5 resulted in an immediate FSH increase (group-by-day interaction, $P < 0.003$). For LH, ablation on Day 0.5 resulted in an interaction ($P < 0.02$), partially from lower ($P < 0.05$) concentrations on each of Days 15.5 to 18.0 than that in the controls, whereas ablation on Days 6.5 or 12.5 did not result in a significant group effect or interaction. Testosterone concentration, but not progesterone or estradiol concentration, was lower ($P < 0.04$) on Day 2 in the Day-0.5 ablation group than that in the controls. We inferred that follicles did not contain adequate FSH suppressors on Days 0.5 and 6.5 and that they were present only in the Day-12.5 ablation group or after the expected emergence of the ovulatory wave. The hypothesis of an association between low postovulatory concentrations of an ovarian steroid and low concentrations of LH after Day 15 was supported.

Keywords: Gonadotropins; Mares; Ovarian follicles; Testosterone; Ultrasonography

1. Introduction

During the ovulatory follicular wave in monovulatory farm species (cattle, horses), the follicles grow at a similar rate until diameter deviation (reviewed in Refs. [1,2]). Deviation in mares occurs when the largest follicle is a mean of 22.5 mm and is characterized by continued growth rate of the developing dominant follicle and decreased growth rate of subordinate follicles. Follicular waves that form a dominant follicle as a result of the deviation process, whether or not the dominant follicle ovulates, are called major waves [3]. Anovulatory major waves are uncommon in pony mares. Minor follicular waves (no dominant follicle) are common between ovulation and the emergence of the next ovulatory wave. Emergence of both the ovulatory wave and minor waves is stimulated by a surge in follicle-stimulating hormone (FSH) [4]. In major waves, the surge begins to decrease as a result of FSH suppressors from follicles when the largest follicle of the ovulatory wave is 14 to 16 mm [5–7]. Surges of

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FSH occur every 3 to 7 d preceding the surge that stimulates the emergence of the ovulatory wave [8]. Although some surges of FSH are associated with the emergence of minor follicular waves, it is unknown whether FSH suppressors from the follicles of minor waves terminate the surges, as in major waves.

The follicular FSH suppressor that terminates the FSH surge associated with the ovulatory follicular wave is inhibin [1,2,9]. Inhibin begins to have a negative effect on FSH at the peak of the FSH surge. Estradiol begins to increase in the circulation 2 or 3 d after the peak of the wave-inducing FSH surge, or 1 or 2 d before the beginning of follicle deviation [10,11]. Estradiol has a negative effect on FSH, but an essential FSH-suppressing role of estradiol near the time of deviation is doubtful [11]. Testosterone and other androgens are also produced by equine follicles [12,13]. A series of studies has indicated that androgens suppress circulating FSH during estrus by stimulating the accumulation of FSH in the pituitary for release during diestrus [14–16].

The introduction of aspiration of the contents of all follicles ≥5 or 6 mm in diameter to initiate a new follicular wave in mares [5] was followed by extensive use of follicle ablation as a research tool. The procedure has been used for studying the interrelationships among follicles of the ovulatory follicular wave, uncomplicated by the masking effect of follicles from previous anovulatory waves [5–7,10,13,17–20]. In reported studies, follicle ablations were done approximately 10 d after ovulation, and FSH concentrations began to increase immediately after ablation [5,10,18]. A similar ablation approach for study of the interrelationships of follicular waves and hormones other than the interrelationships associated with the ovulatory wave has not been reported.

Concentrations of luteinizing hormone (LH) increase immediately after treatment 10 d postovulation with a combination of follicle ablation and administration of prostaglandin $F_{2\alpha}$ (PGF). In contrast, the beginning of an LH increase in controls occurs about 15 d postovulation, which is near the beginning of follicle deviation during spontaneous ovulatory waves. The postablation LH increase is attributable to the sudden decrease in progesterone from the administration of PGF at the time of ablation. This is consistent with the demonstrations of a negative effect of progesterone on LH [17,18] and the beginning of an LH increase when progesterone reaches low concentrations toward the end of luteolysis [21]. In this regard, when PGF was not given in association with ablation 10 d postovulation, LH did not increase until 5 d after ablation [18], implicating the PGF treatment alone in the immediate LH increase. These results indicate that study of the effect of the follicles on gonadotropin concentrations can be complicated by the induction of luteolysis at the time of follicle ablation. Estradiol has a negative effect on circulating LH concentrations throughout the ovulatory LH surge [22]; therefore, in the absence of estradiol, the ovulatory LH surge apparently would be more prominent. Estradiol also has been shown to be a potent stimulator of pituitary storage of LH, in the absence of progesterone and testosterone in ovariectomized mares [16].

The current study involved follicle ablations at various times during the first half of the interovulatory interval to determine if small antral follicles (approximately 6 to 20 mm) have an effect on circulating FSH and LH concentrations before emergence of the ovulatory follicular wave. In addition, it was observed that ablation of follicles on the day of ovulation was followed by lower concentrations of LH beginning 15.5 d after ovulation. Therefore, the hypothesis was tested that the reduction in LH near the end of the estrous cycle was related to a lower circulating concentration of a follicular steroid (estradiol, progesterone, or testosterone) early in the estrous cycle.

2. Materials and methods

2.1. Animals and ultrasonography

The mares were mixed breeds of large ponies and apparent pony-horse crosses weighing 250 to 400 kg and aged 7 to 20 yr. Mares with a docile temperament, a single ovulation, and no apparent abnormalities of the reproductive tract as determined by ultrasound examination [23] were used during April to June (Northern Hemisphere). The lengths of the pre-experimental interovulatory intervals were 20 to 28 d, indicating that the lengths were not reduced as in association with intrauterine fluid collections (metritis [24,25]). The mares were kept under natural light in an open shelter and outdoor paddock and were maintained by ad libitum access to water, trace-mineralized salt, and a mixture of grass and alfalfa hay. Mares were handled according to the U.S. Department of Agriculture Guide for Care and Use of Agricultural Animals in Agricultural Research.

Transrectal B-mode ultrasonographic examinations of the ovaries and measuring of follicles were done with a real-time ultrasound scanner (Aloka SSD-3500; Aloka America, Wallingford CT, USA) and a linear-array 7.5-MHz transducer. Examinations were done as described [23]. Follicles ≥6 mm were ablated by transvaginal