Journal of Equine Veterinary Science 33 (2013) 607-614

Journal of Equine Veterinary Science

journal homepage: www.j-evs.com

Original Research

Estradiol Effects on Secretagogue-Induced Prolactin Release: Disparity in Responses to Sulpiride, Exercise, Epinephrine, Prostaglandin-$F_{2\alpha}$, and Thyrotropin-Releasing Hormone

Donald L. Thompson Jr. PhD, Sarah C. Clavier MS, Pamela B. Mitcham PhD, Lisa R. Earl MS

School of Animal Sciences, Louisiana Agricultural Experiment Station, LSU Agricultural Center, Baton Rouge, LA

ARTICLE INFO

Article history:
Received 29 June 2012
Received in revised form
19 September 2012
Accepted 28 September 2012
Available online 13 November 2012

Keywords:
Estradiol
Prolactin
Exercise
Secretagogue
Sulpiride

ABSTRACT

Three experiments were conducted (1) to assess the effects of estradiol pretreatment on the prolactin response to various secretagogues, and (2) to determine whether elevated plasma thyroxine concentrations altered the prolactin responses to those secretagogues. Geldings were available and were used because their prolactin and luteinizing hormone responses to estradiol and dopamine antagonists are known to be similar to those in seasonally anovulatory mares. In the first experiment, performed in summer, estradiol cypionate (ECP; 100 mg) treatment of geldings increased ($P = .07$) plasma prolactin concentrations before the onset of exercise, and repeated exercise bouts stimulated ($P < .001$) plasma prolactin concentrations after each bout; there was no interaction with estradiol pretreatment. Epinephrine injection (5 μg/kg of body weight) did not alter prolactin concentrations. Prostaglandin-$F_{2\alpha}$ administration (10 mg Lutalyse) stimulated ($P < .001$) prolactin concentrations, but there was no interaction with ECP pretreatment. Sulpiride administration (0.1 mg/kg of body weight) stimulated ($P < .001$) prolactin concentrations, and there was a greater ($P = .038$) response in ECP-treated geldings relative to controls. In the second experiment, performed in winter, ECP (50 mg) pretreatment of geldings before 21 days of daily thyrotropin-releasing hormone (TRH; 1.5 mg) injections did not alter prolactin secretion ($P > .1$); TRH stimulated prolactin secretion only after the very first injection. In the third experiment (performed in July), pretreatment of geldings with 50 mg of thyroxine in biodegradable particles (day 0) raised ($P < .001$) plasma thyroxine concentrations in plasma for the duration of the experiment, but had no effect on the prolactin responses to two exercise bouts on day 5, to an injection of prostaglandin-$F_{2\alpha}$ on day 9, or to an injection of sulpiride on day 13. The previously reported stimulation of plasma prolactin concentrations by estradiol pretreatment and subsequent sulpiride administration in mares, as evidenced herein in geldings, does not occur when prolactin is stimulated by exercise, prostaglandin-$F_{2\alpha}$, or TRH. The practical impact of these data is that stimulation of prolactin concentrations after ECP treatment in winter, in an effort to stimulate ovarian activity in seasonally anovulatory mares, is likely limited to dopamine antagonists. Results of the third experiment indicate that TRH is not likely the mediator in the prolactin response to exercise or prostaglandin-$F_{2\alpha}$ injection.

1. Introduction

Estradiol pretreatment of seasonally anovulatory mares greatly enhanced the prolactin response to the daily injection of the dopamine antagonist, sulpiride [1], as well

Approved for publication by the Director of the Louisiana Agricultural Experiment Station as manuscript number 2012-230-7524.

Corresponding author at: Donald L. Thompson Jr., PhD, School of Animal Sciences, Louisiana State University, S. Campus Drive, Baton Rouge, LA 70803-4210.

E-mail address: dthompson@agctr.lsu.edu (D.L. Thompson).

0737-0806/$ - see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jevs.2012.09.014

as the prolactin response to thyrotropin-releasing hormone (TRH), and resulted in a hastened ovulation relative to sulpiride treatment alone. This same stimulatory effect of estradiol was observed for geldings in November [2,3]. Although treatment with estradiol alone for 21 days increased pituitary prolactin content in ovariectomized pony mares in summer by approximately 250%, the effect on plasma prolactin concentrations was temporary (lasting <10 days) and minimal (approximately 30% above control values) [4].

Clavier et al. [3] showed that estradiol treatment of geldings increased the prolactin response to injections of sulpiride but had no effect on the dose of sulpiride required to cause 50% of maximal response. It has been well documented that exercise and other forms of sympathetic stimulation (e.g., twitching) result in an immediate increase in plasma prolactin concentrations [5-8], although the mechanism for this is unknown. The generally accepted model for the regulation of prolactin production and secretion is a tonic suppression by dopamine secreted by neurons of the tuberoinfundibular portion of the hypothalamus [9]. Thus, any rapid stimulation of prolactin secretion could be due to a brief interruption of dopamine input to the pituitary gland (such as is the case with sulpiride antagonism), or it could be due to some unknown stimulatory agent from the hypothalamus. Although prolactin-releasing peptides have been described [10,11], administration of the bovine factor to horses did not alter plasma prolactin concentrations (D. L. Thompson Jr, unpublished data).

The present experiments were designed (1) to determine whether the stimulatory effect of estradiol pretreatment would be evident after administration of prolactin secretagogues other than dopamine antagonists, and (2) to assess the possibility that TRH is the mediator of the prolactin responses to exercise and prostaglandin-$F_{2\alpha}$ injection. Geldings were available and were used because their prolactin and luteinizing hormone (LH) responses to estradiol and dopamine antagonists are known to be similar to those of seasonally anovulatory mares. Our working hypothesis was that if estradiol simply stimulates the intracellular mechanisms responsible for prolactin production in the lactotropes, then the response to any stimulus should result in a greater response in estradiol-primed horses relative to controls. The first experiment compared the effect of estradiol pretreatment on the short-term prolactin response in geldings to exercise, prostaglandin-$F_{2\alpha}$ injection, epinephrine injection, and sulpiride injection. The second experiment assessed whether estradiol pretreatment would stimulate prolactin secretion in geldings receiving daily injections of TRH for 21 days in the winter. Our premise in the third experiment was that pretreatment with thyroxine in biodegradable particles would suppress endogenous TRH secretion and thus alter the prolactin response to exercise and prostaglandin-$F_{2\alpha}$ injection, if indeed TRH was the mediator of prolactin release in response to those stimuli.

2. Materials and Methods

All procedures described herein were approved by the Institutional Animal Care and Use Committee of the LSU Agricultural Center. In all, 19 geldings of light horse breeds were used in the three experiments. They ranged in age from 6 to 16 years and had body weights (BWs) between 520 and 565 kg and body condition scores [12] between 5.5 and 8. They were routinely housed on pasture, consuming native grasses most of the year, winter ryegrass in the winter, and supplemental native grass hay as needed in the transition period in the fall.

2.1. Experiment 1

The first experiment, conducted in summer of 2009, compared the effect of estradiol pretreatment on the short-term prolactin responses in geldings to exercise, prostaglandin-$F_{2\alpha}$ injection, epinephrine injection, and sulpiride injection. Twelve geldings were allotted to two groups of six such that average ages, BWs, and body condition scores were similar for the two groups. One group was then randomly chosen to receive estradiol pretreatment and the other group served as the control.

On day 0 (June 26, 2009), the six geldings in the estradiol pretreatment group each received a single injection of 100 mg of estradiol cypionate (ECP; Bio-Release estradiol cypionate LA; BET Pharm, Lexington, KY, www.BETPharm.com) intramuscularly in the neck, and control geldings received an equivalent injection of vegetable oil (2 mL). The standard routine for the subsequent administration of the prolactin secretagogue challenges was as follows: for each challenge, all geldings were brought from pasture at approximately 07:00 and were tethered loosely under an open-sided shed. A 14-ga catheter was inserted in one jugular vein and was held in place with cyanoacrylate-based glue. An aqueous solution of 6% sodium citrate (w/v) was used to keep the catheters patent. After a minimum of 1 hour, the geldings were each administered the challenge (the order in which the geldings were challenged was randomized in each case), and blood samples (5 mL) were collected from the catheter at predetermined times and placed into tubes containing sodium heparin (20 U/mL of blood). At the end of all blood sampling, the geldings were returned to pasture. All blood samples were placed at 5°C until centrifugation (within 30 minutes or less), which was at 1,200 × *g* for 15 minutes; plasma was stored at −15°C.

On day 5, all geldings were exercised at a trot for 5 minutes in a round pen for a total of four bouts, 1 hour apart (0, 60, 120, and 180 minutes). Blood samples were collected at −10, 0, 10, 20, 30, 45, 60, 70, 80, 90, 105, 120, 130, 140, 150, 165, 180, 190, 200, 210, 225, and 240 minutes relative to the first exercise bout. On day 7, all geldings received an intravenous injection of epinephrine (Sigma Chem. Co., St. Louis, MO) in saline at 5 μg/kg of BW through the jugular catheter. Blood samples were collected at −10, 0, 10, 20, 30, 45, 60, 90, and 120 minutes relative to the injection. On day 10, all geldings received an intramuscular injection of 10 mg of prostaglandin-$F_{2\alpha}$ (Lutalyse; Pfizer Animal Health, New York, NY, www.lutalyse.com) in the neck. Blood sampling times were the same as for epinephrine injection. On day 13, all geldings received an intravenous injection of sulpiride (0.1 mg/kg of BW of the racemic mixture; Sigma) in saline through the jugular catheter; blood sampling times were the same as for epinephrine injection.