

# Comparison of Vitex agnus castus Extract and Pergolide in Treatment of Equine Cushing's Syndrome

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Vitex agnus castus Extract<sup>a</sup> does not decrease elevated plasma adrenocorticotrophic hormone (ACTH) concentrations or ameliorate clinical signs of disease in horses with Equine Cushing's Syndrome. Authors' address: University of Pennsylvania, New Bolton Center, 382 West Street Road, Kennett Square, PA 19348. © 2002 AAEP.

## 1. Introduction

Pituitary pars intermedia hyperplasia, which causes Equine Cushing's Syndrome, has been treated with dopaminergic agonists such as pergolide. Vitex agnus castus (Chaste Berry) extract has been used medicinally for centuries for various human female cycle disorders, and a lay article claimed its therapeutic efficacy in horses with pituitary hyperplasia and other hormonal dysfunction.<sup>1</sup> Ethanol extracts of the seeds have been demonstrated to bind to the D2 receptor of rat pituitary cells and inhibit prolactin secretion.<sup>2,3</sup> To our knowledge it is unknown whether Vitex agnus castus extract affects secretion of plasma ACTH or pro-opiomelanocortin (POMC)s. Pergolide is a dopaminergic agonist at D2 receptor sites in vitro, although there are no specific studies in horses. Elevated concentrations of POMCs and plasma ACTH have been measured in horses with pituitary hyperplasia.<sup>4-6</sup> Pergolide has been shown to affect plasma POMC and plasma ACTH concentrations in horses.<sup>4,5,7</sup> Because of increasing interest in the use of Vitex agnus castus in horses, we conducted a study on the effects of a commer-

cially available product marketed for use in horses (Vitex agnus castus Extract) and compared it with the effect of pergolide.

## 2. Materials and Methods

Fourteen horses were selected for treatment with Vitex agnus castus Extract based on clinical signs of pituitary dysfunction and elevated plasma ACTH concentrations (n = 12) or dexamethasone suppression testing (n = 4). Only three of the horses were less than 20 yr of age. There were eight castrated males and six females. Individual clinical signs varied but included hirsutism and failure to seasonally shed, abnormal fat distribution, weight loss, laminitis, lethargy, and abnormal estrus cycles. Because we had observed variability of baseline plasma ACTH and insulin values, two to three blood samples were taken at about the same time of day for several days at each testing period; all samples were assayed by the Diagnostic Laboratory at Cornell University. Plasma prolactin concentrations are pending. All horses were maintained and medicated by their owners without any changes in their environment. The manufacturer's recommended

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## NOTES

## MEDICINE II

dose of Vitex agnus castus Extract was administered throughout the trial; details on the active ingredient(s) and concentration in the extract were not available. The original protocol for evaluating Vitex agnus castus was treatment for 6 mo, but this was shortened in some horses because of deterioration in clinical signs and/or endocrinologic test values. Four horses were treated for 2 mo, four were treated for 4 mo, and six were treated for 6 mo. After Vitex agnus castus Extract was discontinued, nine of these horses (five females and four males) were treated with pergolide (0.002–0.006 mg/kg, q 24 h, PO); at this time, seven horses have been treated for 3 mo and two for longer than 4 mo. Three of these horses had two trials of pergolide treatment before and after the Vitex agnus castus Extract trial, separated by approximately 1 yr.

### 3. Results

Before medication, ACTH concentrations values varied greatly for the 12 horses with elevated plasma ACTH (47 to >1250 pg/ml versus the normal range of 9–35 pg/ml). Four horses, including two with normal plasma ACTH concentrations, failed to show normal suppression of resting cortisol concentration to <1 µg/dl after a standard dexamethasone suppression test.

Only 1 of 14 horses was thought to remain stable and not deteriorate clinically during treatment with Vitex agnus castus. This mare's plasma ACTH concentrations (427, 45, and 72 pg/ml) returned to normal (18, 26, and 21 pg/ml) at 2 mo and remained normal or very minimally elevated (36, 44, 51, and 41 pg/ml) for the next 3 mo, during which she received no treatment. Her insulin concentrations were normal at all times. Of the other three horses treated for 2 mo, plasma ACTH concentrations increased. After 4 mo of Vitex agnus castus Extract treatment, plasma ACTH concentrations approximately doubled in two horses, and the dexamethasone suppression test remained abnormal in the two horses with normal plasma ACTH concentrations. Of the six horses treated for 6 mo, one showed no significant decrease in highly elevated plasma ACTH concentrations (514, >1250, and 1094 pg/ml versus 1032, 960, and 453 pg/ml). The plasma ACTH concentration increased more than twofold in four horses, and the dexamethasone suppression test remained abnormal in one horse. Plasma insulin concentrations were measured in 12 horses and did not significantly change.

Of the nine horses treated with pergolide, three horses with abnormal dexamethasone suppression tests before the treatment showed normal suppression; however, in one mare tested at monthly intervals, normalization did not occur until 3 mo after initiating 3 mg, q 24 h, PO. Approximately 6 wk later, when the dose was decreased to 2 mg and the dexamethasone suppression test was repeated, it was again abnormal. In the three horses treated twice with pergolide, the dexamethasone suppres-

sion tests were abnormal in the interval when they were not treated. In one horse (~500 kg body weight), the dexamethasone suppression test remained abnormal after 1 mo of 1 mg, q 24 h, PO, and 2 mo of 2 mg, q 24 h, PO. Because he also seemed lethargic, the drug was discontinued; the owner thought that his attitude subsequently improved. Evaluation of elevated plasma ACTH concentrations in six horses after 1-mo pergolide treatment showed no change in two horses, but in four horses, the values declined to less than 50% of pre-treatment values; some values declined to 20% of pre-treatment levels, although still above normal range. After 2 mo, plasma concentrations of ACTH had further declined in these horses. By 3 mo, one horse's plasma ACTH concentrations were normal, three horses had only slightly elevated concentrations (highest value, 60 pg/ml), and one horse's concentrations remained between 240–363 pg/ml (That horse's pre-treatment values were 1032, 960, and 453 pg/ml). One horse not evaluated at 3 months, but evaluated at 6, 8, and 9 mo, had plasma ACTH concentrations ranging from 40–61 pg/ml (versus pre-treatment values of 161 and 180 pg/ml). Insulin concentrations were normal in seven of eight horses before and during pergolide treatment; one horse's elevated insulin concentrations declined (47, 145, and 91 µIU/ml to 11, 70, and 41 µIU/ml). With the exception of one horse, clinical signs generally improved.

### 4. Discussion

Our study showed that Vitex agnus castus Extract, the commercially available form of Vitex agnus castus, did not have a beneficial effect in horses with pituitary pars intermedia hyperplasia (Equine Cushing's Syndrome); clinical signs sometimes worsened, plasma ACTH concentrations decreased in only 1 of 12 horses, and the dexamethasone suppression test remained abnormal in the horses tested. In contrast, with the exception of one horse, pergolide had a beneficial effect, although individual horses often required dosages above what many practitioners customarily use. Whether higher doses of Vitex agnus castus would have an effect is speculative. Also, as with many herbal or plant medicinals, standardization of the active ingredients can be difficult; environmental conditions and ripeness of fruits can affect their chemical composition. Proprietary concerns of the manufacturer and lack of tests to measure the essential oils, biologic activity, or bioavailability hinder conclusions about Vitex agnus castus itself. In vitro studies on effects of pure Vitex agnus castus extracts on equine pituitary cells would demonstrate whether hormone secretion is affected. Until there is more information, the authors do not advise using Vitex agnus castus for treating Equine Cushing's Syndrome.

The authors thank Emerald Valley Botanicals for providing Hormonise®. The authors gratefully ac-

knowledge J. F. Roser for assay of Prolactin concentrations.

#### References and Footnote

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<sup>a</sup>Hormonise®, The Animal Health Co., Ltd., Halstead, England.