Management of Early PPID in Horses[1]

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Introduction

Pituitary Pars Intermedia Dysfunction (PPID) has previously been diagnosed and managed as an older horse disease with advanced clinical signs. However, the early clinical signs of PPID are typically more subtle.[2] Early clinical signs include: decreased athletic performance, change in attitude/lethargy, delayed hair coat shedding (subtle), regional hypertrichosis, loss of epaxial muscle mass (topline), regional adiposity and laminitis.[2] Most equine practitioners easily diagnose advanced cases of PPID in horses with generalized hypertrichosis. Unfortunately, generalized hypertrichosis is not an early clinical sign of PPID; and veterinarians remain challenged when asked to examine these horses. One of the major limitations of diagnostic testing for PPID is the sensitivity of available diagnostic assays. Resting ACTH has been shown to have a decreased sensitivity in horses with early signs compared to advanced PPID.[3] Thyrotropin-releasing hormone (TRH) stimulation test has been shown to have an increased sensitivity of detecting horses with early signs compared to resting ACTH.[2] Few studies exist concerning endocrinologic testing and follow-up monitoring the clinical progression and diagnostic assay results following treatment in horses with early PPID.

Study Purpose

The purpose of this study was to identify cases with early clinical signs of PPID based on clinical signs and laboratory testing, then determine improvements in ACTH levels using resting ACTH, TRH stimulation test and clinical signs over time.

Materials and Methods

Sixteen horses (followed from January through December) were enrolled with at least one early clinical sign of PPID listed above, and diagnostically confirmed by the TRH stimulation test measuring ACTH at 0 (T0ACTH; pre-TRH) and 10 (T10ACTH) min following 1mg i.v. TRH administration. Fasting insulin and glucose was also determined pre-treatment and at each follow-up visit. Beginning in January, each horse was administered Prascend® (pergolide tablets) orally at a starting dosage of 2 mcg/kg once daily, dosage adjusted to effect if required, but not to exceed 4 mcg/kg daily, per manufacturers label recommendations. A history, physical examination, and TRH stimulation test evaluating T0ACTH and T10ACTH was conducted monthly for 5 months, following initial treatment administration, then every other month until study completion.

Statistical Analysis

The comparative changes to the baseline ACTH levels over time were evaluated using descriptive statistics. The statistical significance of the change in ACTH levels were evaluated using a confidence interval of 95%.

Important Safety Information

PRASCEND is for use in horses only. Treatment with PRASCEND may cause loss of appetite. If severe, a temporary dose reduction may be necessary. PRASCEND has not been evaluated in breeding, pregnant or lactating horses. PRASCEND tablets should not be crushed due to the potential for increased human exposure. Refer to the package insert for complete product information.

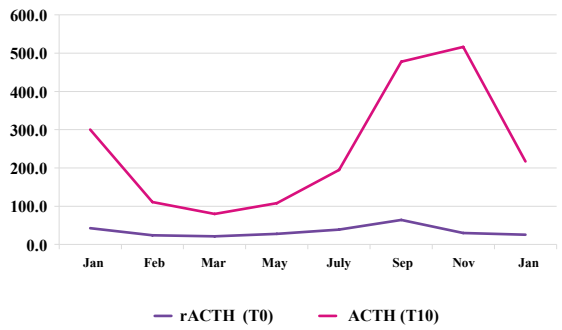
Results

At initial examination, the most common clinical signs at initial diagnosis were regional hypertrichosis (9/16), delayed shedding (5/16) and muscle wasting (4/16). The baseline (arithmetic mean) for T0ACTH and T10ACTH for all horses was 44.6 mg/mL and 360.5 pg/mL, respectively. Following 6 months of treatment, the resting T0ACTH in 12 of 16 (75%) horses was less than normal reference range (35 pg/mL), whereas 7 of 16 (44%) of horses had T10ACTH less than the recommended T10ACTH reference range (110 pg/mL). In June, the decrease from baseline for T0ACTH was 7.1%; whereas the decrease from baseline for T10ACTH was 49.1%. All horses with regional hypertrichosis and delayed shedding were considered improved or resolved, whereas body condition and muscle wasting was slightly improved. Four adverse events not related to treatment were reported and considered resolved within 24 hours.

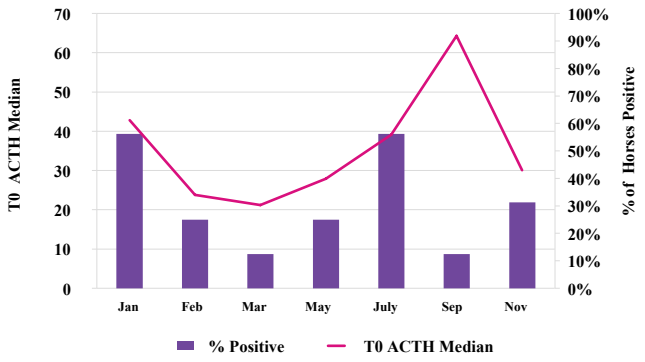
T0 ACTH and T10 ACTH

	Day	Number Positive	Percent Positive	T0 ACTH Minutes Median	Number Positive	Percent Positive	T10 ACTH Minutes Median	n
Jan	0	9	56.25	42.8	12	75.00	300.5	16
Feb	30	4	25.00	23.8	8	50.00	111.1	16
Mar	60	2	12.50	21.2	6	37.50	79.7	16
May	120	4	25.00	27.9	8	50.00	107.5	16
July	**180**	**9**	**56.25**	**39.1**	**13**	**81.30**	**194.5**	**16**
Sep	**240**	**2**	**12.50**	**64.3**	**16**	**100.00**	**477.5**	**16**
Nov	**300**	**5**	**31.25**	**30.1**	**16**	**100.00**	**516.5**	**15**
Jan	360	6	40.00	25.1	11	73.30	217.0	16

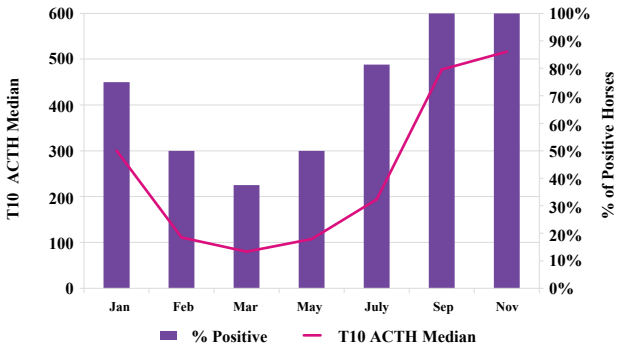
ACTH (Median)



Horses Positive & T0ACTH (Median)



Horses Positive & T10ACTH (Median)



Discussion

All horses had improvements in clinical signs following treatment. No significant changes from baseline were observed in insulin or glucose parameters. Following 5 months of treatment, 12 of 16 (75%) horses T0ACTH decreased below normal range compared to 7/16 (44%) T10ACTH that decreased below the recommended reference range. Although all horses responded clinically, the T10ACTH in 9/16 (54%) horses remained positive. Even though T10ACTH did not decrease below reference range, the option to hold the treatment dosage at the same level is justifiable based on clinical sign improvement. Further long-term studies in large numbers of horses should be conducted in horses with early clinical signs of PPID.

Take Home Message

PPID horses that were initially diagnosed using the TRH stimulation procedure should be retested utilizing the same diagnostic test [TRH stimulation procedure (T10ACTH) measuring ACTH]. In this study, even though all horses responded clinically, only approximately 50% of the T10ACTH levels decreased within normal reference range. Even though the T10ACTH may not decrease within the normal T10ACTH reference range, the option to hold the treatment dosage at the same level is justifiable, based on clinical sign improvement.

References

1. Haffner J, Cocquyt C, Neal D, Grubbs S, Keefe T. Management of early PPID in horses. *J Vet Intern Med* 2016; 30: 1502.

2. Equine Endocrinology Group. 2017 Recommendations for the diagnosis and treatment of pituitary pars intermedia dysfunction (PPID).

3. Durham A, McGowan C, Fey K, Tamzil Y, van der Kolk J. Pituitary pars intermedia dysfunction: diagnosis and treatment. *Equine Vet. Educ.* 2014; 26 (4) 216-223.