A Comparison of the Relative Efficacies of Domperidone and Reserpine in Treating Equine “Fescue Toxicosis”

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After the parenteral administration of bromocriptine (simulating “fescue toxicosis”), oral domperidone was effective in resolving pre- and postpartum agalactia and prolonged gestation in pregnant pony mares. Oral reserpine was ineffective in treating prepartum agalactia and prolonged gestation; however, it did resolve postpartum agalactia. Unlike domperidone, reserpine induced sedation and diarrhea as side effects. Authors’ Addresses: Dept. of Veterinary Pathobiology (Evans), Dept. of Veterinary Medicine and Surgery, College of Veterinary Medicine, University of Missouri-Columbia, Columbia, MO 65211 (Youngquist), Animal Sciences Unit, College of Agriculture, Food, and Natural Resources, University of Missouri-Columbia, Columbia, MO 65211 (Loch), Dept. of Animal, Dairy, and Veterinary Sciences, Poole Agricultural Center, Clemson University, Clemson, SC 29634-0361 (Cross).

1. Introduction

Equine “fescue toxicosis” is characterized by agalactia, prolonged gestation, abortion, dystocia, thickened placentas, and foal dysmaturity and is associated with the ingestion of endophyte-infected tall fescue (Festuca arundinacea). The DA2 dopamine receptor agonistic activity of ergopeptide alkaloids, produced by the tall fescue endophyte, Neotyphodium coenophialum (formerly Acremonium coenophialum), is thought to be responsible for the depressions in circulating, maternal levels of prolactin and progestins, which contribute to the development of the clinical signs of this syndrome. With more than thirty-five million acres of tall fescue pasture (over 75% of it endophyte-infected) in the United States, and more than 688,000 horses grazing those pastures, “fescue toxicosis” is extremely significant to the US horse industry in terms of economics and horse wellbeing.1,2 Ireland et al. reproduced the clinical signs of “fescue toxicosis” in late-gestational ponies, using the semisynthetic ergopeptine alkaloid, bromocriptine, and demonstrated the utility of a DA2 dopamine receptor antagonist, perphenazine, in the prevention of the clinical signs of this syndrome.3 Redmond et al. later introduced the use of the DA2 dopamine receptor antagonist, domperidone in the prophylaxis of equine “fescue toxicosis” and suggested the occurrence of fewer side effects with this preparation because of its failure to cross the blood–brain barrier.4 The Rauwolfian alkaloid, reserpine, depletes serotonin, dopamine, and norepinephrine depots in the brain and other tissues.
and has been used in the treatment and prevention of equine “fescue toxicosis.”

The objective of this study was to compare the relative efficacies of domperidone and reserpine in the treatment of prolonged gestation, pre- and postpartum agalactia, and other clinical signs associated with this syndrome in pregnant mares.

2. Materials and Methods

Eighteen pregnant pony mares of various ages, bred to a single stallion, were injected intramuscularly twice daily (beginning day 300 of gestation) with either bromocriptine (n = 13), prepared in solution as described by Ireland et al., or with an equal volume of saline (n = 5). The dosage of bromocriptine was 0.08 mg/kg, divided into 2 equal doses administered at 07:00 and 17:00 hours. Treatment continued until parturition or until the establishment of normal lactation in mares, which were agalactic at the time of parturition. Maternal levels of immunoassayable prolactin and progestins were measured in plasma and serum, respectively, every other day up to day 320 of gestation and then daily until the bromocriptine was discontinued. The treatment groups consisted of five saline-treated controls (group 1) and thirteen bromocriptine-treated pony mares subdivided into six groups. These subdivisions included groups 2 and 3 (stillbirths and short gestations, respectively; n = 3), group 4 (postpartum agalactia-treated with domperidone; n = 3), group 5 (postpartum agalactia-treated with reserpine; n = 2), group 6 (337 + days/prolonged gestation-treated with domperidone; n = 3), and group 7 (337 + days/prolonged gestation-treated with reserpine; n = 2).

Domperidone and reserpine were administered orally at dosages of 1.1 mg/kg q 24 h and 0.01 mg/kg q 24 h, respectively, and the mares were weighed weekly to adjust the doses of medication. The mares were observed prior to foaling and assisted, as necessary, during parturition. Mammary development was monitored pre- and postpartum, and mares were considered agalactic in the absence of normal amounts of mammary secretions. Foals were examined postpartum for signs of dysmaturity and treated accordingly. Statistical analyses of the data were performed using a one-way ANOVA. Fischer’s least significant difference test was utilized for pairwise group comparisons with a value of p < 0.05 considered statistically significant.

3. Results

All bromocriptine-treated mares had significantly lower circulating maternal blood levels of prolatin and progestins and were agalactic prior to the administration of domperidone or reserpine. The mean gestational lengths of the bromocriptine treatment groups 2, 3, 6, and 7 were different from those observed for the control mares (mean gestational length 332.3 ± 2.03 days). Dystocias, placental ab-normalities, and foal dysmaturity were observed in all bromocriptine treatment groups, except for the mares with prolonged gestation receiving domperidone (group 6). Group 6 mares (mean gestational length 343.3 ± 2.62 days) demonstrated significantly elevated blood levels of progestins and prolactin and increased lactogenesis following the commencement of domperidone therapy as compared to the group 7 reserpine-treated mares (mean gestational length 350.0 ± 3.20 days). Reserpine did not appear to alter prepartum agalactia or prepartum circulating, maternal levels of prolactin or progestins, and these mares exhibited mild to moderate sedation and diarrhea. Postpartum agalactic mares treated with domperidone and reserpine (groups 4 and 5, respectively) exhibited similar elevations in maternal blood levels of prolactin and normal lactogenesis, although the reserpine treated mares exhibited some sedation and diarrhea.

4. Discussion

The relative efficacies of domperidone and reserpine in treating the clinical signs of equine “fescue toxicosis” have not been previously reported. In this study, using parenteral administration of bromocriptine to simulate “fescue toxicosis” in pregnant pony mares, oral domperidone was effective in resolving pre- and postpartum agalactia and prolonged gestation. This efficacy of domperidone further substantiates the role of maternal and/or fetal DA2 dopamine receptors in the pathogenesis of equine “fescue toxicosis.” Although it induced sedation and diarrhea as side effects, oral reserpine, at the dose administered, was ineffective in treating prepartum agalactia and prolonged gestation. However, the depletion of dopamine and possibly other neurotransmitters (from depots in the brain or other tissues), which was induced by reserpine, was sufficient to resolve postpartum agalactia observed in pony mares. These data should be useful in making clinical decisions regarding a therapeutic approach to equine “fescue toxicosis.”

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References and Footnotes


\(^a\)2-bromo-\(\alpha\)-ergocryptine, Sigma Chemical Company, P.O. Box 14508, St. Louis, MO 63178.

\(^b\)Homologous equine prolactin RIA kit, Dr. A.F. Parlow, Harbor-UCLA Medical Center, 1000 W. Carson Street, Torrance, CA 90509.

\(^c\)Coat-A-Count progesterone, Diagnostic Products Corporation, 5700 West 96th Street, Los Angeles, CA 90045-5597.

\(^d\)Equi-tox, 500 mg domperidone prepared in 5 ml of molasses, Equi-tox, Inc., Center for Applied Technology, 511 Westinghouse Rd, Pendleton, SC 29670-1103.

\(^e\)Reserpine, 0.25 mg tablets, United Research Laboratories, Inc., P.O. Box 8546, Philadelphia, PA 19124.