

Semen, Testicular Volume, Sperm Production Efficiency, and Sexual Behavior of Stallions Treated with Trimethoprim-Sulfamethoxazole and Pyrimethamine

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The treatment of normal breeding stallions with recommended dosages of trimethoprim-sulfamethoxazole and pyrimethamine did not affect semen quality, testicular function, or sexual behavior. There was evidence of transient musculoskeletal or neurologic deficits (30 days into treatment through 30 days after treatment) that affected copulatory form and ejaculation pattern. Authors' address: Section of Medicine and Reproduction, Dept. of Clinical Studies, School of Veterinary Medicine, New Bolton Center, University of Pennsylvania, 382 W. Street Rd., Kennett Square, PA 19348. Dr. Bedford's current address is Dept. of Veterinary and Animal Sciences, Paige Lab, University of Massachusetts at Amherst, Amherst, MA 01003. © 1998 AAEP.

1 Introduction

Equine protozoal myeloencephalitis is a neurologic disease caused by the migration of the protozoon *Sarcocystis neurona* (*falcatula*) into the central nervous system. Clinical signs result from diffuse and asymmetric central nervous system involvement.^{1,2} Currently, no antemortem diagnostics can confirm this disease.³ Treatment includes the administration of trimethoprim-sulfamethoxazole or sulfadiazine and pyrimethamine (TMS-Pyr).^{1,2} In breeding stallions, anecdotal evidence suggests that there are possible adverse effects of trimethoprim-sulfamethoxazole and pyrimethamine on semen quality, sexual behavior, and ejaculatory function. In treated stallions, it is difficult to determine whether changes in reproductive function are due to the disease or to the treatment. In male rats and mice, treatment with

pyrimethamine has reduced testis and epididymal weights, testicular and epididymal sperm counts, and fertility.^{4,5} Decisions concerning the therapeutic or prophylactic treatment of valuable breeding stallions rest on a clear understanding of potential side effects. The objective of this study was to evaluate the effects of TMS-Pyr on semen characteristics, testicular function, sexual behavior, and ejaculatory function in otherwise normal pony stallions.

2. Materials and Methods

Twelve mature (ages 3-18 years) pony stallions (125-300 kg) were used. These stallions were kept at pasture throughout the study. Six stallions were treated with trimethoprim-sulfamethoxazole^a (20 mg/kg, PO q 12 h) and pyrimethamine^b (1 mg/kg, PO q 24 h) for 90 days during the summer and fall (June

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through September).² Six stallions matched for age, semen quality, sexual behavior, and ejaculatory efficiency were used as untreated controls. Semen quality measures (gel-free and gel volumes, sperm concentration, total number of spermatozoa, percent of progressively motile sperm, percent of morphologically normal sperm, and pH, in two ejaculates collected 1 h apart as an estimate of daily sperm output), sexual behavior (erection latency, mount readiness latency, erection rigidity score, copulatory form, and agility), and ejaculatory efficiency (number of mounts and number of thrusts to ejaculation, ejaculation latency, and number of ejaculatory pulses) were evaluated in semen collection trials at 30-day intervals immediately before, during, and for 60 days after the course of the treatment. Testicular volume and sperm production efficiency (millions of sperm per cubic centimeter of testicular parenchyma at estimated daily sperm output) were concurrently estimated. Blood cell counts were monitored monthly.

The handling of stallions and all measures were conducted blind to treatment status. Stallions were compared with themselves over time and as control and treatment groups by using within- and between-subjects repeated measures analyses of variance.

3. Results

All measures of semen quality, except percent of progressively motile sperm, were similar ($p > 0.10$) for untreated and treated stallions during baseline and throughout the study. The percent of progressively motile sperm was significantly greater for treated stallions than for untreated stallions ($p < 0.05$) at the beginning and again 60 days after the initiation of treatment. Testicular volume and sperm production efficiency were not affected by treatment ($p > 0.05$). There were no differences that were due to treatment in the erection latency, mount readiness latency, or erection rigidity score. At 30, 60, and 90 days into treatment and at 30 days after treatment, four of the six treated stallions displayed changes in copulatory form or ejaculation pattern. These changes consisted of unsteadiness upon mounting the dummy, clumsy or weak thrusting, failure to flex the back and wrap closely around the dummy mount, and thready or absent ejaculatory pulses, resulting in a dribbling rather than a forceful expulsion of semen. All of these functions were again normal at 60 and 90 days after treatment had ended. The number of mounts, number of thrusts on the ejaculatory mount, and the number of ejaculatory pulses did not differ with treatment ($p > 0.05$). Blood counts were within the range of normal throughout the study, with no differences that were due to treatment ($p > 0.05$).

4. Discussion

Results are encouraging, but the arbitrary treatment of stallions is not recommended. The major problem in four treated stallions concerned transient changes in mounting position, which appeared to reflect musculoskeletal stiffness across the back and possible neurologic changes in the hindlimbs and ejaculatory apparatus. Interestingly, this same pattern of copulatory form was observed in one treated stallion who was positive for equine protozoal myeloencephalitis and three of six prophylactically treated stallions on one well-managed farm in our practice all during the 1997 breeding season. In each case the signs developed at approximately 5-6 weeks into treatment and subsided within approximately 3 weeks, though treatment continued. In association with this behavior, all four of these stallions experienced ejaculatory difficulty and falling during semen collection. In humans, there is some evidence that folic acid deficiency may result in spinal-cord-related neurologic problems.⁶ However, there was no other evidence of folic acid deficiency in any of the treated stallions. As a result of the findings in this study, we recommend caution in continuing to breed a stallion if neurologic signs worsen or arise, especially in stallions not confirmed to have the disease.

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