

Diclazuril and Equine Protozoal Myeloencephalitis

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Equine protozoal myeloencephalitis is an infectious disease of equines. Subjective nonmasked evaluations of four affected Thoroughbreds suggest clinical improvement after oral diclazuril. These horses had relapsed following standard therapy; they have shown no signs of relapse since diclazuril administration ceased. A rigorous evaluation of the therapeutic potential of benzene acetonitrile derivatives in equine protozoal myeloencephalitis appears warranted. Authors' addresses: School of Veterinary Medicine, Ohio State University, Columbus, OH 43210 (Saville) and Maxwell H. Gluck Equine Research Center and Dept. of Veterinary Science, University of Kentucky, Lexington, KY 40506 (all other authors). © 1997 AAEP.

1. Introduction

Equine protozoal myeloencephalitis (EPM) is a disease of the horse that affects the brain and spinal chord. It is caused by *Sarcocystis neurona*. *S. neurona* has a two-host life cycle¹; opossums are the definitive hosts, and avians are the intermediate hosts.²

Current therapy consists of long-term treatment with pyrimethamine and sulfonamides. Although this is successful in many cases, occasional relapses occur. Diclazuril is a triazine derivative used in the prophylaxis of coccidiosis in poultry. A review of the literature suggested to us (Granstrom and Tobin) that triazine-based agents were worth evaluating for the treatment of EPM.

2. Materials and Results

EPM was diagnosed based on clinical signs, a positive spinal tap, exclusion of other causes, and, for horses 1-3, response to current therapy followed by relapse when therapy was withdrawn. All clinical

evaluations were subjective and nonmasked (SN-M). Unless otherwise stated, treatment was with oral diclazuril (5 mg/kg q 24 h) for 21 days.^a

A 12-year-old Thoroughbred mare with severe spinal ataxia was treated with oral pyrimethamine and trimethoprim-sulfamethoxazole. She was donated to the University of Kentucky following her third relapse. This mare was barely ambulatory (grade 4+) and was confined in a stall. After 11 days of treatment, marked improvement was observed. Toward the end of treatment, she showed some regression, but she has since steadily improved. Some muscle atrophy and signs of permanent neurologic damage remain; however, no signs of relapse have been observed since treatment ceased more than 1 year ago.

A 4-year-old Thoroughbred gelding in training had symmetric posterior ataxia and was graded a 3 out of 5 on a neurological exam. Deficits were apparent at rest and at all gaits 3 months after standard therapy. On the second day of diclazuril treatment, the horse

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fell and was maintained in a sling throughout treatment. When removed from the sling at 8 weeks, he showed signs of weakness in the hindquarters. Over the subsequent 5 months he has regained strength and muscle tone and continues to show improvement with no indications of relapse.

A 12-year-old Thoroughbred mare with grade 4 out of 5 asymmetric posterior ataxia had relapsed three times following conventional treatment. Treatment with diclazuril ended 5 months ago, and the horse continues to show slow improvement.

A 2-year-old Thoroughbred colt in training with acute cranial nerve signs and grade 3/5 ataxia was treated for 4 weeks with diclazuril. After 5 days of diclazuril treatment, the ataxia had improved. Treatment ended 12 weeks ago and the colt has returned to light exercise.

Horses 1-3 remain cerebrospinal fluid positive for *S. neurona*; horse 4 has not yet been retested.

3. Discussion

The subjective, nonmasked clinical responses reported here suggest that triazine-based agents may have potential for treatment of EPM. Many apicomplexans contain a plastid-like organelle of photosynthetic origin. Sensitivity of apicomplexans to triazine derivatives may relate to this organelle, and such a mechanism of action is consistent with the apparently low toxicity of these agents in mammals and birds.

The apparent absence of relapse or recurrence (SN-M evaluations) may be significant. Based on

the clinical histories, relapses or recurrences were expected, either because of regrowth of residual *S. neurona* or reinfection.

Although these results are of interest, one must keep in mind that these are SN-M experiments in a very small number of horses. Rigorous scientific evaluation is required to determine whether or not diclazuril has therapeutic efficacy and to establish its therapeutic window, its potential for adverse reactions, and its relationship to current therapies.

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References and Footnotes

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2. Fenger CK, Granstrom DE, Langemeier JL, et al. Identification of opossums (*Didelphis virginiana*) as the putative definitive host of *Sarcocystis neurona*. *J Parasitol* 1995;81:916-919.

*Clinacox, Janssen Pharmaceuticals, Beerse, Belgium.