Comparison of intratumoral administration of cisplatin versus bleomycin for treatment of periocular squamous cell carcinomas in horses

A. P. Théon, DVM, MS; J. R. Pascoe, DVM, PhD; J. E. Madigan, DVM, MS; G. Carlson, DVM, PhD; L. Metzger, MS

Objective—To compare therapeutic benefits of intratumoral administration of cisplatin and bleomycin for squamous cell carcinoma of the eyelids in horses.

Animals—25 horses with 27 T2-stage periocular squamous cell carcinomas.

Procedure—Horses were treated 4 times at 2-week intervals with a slow-release formulation of cisplatin (1 mg/cm^3 of tissue) or bleomycin (1 IU/cm^3 of tissue). A two-stage design was used to minimize the sample size in each treatment arm.

Results—The local control rate at 1 year for lesions treated with cisplatin was 93 ± 6%, and with bleomycin was 78 ± 10%. Difference in local control duration between the 2 treatment groups was not significantly different. A high tumor proliferative fraction index value was associated with a higher local (in-field) control rate, but also with a higher risk of marginal and regional recurrences. Tumors with a low proliferative fraction index value (< 28%) had 9.5-times higher (P = 0.0411) risk of recurrence than those with a high index value. Local acute reactions were similar in the 2 treatment groups, and chronic reactions were not observed.

Conclusions—Cisplatin and bleomycin were effective anticancer agents for carcinoma of the eyelid in horses. Based on therapeutic benefit and treatment cost, cisplatin was found to be a better choice for intratumoral chemotherapy of eyelid carcinomas.

Clinical Relevance—Results of this study confirm the value of intratumoral chemotherapy, using cisplatin, for treatment of cutaneous squamous cell carcinomas in horses. (*Am J Vet Res* 1997;58:431–436)

Intratumoral administration of anticancer agents is used for treatment of tumors in dogs, cats, horses, and human beings.[1-4] Route and schedule of administration of anticancer agents, as well as the use of slow-release formulations, result in protracted high tumor-to-plasma drug concentration ratios. As a result, this treatment technique is particularly appropriate for anticancer drugs for which efficacy is concentration dependent.[5] Cisplatin,[a] an anticancer drug without cell-cycle specificity, is used for intratumoral administration because of its high concentration-response relationship.[6] Therapeutic benefit of cisplatin is optimized by manipulation of the release rate in tissue and time interval between treatments.[3,7] Intratumoral administration of anticancer drugs is also appropriate for drugs with cytokinetic specificity.[8] Because of differences in cellular proliferative activity among carcinomas in the horse,[9] the efficacy of intratumoral administration may be improved by the use of drugs with cell-cycle specificity.

The goal of the study reported here was to test the hypothesis that the use of a cycle-specific drug may improve the therapeutic ratio of intratumoral chemotherapy. Therapeutic benefits of intratumoral administration of cisplatin and bleomycin sulfate[b] in water-sesame-oil emulsion for treatment of periocular squamous cell carcinomas in horses were compared by use of a two-stage plan. Bleomycin was chosen as an anticancer drug for this trial because of its cell-cycle specificity and its selective toxicity for epithelial tumors.[10] In addition, intratumoral administration of bleomycin in sesame oil is effective for treatment of cutaneous warts and squamous cell carcinomas in human beings.[11,12] Although 5-fluorouracil has shown some activity against carcinomas, it was not chosen for this study because intratumoral administration of 5-fluorouracil was not found to be effective as a single agent for treatment of carcinoma in horses.[13]

Materials and Methods

Design—Horses considered eligible for enrollment in the study were those with World Health Organization T2-stage carcinoma, good general health, and without clinical evidence of regional or systemic dissemination of eyelid tumors. Horses were randomly administered cisplatin or bleomycin intratumorally. A two-stage design was used to allow for early termination of the trial in the face of negative treatment results.[14] The criterion for conducting the 2-stage trial was a 30% higher 1-year local control rate by use of bleomycin compared with cisplatin. In the first stage of the trial, the minimum number of lesions necessary to detect a difference between treatments (power = 0.8 and type-I error rate = 5%), using a local control rate of at least 60% for cisplatin,[3] was 26 lesions (13 lesions in each treatment arm). If the 1-year local-control rate for bleomycin was not significantly different than that for cisplatin, the study would be stopped. If there was a significant difference between the 1-year local-control rates, a second group of horses would be entered in the study until a total of 62 lesions were treated (31 in each treatment arm) to obtain an accurate estimate of the difference.

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From the Departments of Surgical and Radiological Sciences (Théon, Pascoe, Metzger) and Medicine and Epidemiology (Madigan, Carlson), School of Veterinary Medicine, University of California, Davis, CA 95616-8745.

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