The Effects of Intravenous Formaldehyde on Hemostasis in Normal Horses

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IV formaldehyde has been advocated for treatment of hemorrhaging in horses. However, at recommended doses, formaldehyde had no effect on coagulation parameters or template bleeding times in normal horses. At twice the recommended dose, horses experienced muscle fasciculations, hypersalivation and distress without evidence of renal or hepatic damage. Authors’ address: Dept. of Veterinary Clinical Sciences, College of Veterinary Medicine, Washington State University, Pullman, WA 99164. © 1999 AAEP.

1. Introduction
For many years, IV formaldehyde therapy has been advocated for use in horses for control of purpura hemorrhagica and other forms of hemorrhaging. However, few scientific reports support its efficacy or safety. In 1940, Roberts reported administration of 4 to 50 ml of 4% to 12% formalin solution in 400 to 500 ml distilled water to horses, with an average decrease in coagulation time of 75.2%. Higher doses were associated with adverse reactions including restlessness, lacrimation, salivation, nasal discharge, frequent defecation, sweating, muscle tremors and abdominal pain.

Administration of 5% formalin to goats at 1.1 ml/kg markedly decreased clotting time and bleeding time for approximately 30 minutes postinjection. Decreases in bleeding time occur with enhanced primary hemostasis, usually indicative of a platelet or endothelial change. Formaldehyde is useful as a tissue fixative because it cross-links proteins. This cross-linking might alter platelet or endothelial cell surface proteins, resulting in activation of platelets or decreased endothelial permeability.

For horses, doses of approximately 10 ml of 37% formaldehyde or 30 to 150 ml of 10% buffered formalin in 1 l of isotonic fluids have recently been recommended for control of bleeding. In addition to the gross behavioral changes observed by Roberts in formaldehyde-treated horses, formaldehyde is potentially hepatotoxic; high concentrations of formaldehyde dehydrogenase in the liver are responsible for catabolism of formaldehyde.

We investigated the effects of IV formaldehyde administration on coagulation parameters and bleeding time in normal, healthy horses and horses with prolonged bleeding times secondary to aspirin administration to determine if formaldehyde is safe and efficacious for enhancement of hemostasis.

2. Materials and Methods
For all experiments, six horses were used in a blinded, two-way cross-over design. Before use, each horse was determined to be in good health by
general physical examination, complete blood count (CBC) and serum biochemical profile. Horses were housed in individual box stalls with freely available grass hay and water.

In Experiment 1, 10 ml of 37% formaldehyde diluted in 1 l of lactated Ringer’s solution (LRS) was administered IV over 15 minutes. Control horses received LRS without formaldehyde. Horses were monitored for 24 hours after infusion for changes in coagulation parameters (activated partial thromboplastin time [APTT], prothrombin time [PT], activated clotting time [ACT], platelet counts and fibrin degradation products [FDPs]), template bleeding time, CBC, serum biochemical profile and physical examination parameters (temperature, heart rate, respiratory rate, gastrointestinal sounds, behavior). After a 1-week wash-out period, the protocol was repeated with each horse receiving the opposite treatment.

In Experiment 2, treated horses received 20 ml of 37% formaldehyde in 1 l of LRS over 15 minutes. In Experiment 3, horses were pretreated with aspirin at 20 mg/kg once daily for 3 days before treatment with 10 ml of 37% formaldehyde in LRS or LRS alone. Data were analyzed using two-way analysis of variance for repeated measurements with Bonferroni’s post hoc test.

3. Results
Formaldehyde-treated horses had no significant differences in physical examination parameters, coagulation parameters, CBC or serum biochemical profile compared with LRS-treated control horses. Template bleeding times were not significantly different between treated and control horses at 20 minutes (3.04 ± 0.86 min versus 3.54 ± 1.35 min) or 60 minutes (2.64 ± 0.70 min versus 2.80 ± 0.43 min). Horses had no adverse effects during or after infusion. When the dose of formaldehyde was doubled, horses exhibited lacrimation, salivation, muscle fasciculations, tachycardia, tachypnea and mild to moderate distress after administration of 250 to 750 ml. This reaction ended within 5 to 10 minutes of discontinuation of the infusion in each horse, and there were no long-term negative effects on physical examination parameters, CBC or serum biochemical profile. Despite these adverse behavioral effects, there was no effect of formaldehyde treatment on coagulation parameters or template bleeding time. Administration of aspirin resulted in prolonged template bleeding times (control, 3.66 min; aspirin, 6.04 min). However, in these aspirin-treated horses, formaldehyde administration did not result in any significant differences in template bleeding times between treated and control horses at 20 minutes (6.64 ± 1.53 min versus 5.59 ± 1.42 min) or 60 minutes (5.10 ± 1.55 min versus 5.33 ± 1.16 min).

4. Discussion
IV formaldehyde administration had no significant effect on the measured parameters of primary or secondary hemostasis in normal or aspirin-treated horses. Higher doses resulted in adverse behavioral effects, tachycardia, lacrimation, salivation and muscle fasciculations, without evidence of long-term hepatic or renal toxicity. Unless the effects of formaldehyde differ in horses that are actively hemorrhaging, it is difficult to recommend formaldehyde as a hemostatic agent.

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References
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