Influence of general anesthesia on pharmacokinetics of intravenous lidocaine infusion in horses

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Objective—To compare the disposition of lidocaine administered IV in awake and anesthetized horses.

Animals—16 horses.

Procedure—After instrumentation and collection of baseline data, lidocaine (loading infusion, 1.3 mg/kg administered during 15 minutes (87 µg/kg/min); constant rate infusion, 50 µg/kg/min) was administered IV to awake or anesthetized horses for a total of 105 minutes. Blood samples were collected at fixed times during the loading and maintenance infusion periods and after the infusion period for analysis of serum lidocaine concentrations by use of liquid chromatography with mass spectral detection. Selected cardiopulmonary parameters including heart rate (HR), mean arterial pressure (MAP), arterial pH, PaCO₂, and PaO₂ were also recorded at fixed time points during lidocaine administration. Serum lidocaine concentrations were evaluated by use of standard noncompartmental analysis.

Results—Serum lidocaine concentrations were higher in anesthetized than awake horses at all time points during lidocaine administration. Serum lidocaine concentrations reached peak values during the loading infusion in both groups (1,849 ± 385 ng/mL and 3,348 ± 602 ng/mL in awake and anesthetized horses, respectively). Most lidocaine pharmacokinetic variables also differed between groups. Differences in cardiopulmonary variables were predictable; for example, HR and MAP were lower and PaO₂ was higher in anesthetized than awake horses but within reference ranges reported for horses under similar conditions.

Conclusions and Clinical Relevance—Anesthesia has an influence on the disposition of lidocaine in horses, and a change in dosing during anesthesia should be considered. (Am J Vet Res 2005;66:574–580)
Serum lidocaine concentrations measured at this lower dose during anesthesia were similar to those reported for unanesthetized horses receiving twice the dose (as recommended by Malone et al), but the reported range was broad, and study conditions were not standardized to account for other variables that could influence drug concentrations.

The purpose of the study reported here was to expand on those earlier studies and compare the serum concentration and pharmacokinetics of lidocaine administered IV in healthy awake and anesthetized horses during a defined range of study conditions. In an effort to standardize study conditions and observe adverse effects of lidocaine, selected cardiopulmonary parameters were also assessed.

Materials and Methods

Horses—The study protocol was reviewed and approved by the Colorado State University Animal Care and Use Committee (ACUC). Two groups of 8 horses were studied. Group 1 horses included 8 mares (mean ± SD weight, 546 ± 63 kg) that did not receive any additional drugs (awake) for the duration of the study. Group 2 horses were anesthetized for routine arthroscopy of the shoulder joint. As part of another study and included 8 horses representing both sexes (2.3 ± 0.4 years and 424 ± 32 kg). Both groups of horses were considered healthy on the basis of results of physical examination, CBC, and serum biochemistry analyses. Food was withheld from horses for 12 hours prior to the morning of the study; water was available ad libitum. Horses were weighed the morning of the study.

Instrumentation—Horses were instrumented with a 14-gauge, 5-inch jugular venous catheter dedicated to IV fluid and lidocaine administration and a 20-gauge, 2-inch percutaneous arterial catheter for blood pressure measurements and collection of blood samples for pH, blood gas, and PCV measurements and total protein (TP) and serum lidocaine concentrations. Approximately 2 to 10 mL of 2% lidocaine solution was administered SC at least 30 minutes prior to sample collection to facilitate percutaneous arterial catheter placement in awake horses because they were unsedated and inconsistent in their response to physical restraint (eg, nasal twitch) and in anesthetized horses to facilitate venous catheter placement prior to anesthesia. Arterial catheters were placed in standing horses in the transverse facial (6 horses) or carotid (2 horses) artery. Arterial catheters in all anesthetized horses were placed in the facial artery (8 horses). In circumstances in which the arterial catheter was unable to be maintained (eg, during recovery from anesthesia), a second dedicated catheter was placed in the opposite jugular vein for blood collection. Polyionic fluids (5 mL/kg/h, IV) were administered to horses in both groups.

Anesthetic protocol—All horses were weighed and instrumented with a jugular venous catheter, as described. Horses received xylazine (0.87 ± 0.2 mg/kg, IV), followed 5 minutes later by administration of guaifenesin (36 ± 13 mg/kg, IV) and ketamine (2.1 ± 0.1 mg/kg, IV) for induction of anesthesia, according to the protocol of the concurrent ACUC-approved orthopedic study. Horses were placed in dorsal recumbency and instrumented as described previously. Additionally, an ECG (base-apex lead) and nasopharyngeal temperature probe were placed. Anesthesia was maintained with sevoflurane in oxygen, as determined to be appropriate on the basis of clinical signs of anesthetic depth; vaporizer settings were recorded at times corresponding to lidocaine sampling. Body temperature was maintained at 36.5 ± 1°C, and ventilation was controlled to a PaCO₂ of 55 ± 5 mm Hg with mechanical ventilation. Mean arterial blood pressure was maintained > 65 mm Hg with administration of dobutamine as necessary.

Experimental protocol—Horses in both groups received a loading infusion of lidocaine (1.3 mg/kg, IV) during 15 minutes (87 μg/kg/min), followed immediately by a maintenance infusion of lidocaine (50 μg/kg/min) for an additional 90 minutes, for a total consecutive lidocaine administration time of 105 minutes. Lidocaine was administered with a calibrated syringe infusion pump. For anesthetized horses, lidocaine administration was initiated within 10 to 15 minutes after induction of anesthesia, following instrumentation, establishment of study conditions, and collection of baseline data.

Twenty milliliters of arterial blood was collected prior to, at the midpoint (7.5 minutes), and at completion (15 minutes) of the loading infusion of IV lidocaine administration, then at 15-minute intervals throughout the maintenance infusion. Lidocaine administration was discontinued at 105 minutes, and arterial blood samples were collected at 30-minute intervals for the first 2 hours after lidocaine infusion, then at 60-minute intervals for 4 hours, totaling 465 minutes (7.75 hours) of sample collection.

Twenty milliliters of venous blood was collected at various times when the arterial catheter could not be maintained (4 samples in awake horses and 8 samples in anesthetized horses, all in the period after lidocaine infusion). Results of a concurrent study simultaneously comparing serum lidocaine concentrations of venous and arterial blood from 3 horses in the awake group indicated no difference between blood collection sites. Samples were centrifuged, and the serum supernatant was collected, placed in tubes, and stored at –40°C until analysis.

Heart rate (HR) and rhythm, respiratory rate (RR), mean arterial pressure (MAP), and temperature (rectal for awake and nasopharyngeal for anesthetized horses) were recorded prior to and at each blood sample collection time throughout loading and maintenance infusions of lidocaine. Heart and respiratory rates were determined via auscultation in standing horses and via ECG and mechanical ventilation rates, respectively, in anesthetized horses. Mean arterial pressure was determined directly with an aneroid manometer in standing horses and a calibrated pressure transducer in anesthetized horses. The zero level in the manometer and transducer was set at the presumed level of the heart base (point of shoulder). Three milliliters of arterial blood was collected in a heparinized syringe (needle and syringe flushed with heparin [1,000 U/mL], and then the heparin was discarded) for pH and blood gas analysis (Paco₂ and PacO₂) and PCV measurements and TP concentrations prior to and at 15 and 75 minutes during lidocaine administration and at 165 minutes (60 minutes after end infusion). Samples were stored in ice water and analyzed within 60 minutes of collection; pH and blood gas values were corrected for rectal and body temperatures. Observation of CNS signs of lidocaine toxicosis in awake horses involved assessment of mental status (depression or excitement) and the presence of muscle fasciculations. Cardiovascular effects were assessed on the basis of HR, heart rhythm, and MAP.

Determination of serum lidocaine concentrations—Serum lidocaine concentrations were measured in duplicate by use of high-performance liquid chromatography with mass spectral detection by use of a technique validated at the Equine Analytical Chemistry Laboratory at the University of California, Davis. Briefly, reference, calibration, and test samples were pipetted into autosampler vials and vortexed for 5 to 10 seconds. A mixture containing acidic acetonitrile (ace-
tonitrite and 1M acetic acid mixed in a ratio of 9:1) including mepivacaine (200 ng/mL; internal standard) was added to each sample vial. After addition of the internal standard, the contents of each vial were again mixed for 1 minute on a multipulse rack vortex mixer (speed, 60 to 70; pulse, 60), and all samples were refrigerated for 30 minutes at 4°C, then centrifuged at 1,580 × g for 10 minutes at 4°C. The vials were transferred to an autosampler rack, and the supernatant was injected for analysis.

Quantitative analyses were performed by use of a mass spectrometer equipped with a liquid chromatograph system. The mobile phase was composed of a solvent mixture of acetoniitrite with 0.05% trifluoroacetic acid (TFA; solvent A) and water with 0.05% TFA (solvent B). The liquid chromatograph pump provides a gradient of the acetoniitrite from 30% to 90% at a flow rate of 0.9 mL/min. The concentration of lidocaine in each sample was determined in duplicate by the internal standard method by use of the peak area ratio and linear regression analysis.

Pharmacokinetic analysis—Serum lidocaine concentrations were evaluated by use of standard noncompartmental analysis. Maximum concentration (C_{max}) of serum lidocaine and time of C_{max} (T_{max}) were estimated from the data. The elimination rate constant (k_{el}) was calculated as the slope of the terminal phase of the serum concentration curve that included a minimum of 3 points. Terminal half-life (t_{1/2}) was calculated as t_{1/2} = 0.693/k_{el}. Linear trapezoidal areas were used in calculating the area under the serum lidocaine concentration versus time curve (AUC) from 0 to 15 minutes (AUC_{0–15}), from 15 to 105 minutes (AUC_{15–105}), from 105 to 465 minutes (AUC_{105–465}), and extrapolated to infinity (AUC_{∞}). Other pharmacokinetic parameters (eg, clearance [Cl], volume of distribution during steady state [V_{d(ss)}], and mean residence time [MRT]) were determined by statistical software by use of standard noncompartmental equations.

Statistical analyses—Data were summarized as mean ± SD. The significance and magnitude of treatment group (awake vs anesthetized) differences for observations with a single measurement were assessed by use of a restricted maximum likelihood–based mixed-effect model that included the categorical, fixed effect of treatment and a random animal effect (horse within treatment). For repeated observations, the statistical model included the fixed effects of treatment, time, and the interaction of treatment and time. An autoregressive correlation structure (for cardiopulmonary variables) or a first-order Toeplitz correlation structure (for lidocaine concentrations) allowing for heterogeneous variances was used to model the within-subject effects. The Kenwardroger approximation was used to estimate denominator degrees of freedom. Analysis was performed by use of a software option for fitting linear models. Where differences were detected, least squares means were reported, and all hypotheses were tested by use of a 2-sided level of significance of 0.05.

Results
The disposition profile differed between groups during and after IV lidocaine administration (Figure 1). Despite higher baseline concentrations in the awake horses (130 ± 229 ng/mL), compared with anesthetized horses (19 ± 53 ng/mL), the mean serum lidocaine concentrations of awake horses were significantly less than anesthetized horses during loading and maintenance infusion periods. The highest serum lidocaine concentrations were reached during the loading infusion for both groups (1,849 ± 385 ng/mL and 3,348 ± 602 ng/mL for the awake and anesthetized groups, respectively).

Most of the lidocaine pharmacokinetic variables derived from measured lidocaine concentrations differed significantly between groups (Table 1). Differences were recorded for C_{max}, V_{d(ss)}, Cl, (AUC_{0–15}), (AUC_{15–105}), (AUC_{105–465}), and (AUC_{∞}) but not for T_{max}, t_{1/2}, or MRT between awake and anesthetized horses.

Horses in the anesthetized group were younger than awake horses, with a proportional difference in body weight between groups. Heart rate, RR, temperature, and MAP differed between groups at baseline and...
Table 1—Mean ± SD values for pharmacokinetic parameters after administration of lidocaine (loading infusion, 87 µg/kg/min, IV, for 15 minutes; constant rate infusion, 50 µg/kg/min, IV, for 90 minutes) to awake (n = 8) and anesthetized (8) horses.

<table>
<thead>
<tr>
<th>Kinetic variable</th>
<th>Awake</th>
<th>Anesthetized</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>C_max (µg/mL)</td>
<td>2.0 ± 0.27</td>
<td>3.8 ± 0.95</td>
<td>0.001</td>
</tr>
<tr>
<td>t_{1/2} (min)</td>
<td>79 ± 41</td>
<td>54 ± 14</td>
<td>0.132</td>
</tr>
<tr>
<td>Cl (mL/min/kg)</td>
<td>29 ± 7.6</td>
<td>15 ± 3.3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Vd (L/kg)</td>
<td>0.79 ± 0.16</td>
<td>0.40 ± 0.09</td>
<td>0.001</td>
</tr>
<tr>
<td>AUC_{0–15} (µg min/mL)</td>
<td>21 ± 2.6</td>
<td>37 ± 6.5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>AUC_{105–465} (µg min/mL)</td>
<td>130 ± 72</td>
<td>260 ± 50</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>AUC_{0–15} (µg min/mL)</td>
<td>55 ± 27</td>
<td>110 ± 37</td>
<td>0.003</td>
</tr>
<tr>
<td>AUC_{0–15} (µg min/mL)</td>
<td>210 ± 52</td>
<td>410 ± 84</td>
<td>0.001</td>
</tr>
<tr>
<td>MRT (min)</td>
<td>28 ± 7.8</td>
<td>27 ± 5.4</td>
<td>0.835</td>
</tr>
</tbody>
</table>

C_max = Maximum observed serum drug concentration. \( t_{1/2} \) = Terminal half-life. Cl = Total body clearance. Vd = Apparent volume of distribution. AUC_{0–15} = Area under the serum concentration-time curve from zero to 15 minutes. AUC_{105–465} = Area under the serum concentration-time curve from 105 to 465 minutes. AUC_{0–15} = Area under the serum concentration-time curve extrapolated to infinity. MRT = Mean residence time.

at all times during lidocaine infusion (Table 2). Heart rate ranged from 43 to 46 beats/min in the awake group, compared with 29 to 36 beats/min in the anesthetized group. Dobutamine was used periodically during sevoflurane anesthesia in all 8 horses at a dosage of 0.25 to 2.0 µg/kg/min (most commonly 0.5 to 1.0 µg/kg/min) to maintain MAP > 65 mm Hg. The vaporizer setting for sevoflurane was 3.88 ± 0.44 (mean ± SD) at the start of the loading infusion, 3.78 ± 0.41 at the end of the loading infusion and beginning of maintenance infusion, 3.13 ± 0.27 midway through the maintenance infusion, and 2.88 ± 0.19 at the end of the infusion.

Differences between arterial pH, PaCO₂, and PaO₂ were also observed between the 2 groups (Table 3). During lidocaine infusion, PaCO₂ and PaO₂ values were consistently lower in the awake group than in the anesthetized group. The PCV and TP concentrations did not differ between groups; mean ± SD values for PCV and TP concentration were 33 ± 4% and 6.5 ± 0.4 g/dL, respectively, for awake horses and 35 ± 4% and 6.3 ± 0.5 g/dL, respectively, for anesthetized horses.

Table 2—Mean ± SD values for selected parameters in awake (n = 8) and anesthetized (8) horses in which lidocaine (loading infusion, 87 µg/kg/min, IV, for 15 minutes; constant rate infusion, 50 µg/kg/min, IV, for 90 minutes) was administered.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>7.5</th>
<th>15</th>
<th>30</th>
<th>45</th>
<th>60</th>
<th>75</th>
<th>90</th>
<th>105</th>
</tr>
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<tbody>
<tr>
<td>HR* (beats/min)</td>
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</tr>
<tr>
<td>Awake</td>
<td>44 ± 7</td>
<td>43 ± 6</td>
<td>43 ± 4</td>
<td>45 ± 5</td>
<td>46 ± 4</td>
<td>44 ± 4</td>
<td>45 ± 7</td>
<td>46 ± 6</td>
<td>43 ± 8</td>
</tr>
<tr>
<td>Anesthetized</td>
<td>32 ± 4</td>
<td>29 ± 2</td>
<td>31 ± 3</td>
<td>33 ± 4</td>
<td>34 ± 2</td>
<td>34 ± 2</td>
<td>34 ± 4</td>
<td>36 ± 5</td>
<td>36 ± 6</td>
</tr>
<tr>
<td>RRT* (breaths/min)</td>
<td></td>
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<td></td>
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<td></td>
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<td></td>
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</tr>
<tr>
<td>Awake</td>
<td>12 ± 2</td>
<td>11 ± 1</td>
<td>11 ± 1</td>
<td>11 ± 1</td>
<td>11 ± 1</td>
<td>12 ± 2</td>
<td>11 ± 1</td>
<td>11 ± 1</td>
<td>11 ± 1</td>
</tr>
<tr>
<td>Anesthetized</td>
<td>4 ± 0</td>
<td>4 ± 1</td>
<td>4 ± 1</td>
<td>4 ± 1</td>
<td>5 ± 1</td>
<td>5 ± 1</td>
<td>5 ± 1</td>
<td>4 ± 1</td>
<td></td>
</tr>
<tr>
<td>Temperature* (°C)</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Awake</td>
<td>38 ± 0.4</td>
<td>38 ± 0.4</td>
<td>38 ± 0.4</td>
<td>38 ± 0.4</td>
<td>38 ± 0.4</td>
<td>38 ± 0.4</td>
<td>38 ± 0.4</td>
<td>38 ± 0.4</td>
<td>38 ± 0.4</td>
</tr>
<tr>
<td>Anesthetized</td>
<td>37 ± 0.3</td>
<td>37 ± 0.3</td>
<td>37 ± 0.3</td>
<td>37 ± 0.4</td>
<td>37 ± 0.5</td>
<td>37 ± 0.5</td>
<td>37 ± 0.4</td>
<td>36 ± 0.5</td>
<td>36 ± 0.6</td>
</tr>
<tr>
<td>MAP* (mm Hg)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Awake</td>
<td>140 ± 20</td>
<td>139 ± 16</td>
<td>138 ± 20</td>
<td>138 ± 16</td>
<td>135 ± 15</td>
<td>136 ± 13</td>
<td>137 ± 10</td>
<td>136 ± 12</td>
<td>131 ± 12</td>
</tr>
<tr>
<td>Anesthetized</td>
<td>78 ± 19</td>
<td>72 ± 4</td>
<td>66 ± 3</td>
<td>68 ± 12</td>
<td>70 ± 17</td>
<td>73 ± 2</td>
<td>72 ± 6</td>
<td>74 ± 4</td>
<td>72 ± 5</td>
</tr>
</tbody>
</table>

Baseline was recorded after induction of anesthesia, immediately prior to lidocaine administration in anesthetized horses. Rectal temperature was monitored in awake horses, and nasopharyngeal temperature was monitored in anesthetized horses.

*Significantly (P < 0.05) different between groups at all times.

HR = Heart rate. RR = Respiratory rate. MAP = Mean arterial pressure.

Table 3—Mean ± SD values for selected respiratory parameters in awake (n = 8) and anesthetized (8) horses in which lidocaine (loading infusion, 87 µg/kg/min, IV, for 15 minutes; constant rate infusion, 50 µg/kg/min, IV, for 90 minutes) was administered.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline*</th>
<th>15*</th>
<th>75*</th>
<th>End plus 60†</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Awake</td>
<td>7.44 ± 0.02</td>
<td>7.43 ± 0.02</td>
<td>7.43 ± 0.01</td>
<td>7.42 ± 0.02</td>
</tr>
<tr>
<td>Anesthetized</td>
<td>7.36 ± 0.03</td>
<td>7.38 ± 0.04</td>
<td>7.36 ± 0.04</td>
<td>7.46 ± 0.03</td>
</tr>
<tr>
<td>PacO₂ (mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Awake</td>
<td>42.0 ± 2.4</td>
<td>43.6 ± 1.3</td>
<td>43.0 ± 1.5</td>
<td>42.2 ± 1.9</td>
</tr>
<tr>
<td>Anesthetized</td>
<td>49.3 ± 3.2</td>
<td>50.2 ± 5.3</td>
<td>55.3 ± 7.1</td>
<td>49.9 ± 2.2</td>
</tr>
<tr>
<td>PacO₂ (mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Awake</td>
<td>68.5 ± 5.9</td>
<td>67.3 ± 3.8</td>
<td>67.9 ± 4.8</td>
<td>69.1 ± 5.7</td>
</tr>
<tr>
<td>Anesthetized</td>
<td>279.3 ± 25.0</td>
<td>316.1 ± 42.1</td>
<td>287.8 ± 78.3</td>
<td>66.2 ± 6.9</td>
</tr>
</tbody>
</table>

*Significantly (P < 0.05) different between treatment groups at baseline and 15 and 75 minutes for all variables. All horses were breathing room air at sample collection.
Discussion

Results support the hypothesis that general anesthesia has a profound effect on lidocaine disposition in horses. Although it would have been ideal to obtain awake and anesthetized data from the same horses, this was not feasible. Instead, 2 groups of horses were studied, and attempts were made to standardize factors known to influence drug disposition. For example, food was withheld in both groups of horses for a similar duration because withholding food has been found to decrease plasma clearance of lidocaine by the liver. Horses in both groups were considered adults with presumed normal hepatic function; measured serum biochemical values, including values for hepatic enzymes, were within reference limits in horses in both groups. Intravenous fluid administration and lidocaine dosing, administration, and sampling schedules were standardized. Other factors that may have influenced lidocaine disposition include different body mass composition and free water distribution given the different age, sex, and weight of horses in the 2 groups. Results of a study in humans suggest that there is no difference in the pharmacokinetics of lidocaine between adults and children > 6 months of age. Similar data are not available for horses. Plasma protein binding differences can also influence drug disposition; this was not thought to play a role in this study because TP concentrations did not differ between groups.

The lidocaine administration protocol was based on results of a clinical study in which effects of lidocaine toxicity were not observed. Mean serum lidocaine concentrations measured at baseline, prior to IV lidocaine administration, were consistently higher in awake than anesthetized horses. Despite this, concentrations during lidocaine administration were higher in the anesthetized than the awake group. The deviation from zero at baseline is explained by the SC administration of lidocaine to facilitate arterial (in awake horses) and venous (in anesthetized and awake horses) catheter placement in horses prior to treatment and is largely attributed to 2 horses in the awake group and 1 in the anesthetized group in which > 1 site was attempted for catheter placement. Pharmacokinetic parameters did not vary significantly when analyzed without data from these 3 horses; hence, the values provided represent data from 8 horses in both groups.

Noncompartmental analyses of the data were performed because this method best fit individual horse concentration versus time data, given the limited number of data points immediately following the end of lidocaine administration. The pharmacokinetics of lidocaine administered IV have been described in dogs, rabbits, humans, and horses by use of a 2-compartment model. The clearance of lidocaine in fed horses was approximately twice that reported from the circulation because it is almost exclusively dependent on hepatic blood flow. Although the specific site of lidocaine metabolism in horses is not known, it is possible that the decreased Cl of lidocaine in anesthetized horses was in part caused by enzyme inhibition or competition by sevoflurane, which is metabolized (5% in the horse) by the cytochrome P-450 enzyme system.

As suggested previously, adverse effects of lidocaine on the cardiovascular system, such as hypotension and bradycardia, were not observed in awake horses, as indicated by consistent HR and MAP measurements before and during lidocaine administration. This was consistent with results of Meyer et al, who found that clinically significant cardiovascular effects are not observed with serum lidocaine concentrations below those resulting in signs of CNS toxicosis (3,240 ± 740 ng/mL) in standing horses. Distinguishing between the effects of general anesthesia and the effects of systemic lidocaine on HR and MAP in the anesthetized group was more challenging, as both may...
influence these variables. However, the consistency of these values during the anesthetic period and the inter-
mittent requirement for low-dose inotropic (dobutam-
ine) support suggested the effect of lidocaine on these variables was minimal.

The PaO₂ in awake horses was within the reference range²⁶ (62 to 96 mm Hg) for horses at approximately 1,515 m (5,000 ft) above sea level, as was PaCO₂ (reference range, 35 to 47 mm Hg) and pH (reference range, 7.38 to 7.44). Although anesthetized horses had significantly higher mean PaO₂ values, as would be expected during mechanical ventilation with 100% oxygen, compared with awake horses, this should not have affected serum lidocaine concentrations. The PaCO₂ and resultant change in pH can have an effect on lidocaine disposition in the body.⁵⁰ Although the PaCO₂ was significantly higher during anesthesia, compared with awake horses, both PaCO₂ and pH values remained within a clinically acceptable range and were not likely to have influenced lidocaine disposition. Body temperature was significantly higher in awake versus anesthetized horses but within reference ranges in both groups.

Results of the study reported here confirmed the profound effect of general anesthesia on serum lidocaine concentration in horses and suggested that an alteration in dosing during anesthesia may be appropriate when a specific serum concentration of lidocaine is desired. Despite alterations in lidocaine disposition between awake and anesthetized groups, no adverse cardiopulmonary effects or behavioral signs of toxicosis were observed. Further investigation is needed to determine the appropriate target serum lidocaine concentration for different disease conditions and the influence of concurrently administered pharmacologic agents and disease conditions on the disposition of lidocaine in horses.

References


