Effects of acepromazine on renal function in anesthetized dogs

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Objective—To investigate the effects of IM administration of acepromazine on indices of relative renal blood flow and glomerular filtration rate (GFR) by means of scintigraphy, as well as the effects on physiologic, hematologic, and serum biochemical variables in anesthetized dogs, compared with effects of administration of saline.

Animals—6 healthy Beagles.

Procedure—Acepromazine (0.1 mg/kg) or physiologic saline (0.9 NaCl) solution was administered IM 30 minutes prior to induction of anesthesia with thiopentone; anesthesia was maintained with inspired isoflurane for 2.25 hours. Blood gases and circulatory and ventilatory variables were monitored. Renal function was evaluated by scintigraphic measurements of GFR and relative renal blood flow and analyses of serum and urine. Statistical analyses used ANOVA or Friedman ANOVA.

Results—Values of relative renal blood flow and GFR remained high despite low blood pressures. After administration of acepromazine, mean ± SD arterial blood pressure was 66 ± 8 mm Hg during anesthesia; this value was below the threshold (80 mm Hg) for renal autoregulation of GFR. In comparison, mean arterial blood pressure after administration of saline was significantly higher (87 ± 13 mm Hg). However, between treatments, there were no significant differences in GFR, relative renal blood flow, or other indices of renal function.

Conclusions and Clinical Relevance—Measurements of renal function and blood flow in dogs during anesthesia with thiopentone and isoflurane did not differ significantly between treatments, which suggested that acepromazine protects renal function despite inducing reduction in blood pressure, compared with effects of administration of saline. (Am J Vet Res 2003; 64:590–598)

Acepromazine maleate is a phenothiazine derivative that blocks peripheral actions of catecholamines, causing arterial hypotension via vasodilation. It is commonly used as a preanesthetic sedative; its central effect is blockage of the effects of dopamine, a catecholamine neurotransmitter in the CNS. Other useful effects of acepromazine include prevention of epinephrine-induced arrhythmia and ventricular fibrillation in dogs during administration of halothane. Acepromazine decreases respiratory rate in dogs without causing notable alterations in pulmonary gas exchange and acid-base balance. Acepromazine also causes hypothermia and decreases in PCV and hemoglobin concentration through storage of blood in the spleen.

In studies by Boström et al., effects of nonsteroidal anti-inflammatory drugs (NSAIDs) on indices of renal function were evaluated in dogs that had low blood pressure induced by acepromazine-thiopentone-isoflurane anesthesia. Although mean systemic blood pressures ranged from 41 to 82 mm Hg in those dogs, the glomerular filtration rate (GFR) observed after administration of NSAIDs was not different from that observed after administration of saline solution; furthermore, there was no difference in GFR observed in anesthetized and nonanesthetized dogs. Because mean renal arterial blood pressure of 80 mm Hg has been reported as the lower threshold of renal autoregulation of GFR, the question arose whether peripheral vasodilation caused by acepromazine provided protection of renal function. The purpose of this study was to investigate the effect of IM administration of acepromazine on relative renal blood flow and GFR by means of scintigraphy, as well as on results of hematologic and serum biochemical analyses and measurements of physiologic variables in anesthetized dogs, compared with effects of administration of saline.

Materials and Methods

Animals—Six healthy Beagle dogs (3 males and 3 females) were used in the study. Dogs were between 15 and 48 months of age (mean ± SD, 22 ± 13 months) and weighed between 11.6 and 18.4 kg (mean, 15.2 ± 2.5 kg). Throughout the study, housing and care of the dogs was provided by the Department of Small Animal Sciences, Faculty of Veterinary Medicine at the Swedish University of Agricultural Sciences. The dogs remained at that facility after completion of the study. Approval of the study was obtained from the local Ethical Committee on Animal Experiments.
**Study design and procedure**—The study had a nonrandomized crossover design. Dogs were administered either acepromazine (0.1 mg/kg, IM) or physiologic saline (0.9% NaCl) solution (0.01 mL/kg, IM) at an interval of 8 weeks so that all dogs received both treatments during the course of the study.

The dogs’ treatment with acepromazine was conducted as part of a previous study; after completion of that study, the dogs received the saline treatment. To adhere to the same protocol, saline solution (0.08 mL/kg, IV) was administered twice (once immediately before administration of the study treatment and again after 30 minutes of anesthesia and completion of all measurements at that time point). On the day of the anesthetic procedure, the dogs were not given food and water was withheld for 2 hours prior to induction of anesthesia. Blood and urine samples were collected on the morning of the anesthetic procedure and used for serum biochemical analyses, determination of hormone concentrations, and urinalysis. An IV catheter was placed in the cephalic vein before collection of the preanesthetic blood sample. Glomerular filtration rate and relative renal blood flow were measured by use of scintigraphy.

After administration of acepromazine, a 20-gauge catheter was inserted in the femoral artery by use of the Seldinger technique. The catheter was used for invasive measurement of arterial blood pressure and collection of blood samples for serum biochemical analyses, blood gas determinations, and assessment of acid-base balance during the anesthetic procedure. Arterial blood pressure and blood gases were measured before administration of acepromazine or saline. Baseline values for heart and respiratory rates and rectal temperature were obtained. A baseline ECG was also recorded.

**Sedation and anesthesia**—Thirty minutes before induction of anesthesia, acepromazine or saline was administered IM in the right triceps brachii muscle. Anesthesia was induced with thiopentone (25 mg/mL) administered slowly IV as needed to enable endotracheal intubation. Anesthesia was maintained with isoflurane (measured inspired concentration of 2%) in oxygen (150 mL/kg/min) in a Bain coaxial breathing system. The time at which thiopentone was administered as well as the start and end of administration of isoflurane were recorded. The volume thiopentone administered to each dog was recorded. Each dog was anesthetized for 2.25 hours. Dogs were covered with a blanket during anesthesia, except during the scintigraphic examination and insertion of a urinary catheter.

Heart and respiratory rates, arterial blood pressure, ECG variables, fraction of inspired oxygen (FiO₂), end-tidal CO₂ (ETCO₂), concentration of inhaled isoflurane, and arterial oxygen saturation of hemoglobin (SaO₂) were monitored continuously throughout anesthesia. Values were recorded at 30, 90, and 120 minutes after induction of anesthesia. Respiratory minute volume was measured at 30, 90, and 120 minutes after induction of anesthesia. Rectal temperature was also measured at the same time points. The arterial catheter was flushed repeatedly with small amounts of saline solution; the volume used for each flush was recorded. Thirty minutes after extubation, a blood sample was collected for blood gas analysis, and arterial blood pressure, ECG variables, respiratory rate, and rectal temperature were recorded.

Thirty minutes after the start of maintenance of anesthesia by the administration of isoflurane, samples were obtained for serum biochemical analyses, determination of hormone concentrations, measurement of blood gases, and urinalysis; the GFR and relative renal blood flow were also measured. At 120 minutes after onset of isoflurane administration, another set of samples was obtained for serum biochemical analyses, determination of hormone concentrations, measurement of blood gases, and urinalysis; the GFR and relative renal blood flow were measured.

Monitoring during anesthesia—Arterial blood samples for blood gas analysis and assessment of acid-base balance, including arterial pH (pHₐ), PaCO₂, and PaO₂, were obtained anaerobically from the femoral artery and stored in airtight syringes on ice until assayed by means of a standard electrode technique at an electrode temperature of 37°C. Arterial blood pressure was measured by use of a pressure transducer positioned at the level of the sternum and connected to the catheter in the femoral artery via a line filled with saline solution. Each dog was maintained in left lateral recumbency. Arterial blood pressure was monitored with a cardiovascular monitor and recorded with an ink-jet recorder. A lead II ECG was monitored and also recorded. Heart rate was calculated from the ECG, and respiratory rate was measured by use of a gas monitor. End-tidal CO₂, FiO₂, concentration of inhaled isoflurane, and SpO₂ were measured by means of the gas monitor. Tidal volume was calculated from the respiratory rate and minute volume (measured with a spirometer that was connected to the endotracheal tube). Rectal temperature was measured with a battery-powered thermometer.

**Hematologic examination, serum biochemical analyses, and urinalysis**—Blood samples were collected by venipuncture for the baseline sample, and the sample was obtained 20 hours after the end of the anesthetic episode; all other samples were collected via the indwelling arterial catheter. When possible, voided urine samples were obtained before and 20 hours after the end of the anesthetic episode; free-catch urine samples were preferred to avoid the need for additional catheterizations and an increased risk of urinary tract infection. During anesthesia, urine was collected via the indwelling arterial catheter that was allowed to remain in place until the final sample was collected on that day. Concentration of creatinine and activity of alkaline phosphatase (ALP) in urine were determined on a selective analyzing system; serum activity of alanine aminotransferase (ALT) and ALP was determined on the same selective analyzing system. Serum concentrations of creatinine, potassium, inorganic phosphate, and calcium and ALP and ALT activities were measured by use of standard reagent kits. A CBC was performed with an automated hematology analyzer.

**Hormonal analysis**—Immunoreactive angiotensin II and arginine-vasopressin (antidiuretic hormone) concentrations were measured in plasma after extraction with acetone and petroleum benzene (boiling range, 40 to 60°C; recovery of 92%). Both hormones were then analyzed by use of radioimmunoassays. The methods have been described. The limits of detection for the methods and interassay coefficient of variation (CV) were 0.62 pmol/L and 13 to 19%, respectively, for the arginine-vasopressin assay and 2.0 pmol/L and 1 to 10%, respectively, for the angiotensin-II assay. Intra-assay CV was <10% for the range of 1.3 to 59 pmol/L for the arginine-vasopressin assay and 6.3 to 300 pmol/L for the angiotensin-II assay. Immunoreactive aldosterone concentration was determined in plasma by means of a commercially available radioimmunoassay. This assay has been serum for use on
canine plasma samples. The limit of detection for the method is 32 pmol/L, and recovery ranged from 71 to 98%. The intra- and interassay CVs were 8% and 10%, respectively.

Renal scintigraphy—Relative blood flow to each kidney was measured with a computer program that calculates the fraction of cardiac output that flows to each kidney. Radioactive compounds that are injected IV pass through an arterial reference region, and for each kidney, time-activity curves (TACs) of the first pass of the bolus of radioactive compounds (activity) through the kidney are generated by a gamma camera and computer. Renal blood flow was calculated from TACs with the assumption that the activity was equivalent to radiolabeled microspheres that were completely trapped in the kidneys on first pass. Because of their capillary beds, all of the radioactive compound is localized and remains in the kidneys for a short period before any of the product exits via renal veins. Thus, the upslope region of the kidney TAC represents only inflow of the compound, and only the upslope of the kidney curve is required to calculate renal blood flow. This method of renal blood flow measurement has been validated in dogs by comparison with the radiolabeled microspheres technique.

In our study, diethylene-triaminepentacetic acid (DTPA) was used as a radiolabeled tracer. With the dog in left lateral recumbency, technetium99m-labeled DTPA (approx 70 MBq in a volume of < 1 mL) was injected in the cephalic vein via the catheter tubing; a bolus of saline solution (5 mL) was used to flush the catheter. The gamma camera was positioned against the dorsum of the dog to obtain a view that included the thorax and kidneys. The flow was recorded during 1 minute as a sequence of images at a rate of 1 frame/s. The flow through the right lung and kidneys was recorded as TACs from regions of interest (ROIs) drawn around these organs. To ensure sufficient resolution to define the edges of these organs, frames that indicated activity in the organs were summed to create a composite image. In our experience, the right lung had the most consistent results of the arterial ROIs that were used by Peters et al as the arterial reference region. The left lung was more compressed and consequently poorly aerated and had little blood flow; in the right lung, the ROI was easily and accurately drawn without inclusion of the aorta and heart (Fig 1). The descending limb of the first pass lung (arterial) TAC is distorted by the recirculating blood from the systemic circulation. This part was subtracted by use of a gamma function fit to the curve. This recirculation-corrected curve was integrated. The maximum slopes of the integrated arterial curve and kidney curves were measured by placing cursors at the start and end of the upslope regions of the curves (Fig 2).
The integrated arterial TAC was recalculated so that its slope was the same as that of the kidney TAC, after this recalculation, the height of the plateau (H) of the integrated and recalculated arterial curve represented the relative flow through the kidney, which was compared with the height (A) of the integrated arterial TAC by use of the following equations:

$$HxD = \frac{OF/B}{CO}$$

After integration of the arterial TAC,

$$\frac{H}{A} = \frac{gK}{gA}$$

Substituting for H in preceding equation

$$\frac{OF}{CO} = \frac{gK}{gA} \cdot \frac{A}{D} \cdot \frac{1}{H}$$

where H is the height of the curve recorded over the kidney after entrapment of radiolabeled microspheres, D is a correction factor (accounting for camera sensitivity, conversion of counts/s to MBq, and photon attenuation), D is the injected dose (counts/s), OF is organ blood flow, CO is cardiac output, A is the area under the recirculation-corrected arterial TAC and the height of the integrated arterial TAC, gK is the maximum upslope of the organ first pass curve (counts/s), and gA is the maximum upslope (counts/s) of the integrated arterial TAC. Attenuation of radiation in tissues located between each kidney and the camera was calculated from the measurement (by use of calibrated pixels) of the distance of the kidney from the dog’s back in a lateral view obtained immediately after the study and the attenuation coefficient of technetium99m in tissue (0.153/cm). The curves from the injections during anesthesia were corrected by subtracting the stable baseline counts associated with previous injections. The relative renal blood flow from each injection was measured 3 times, and the mean value was calculated. Glomerular filtration rate was determined by scintigraphic measurements via the method of Krawiec et al., with slight modifications to make the measurements more reproducible. The method measures the renal uptake of DTPA, which is excreted only by glomerular filtration; the DTPA is radiolabeled with technetium99m. In our study, the same renogram was used for GFR and blood flow measurements. With the gamma camera, the uptake of technetium99m-labeled DTPA between 30 and 120 seconds after the bolus injection was measured by use of ROIs drawn automatically around each kidney. The frames from 60 to 120 seconds were added to create an image with sufficient activity counts and resolution to draw the ROIs. Activity measurements were corrected for extrarenal background activity by use of circumferential ROIs that were automatically drawn (1 pixel in width) at a location 1 pixel from the edge of each kidney ROI and for the attenuation of activity in the tissues between the kidney and the camera. The distance of the kidney to the surface of the skin was measured on the lateral view obtained after the renogram, as described. Any stable background activity evident after a preceding injection was subtracted from the kidney TAC by setting the baseline of residual activity before the newly injected radioactive compound reached the kidney. The corrected uptake was expressed as a fraction of measured activity of the injection and was correlated with GFR by means of a correlation coefficient derived from plasma clearance of DTPA measured in clinically normal dogs at the Department of Clinical Radiology.

Statistical analyses—Data were analyzed with a repeated measure ANOVA, with treatment and time as within-dog factors. Missing observations were substituted with estimated values that were calculated via a formula by Kirk.

Results

Monitoring during anesthesia—The value of mean arterial blood pressure was significantly (P < 0.001) lower in dogs during anesthesia than when the dogs were conscious. Values of MAP differed significantly (P < 0.05) between treatments (acepromazine vs saline solution) during and after anesthesia and with time (P < 0.001). However, there was not significant difference between the treatments at all time points (Fig 3). Heart rate differed significantly (P < 0.01) between treatments at 30 minutes of anesthesia. There was also a significant (P < 0.001) change in heart rate with time for both treatments (Fig 4). After saline treatment, heart rate was significantly (P < 0.05) higher at 30 minutes of anesthesia, compared with 90 and 120 minutes of anesthesia. Rectal temperature decreased during anesthesia with both treatments, and there was a significant (P < 0.05) difference between the treatments after anesthesia. In dogs treated with acepromazine, temperature decreased from 38.6 ± 0.2°C before anesthesia to 36.1 ± 0.9°C after 120 minutes of anesthesia; in dogs treated with saline, temp...
temperature decreased from 38.4 ± 0.4°C before anesthesia to 36.1 ± 0.8°C after 120 minutes of anesthesia. After anesthesia, temperature remained lowered (36.1 ± 0.8°C) in the acepromazine-treated dogs, but had increased in saline-treated dogs (37.3 ± 0.4°C).

Compared with dogs that received saline treatment, less thiopental had to be administered to dogs treated with acepromazine to achieve intubation (18.8 ± 0.8 mg thiopental/kg and 9.7 ± 0.9 mg thiopental/kg, respectively). Mean respiratory rate decreased with both treatments during anesthesia to 4 ± 3 breaths/min at 30 minutes of anesthesia, compared with pre- and postanesthetic mean rates, which were more than 13 breaths/min in all dogs (P < 0.001). Two dogs treated with saline required assisted-ventilation intermittently during anesthesia. There was no difference in tidal volume during anesthesia between treatments or among time points. Arterial CO₂ tension in the blood was increased with both treatments during anesthesia, compared with pre- and postanesthetic mean values (P < 0.001). Mean values before and after anesthesia were 34 ± 4 mm Hg, and values during anesthesia were 66 ± 9 mm Hg. There was a significant (P < 0.05) difference between the treatments with time, with the largest difference between the treatments at 30 minutes of anesthesia. However, there was no significant difference between the treatments at any specific time point. Mean pHₐ before anesthesia was 7.40 ± 0.02 with both treatments. After 30 minutes of anesthesia, pHₐ declined to 7.21 ± 0.04 in dogs treated with acepromazine, compared with 7.15 ± 0.03 in dogs treated with saline treatment; this difference was significant (P < 0.01). However, at 90 and 120 minutes of anesthesia, no differences between the treatments were observed. Arterial O₂ tension was significantly (P < 0.001) higher in dogs during anesthesia than in conscious dogs with FiO₂ of 0.97; the pre- and postanesthetic mean value was 100 ± 8 mm Hg, whereas the mean value during anesthesia was 571 ± 25 mm Hg with both treatments.

Hematologic examinations, serum biochemical analyses, and urinalysis—Serum creatinine concentration was significantly (P < 0.01) decreased with both treatments during anesthesia, compared with baseline values, and remained within reference range (40 to 130 µmol/L). Overall, the ALP-to-creatinine ratio in urine did not differ between or within treatments at any time point. However, in 2 male dogs treated with saline, there was a slight increase in the ALP-to-creatinine ratio (from < 0.1 to 0.7 and 0.1, respectively; reference limit, < 0.1) during anesthesia, and in 1 dog treated with acepromazine, there was a slight increase in this variable (from < 0.1 to 0.3) recorded the day after anesthesia. Baseline values of hemoglobin concentration and Hct were significantly (P < 0.05) higher with saline treatment (184 ± 11 g/L and 53 ± 3%, respectively) than with acepromazine treatment (165 ± 21 g/L and 46 ± 6%, respectively). Hemoglobin concentration and Hct were decreased (P < 0.001) during anesthesia with mean values for both treatments of 121 ± 24 g/L and 33 ± 7%, respectively. Compared with values before anesthesia, WBC concentration decreased significantly (P < 0.001) with both treatments during anesthesia and increased on the day after the anesthetic episode. Activity of ALT did not differ significantly during anesthesia, compared with conscious dogs, or between treatments at any time point; however, in 1 male dog treated with saline, ALT activity was high during anesthesia. In that dog, activity of ALT was 36, 108, and 114 U/L (reference range, < 72 U/L) before anesthesia, after 30 minutes of anesthesia, and after 120 minutes of anesthesia, respectively. The day after the anesthetic episode, ALT activity was 102 U/L.

Serum potassium concentration was significantly (P < 0.001) lower after 30 minutes of anesthesia (3.9 ± 0.2 mmol/L; reference range, 4.2 to 5.5 mmol/L), compared with values before anesthesia (4.4 ± 0.2) and after 120 minutes of anesthesia (4.8 ± 0.4 mmol/L). On the day after the anesthetic episode, serum potassium concentration decreased to approximately baseline value (4.2 ± 0.3 mmol/L). Serum calcium concentration did not differ between treatments or between con-
sciou and anesthetized dogs. Serum inorganic phosphate concentration increased significantly (P < 0.001) with both treatments during anesthesia, compared with baseline values, with a maximum value after 120 minutes of anesthesia (2.44 ± 0.23 mmol/L; reference range, 0.80 to 2.00 mmol/L).

Hormonal analysis—Concentrations of angiotensin II and vasopressin increased significantly (P < 0.001) during anesthesia, compared with baseline values for both treatments. There was a significant (P < 0.05) slight difference in angiotensin II concentrations between the treatments with time; however, there was no significant difference between the treatments at any specific time point (Fig 5). In dogs treated with acepromazine and those treated with saline, mean values for vasopressin concentration before and after anesthesia were 0.1 ± 0 and 0.3 ± 0 pmol/L, respectively; at 30 minutes of anesthesia, mean concentrations were 13.8 ± 8 and 9.1 ± 6 pmol/L, respectively; and at 120 minutes of anesthesia, mean concentrations were 16.6 ± 11 and 14.4 ± 6 pmol/L, respectively. In dogs treated with acepromazine or saline, aldosterone concentration did not change from baseline value (mean concentration, 219 ± 100 and 328 ± 216 pmol/L, respectively) at 30 minutes of anesthesia, but increased significantly (P < 0.001) from baseline value at 120 minutes of anesthesia (mean concentration, 1,651 ± 1,051 and 1,162 ± 397 pmol/L, respectively).

Renal scintigraphy—No significant difference in relative renal blood flow was detected between or within treatments at any time point. Relative blood flow was 16.1 ± 3.0, 16.4 ± 3.5, and 17.6 ± 5.3% of CO before anesthesia, during anesthesia, and the day after the anesthetic procedure, respectively. Similarly, there were no differences in GFR between or within treatments at any time point. Glomerular filtration rate was 3.60 ± 0.48, 4.02 ± 0.55, and 3.97 ± 0.50 mL/min/kg before anesthesia, during anesthesia, and the day after the anesthetic episode, respectively. During anesthesia, there was no association between mean arterial blood pressure and relative renal blood flow (Fig 6) or between mean arterial blood pressure and GFR (Fig 7).

Discussion

The purpose of the study was to compare the effects of acepromazine on renal function with those of saline in dogs anesthetized with thiopentone and isoflurane. Low systemic arterial blood pressure, both between and within individual dogs, was reproducibly achieved with acepromazine treatment. In those dogs, mean arterial blood pressure was < 80 mm Hg, which is the lower threshold value for GFR autoregulation in conscious dogs.2 With saline treatment, mean arterial blood pressure was approximately 20 mm Hg higher (within the threshold range for GFR autoregulation). High concentrations of angiotensin II and vasopressin during anesthesia with both treatments may signify that the blood pressure was low enough to produce a response from compensatory mechanisms.7,18 Glomerular filtration rate in dogs with low arterial blood pressure measurements after acepromazine treatment did not differ from GFR in dogs with higher blood pressure after saline treatment; all GFR measurements were within reference range (2.53 to 5.41 mL/min/kg, as determined in our laboratory in 18 conscious, healthy Beagles of both sexes19).

The finding that renal blood flow and GFR did not decrease with low blood pressure induced by acepromazine treatment may be explained by the fact that the measured renal blood flow is relative to CO. If CO and absolute renal blood flow decreased equally as blood pressure decreased, no difference in the relative renal blood flow would be seen. Glomerular filtration rate (an absolute value) would then be expected to decrease because of low perfusion pressure caused by the decrease in absolute renal blood flow and the low systemic blood pressure. In our study, GFR did not decrease, which suggested that CO was maintained by acepromazine despite the effect of low blood pressure. Many anesthetics decrease the systemic blood pressure and CO.20,21 However, acepromazine may increase CO...
and stroke volume in anesthetized animals despite lowering the blood pressure. In horses anesthetized with halothane, IV administration of acromepazine resulted in increased CO through increased stroke volume. In dogs anesthetized with halothane, IM administration of acromepazine resulted in increased cardiac index and stroke index, but only the increase in stroke index was significant.

The dogs in our study may have been more stressed at induction of anesthesia when they had received saline treatment (ie, no sedative). This is supported by significantly higher heart rate during anesthesia in saline-treated dogs, compared with heart rate recorded during anesthesia in acromepazine-treated dogs. Also in the dogs treated with saline, heart rate was significantly increased at 30 minutes of anesthesia, compared with other time points during anesthesia; during the period of anesthesia, the lower heart rate noted in these dogs at 90 and 120 minutes of anesthesia, compared with the 30-minute value, may have been caused by decreased sympathetic stimulation. After administration of saline, respiratory rate was also decreased to a greater extent at 30 minutes of anesthesia than at other time points, which probably results from administration of larger amounts of thiopental to achieve intubation than that needed in dogs treated with acromepazine. The larger doses of thiopental were likely to have depressed respiration at the start of anesthesia with more extreme respiratory acidosis. Although acromepazine can decrease respiratory rate when given alone, the decrease is not always apparent when acromepazine is administered in combination with other anesthetic agents. The amount of other agents required to achieve anesthesia is reduced when acromepazine is administered; therefore, respiratory depression during anesthesia is also reduced. Respiratory depression causes increases in arterial CO2 pressure and hydrogen ion concentration that may raise arterial blood pressure and cardiac output through stimulation of vasomotor center. Stress and respiratory acidosis also stimulate the sympathetic nervous system. Sympathetic stimulation increases heart rate, force of muscle contractions, and total peripheral resistance directly and indirectly through release of norepinephrine, an α-receptor agonist. These effects increase CO, arterial blood pressure, and venous return.

Nevertheless, increased sympathetic stimulation may reduce renal blood flow. Direct sympathetic stimulation of the kidneys and actions of the adrenal hormones norepinephrine and epinephrine can constrict afferent and efferent renal arterioles and thereby reduce renal blood flow and GFR. Dogs anesthetized without prior acromepazine sedation, may therefore, have adequate systemic blood pressure and flow, but may have reduced renal blood flow under anesthesia. As long as renal autoregulation is not compromised, no renal damage is likely to occur. Other effects, however, increase the risk of renal damage. The lower limit of renal autoregulation may be raised by anesthesia; further decrease in blood pressure, stimulation of the sympathetic system because of inadequate analgesia during surgery, or administration of prostaglandin inhibitors may cause the hemodynamics of the kidneys to alter rapidly. Results of the study reported here and from our previous studies have indicated that in dogs treated with acromepazine, GFR and relative renal blood flow were maintained, although the blood pressure is below the lower threshold limit of renal autoregulation. In conscious dogs, as arterial blood pressure decreases to < 80 mm Hg, GFR decreases but blood flow is maintained until the mean renal arterial blood pressure is < 66 mm Hg. It is possible that the positive effects of acromepazine on GFR and renal blood flow are mediated through blockage of α-adrenoceptors in the renal vasculature. In a study by Henrich et al in which a volume of blood was removed from dogs with denervated kidneys to achieve mean arterial pressure of 100 mm Hg, α-receptors in kidneys were blocked with unilateral renal infusion of phenoxybenzamine, an α-adrenoceptor antagonist. After inhibition of prostaglandin synthesis by meclofenemate or indomethacin, the phenoxybenzamine infusion maintained renal blood flow and GFR at higher values than in uninfused kidneys during hemorrhage.

Concentrations of angiotensin II were increased in both treatments during anesthesia in the study reported here. Mean renal artery pressure of 95 mm Hg has been indicated as the threshold pressure for release of the enzyme renin. Below this pressure, renin concentration in renal venous blood rise rapidly. Release of renin results in formation of angiotensin II via a series of reactions. Angiotensin II contributes to maintenance of GFR when blood pressure decreases by raising the glomerular hydrostatic pressure through constriction of arterioles in the kidney. Assuming that acromepazine reduced the renin release response, vasconstriction caused by angiotensin II might have been less pronounced in dogs treated with acromepazine than would have been expected at the blood pressures achieved. In a study by Kopp et al, phenoxybenzamine reduced the renin release response to high level renal nerve stimulation in anesthetized dogs. In the study reported here, no significant difference in angiotensin II concentration at any time point was noted between treatments, which indicated that acromepazine may have reduced the renin release response to low blood pressures. However, as angiotensin II preferentially acts on the efferent arteriole in kidneys to maintain filtration pressure, decreases in its concentrations by administration of acromepazine may lead to less improvement in perfusion pressure despite increased renal blood flow.

In the study reported here and in previous studies, individual male dogs after saline treatment had a slightly increased urine ALP-to-creatinine ratio without any other sign of renal damage. Increased activity of ALP in urine is considered an early indication of renal damage. In male dogs, however, secretions from the prostate gland are a possible source of ALP in urine; this is supported by findings of our studies in which only male dogs had an increased urine ALP-to-creatinine ratio. Fluctuations in serum concentrations of electrolytes during anesthesia were detected in the study reported here; these fluctuations did not differ between
treatments, which is in agreement with results of an earlier study. Serum calcium concentration was the only variable that differed between results of the study presented here and another study of Boström et al. Serum calcium concentration seems to be less reliably affected by anesthesia and changes in acid-base balance. Similar to findings of other studies, I dog had a transient change in liver enzyme activities during anesthesia; it is possible that anesthesia is associated with slight increases in liver enzyme activities in susceptible individuals.

Although surgery was not performed on any of the dogs in our study, rectal temperature was considerably lowered in all dogs during anesthesia. The flow of oxygen in the nonbreathing system may have contributed to low body temperature, as may have thiopental and isoflurane administration. Hypothermia is a known adverse effect of acepromazine, as demonstrated by the increase in body temperature after anesthesia in dogs treated with saline in our study; temperature remained low at this time point in dogs that received acepromazine, because the plasma half-life of acepromazine in dogs is approximately 4 to 5 hours.

From our data, the lack of differences in measurements of renal function and blood flow between the treatments, despite low blood pressure detected with administration of acepromazine in healthy Beagles, suggested that acepromazine exerts a protective effect on renal blood flow and GFR during thiopentone-isoflurane anesthesia

References


