Comparison of Acute Hemodynamic Effects of Lidocaine and Procainamide for Postoperative Ventricular Arrhythmias in Dogs

Heart rate and systolic, diastolic, and mean pressures were measured in two groups of dogs during treatment of postoperative ventricular arrhythmias either with intravenous (IV) 2% lidocaine hydrochloride or procainamide hydrochloride. Hemodynamic parameters were not significantly changed after IV administration of either drug. Additionally, changes in hemodynamic parameters for dogs treated with 2% lidocaine were not significantly different from those of dogs treated with procainamide. When dosed appropriately in the clinical setting, one bolus of IV procainamide was safe for the treatment of postoperative ventricular arrhythmias. J Am Anim Hosp Assoc 2006;42:262-268.

Introduction

Ventricular arrhythmias in the dog may arise from cardiac or noncardiac causes. Noncardiac causes are gastric dilatation-volvulus (GDV), shock, multiple trauma, pain, serum electrolyte abnormalities, mass lesions of the spleen, and hypoxia.1-7 These arrhythmias can significantly increase morbidity and mortality. Lidocaine and procainamide are two common treatments for ventricular arrhythmias.1,5,7-9 They are class I (Vaughn-Williams classification) antiarrhythmic drugs, which are considered membrane stabilizers.9 Their antiarrhythmic action is from the blockade of fast sodium channels in the myocardium, resulting in decreased upstroke (phase 0) velocity of the action potential in the ventricular myocardium and Purkinje cells.9 This decrease in upstroke velocity ultimately decreases conduction velocity, thereby facilitating abolishment of the arrhythmia. Additionally, these drugs lead to an increase in refractoriness of the myocardium.

Differences exist between procainamide and lidocaine, and they are subcategorized into classes Ia and Ib, respectively.9 The major difference is that class Ib drugs only depress phase 0 of the action potential and decrease conduction velocity in diseased cardiac tissue, therefore having little effect on normal cardiac tissue. Class Ia drugs affect both normal and diseased cardiac tissue.9,10 Another reported difference between lidocaine and procainamide, which may be clinically significant, is that procainamide can cause hypotension when administered by intravenous (IV) bolus.8-14 Unlike lidocaine, which usually causes hypotension only when dosed inappropriately, IV procainamide has caused this side effect even when appropriately dosed.8-11 However, there are no reported cases of hypotension-related complications of procainamide in the clinical setting. Lidocaine has been considered by some to be the treatment of choice in the emergency treatment of ventricular arrhythmias secondary to splenectomy, GDV, and trauma.8

In dogs where persistent ventricular tachycardia persists beyond the postoperative period, it may be necessary to continue antiarrhythmic
therapy beyond discharge from the hospital. Because lidocaine has no oral formulation, oral procainamide is often utilized for maintenance antiarhythmic therapy. It is recommended that therapeutic levels of procainamide be achieved prior to administering maintenance doses. In order to avoid the perceived risk of hypotension, procainamide is generally delivered intramuscularly or orally, rather than by IV bolus or constant-rate infusion (CRI). In dogs, it can take up to 16 hours to obtain therapeutic levels with orally administered procainamide, and 6 to 8 hours with intramuscular procainamide.\(^{9,10}\) Therapeutic levels of procainamide can be obtained within minutes with a slow, IV bolus, and these levels can be maintained with administration via CRI. In humans, procainamide has been given as an IV bolus without significant hypotension.\(^{15,16}\)

Intravenous delivery of procainamide as a bolus in dogs would provide faster therapeutic levels than intramuscular or oral administration. Once therapeutic levels have been maintained for several hours, oral procainamide can be administered for long-term maintenance.

The purpose of this study was to examine the immediate effects of lidocaine and procainamide, administered as IV boluses and short-term CRI at currently recommended doses, on heart rate (HR) and systemic blood pressures in dogs with ventricular arrhythmias.

**Materials and Methods**

Client-owned dogs having no known previous myocardial disease, yet considered to be at risk for postoperative ventricular arrhythmias, were identified. Each dog was closely observed in an intensive care setting with continuous electrocardiography (ECG) and continuous direct blood pressure monitoring. Dogs noted to be suffering from postoperative ventricular arrhythmias requiring medical treatment were randomized to two treatment groups. Elimination of preexisting myocardial disease was based on historical findings, cardiac auscultation, preoperative ECG, and thoracic radiography. Dogs with evidence of myocardial disease were excluded from the study. Ventricular arrhythmias were defined as requiring medical attention if ventricular premature contractions (VPCs) were >20 per minute, sustained ventricular tachycardia was present, R on T phenomenon was noted, or VPCs were multifocal or multiform. Ventricular tachycardia was defined as a HR of ≥140 beats per minute. Breed, age, weight, and surgical procedure were recorded for each dog.

Dogs with postoperative ventricular arrhythmias requiring treatment were randomly assigned to one of two groups. The dogs in group 1 were treated with 2% lidocaine hydrochloride.\(^6\) A bolus of lidocaine (2 mg/kg IV) was administered over 5 minutes via an IV pump and was followed by a CRI of lidocaine (60 µg/kg per minute IV).\(^{9,10}\) The dogs in group 2 were treated with procainamide hydrochloride.\(^9\) A bolus of procainamide (10 mg/kg IV) was administered over 5 minutes via an IV pump and was followed by a CRI (20 µg/kg per minute IV).\(^{10}\)

Direct blood pressure measurements were taken via an IV catheter (20 gauge, 2 inch) placed in the dorsal pedal artery prior to surgery. Arterial pressure was measured with a fluid-filled pressure transducer, zeroed at the level of the right atrium. Heart rate measurements were obtained by ECG. Baseline HR, systolic arterial pressure (SAP), diastolic arterial pressure (DAP), and mean arterial pressure (MAP) were measured prior to, every minute for the first 5 minutes, and then 10 minutes after the bolus injection. Constant-rate infusion was started immediately after the end of the IV bolus, and the last measurements were taken during the CRI of both drugs. Effects were measured for 10 minutes in an attempt to identify transient hypotension following bolus administration. Intravenous crystalloid administration was maintained at a constant rate during the study. Continuous ECG was performed throughout the 10-minute treatment period. Additionally, serum sodium, potassium, and pH were measured and recorded prior to treatment. Electrolyte and blood pH values were measured from arterial blood samples. All dogs received supplemental potassium in the IV crystalloid fluids postoperatively, with the amount of supplementation determined by the serum potassium level.

Data were analyzed using statistical software programs.\(^3,4\) An analysis of variance (ANOVA) test for repeated measurement was utilized to compare the effects of lidocaine and procainamide on hemodynamic parameters over time. A one-way ANOVA was used to compare serum sodium, potassium, and pH measurements between the two groups. Chi-square analysis was used to compare the effects of lidocaine and procainamide on the rate of conversion of arrhythmias between the two groups. Data were tested for normalcy (Kolmogorov-Smirnov test) and homoscadicity (Mauchly criterion). Data are reported as means ± standard deviation. The level of significance was defined as \(P<0.05\).

Power for each hemodynamic parameter was calculated using a conservative difference between the means for each data point in each group.

**Results**

Sixteen client-owned dogs with treatable, postoperative ventricular arrhythmias were identified and randomized into two treatment groups. Dogs from group 1 (n=6) had a mean age of 10.2±3.3 years (range 6 to 14 years) and a mean weight of 33.0±11.4 kg (range 23.0 to 49.4 kg). Dogs from group 2 (n=10) had a mean age of 9.2±3.8 years (range 1 to 15 years) and a mean weight of 36.5±14.1 kg (range 13.6 to 61 kg). Five dogs were Labrador retrievers or Labrador retriever-crosses. Preexisting myocardial disease was ruled out in all cases. Thoracic radiography was also performed on 13 cases. Four dogs initially included in group 1 did not meet all inclusion criteria and were later removed from the group. Two cases did not meet the criteria to treat ventricular arrhythmias, and preexisting myocardial disease could not be completely ruled out in two cases. Therefore, group 1 had only six cases available for analysis. Surgical procedures included splenectomy for a mass lesion (n=8), derotation and gastropexy for GDV (n=4), portosystemic shunt attenuation (n=1), liver lobectomy for a mass lesion (n=1),...
thoracoscopic pericardectomy for pericardial effusion (n=1), and thoracotomy for treatment of trauma-induced hemothorax (n=1). Procedures performed on dogs in group 1 included splenectomy (n=3), liver lobectomy (n=1), GDV treatment (n=1), and thoracotomy (n=1). Procedures for group 2 were splenectomy (n=5), GDV correction (n=3), portosystemic shunt attenuation (n=1), and pericardectomy (n=1).

Mean serum potassium concentrations in group 1 and group 2 were 3.6±0.8 mEq/L and 3.4±0.6 mEq/L (reference range 3.5 to 5.2 mEq/L), respectively ($P=0.51$). Mean serum sodium concentrations in group 1 and group 2 were 150±6 mEq/L and 147±3 mEq/L (reference range 142 to 152 mEq/L), respectively ($P=0.38$). Additionally, blood pH values (reference range 7.35 to 7.45) for group 1 (pH=7.42±0.13) and group 2 (pH=7.32±0.15) were not significantly different ($P=0.26$).

The arrhythmia was abolished in all (100%) dogs treated with lidocaine (group 1) and in 9/10 (90%) dogs treated with procainamide (group 2). One dog treated with procainamide was refractory to the IV bolus and 10 minutes of CRI. This dog subsequently responded favorably to lidocaine but was not included in the lidocaine group. No significant difference ($P>0.99$) was noted between the two groups regarding response to treatment. For both groups, mean HR, SAP, DAP, and MAP for each time point are shown in the Table. There were no significant differences between group 1 and group 2 with regard to HR ($P=0.84$), SAP ($P=0.64$), DAP ($P=0.98$), or MAP ($P=0.91$) over time. Comparisons of mean hemodynamic parameters are shown in Figures 1 through 4. The power calculations (i.e., the chances that a correct conclusion has been made when considering statistical insignificance) for the hemodynamic

**Figure 1**—Comparison of mean heart rates at various times for dogs treated with procainamide (n=10) and lidocaine (n=6). No statistical difference was noted over time ($P=0.84$). bpm=beats per minute

**Figure 2**—Comparison of mean systolic arterial pressures at various times for dogs treated with procainamide (n=10) and lidocaine (n=6). No statistical difference was noted over time ($P=0.64$).
parameters (i.e., HR, SAP, DAP, MAP) were 0.85, 0.66, 0.99, and 0.98, respectively.

**Discussion**

Ventricular arrhythmias were rapidly abolished in this study by both lidocaine and procainamide injected IV as a bolus. Hypotension did not occur in any dog, and HR was maintained. Conflicting data exist as to the degree of hypotension caused by IV procainamide; however, most studies in dogs have agreed that significant hypotension can occur.8,10,12-14,17,18 In contrast, no arterial hypotension or tachycardia occurred after IV procainamide in the dogs of this study. It has been shown that the hypotension produced in dogs by procainamide is dose dependent, possibly from a vasodilator effect caused by an inhibition of ganglionic transmission.12,14,17 Many of the early studies performed on dogs measured the effects of procainamide given as an IV bolus in doses ranging from 18 to 30 mg/kg, which are much higher than the recommended dosages for clinical cases (2 to 8 mg/kg IV).1,11,12,14 Constant-rate infusion doses used in earlier studies were also higher (up to 87 µg/kg per minute) than the currently recommended dose of 20 to 50 µg/kg per minute.9,10,13

Early pharmacological studies compared the effects of procainamide to the effects of N-acetylprocainamide (NAPA), and dosages for dogs were initially extrapolated from results in humans.9-11,13 N-acetylprocainamide is a functional, antiarrhythmic metabolite of procainamide that may have less detrimental side effects.9,19 Since this metabolite is functional, arrhythmias may be controlled longer and at relatively lower doses in people. However, researchers found ventricular arrhythmias in dogs were
<table>
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<th>Parameter</th>
<th>Lidocaine Group (n=6)</th>
<th>Procainamide Group (n=10)</th>
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<table>
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<tr>
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<tr>
<td>Baseline</td>
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<td>Systolic pressure (mm Hg)</td>
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<tr>
<td>Mean pressure (mm Hg)</td>
<td>82.1±16.1</td>
<td>86.7±20.6</td>
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more difficult to control with procainamide; therefore, doses were increased. Papich and others later showed that dogs are unable to acetylate procainamide to NAPA and may require higher plasma concentrations of procainamide than humans to control some cardiac arrhythmias.19,20 Another reason large doses of procainamide were used in early studies is that these studies were performed on dogs with ouabain-induced arrhythmias. Ouabain produces delayed afterdepolarizations similar to those seen with digitalis intoxication. In dogs, procainamide is not effective or recommended for treatment of delayed afterdepolarizations produced by means other than digitalis intoxication, because a very high serum concentration is required to suppress these arrhythmias.9,20 A relatively low serum concentration is needed to suppress spontaneous, clinical ventricular arrhythmias.10

The rate of administration of procainamide also influences the development of hypotension in dogs, as it has been shown that rapid IV administration can cause a transient hypotension.9,10,17 In earlier studies, a large dose of procainamide was often infused as quickly as 2 seconds.14,21 In the study reported here, procainamide was infused over a longer time period (i.e., 5 minutes), and no hypotension was observed. Slow IV injections of procainamide may avoid hypotension by preventing circulatory collapse from peripheral vasodilation and decreased cardiac contractility.9

Arrhythmias were abolished at the end of 10 minutes in all but one dog treated with procainamide. Electrolytes and blood pH were similar in both treatment groups. Mean pH levels were similar between groups; however, the mean pH for group 2 was slightly below the normal reference range. Mean serum sodium concentrations were normal for both treatment groups. Mean serum potassium levels were identical and slightly below normal (3.5 to 5.2 mEq/L) for both treatment groups. The actions of both lidocaine and procainamide are affected by extracellular potassium levels.8,10 Both antiarrhythmics are less effective during hypokalemia, and both cause increased myocardial depression during hyperkalemia.8,10 Additionally, acidosis can lead to increased myocardial depression.8,10 The dog that did not respond to procainamide had normal serum sodium (147 mEq/L) and potassium (4.0 mEq/L) levels, and serum pH was only slightly decreased (pH=7.33) in this dog. Serum sodium and potassium levels were also normal in the same dog at the onset of treatment with lidocaine.

Many authors recommend choosing lidocaine over procainamide as a first choice in treating ventricular arrhythmias postoperatively, or they only recommend selecting procainamide to control arrhythmias that are refractory to lidocaine.8-10,18 These recommendations may have arisen from lack of adverse side effects of IV lidocaine or the perceived risk of side effects with IV procainamide. Alternatively, some may believe that IV lidocaine is more effective than IV procainamide. In the study reported here, most arrhythmias were suppressed after one IV bolus dose of the antiarrhythmic drug, and procainamide appeared to be as effective as lidocaine. As with many clinical studies, some limitations existed in the present study. Only a small number of cases were entered in the study, which had an effect on the power of a statistical analysis. However, even with the small study population, the power calculations were 0.66 for the SAP, 0.85 for HR, and >0.90 for all other parameters, which are recognized as acceptable powers.24 A power of 0.90 means that there is only a 10% chance that a type II error (i.e., there is a treatment effect, yet it is concluded that no treatment effect occurred) has been committed.24 A second limitation was that only a single dose of each drug was tested, despite the existence of acceptable dosage ranges. Although dose-related side effects may occur with both drugs, the objective of this study was to determine changes in hemodynamic parameters at a single, clinically effective dose. Further studies regarding changes in hemodynamic parameters would be beneficial in establishing the overall safety and effectiveness of these drugs at higher doses. Another limitation to the study was that the hemodynamic parameters were measured for only 10 minutes. Although evaluation of data over a longer time period may have added to the study, a lack of control over the variables of each clinical case (e.g., changes in opioid or IV fluid rate, confounding drug interactions) would have made interpretation of the results difficult. The authors chose a 10-minute time period because changes in the measured parameters after IV bolus administration typically occur within this time frame. A final limitation was that none of the dogs had echocardiography to evaluate their cardiac function prior to treatment, and the absence of cardiac disease was based on history, auscultation, a preoperative ECG, and failure to detect cardiomegaly on thoracic radiographs.

Conclusion
Slow IV bolus administration of procainamide appeared to be a safe alternative to lidocaine for the acute treatment of postoperative ventricular arrhythmias in dogs in this study. No changes occurred in HRs or blood pressure after an IV bolus of procainamide was delivered over 5 minutes, or during the first 10 minutes of administration of CRI procainamide. No significant differences in HRs or blood pressures were noted between the lidocaine and procainamide treatment groups. Although procainamide has been reported to cause hypotension with IV administration, hypotension was not demonstrated in the study reported here.

References

a 2% lidocaine hydrochloride; Abbott Laboratories, North Chicago, IL 60064
b Procainamide hydrochloride; Abbott Laboratories, North Chicago, IL 60064
c Statview 5.0.1; SAS Institute, Cary, NC 27511
d JMP 5.1; SAS Institute, Cary, NC 27511


