Evaluation of the urodynamic and hemodynamic effects of orally administered phenylpropanolamine and ephedrine in female dogs

Francesca Carofiglio, DVM; Annick J. Hamaide, DVM, PhD; Frédéric Farnir, PhD; Marc H. Balligand, DVM, PhD; John P. Verstegen, DVM, PhD

Objective—To compare the urodynamic and hemodynamic effects of different dosages of phenylpropanolamine and ephedrine and determine effective dosages in increasing urethral resistance in female dogs.

Animals—20 sexually intact female Beagles.

Procedure—Dogs were allocated into 4 groups and received phenylpropanolamine once, twice, or 3 times daily, or ephedrine twice daily, for 14 days. On days 0, 7, and 14, urethral pressure profiles were performed while dogs were anesthetized with propofol. Variables recorded included maximum urethral pressure, maximum urethral closure pressure, integrated pressure, functional profile length, anatomic profile length, plateau distance, distance before maximum urethral pressure, and maximum meatus pressure. Arterial and central venous pressures were measured before anesthetic induction and 10 and 35 minutes after induction.

Results—Administration of phenylpropanolamine once daily or ephedrine twice daily significantly increased maximum urethral pressure and maximum urethral closure pressure. Values for integrated pressure were significantly increased after 14 days of once-daily administration of phenylpropanolamine. Variables did not change significantly from day 7 to day 14. Diastolic and mean arterial blood pressures increased significantly during the treatment periods, and arterial pressure decreased during propofol infusion.

Conclusions and Clinical Relevance—Oral administration of phenylpropanolamine once daily or ephedrine twice daily increased urethral resistance in clinically normal dogs and may be recommended for management of urethral sphincter mechanism incompetence. Treatment efficacy may be assessed after 1 week. Dogs with concurrent cardiovascular disease should be monitored for blood pressure while receiving α-adrenergic agents because of the effects on diastolic and mean arterial pressure. (Am J Vet Res 2006;67:723–730)

Urethral sphincter mechanism incompetence is the most common cause of urinary incontinence in mature spayed dogs and most commonly affects dogs of medium to large breeds. The term refers to weakness of the urinary sphincter mechanism, a condition that predisposes affected dogs to urinary incontinence.

Structures or factors contributing anatomically to the urethral sphincter closure mechanism include urethral fibroelastic connective tissue, the urethral submucosal vascular plexus, urethral striated and smooth muscle, and the position of the neck of the bladder. In humans, urethral tone is maintained primarily by activation of postsynaptic α-adrenoceptors, whereas in rabbits and dogs, urethral tone is mediated primarily by an α₁-adrenergic receptor subtype that corresponds to the human α₁c-adrenergic receptor.

On the basis of that knowledge, α₁-adrenergic receptor agonists (most commonly phenylpropanolamine and ephedrine) have been used for treatment of stress incontinence in women and for treatment of USMI in dogs. Results of experimental and clinical studies in humans and dogs indicate that an increase in MUP (ie, the difference between MUP and bladder pressure) develops in association with administration of α-adrenoceptor agonists. However, adverse effects such as increased blood pressure, tachycardia, headaches, and dizziness have been reported in humans taking phenylpropanolamine or ephedrine, which were available in many over-the-counter dietetic preparations. In other studies in humans, rabbits, and dogs, investigators reported increases in blood pressure and decreases in heart rate, in addition to an increase in MUP, after administration of phenylpropanolamine or ephedrine. Despite these observations, the use of orally administered α-adrenoceptor agonists for treatment of female dogs with USMI has been rewarding. The success rate associated with the use of these drugs is high; moreover, they are inexpensive, and no important adverse effects associated with their use have been reported in dogs. However, there is a lack of information regarding cardiovascular effects of long-term oral administration of low dosages of

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<th>ABBREVIATIONS</th>
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<td>USMI</td>
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<td>MUCP</td>
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Received July 14, 2005.
Accepted September 20, 2005.

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phenylephrine or ephedrine; previously cited experimental studies were mostly performed in anesthetized dogs after administration of a single high dose of either drug, usually by the IV route.

Although treatment protocols for use of phenylephrine and ephedrine in dogs with USMI have been reported, to the authors’ knowledge there are no published data describing urodynamic and hemodynamic effects of these drugs in unanesthetized or anesthetized dogs. The duration of oral administration required before maximum urodynamic effects are reached is also unknown.

The purpose of our study was to compare the urodynamic and hemodynamic effects of a 14-day course of orally administered phenylephrine (dose, 1.5 mg/kg) given once, twice, or 3 times daily and orally administered ephedrine (dose, 1.5 mg/kg) given twice daily in sexually intact female Beagles. Specific objectives were to determine effective dosages and the duration of treatment needed to reach the maximum urodynamic response.

Materials and Methods

Dogs—Twenty adult sexually intact female Beagles were used. All dogs were born and housed at the Small Animal Theriogenology facilities at the Department of Clinical Sciences of the College of Veterinary Medicine, University of Liege. Animal housing, care, and experimentation were conducted in accordance with Belgian governmental regulations and with the National Institutes of Health Guide for Care and Use of Laboratory Animals. Complete physical examinations were performed each week. Dogs were housed in groups of 2 to 5 in indoor-outdoor runs (2.5 × 10 m), had exposure to natural light, were fed a commercial dry food once daily in amounts sufficient to maintain body weight, and were provided water ad libitum. Dogs were in anestrus during the study, as determined by vaginal cytologic examination. Prior to initiation of each experiment, a physical examination that included measurements of heart rate, respiratory rate, and rectal temperature was performed and a urine sample was obtained via cystocentesis for urinalysis and bacteriologic culture. Urinalysis included determination of specific gravity and pH and detection of urinary blood, protein, bilirubin, and glucose. Dogs included in the study had no clinical signs of disease of the lower portion of the urinary tract and no abnormalities on urinalysis.

Study design—Dogs were randomly allocated to 1 of 4 groups (3 dogs/group). Dogs in group I received phenylephrine hydrochloride in an immediate-release form at a dosage of 1.5 mg/kg, PO, every 24 hours for 14 days. Dogs in group II received the same dose every 12 hours for 14 days; dogs in group III were treated every 8 hours for 14 days; and dogs in group IV received ephedrine at a dosage of 1.3 mg/kg, PO, every 12 hours for 14 days.

Urodynamic and hemodynamic measurements were performed in each dog on days 0, 7, and 14 within 2 to 5 hours of the first daily drug administration. Dogs were selected to undergo the procedures in random order. Prior to induction (T0), a 21-gauge IV catheter was placed in the dor- sal pedal artery 5 minutes after SC injection of 10 mg of lido- caine; another 21-gauge jugular catheter was placed in a jugular vein. Dogs were allowed to rest for 15 minutes. Measurements of systolic and diastolic blood pressure, MAP, and central venous pressure were recorded by use of a monitor connected to a pressure transducer.

Anesthesia was induced with an IV bolus of propofol (dose, 5 mg/kg) and was maintained via continuous IV propofol infusion (dosage, 30 mg/kg per hour). All dogs were intubated and monitored by use of a pulse oximeter. Supplemental oxygen was administered if oxygen saturation was < 95%. When dogs were in a stable anesthetic plane, they were positioned in right lateral recumbency. Cystocentesis was performed, and 3 successive urethral pressure profiles were obtained according to a described protocol. Cystocentesis, diastolic, central venous, and MAP measurements were recorded 10 and 35 minutes (T10 and T35) after anesthetic induction.

### Table 1—Mean ± SE values for urodynamic variables in 20 sexually intact female Beagles that received 1 of 3 regimens of orally administered phenylephrine or a regimen of orally administered ephedrine for 14 days.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group I</th>
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<th>Group II</th>
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<th>Group III</th>
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<th>Group IV</th>
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<tr>
<td></td>
<td>Day 0</td>
<td>Day 7</td>
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<tr>
<td>MUP (cm H2O)</td>
<td>21 ± 6</td>
<td>35 ± 6*</td>
<td>37 ± 6†</td>
<td>40 ± 5</td>
<td>44 ± 5</td>
<td>47 ± 5</td>
<td>32 ± 6</td>
<td>33 ± 6</td>
<td>31 ± 6</td>
<td>34 ± 6</td>
<td>46 ± 6*</td>
<td>51 ± 6†</td>
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<td>MUCP (cm H2O)</td>
<td>17 ± 6</td>
<td>30 ± 6*</td>
<td>35 ± 6†</td>
<td>34 ± 5</td>
<td>38 ± 5</td>
<td>40 ± 5</td>
<td>25 ± 6</td>
<td>26 ± 6</td>
<td>27 ± 6</td>
<td>30 ± 6</td>
<td>41 ± 6</td>
<td>45 ± 6*†</td>
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<td>IP (cm × cm H2O)</td>
<td>72 ± 21 112 ± 21 135 ± 21*</td>
<td>122 ± 17 134 ± 17 141 ± 17</td>
<td>88 ± 21 110 ± 21 121 ± 21</td>
<td>95 ± 21 138 ± 21 130 ± 21</td>
<td>95 ± 21 138 ± 21 130 ± 21</td>
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<td>FPL (mm)</td>
<td>79 ± 6</td>
<td>81 ± 6</td>
<td>72 ± 6</td>
<td>68 ± 5</td>
<td>79 ± 5</td>
<td>74 ± 5</td>
<td>77 ± 6</td>
<td>80 ± 6</td>
<td>84 ± 6</td>
<td>69 ± 6</td>
<td>68 ± 6</td>
<td>66 ± 7</td>
<td>67 ± 6</td>
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<td>APL (mm)</td>
<td>100 ± 4 104 ± 4 95 ± 4</td>
<td>95 ± 4 98 ± 4 95 ± 4</td>
<td>97 ± 4 103 ± 4 104 ± 4</td>
<td>85 ± 4 86 ± 4 86 ± 4</td>
<td>85 ± 4 86 ± 4 86 ± 4</td>
<td>85 ± 4 86 ± 4 86 ± 4</td>
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<td>BMUP (mm)</td>
<td>46 ± 5 50 ± 5 50 ± 5</td>
<td>52 ± 4 54 ± 4 50 ± 4</td>
<td>54 ± 5 50 ± 5 52 ± 4</td>
<td>46 ± 5 45 ± 5 47 ± 5</td>
<td>46 ± 5 45 ± 5 47 ± 5</td>
<td>46 ± 5 45 ± 5 47 ± 5</td>
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<td>MMP (cm H2O)</td>
<td>12 ± 6 12 ± 6 17 ± 6</td>
<td>20 ± 5 11 ± 5 10 ± 5*</td>
<td>5 ± 6 10 ± 7 11 ± 7</td>
<td>19 ± 7 16 ± 6 10 ± 6</td>
<td>19 ± 7 16 ± 6 10 ± 6</td>
<td>19 ± 7 16 ± 6 10 ± 6</td>
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<td>Plateau (mm)</td>
<td>21 ± 3 23 ± 3 22 ± 3</td>
<td>24 ± 3 19 ± 3 21 ± 2</td>
<td>19 ± 3 19 ± 3 18 ± 3</td>
<td>17 ± 3 18 ± 3 19 ± 3</td>
<td>17 ± 3 18 ± 3 19 ± 3</td>
<td>17 ± 3 18 ± 3 19 ± 3</td>
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Dogs in group I received orally administered phenylephrine at a dosage of 1.5 mg/kg every 24 hours, dogs in group II received phenylephrine at a dosage of 1.5 mg/kg every 12 hours, dogs in group III received phenylephrine at a dosage of 1.5 mg/kg every 8 hours, and dogs in group IV received orally administered ephedrine at a dosage of 1.5 mg/kg every 12 hours.

*Values were significantly (P < 0.05) different from those obtained on day 0. †Values were significantly (P < 0.01) different from those obtained on day 0.

IP = Integrated pressure (ie, area under the functional profile). APL = Anatomical profile length (ie, the distance between the point in the urethra where intravesical pressure exceeded the total urinary bladder pressure and the point where it reached atmospheric pressure). MMP = Maximum urethral pressure (ie, maximal pressure measured at the level of the external urethral orifice). Plateau = Distance between the end of the functional profile length and the point at which intravesical pressure decreased to atmospheric pressure.
Data interpretation—The following variables were calculated from the urethral pressure profile measurements: MUP, MUCP, anatomic profile length (ie, the distance between the point in the urethra at which intraurethral pressure exceeded total bladder pressure and the point at which intraurethral pressure equalled atmospheric pressure), and integrated pressure (ie, integrated pressure under the urethral functional profile, calculated as MUCP × functional profile length). Definitions are in accordance with those of the International Continence Society.38 In the present study, the FPL was defined as the distance between the point in the urethra at which intraurethral pressure exceeded bladder pressure and the point at which either a pressure plateau was observed or intraurethral pressure became less than bladder pressure. The plateau was defined as the distance between the end of the FPL and the point at which intraurethral pressure exceeded atmospheric pressure. The distance between maximum urethral pressure was defined as the distance between the point in the urethra at which intraurethral pressure exceeded total bladder pressure and the point of MUP. The maximum meatus pressure was defined as the maximal pressure at the level of the external urethral orifice.

The following variables were calculated from hemodynamic measurements: SAP, diastolic arterial pressure, MAP, heart rate, and mean central venous pressure.

Statistical analysis—Data were expressed as mean ± SE, except for those pertaining to dogs’ age and weight, which were expressed as mean ± SD. Differences in age and weight among groups were determined by use of 1-way ANOVA. Two-way ANOVA with interaction for repeated measures (treatment and time) was performed by use of statistical software. Within-treatment (ie, differences between data obtained at successive test times) and between-treatment comparisons were made. For all analyses, values of P < 0.05 were considered significant.39

Results
There were no significant differences in age or weight among treatment groups. Mean ± SD age of dogs was 7.7 ± 1.7 years, and body weight ranged from 12 to 17 kg (mean ± SD, 14.4 ± 1.6 kg).

Urodynamic measurements—On day 0, MUP and MUCP were significantly lower in dogs in group I, compared with dogs in group II (Table 1). On day 7, values for distance before maximum urethral pressure were significantly higher in dogs in group I, compared with dogs in group IV. On days 0 and 7, values for anatomic profile length were significantly lower in dogs in group IV, compared with dogs in group I. On day 14, there were no significant differences in any variables among treatment groups.

In dogs in group I, values for MUP and MUCP were significantly higher on days 7 and 14, compared with day 0, and values for integrated pressure were significantly higher on day 14, compared with day 0 (Figures 1 and 2). In dogs in group II, values for maximum meatus pressure were significantly higher on day 14, compared with day 0. In dogs in group IV, MUP was significantly higher on days 7 and 14, compared with day 0, and MUCP was significantly higher on day 14, compared with day 0.

No significant differences in FPL, anatomic profile length, distance before maximum urethral pressure, and plateau values were observed during the treatment period (Figure 3). Values of SAP were significantly higher on days 7 and 14, compared with day 0, but only in dogs in group II.

Diastolic arterial pressures were significantly higher on day 14, compared with day 0 (P < 0.001) and day 7 in group I (in group I, values were not significantly different between days 0 and 7). In group III, diastolic arterial pressures were significantly higher on days 7 and 14, compared with day 0 (values for days 7 and 14 were not significantly different), whereas in group IV, diastolic arterial pressures were significantly higher on day 7, compared with day 0 (there were no significant differences between values for days 0 and 14 or between days 7 and 14).

Values for MAP were significantly higher on days 7 and 14, compared with those on day 0, in all treatment groups (no significant difference in values was
observed between days 7 and 14). Heart rates were significantly lower on day 14, compared with those on days 0 and 7, in all treatment groups. No significant difference was observed in mean central venous pressure during any of the treatment periods (range of mean ± SE values at T0, 7.7 ± 0.84 mm Hg to 8.71 ± 0.84 mm Hg).

In all treatment groups and on each test day, MAP decreased while dogs were anesthetized. Values for SAP, diastolic arterial pressure, and MAP were significantly lower at T10 and T35, compared with values at T0 (P < 0.001). No significant differences were observed between pressures at T10 and T35 except in dogs in group II, in which SAP was significantly higher at T10, compared with SAP at T35. For all treatment groups, arterial pressure values at T10 and T35 were not significantly different among days 0, 7, and 14.

In dogs in groups I and IV, central venous pressure decreased significantly while dogs were anesthetized with propofol on days 7 and 14, with values obtained at T10 and T35 significantly less than values at T0. In dogs in group III, central venous pressure at T10 and T35 decreased significantly while dogs were anesthetized on day 7.

Discussion
The first purpose of the present study was to determine the most effective treatment for increasing urethral resistance in clinically normal female dogs by comparing the efficacy of 3 regimens involving administration of phenylpropanolamine hydrochloride and 1 regimen involving administration of ephedrine. We wished to compare the effects of phenylpropanolamine with those of ephedrine because use of the latter α-adrenergic agent in treatment of urinary incontinence has been widely described in humans and investigated in dogs. Dosages administered in the present study have been evaluated previously.

In the present study, phenylpropanolamine administered once daily and ephedrine administered every 12 hours significantly increased urethral resistance, as indicated by increases in MUP and MUCP. Interestingly, integrated pressure values were significantly increased after once-daily administration of phenylpropanolamine. The value for integrated pressure defines the functional area (ie, the segment of the urethral length in which the resistance is enough to prevent urine leakage) and may be a better measure of urethral sphincter competence than MUCP or FPL because it more fully characterizes sphincter deficiency in humans and is useful for assessing urethral function. A striking finding associated with once-daily administration of phenylpropanolamine in the present study was the change in shape of the urethral pressure curve; that is, there was a substantial increase in
the area under the curve, representing the functional area (Figure 3).

Pharmacokinetic studies\(^2\)\(^{-47}\) of phenylpropanolamine have been conducted in humans, dogs, and rats. The elimination half-life of phenylpropanolamine after oral administration ranges from 4 to 7 hours and is longer in humans than in rats.\(^44\)\(^{,}56\) That finding constituted the rationale for our use of twice- and 3-times-daily administration protocols for phenylpropanolamine. In 1 experimental study\(^4\) in humans, steady-state plasma concentrations of phenylpropanolamine were achieved after 1 to 2 days of administration at a dosage of 50 mg/person, every 12 hours; steady-state concentrations ranged from 30 to 200 ng/mL. The authors are not aware of published information pertaining to the pharmacokinetics of phenylpropanolamine with chronic administration. In our study, administration of phenylpropanolamine once daily for 7 days induced a significant increase in urethral resistance that was still observable several hours after oral administration.

One limitation inherent in the present study was the absence of a concurrent pharmacokinetic analysis with the urodynamic testing. Such data would have provided useful information for interpreting the urodynamic effects associated with different frequencies of drug administration. Determinations of plasma phenylpropanolamine concentrations were not performed because of laboratory technical difficulties.

Although successful treatment of USMI with phenylpropanolamine administered every 8 or 12 hours has been described,\(^10\)\(^{,}33\) MUP and functional area in the present study were not significantly higher after 7 or 14 days of phenylpropanolamine administered every 8 or 12 hours, compared with once-daily administration during an identical treatment time. Other studies\(^15\)\(^{,}47\)\(^{,}48\) in humans have revealed similar findings; in 1 study,\(^17\) there was no correlation between plasma phenylpropanolamine concentration and number of hours after drug intake. An absence of correlation between serum concentrations of the drug and MUCP has also been reported.\(^3\)\(^{,}48\) The range of therapeutic plasma concentrations of phenylpropanolamine in veterinary species is unknown.

On the basis of our results, it is reasonable to suspect that desensitization of urethral \(\alpha\)-adrenergic receptors may occur in dogs treated multiple times daily with phenylpropanolamine or in dogs receiving prolonged treatment. Whether desensitization of urethral \(\alpha\)-adrenergic receptors develops is controversial.\(^2\)\(^{,}3\)\(^{,}45\)\(^{,}56\) Prolonged administration of \(\alpha\)-adrenoceptor agonists may cause a right shift in the dose-response curve and reduce the maximum response.\(^5\)\(^{,}10\) However, other investigators\(^3\) have disputed that finding and contended that repetitious administration of an agonist at a dose that significantly increases the urethral pressure does not desensitize functional urethral \(\alpha\)-adrenergic receptors in vivo.

Pharmacokinetic studies\(^2\)\(^{,}3\)\(^{,}55\)\(^{,}57\) of acute and chronic administration of ephedrine have been conducted in humans. The elimination half-life of ephedrine after oral administration in humans is approximately 6 hours.\(^5\) In the present study, administration of ephedrine at a dosage of 1.5 mg/kg every 12 hours was effective at increasing urethral pressure. This observation corroborated published observations\(^6\) in the human medical literature, in which ephedrine administered for treatment of stress incontinence increased MUCP in women.

The present study was conducted on normally continent, sexually intact dogs that had appropriate urethral resistance, making clinical evaluation of these treatments impossible. Although the use of sexually intact dogs could be considered a limitation for making comparisons with the drugs’ effects on spayed dogs, our dogs were used because they permitted acquisition of data from a larger and more uniform group of subjects, with regard to age and weight, than would have been possible with spayed females. It is also possible that the increases in MUP, MUCP, and integrated pressure that were observed in our dogs would not necessarily elicit clinically apparent improvement in dogs with incontinence. However, results of studies\(^12\)\(^{,}13\) in humans indicate that there is a correlation between subjective assessments of improvement and increased MUCP. Clinical studies in dogs with USMI are needed to confirm that the significant increases in MUP, MUCP, and integrated pressure observed in the present study in association with administration of the \(\alpha\)-adrenergic drugs (particularly once-daily administration of phenylpropanolamine) would also be observed in incontinent dogs and would be curative or result in improved clinical signs when used for treatment of USMI.

During the course of each treatment regimen, we detected no significant differences in FPL distance before maximum urethral pressure, or plateau values, which is in accordance with results of studies\(^12\)\(^{,}13\) in humans. For FPL measurements, we considered that the pressure plateau frequently detected in the distal segment of the urethral pressure profile, although superior to urinary bladder pressure, does not reflect true sphincter activity but only corresponds to mechanical pressure resulting from apposition of the distal aspect of the urethral wall with the walls of the catheter. This observation can be related to the histologic composition of the urethra in female dogs and pigs\(^2\)\(^{,}32\) in that the proximal three fourths of the urethra is comprised of connective tissue and smooth muscle (ie, the segment corresponding to the FPL measurement) and the distal one fourth is comprised of striated muscle (ie, the segment corresponding to the pressure plateau) and therefore does not directly contribute to the resting urethral sphincter mechanism evaluated when the dogs were anesthetized.

It is possible that the absence of change in plateau values during the treatments indicates an absence of \(\alpha\)-adrenergic receptor stimulation in the distal part of the urethra. However, that observation does not corroborate results of an earlier study,\(^6\) in which intra-aortic injection of norepinephrine resulted in constriction of the distal portion of the urethra. The anatomic profile lengths were significantly shorter in dogs in group IV, that observation cannot be explained by the smaller size of dogs treated with ephedrine because dogs’ weights were not significantly different among groups.

The second purpose of the study was to determine the duration of treatment needed to attain maximum
urometric responses. Maximum urodynamic effects were observed by 7 days of treatment, and there were no further increases in measured variables at reevaluation on day 14. This finding correlates with that from a previous report in which investigators observed urethral pressure to be increased to an equal extent on all days of a 5-day course of phenylpropanolamine administration, with no increase in pressures measured during the treatment period.

Lastly, the hemodynamic effects of orally administered phenylpropanolamine and ephedrine were evaluated to determine the safety of these α-adrenergic agents at the described doses. Conclusions from previous studies are contradictory; although increases in systolic and diastolic arterial pressures and moderately severe headaches have been reported in humans after administration of phenylpropanolamine at recommended doses, other investigators reported no hypertension and a low frequency of adverse effects, such as hyperexcitability, after administration of phenylpropanolamine or ephedrine at recommended doses in humans, dogs, and rabbits. However, increased heart rates have been observed for as long as 12 hours after orally administered ephedrine in animals receiving α-adrenergic agents should be contemplated with caution, and combinations causing further increases in arterial blood pressure should be avoided. α-adrenergic agents should also be used with caution in dogs that are susceptible to exaggerated vagal tone (such as those of brachycephalic breeds) because such dogs could overrespond to arterial hypertension and have vagally mediated syncope.

Arterial and venous blood pressures decreased significantly during propofol infusion (administration rate, approx 30 mg/kg per hour), even during the treatment periods with α-adrenoceptor agonists. The hypotensive effect of propofol is primarily a result of reduction in systemic vascular resistance, with or without a reduction in cardiac output, that results from a combination of venous and arterial vasodilation. It was therefore expected that stimulation of α-adrenergic receptors would ameliorate any associated hypertension. Propylphylactic IV injection of ephedrine significantly attenuated the decrease in blood pressure associated with anesthetic induction with propofol and fentanyl in 1 study. Whether oral administration of phenylpropanolamine or ephedrine attenuated the level of hypotension resulting from propofol infusion in dogs in the present study is not clear because the arterial pressures recorded in our study correlated with those described by other investigators after 30 minutes of propofol infusion at a rate of 21 mg/kg per hour.

In the present study, administration of phenylpropanolamine every 8 or 12 hours did not significantly increase urethral pressure above baseline values and did not increase urethral resistance over measurements obtained with once-daily administration. Until use of the drug in veterinary patients with USMI is tested, the use of phenylpropanolamine at a dosage of 1.5 mg/kg, PO, every 24 hours may be recommended for treatment of dogs with USMI. Ephedrine also increased urethral resistance and could be used as an alternative to phenylpropanolamine. However, in the present protocol, ephedrine was administered twice daily, which may make it a less attractive option than once-daily phenylpropanolamine. On the basis of our results, the effectiveness of treatment with α-adrenergic agents can rapidly be assessed because no important increases in urethral resistance were observed after 1 week of administration of the drugs in clinically normal dogs. Increases in arterial blood pressures were observed in dogs in all treatment groups, a finding which supports the indication for caution and serial blood pressure measurements.
monitoring in dogs with concurrent cardiovascular disease that are receiving α-adrenergic agents.

Further studies on a larger number of dogs, including dogs with incontinence, are needed to confirm the efficacy of the administration of a once-daily dose of phenylpropanolamine for treatment of USMI.

a. Propalin, Vetoquinol SA-BP, Lure Cedex, France.
b. Ephedrine preparation (capsules containing 22 mg), provided by AstraZeneca S.A., Brussels, Belgium.
c. Linisol 2%, Braun, Melsungen, Belgium.
e. Siemens 6802 XL, Electro Medical System Group, Danvers, Mass.
g. Diprivran, AstraZeneca S.A., Brussels, Belgium.
h. Neclor, Nilcor Puritan Bennett Inc, Pleasanton, Calif.
i. SAS, version 8, SAS Institute Inc, Cary, NC.

References


