

Comparison of the effect of propofol and sevoflurane on the urethral pressure profile in healthy female dogs

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Objective—To compare the effects of propofol and sevoflurane on the urethral pressure profile in female dogs.

Animals—10 healthy female dogs.

Procedure—Urethral pressure profilometry was performed in awake dogs, during anesthesia with sevoflurane at 1.5, 2.0, and 3.0% end-tidal concentration, and during infusion of propofol at rates of 0.4, 0.8, and 1.2 mg/kg/min. A consistent plane of anesthesia was maintained for each anesthetic protocol. Maximum urethral pressure, maximum urethral closure pressure, functional profile length, and functional area were measured.

Results—Mean maximum urethral closure pressure of awake dogs was not significantly different than that of dogs anesthetized with propofol at all infusion rates or with sevoflurane at 1.5 and 2.0% end-tidal concentration. Functional area in awake dogs was significantly higher than in anesthetized dogs. Functional area of dogs during anesthesia with sevoflurane at 3.0% end-tidal concentration was significantly lower than functional area for other anesthetic protocols. Individual differences in the magnitude of effects of propofol and sevoflurane on urethral pressures were observed.

Conclusions and Clinical Relevance—Sevoflurane is an alternative to propofol for anesthesia in female dogs undergoing urethral pressure profilometry. Use of these anesthetics at appropriate administration rates should reliably distinguish normal from abnormal maximum urethral closure pressures and functional areas. Titration of anesthetic depth is a critical component of urodynamic testing. (*Am J Vet Res* 2003;64:1288–1292)

In clinically normal dogs, urethral pressure exceeds intravesical pressure during all phases of bladder filling and during changes in abdominal pressure. Urinary incontinence occurs when urethral pressure is less than intravesical pressure. Urethral pressure profilometry (UPP) is an effective way to evaluate urethral function and its contribution to urinary

incontinence in female dogs. This test measures pressures throughout the urethra from the bladder neck to the external urethral orifice. The maximum urethral closure pressure (MUCP) and functional profile length (FPL) are reliable indicators of urethral competence.¹

In humans, UPP is performed in the awake state. Sedation or restraint usually is required in other animals because of frequent movement during testing and artifacts that can affect urethral pressures. Many anesthetic agents markedly decrease urethral pressure, making it difficult to evaluate differences between clinically normal and abnormal dogs. Mean MUCP in healthy unsedated dogs ranges from 79.7 to 110.1 cm H₂O.^{2,3} Xylazine decreases MUCP as much as 52 to 73%, compared with that measured in unsedated dogs,^{2,4,6} and medetomidine reduces MUCP by 76%.⁴ Use of halothane as a primary anesthetic results in MUCP reductions ranging from 45 to 90%, compared with awake dogs.⁷⁻⁹

Propofol has been reported to have the least effect on UPP in female dogs, lowering closure pressure by approximately 36% (51.0 ± 7.4 cm H₂O), compared with unsedated dogs.^{2,5} Unfortunately, propofol has several adverse effects, including idiosyncratic muscle hypertonicity, that make it less desirable for use as a single anesthetic.^{10,11} Anesthesia with propofol is also difficult to control and can cause inconsistent MUCP measurements.

Newer inhalant anesthetics, such as sevoflurane, have not been evaluated for their suppressive effects on UPP. Sevoflurane may provide a more constant plane of anesthesia and is less expensive to administer to large-breed dogs than propofol. For these reasons, sevoflurane may provide a more reliable and convenient method for restraining patients during UPP, compared with other agents.

The purpose of the study reported here was to compare the effects of sevoflurane and propofol on UPP in clinically normal female dogs. Anesthetic drug concentrations were systematically varied for each agent to determine the effect of anesthetic depth on UPP. Recordings in the awake state also were obtained. We hypothesized that sevoflurane and propofol would not significantly decrease urethral pressures, compared with results obtained in the awake state, and that mean MUCP measures for sevoflurane would not be significantly different from those obtained with propofol. We further hypothesized that significant decreases in MUCP would occur as anesthetic depth was increased.

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Materials and Methods

Dogs—Ten healthy young adult sexually intact female Beagles that weighed from 7 to 10 kg were screened for underlying disease and urogenital abnormalities before UPP was performed. Dogs were considered clinically normal on the basis of results of physical examination, neurologic examination, CBC, serum biochemical analyses, abdominal radiography, urinalysis, and bacteriologic culture of urine. Dogs were observed for 1 week before the study for perineal soiling and exercise-induced urine leakage.

Urodynamic procedure—Urethral pressure profilometry was performed by the perfusion method with a triple lumen 9-F urinary catheter.^{12a} The catheter was placed aseptically in the urethra, and urine was collected for urinalysis and aerobic bacteriologic culture. The catheter was connected to pressure transducers that measured intravesical and urethral pressure. The rectum was evacuated manually, and a balloon catheter^b was placed and advanced to the level of the L6 or L7 vertebra. The balloon was inflated with 3 mL of sterile water, and the rectal catheter was connected to a pressure transducer used to measure intra-abdominal pressure. The urethral catheter was mechanically withdrawn from the urethra at a rate of 1 mm/s, while the urethra was perfused through the urethral pressure ports with warm (42°C) sterile water at a rate of 2 mL/min with an infusion pump.^c Bladder volume was adjusted throughout the procedure to maintain intravesical pressure from 2 to 7 cm H₂O. Abdominal, urethral, and bladder pressures were recorded during catheter withdrawal and stored on a computer for subsequent analysis. All measurements and calculations were performed by use of a urodynamic system and associated software.^d

Maximum urethral pressure (MUP) was recorded during the withdrawal phase of the UPP. The MUCP was calculated as the difference between MUP and perfused intravesical pressure. Traditionally, FPL is calculated as the portion of the UPP tracing during which urethral pressure exceeds intravesical pressure. With the perfusion method, however, initial or baseline urethral pressure is often higher than intravesical pressure, because perfused fluid is delivered through the same catheter port where urethral pressure is measured. Therefore, FPL was measured as the portion of the tracing during which urethral pressure exceeded baseline perfusion pressure. **Functional area (FA)** was calculated as the area under the FPL curve. Amoxicillin^e (22 mg/kg, PO, q 12 h for 7 days) was administered after each procedure.

Study design—The UPP studies were performed on all dogs during 7 conditions: awake; anesthetized with sevoflurane^f at end-tidal (ET) concentrations of 1.5, 2.0, or 3.0%; or anesthetized with propofol^g at constant rate infusion (CRI) rates of 0.4, 0.8, or 1.2 mg/kg/min, IV. The order in which the dogs received the treatments was not randomized; however, each procedure was performed at least 7 days apart in each dog to eliminate interference from previous procedures. During anesthesia, esophageal temperature, percentage oxygen saturation of hemoglobin (SpO₂),^h ET CO₂ concentration,ⁱ and heart and respiratory rates were monitored. In addition, jaw tone and palpebral reflex were used to assess the plane of anesthesia. During anesthesia with sevoflurane, ET sevoflurane concentration was measured.¹ A circulating water blanket and infrared heat lamp were used to maintain esophageal temperature from 36.7 to 37.7°C.

Awake state—Dogs were briefly anesthetized by administration of propofol (4 to 6 mg/kg, IV) to place the urethral and rectal catheters. The dogs were allowed to recover to the point at which they could maintain sternal recumbency without assistance. All dogs were restrained gently in right lateral recumbency during the UPP procedure.

Sevoflurane—An IV catheter was placed in the cephalic vein of each dog, and anesthesia was induced by administration of propofol (4 to 6 mg/kg, IV). The dogs were intubated, connected to a semiclosed circle rebreathing system with sevoflurane as the inhalant, and mechanically ventilated.¹ A capnograph systemⁱ connected to the endotracheal tube measured ET inhalant and CO₂ concentrations (30 to 35 mm Hg) and respiratory rate. After the urinary and rectal catheters were placed, ET sevoflurane concentration was adjusted to 1.5, 2.0, or 3.0%, and a minimum of 10 minutes was allowed for gas equilibration before UPP. At least 30 minutes elapsed between propofol induction and the start of UPP.

Propofol—Dogs were anesthetized, intubated, and ventilated as for sevoflurane. Propofol was administered IV at a rate of 0.4, 0.8, or 1.2 mg/kg/min.^c The UPP measurements were recorded after a minimum of 15 minutes at each infusion rate.

Statistical analyses—Mean MUP, MUCP, FPL, and FA were calculated for each of the 7 conditions in all dogs. Normality testing of each outcome indicated that data were normally distributed. Mean values were analyzed via 1-way ANOVA to determine whether significant differences were evident among anesthetic treatments across all dogs. If significant differences were found, a Bonferroni *t* test was performed to make pairwise comparisons between treatments. A *P* value of < 0.05 was considered significant. All statistical analyses were performed with a statistical software program.^k Data are reported as mean ± SD.

Results

All dogs remained clinically normal throughout the study, and no dogs were observed to have urinary or fecal incontinence. Serial bacteriologic cultures of urine performed at least 3 times on each dog over the study period failed to detect clinically relevant growth of organisms ($\geq 10,000$ cfu/mL). No abnormalities were observed among physical parameters monitored during anesthesia, and all dogs recovered from the procedures without complications. Two dogs became arousable and had voluntary movement during catheter replacement after withdrawal at the lowest infusion rate of propofol (0.4 mg/kg/min). An increase in the number of recorded movement artifacts was observed during the awake studies.

MUP—No significant difference was detected between MUP in awake dogs and that of dogs anesthetized with either sevoflurane at 1.5 or 2.0% or propofol at all infusion rates ($P = 0.388$). Dogs anesthetized with 3.0% sevoflurane had significantly lower MUP than awake dogs ($P < 0.001$) and those anesthetized with 1.5 and 2.0% sevoflurane ($P = 0.047$; Table 1). Standard deviations of MUP measurements ranged from 17.5 to 36.4% of the mean and were greatest for measurements taken at sevoflurane concentration of 3.0%, propofol CRI of 0.8 mg/kg/min, and propofol CRI of 1.2 mg/kg/min.

MUCP—The MUCP of awake dogs (82 ± 16 cm H₂O) was not significantly different ($P = 0.872$) from that of dogs anesthetized with 1.5 or 2.0% sevoflurane or with propofol at all infusion rates. The MUCP of dogs anesthetized with 3.0% sevoflurane (32 ± 15 cm H₂O) was significantly ($P < 0.05$) lower than the MUCP of all other anesthetic groups, except those of

Table 1—Mean \pm SD urodynamic measurements in clinically normal female dogs in the awake state and at various depths of anesthesia induced by use of propofol or sevoflurane

Variable	MUP (cm H ₂ O)	MUCP (cm H ₂ O)	FPL (cm)	FA (cm ² H ₂ O)
Awake	95 (17) ^a	82 (16) ^a	7.51 (1.80)	283 (46) ^a
Propofol (mg/kg/min)				
0.4	84 (18) ^a	72 (19) ^a	6.00 (1.16)	188 (59) ^b
0.8	82 (24) ^a	70 (24) ^a	5.91 (1.07)	165 (47) ^b
1.2	72 (24) ^{a,b}	61 (25) ^{a,b}	6.16 (1.07)	148 (55) ^b
Sevoflurane (%)				
1.5	91 (22) ^a	77 (21) ^a	5.98 (1.15)	205 (56) ^b
2.0	76 (21) ^a	63 (20) ^a	5.88 (1.31)	146 (40) ^b
3.0	46 (17) ^b	32 (15) ^b	5.71 (1.45)	72 (19) ^c

^{a,b,c}Within a column, values with different superscript letters are significantly ($P < 0.05$) different. MUP = Maximum urethral pressure. MUCP = Maximum urethral closure pressure. FPL = Functional profile length. FA = Functional area.

dogs anesthetized with 1.2 mg of propofol/kg/min ($P = 0.065$; Table 1). Standard deviations of MUCP measurements ranged from 19.7 to 40.4% of the mean and were greatest for dogs anesthetized with propofol CRIs of 0.8 and 1.2 mg/kg/min and sevoflurane concentration of 3.0%.

The MUCP of individual dogs anesthetized with propofol at 0.4, 0.8, and 1.2 mg/kg/min was determined. Although MUCP means at all propofol infusion rates were not significantly different, an anesthetic effect on the MUCP was apparent in certain dogs and not others. For example, the MUCP of 1 dog was 89 cm H₂O during the infusion of propofol at 0.4 mg/kg/min, 78 cm H₂O during the infusion of propofol at 0.8 mg/kg/min, and 58 cm H₂O during the infusion of propofol at 1.2 mg/kg/min. The MUCP of another dog was 80, 81, and 78 cm H₂O during the infusions of propofol at 0.4 mg/kg/min, 0.8 mg/kg/min, and 1.2 mg/kg/min, respectively.

FPL—No significant differences were observed among FPL values obtained during any of the anesthetic conditions. However, mean FPL (7.5 cm) was longer for the dogs in the awake state than during any of the anesthetic conditions, and this difference approached significance ($P = 0.06$; Table 1).

FA—Functional area in conscious dogs was significantly ($P = 0.011$) higher than that in anesthetized dogs (Table 1). There was no significant difference in FA among dogs anesthetized with propofol at 0.4, 0.8, or 1.2 mg/kg/min and dogs anesthetized with 1.5 or 2.0% sevoflurane ($P = 0.152$). Pairwise comparisons between 1.5 and 2.0% sevoflurane identified FA mean differences that approached, but did not attain, significance (205 ± 56 and 146 ± 40 cm²H₂O, respectively [$P = 0.152$]). The FA of dogs anesthetized with 3.0% sevoflurane was significantly ($P = 0.028$) lower than the FA for any of the other 6 conditions. The SDs of FA ranged from 16 to 36.7% of the means and were greatest for measurements using all infusion rates of propofol.

Discussion

Assessment of urethral sphincter mechanism incompetence (USMI) is complicated by the effect of anesthetics and sedatives on UPP, but some form of

chemical restraint is usually required in dogs because of excessive movements during the awake state that can interfere with reliable UPP recordings. Urethral sphincter mechanism incompetence results when intravesical pressure exceeds pressures generated along the length of the urethra. Intravesical pressure, however, is secondarily affected by fluctuations in intra-abdominal pressure and by the degree of bladder filling. Increases in abdominal pressure during exercise and bladder filling during sleep are the 2 events that are most highly associated with urine leakage in female dogs with USMI. Consequently, the threshold MUCP at which continence is achieved must be considerably higher than resting intravesical pressure in a laterally recumbent anesthetized patient with a nondistended bladder. Richter and Ling¹³ examined MUCP values in awake, incontinent female dogs by use of methods similar to those in our study. Mean awake MUCP was 37 ± 8 cm H₂O in affected dogs. This value represented a 53.7% reduction of the mean MUCP obtained in awake, healthy, continent female dogs (79.7 cm H₂O).¹³ An ideal method of chemical restraint for UPP would maintain pressures in clinically normal continent dogs greater than the awake incontinence mean of approximately 37 cm H₂O. Otherwise, considerable overlap might occur in the MUCP of continent and incontinent dogs, leading to errors in diagnosis of USMI.

Sevoflurane at 2.0 and 1.5% ET concentration and propofol at all rates of infusion maintained the mean MUCP > 37 cm H₂O in our study. Sevoflurane at 3.0% ET concentration reduced the MUCP to a value less than this continence threshold. Early studies of UPP in dogs used xylazine as the primary agent for restraint. Xylazine, however, reduced mean MUCP in continent dogs to 36.8 cm H₂O¹² and to 23.0 and 23.3 cm H₂O in 2 other studies.^{2,5} The large SDs in each study (from 20 to 46% of the mean) also suggested a variable drug effect among dogs. In later UPP studies^{18,9} that used halothane as the maintenance agent after thiopentone induction, mean MUCPs reported in continent dogs did not exceed 13 cm H₂O. Propofol caused the least effect on MUCP in clinically normal dogs (51 ± 8.0 cm H₂O).⁵ Propofol anesthesia in our study yielded similar MUCPs, ranging from 62 cm H₂O at 1.2 mg/kg/min CRI to 72 cm H₂O at 0.4 mg/kg/min CRI. The awake mean MUCP in the same dogs was 82 cm H₂O.

Propofol maintained urethral pressures in the dogs of our study, but use of propofol anesthesia for UPP recordings has several disadvantages. Although a CRI of propofol was used, variable plasma concentrations of propofol caused by variations in drug metabolism could have affected urethral pressures. Because plasma concentration of propofol cannot realistically or practically be monitored and regulated, planes of anesthesia in different dogs and in individual dogs over time may vary. In a study⁵ in which propofol was used as the anesthetic agent, 2 of 7 dogs had baseline MUCP values that differed by at least 30% from MUCP values recorded on subsequent catheter withdrawals. Lack of reproducibility of UPPs could hinder interpretation of urodynamic function in continent and incontinent dogs. Propofol also can cause an idiosyncratic syndrome characterized by muscle hypertonicity and

tremor that can create movement artifact on UPP recordings.^{10,11} These anesthetic concerns, combined with the high cost of propofol, especially in large-breed dogs that typically have USMI, make propofol a less than ideal agent for urodynamic testing.

Anesthesia with sevoflurane induced a constant plane of anesthesia and permitted reliable UPP measurements to be recorded. At 1.5 and 2.0% ET concentration, mean MUCP values (77 and 63 cm H₂O, respectively) were comparable to those obtained with propofol. A 3.0% ET concentration reduced the mean MUCP to 33 cm H₂O and consequently cannot be recommended for clinical use. A 3.0% ET concentration exceeds the minimum alveolar concentration of sevoflurane (2.4% ET) in dogs and would rarely be necessary in a clinical setting. A major advantage of sevoflurane is that drug delivery and systemic drug concentration can be precisely regulated. In our study, maintenance of constant sevoflurane concentration was achieved by controlling ventilation and by capnographic monitoring of ET concentrations. These procedures can be duplicated in a clinical setting and remove a major confounding variable that hinders comparisons of UPP studies between different laboratories and institutions. Previous studies^{1,7-9,14} with other inhalant anesthetics did not describe use of these methods in UPP evaluations. Imprecise control of anesthetic depth during testing could have contributed to the frequently observed low pressures, increased variability, and poor predictive value of the UPP in these studies.

Despite numerous measures taken to reduce experimental factors associated with variability, biological variability was observed in the dogs of this study. Awake MUCP values ranged from 53 to 110 cm H₂O, indicating considerable differences in peak pressures generated in individual dogs. A wide distribution of MUCP values for anesthetized dogs also was observed. The dog with the lowest MUCP, however, had a long FPL (9.3 cm), and the dog with the highest MUCP had a relatively short FPL (5.6 cm). The combined effect of MUCP and FPL in the latter dog likely contributed to the dog's continence. Two dogs had an anesthetic-related reduction in MUCP for both propofol and sevoflurane that was much more pronounced than that observed in other dogs. In 4 dogs, MUCP decreased in a graded manner as propofol infusion rate increased. In the remaining 6 dogs, a graded effect of propofol concentration was not evident. Individual variability in baseline urethral pressures and variable sensitivity to anesthetic depth among dogs resulted in MUCP SDs that were greater than expected.

Functional area is a calculated measure based on MUCP and FPL and may be a better measure of urethral sphincter competence for this reason. Functional area presently is used to more fully characterize USMI in human patients and is a useful parameter in assessing urethral function.¹⁵ Both MUCP and FPL contribute to urinary continence, and as observed in several dogs of this study, decreases in MUCP often are offset by increases in FPL and vice versa. Functional area values were less variable and more clearly indicated the effects of anesthetic depth on urethral function. Awake mean FA was 50% greater than the highest

mean FA during anesthesia and significantly greater than all other FA values. Propofol at 0.4, 0.8, and 1.2 mg/kg/min resulted in a gradual sequential reduction of the FA to 66, 58, and 53%, respectively, of the mean awake FA, but these values were not significantly different. The reduction in FA with increasing depth of anesthesia with sevoflurane was more pronounced and consistent; 1.5, 2.0, and 3.0% ET sevoflurane concentrations resulted in FA values of 72, 51, and 26% of the mean awake FA. Although only the FA at 3.0% ET was significantly different from other means, differences between FA means at 2.0 and 1.5% ET concentration approached, but did not attain, significance ($P = 0.152$).

Propofol and sevoflurane at clinically relevant rates of administration maintained mean MUCP well above the reported mean¹³ for awake incontinent dogs. Functional area measures were more sensitive in detecting an effect of propofol or sevoflurane on UPP and clearly revealed that administration of either anesthetic will reduce urethral function. An ET sevoflurane concentration of 3.0% in most dogs and CRI of propofol at 0.8 and 1.2 mg/kg/min in some dogs reduced the MUCP to less than the mean MUCP reported for awake incontinent dogs.¹³ Similar findings in a dog with incontinence secondary to other causes would lead to an incorrect diagnosis of USMI. The effect of anesthetic depth on urodynamic measures underscores the necessity of monitoring anesthetic concentrations and standardizing anesthetic delivery to clinical patients. Unlike propofol, ET sevoflurane concentration can be precisely monitored and regulated. Selection of ET sevoflurane concentrations in the 0.65 to 1.0 minimum alveolar concentration range (1.5 to 2.4%) should not adversely affect urethral pressures in clinically normal dogs. Use of other inhalant anesthetics also may not adversely affect urethral pressures, if anesthetic concentrations are titrated to an appropriate concentration. Reliable and repeatable UPP results will allow meaningful comparisons to be made between continent and incontinent dogs and will increase the predictive value of UPP.

^aTriple lumen catheter, model TLC-9M, Life-Tech Inc, Stafford, Tex.

^bAbdominal pressure catheter, model RPC-9PU, Life-Tech Inc, Stafford, Tex.

^cMedfusion syringe infusion pump 2010, Medex Inc, Duluth, Ga.

^dUrolab Primus IV urodynamic system, Life-Tech Inc, Stafford, Tex.

^eAmoxi-tabs, Pfizer Animal Health, Exton, Pa.

^fSevoFlo, Abbott Laboratories, North Chicago, Ill.

^gPropoFlo, Abbott Laboratories, North Chicago, Ill.

^hVetOx, model 4402, Sensor Devices Inc, Fort Collins, Co.

ⁱCapnomac Ultima, Datex Engstrom, Tewksbury, Mass.

^jOhio anesthesia ventilator, Ohio Medical Products, Airco Inc, Madison, Wis.

^kSigmaStat, SPSS Inc, Chicago, Ill.

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