Results of cystometry and urethral pressure profilometry in dogs sedated with medetomidine or xylazine

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Objective—To compare effects of medetomidine and xylazine hydrochloride on results of cystometry and micturition reflexes in healthy dogs and results of urethral pressure profilometry (UPP) in sedated and conscious dogs.

Animals—20 dogs.

Procedures—Urodynamic testing was performed 6 times in each dog (3 times after administration of xylazine [1 mg/kg of body weight, IV] and 3 times after administration of medetomidine (30 µg/kg, IM). Before each episode of sedation, UPP was performed. Heart and respiratory rates and indirect blood pressures were recorded prior to and 5, 10, 20, and 30 minutes after injection of sedative. Cystometry measurements included threshold volume, threshold pressure, and tonus limb. The UPP measurements included maximal urethral closure pressure (MUCP), functional profile length, and, in male dogs, plateau pressure.

Results—Mean MUCP was decreased markedly in xylazine- and medetomidine-sedated dogs. Xylazine and medetomidine also decreased plateau pressure in male dogs. The MUCP measurements were consistent among days for conscious and xylazine-sedated dogs but were inconsistent for medetomidine-sedated female dogs. The proportion of valid cystometry measurements was greater for xylazine (39 of 60) than for medetomidine (27 of 60). Cystometry was considered invalid when bladder pressure reached 30 cm H_2O without initiation of a micturition reflex.

Conclusions and Clinical Relevance—Medetomidine and xylazine have similar effects on measurement of UPP and cystometry. Medetomidine was less consistent among days for UPP in female dogs and produced fewer valid cystometry tests, compared with xylazine. For urodynamic evaluations, medetomidine administered IM cannot be substituted for xylazine administered IV. (*Am J Vet Res* 2001;62:167–170)

Evaluation of urinary tract problems in dogs is accomplished by combining clinical signs with anatomic evaluations, neurologic examination, determination of residual volume after urination, and results of urodynamic tests (**urethral pressure profilometry [UPP]**[1] and **cystometry [CM]**[2]). Typical clinical indications include incontinence resulting from sphincter incompetence after ovariohysterecomy,[3-8] prostatic disease,[6-11] neurologic deficits,[6-8] ectopic ureters,[7,8,12] inflammatory bladder disease,[6] inappropriate behavior, and urethral obstruction.[6-8] The objective of urodynamic testing is to determine whether the urinary dysfunction is in the bladder, urethra, or both. Evaluation of bladder function requires observation of voiding, measurement of residual volume by use of catheterization of the bladder after voiding, and, finally, analysis of results of CM performed during a period of sedation induced by administration of xylazine hydrochloride.[2] Evaluation of the contribution of urethral tone for preventing incontinence is achieved in our laboratory by use of UPP during a separate or urodynamic session when the dog is conscious.[9-11] Other investigators prefer the use of xylazine to sedate dogs for UPP or even the use of general anesthesia for UPP. When UPP is performed during xylazine-induced sedation, **maximal urethral closure pressure (MUCP)** and plateau pressure are reduced, especially in dogs with prostatic disease.[9]

The study reported here was designed to compare the urodynamic effects of xylazine with those of a more selective α_2-agonist, medetomidine, for use as the analgesic or sedation agent in dogs undergoing CM and UPP. It was hoped that the more specific α_2-agonist effects of medetomidine[13] would have less impact on urethral pressures than xylazine, thereby increasing efficiency of the urodynamic diagnostic evaluation by enabling clinicians to perform the UPP and CM during the same sedation episode.

Materials and Methods

Animals—Cystometry and UPP[14] tests were performed in 10 healthy sexually intact male and 10 healthy sexually intact female hound-type dogs. Body weight of male dogs ranged from 12.7 to 28.4 kg (mean ± SD, 23.2 ± 4.6 kg), and body weight of female dogs ranged from 13.1 to 23.0 kg (17.4 ± 3.3 kg). Each dog was evaluated during 6 sessions of sedation (3 after administration of xylazine[a] [1 mg/kg of body weight, IV] and 3 after administration of medetomidine[b] [30 µg/kg, IM]). Sedation sessions and urodynamic tests were separated by an interval of ≥ 4 days.

Procedure—Prior to each urodynamic test, food was withheld from the dogs, and dogs were given 500 mg of ampicillin orally. Urinalysis was performed on a urine specimen obtained via a catheter, and rectal temperature as well as heart and respiratory rates were recorded.

After dogs were sedated, heart and respiratory rates and indirect arterial blood pressures were recorded 5, 10, 20, and

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30 minutes after drug injection. Urodynamic tests were conducted, and effects of medetomidine were reversed by IV administration of atipamezole,[c] whereas effects of xylazine were reversed by IV administration of yohimbine.[d] Intervals from injection to effective sedation, injection of sedative agent to injection of reversal agent, and injection of reversal agent to sternal recumbency were recorded.

Before sedation, a UPP was recorded, using a computer-based urodynamic system.[e] Each dog was gently restrained in right lateral recumbency. A sterile 8-F catheter[f] was inserted via the urethra into the bladder and connected to a pressure transducer positioned at the level of the vulva or prepuce. Fluids were infused through the catheter at a rate of 5 ml/min, with pressure being measured through the inline port. The catheter was connected to a mechanical device that withdrew the catheter at a rate of 0.5 mm/s.

After completion of the UPP and withdrawal of the catheter, a sterile 6-F catheter[g] was inserted via the urethra into the bladder, and medetomidine was administered IM or xylazine was administered IV. Cystometry was performed by infusing fluid at a rate of 20 to 25 ml/min (rate calculated to provide 12 ml/kg with the interval from onset of infusion to micturition being < 5 minutes) until the micturition reflex was detected, or pressure in the bladder increased to 30 cm H_2O. The bladder then was emptied, the 8-F catheter was replaced, and UPP was performed once during the period of sedation.

Cystometry measurements[2] included threshold volume (volume of saline [0.9% NaCl] solution infused when micturition contraction began), threshold pressure (pressure in the bladder when maximal contraction developed), and tonus limb (change from initial pressure to threshold pressure/100 ml of infused fluid). Tonus limb was calculated only when the micturition reflex was detected. When fluid leaked from the urethra of a dog without an increase in bladder pressure or a dog did not develop a micturition reflex by the time bladder pressure reached 30 cm H_2O, CM measurements were considered invalid.

Measurements for the UPP included maximal urethral pressure, MUCP (ie, difference between maximal urethral pressure and intravesical pressure), and **functional profile length (FPL**; ie, length of urethra for which the urethral pressure exceeded intravesical pressure). Plateau pressure was measured in male dogs; it was defined as the approximate mean pressure in the flat portion of the profile.[1]

Statistical analysis—Mean values for the UPP (MUCP and FPL) and CM (threshold volume, threshold pressure, and tonus limb) were calculated for each dog. Mean plateau pressure was determined for male dogs. Using these data, descriptive values (mean ± SD) were calculated for male and female dogs. For each sex, the 4 measurements of UPP (conscious baseline value before administration of xylazine, value during xylazine-induced sedation, conscious baseline value before administration of medetomidine, and value during medetomidine-induced sedation) were compared. Each UPP sequence was compared with other sequences, using a paired *t*-test, and results for all 4 then were compared by use of a 1-way repeated-measures ANOVA. Treatment groups from the ANOVA then were compared, using a Tukey pairwise multiple-comparison procedure. The proportion of tests that had valid CM results was compared between xylazine and medetomidine, using a z-test for proportions. Repeatability of each test was determined by comparing the 6 UPP baseline evaluations for each dog and the 3 UPP and 3 CM evaluations for each drug in each dog, using a 1-way repeated-measures ANOVA when 3 urodynamic tests/dog were being compared or a paired *t*-test when only 2 urodynamic tests/dog were being compared. Threshold volume for each drug and each sex was compared to body weight, using linear regression. To determine whether specific dogs had similar UPP results for each of the sedatives, mean values were used to perform linear regressions between xylazine and medetomidine as well as between conscious and sedated conditions for each drug.

Mean values for heart rate, respiratory rate, and indirect blood pressures for each time period after administration of xylazine for each session were compared by use of a Kruskal-Wallis 1-way ANOVA on ranks. This test also was conducted on the values obtained after administration of medetomidine. Significance was defined as $P < 0.05$.

Results

Dogs were healthy throughout the study period. Urinary tract inflammation was not detected at any time, as determined by results of urinalysis.

Analysis of results did not reveal a significant difference in mean MUCP among the 6 sessions during conscious conditions for male or female dogs (**Table 1**). We did not detect significant differences for mean MUCP between the baseline values in conscious dogs before xylazine and the baseline values in conscious dogs before medetomidine; similarly, we did not detect significant differences among values for male and female dogs given xylazine and medetomidine. Plateau pressure did not differ significantly among male dogs.

Significant differences were detected for mean MUCP and mean plateau pressure between conscious dogs and dogs sedated with xylazine and between conscious dogs and dogs sedated with medetomidine. We did not detect significant differences in mean MUCP among the 3 sessions after administration of xylazine for male or female dogs and after administration of medetomidine for male dogs. In female dogs, MUCP during medetomidine-induced sedation had inconsistent day-to-day values in that the value for the first session (35.2 ± 18.8 cm H_2O) was greater than values for the second (22.3 ± 13.0 cm H_2O) or third (18.9 ± 9.7 cm H_2O) sessions. Regression analyses performed for MUCP between any 2 combinations of conscious, xylazine-sedated, and medetomidine-sedated sessions did not reveal significant associations.

Many of the CM did not provide valid pressure recordings, because urine leaked from the urethra without developing a micturition reflex or pressure in the bladder reached 30 cm H_2O without initiation of a micturition reflex. The proportion of valid CM evaluations during xylazine-induced sedation (39 of 60) was greater than that for medetomidine-induced sedation (27 of 60). Fourteen of 20 dogs given xylazine had at least 2 valid CM of the 3 CM attempted, whereas only 8 of the same 20 dogs had 2 valid CM of the 3 CM attempted when given medetomidine. Two dogs given xylazine and 4 dogs given medetomidine did not have any valid CM recordings. We did not detect significant differences between values for the first 2 CM recordings for any of the CM variables (threshold volume, threshold pressure, and tonus limb) for either drug, nor did we detect significant differences between the recordings for those dogs that had 3 CM recordings. Only mean CM data for each dog were used for analysis (Table 1). When values for male dogs were compared with those for female dogs, significant differences were not detected for either drug. Values for dogs given xylazine did not differ from values for dogs given

Table 1—Results (mean ± SD) of urethral pressure profilometry and cystometry in 20 healthy dogs

Group	Urethral pressure profilometry			Cystometry		
	MUCP (cm H_2O)	Plateau pressure (cm H_2O)	Functional profile length (cm)	Threshold volume (ml)	Threshold pressure (cm H_2O)	Tonus limb (cm H_2O/100 ml)
Male						
Conscious before xylazine	141.8[a] ± 32.9	48.1[c] ± 12.3	21.8 ± 3.1	ND	ND	ND
After xylazine	30.8[b] ± 6.9	23.8[d] ± 4.8	23.2 ± 2.0	188 ± 83.8	34.0 ± 6.5	18.5 ± 6.4
Conscious before medetomidine	135.0[a] ± 25.8	46.3[c] ± 11.6	23.8 ± 1.6	ND	ND	ND
After medetomidine	29.5[b] ± 6.0	23.9[d] ± 3.2	23.4 ± 1.8	236 ± 76.5	33.9 ± 7.4	15.1 ± 7.7
Female						
Conscious before xylazine	105.6[e] ± 39.2	NA	8.5 ± 1.2	ND	ND	ND
After xylazine	28.4[f] ± 13.7	NA	6.6 ± 1.8	204 ± 75	36.2 ± 6.2	22.3 ± 12.1
Conscious before medetomidine	107.9[e] ± 33.4	NA	7.9 ± 1.9	ND	ND	ND
After medetomidine	25.4[f] ± 11.6	NA	6.1 ± 1.1	219 ± 68	36.8 ± 6.5	19.4 ± 11.6

MUCP = Maximal urethral closure pressure. ND = Not determined. NA = Not applicable.
Mean ± SD is reported for each measurement. Within each gender, mean values for MUCP and plateau pressure with different superscript letters differ significantly ($P < 0.05$). Values for cystometry measurements or for functional profile length did not differ significantly ($P < 0.05$).

medetomidine for any of the CM variables in male dogs, female dogs, or the combination of male and female dogs. There was not a significant linear relationship between threshold volume and body weight for either drug, as determined by analysis of combined CM results for male and female dogs.

Results of heart and respiratory rates were similar for dogs given xylazine and medetomidine. Mean rates for dogs after administration of each drug decreased from values obtained before injection at all time periods from 5 to 30 minutes after injection. For example, mean heart rate before xylazine injection was 117.4 beats/min, which decreased to 45.6, 47.1, 47.4, and 47.0 beats/min at 5, 10, 20, and 30 minutes, respectively, after injection. Heart and respiratory rates were similar between dogs after administration of each of the drugs. Significant differences were not detected for blood pressure after injection of either drug for the intervals extending from before drug injection to any of the time periods after injection.

Discussion

Medetomidine given IM has a similar but less consistent effect on results of CM and UPP, compared with the effect of xylazine given IV. Measurements for MUCP during the 3 UPP sessions did not differ for conscious, xylazine, or medetomidine conditions, except that MUCP was inconsistent in female dogs given medetomidine. Consistent day-to-day UPP results are important if a test is to be considered reliable. Because the most common use of UPP is to measure sphincter function in dogs with incontinence after ovariohysterectomy and the subsequent response to treatment,[4-8,15-17] use of medetomidine in female dogs may result in inconsistent clinical signs. Inconsistent UPP results may have been related to inconsistent medetomidine absorption following IM injections. Similar inconsistencies for MUCP measured on the same day, with the value for the first recording being lower than the values for the second and third measurements, have been reported in dogs anesthetized with thiopentone, halothane, and nitrous oxide.[18] In another study,[16] consecutive MUCP measurements obtained in anesthetized dogs on the same day were not different, although none of the MUCP exceeded 2.26 cm H_2O. The MUCP measurements seen during sedation induced by medetomidine and xylazine were approximately a fourth of those recorded for the conscious female dogs. Xylazine consistently produces low MUCP, compared with MUCP for conscious conditions.[1,7,19,20] In the study reported here, MUCP recorded for the conscious female dogs before xylazine (105.6 ± 39.2 cm H_2O) and before medetomidine (107.8 ± 33.4 cm H_2O) compared favorably with the value (110.1 ± 20.2 cm H_2O) reported for healthy female dogs in another study conducted by our laboratory group.[14]

The study reported here further emphasizes differences between conscious and sedated conditions when performing a UPP. Because the study was performed in clinically normal dogs, the debate about drug effects probably will continue, with each laboratory needing to define its own UPP values for clinically normal dogs. Medetomidine administered IM appears to have effects similar to that of xylazine, but the day-to-day variations in female dogs and minority of the CM tests having valid results would imply that a dosage for use in IV administration should be developed for urodynamic testing. Some of the invalid CM results in female dogs may have been reduced by use of a Foley catheter. The lack of a significant association in MUCP among conscious, medetomidine, and xylazine conditions for specific dogs means that clinical recommendations developed on the basis of UPP recorded after use of 1 anesthetic regimen cannot be compared with the clinical interpretation of UPP recorded during other conditions. An example of this disparity was found when clinically normal dogs were studied before and after excisional prostatectomy. Xylazine, compared with the conscious condition, had a much greater depressant effect on MUCP after prostatectomy.[9]

Medetomidine was not as consistent in providing interpretable CM results as xylazine. We did not detect an association between threshold volume and body weight with either drug. This individual variation of bladder distention may be related to urinary tract function of specific dogs or to the fact that dogs had similar body weights. The clinical utility of CM is to determine whether the bladder can distend to a threshold volume

that initiates the micturition reflex without stimulating spastic contractions. A potentially equal useful clinical tool is observation of voiding and measurement of residual volume following urination; however, many animals are reluctant to void while being observed or while hospitalized. A spastic bladder usually is associated with urinary tract infection, a condition that should be evaluated by use of urinalysis and microbial culture. None of the dogs in our study had a urinary tract infection, a condition that could have produced incontinence or altered the response to bladder distention.

Inhibition of micturition induced by both drugs may be a problem when used in some patients. Decom pression of the distended bladder should be accomplished by manual expression or catheterization. Bladder distention is less likely to be a problem with these sedatives than during general anesthesia, because both drugs have a short duration of effect and can be reversed.

Cardiopulmonary and clinical responses to xylazine and medetomidine were similar to that recorded in another study.[21] All dogs were healthy and did not seem to be adversely effected by either drug. Recovery was rapid after administration of reversal agents.

[a]Rompun, Bayer Corp, Shawnee Mission, Kan.
[b]Domitor, Pfizer Animal Health, New York, NY.
[c]Antisedan, Pfizer Animal Health, New York, NY.
[d]Yohimbine, Lloyd Laboratories, Shenadoah, Iowa.
[e]Janus System III (MC394) urodynamic system, Life-Tech Inc, Houston, Tex.
[f]Urethral pressure profile catheter (UPP-8D), Life-Tech Inc, Houston, Tex.
[g]Dual-lumen catheter (DLC-6D), Life-Tech Inc, Houston, Tex.

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