Intravesical application of lidocaine and sodium bicarbonate in the treatment of obstructive, idiopathic lower urinary tract disease in cats

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Abstract: Die idiopathische Erkrankung der unteren Harnwege der Katze (iLUTD) teilt viele Merkmale mit der interstitiellen Zystitis (IC) des Menschen. Bei einigen Menschen mit IC wurde nach der intravesikalen Applikation von alkalisiertem Lidocain eine anhaltende Symptomlinderung festgestellt. Das Ziel dieser Studie war, die Effekte der intravesikalen Instillation von alkalisiertem Lidocain in Bezug auf Rezidivrate und Symptomlinderung bei obstruktiver iLUTD zu evaluieren. Zwölf Katzen wurden in die Fallgruppe (2 oder 4mg/kg Lidocain und Natriumbikarbonat) und 14 in die Kontrollgruppe (Placebo (0.2mL/kg 0.9% NaCl und Natriumbikarbonat) oder Standardtherapie (nur Harnkatheter, ohne Instillation)) aufgenommen. Die Zuteilung zu den Gruppen erfolgte zufällig. Die Instillation wurde einmal täglich für 3 Tage durchgeführt. Bei erfolgreicher Therapie wurde eine Nachkontrolle bis 2 Monate nach Entlassung mittels Fragebogen durchgeführt. Die Rezidivrate betrug 58% (7/12) bei der Fallgruppe und 57% (8/14) bei der Kontrollgruppe. Die Symptomlinderung war bei beiden Gruppen ähnlich. Bei Katzen mit obstruktiver iLUTD hatte die intravesikale Applikation von Lidocain während drei Tagen keine Auswirkung auf die Rezidivrate oder den Schweregrad der Symptome. Idiopathic lower urinary tract disease (iLUTD) in cats shares many features in common with interstitial cystitis (IC) in humans. In human patients intravesical instillation of alkalinized lidocaine sometimes is associated with sustained amelioration of symptoms. The objective of this study was to evaluate whether the intravesical instillation of alkalinized lidocaine reduces recurrence of urethral obstructions and severity of clinical signs in cats with obstructive iLUTD. Twelve cats were included in the case group (2 or 4mg/kg lidocaine and sodium bicarbonate) and 14 cats served as controls (placebo (0.2mL/kg 0.9% NaCl and sodium bicarbonate) or standard therapy (urinary catheter only, without instillation)). Cats were randomly assigned to either group. The intravesical instillation was done once a day for 3 days. A follow-up of the cats with successful treatment was made up to 2 months after discharge using a questionnaire. Recurrence of urethral obstruction occurred in 58% (7/12) of the case group and 57% (8/14) of the control group. The amelioration scores were similar between the groups. The intravesical administration of alkalinized lidocaine for up to 3 days had no effects on recurrence and severity of clinical signs in cats with obstructive iLUTD.

Other titles: Intravesikale Applikation von Lidocain und Natriumbikarbonat bei der Behandlung der obstruktiven, idiopathischen Erkrankung der unteren Harnwege bei Katzen

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SUMMARY

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Idiopathic lower urinary tract disease (iLUTD) in cats shares many features in common with interstitial cystitis (IC) in humans. In human patients intravesical instillation of alkalinized lidocaine sometimes is associated with sustained amelioration of symptoms. The objective of this study was to evaluate whether the intravesical instillation of alkalinized lidocaine reduces recurrence of urethral obstructions and severity of clinical signs in cats with obstructive iLUTD.
Twelve cats were included in the case group (2 or 4mg/kg lidocaine and sodium bicarbonate) and 14 cats served as controls (placebo (0.2mL/kg 0.9% NaCl and sodium bicarbonate) or standard therapy (urinary catheter only, without instillation)). Cats were randomly assigned to either group. The intravesical instillation was done once a day for 3 days. A follow-up of the cats with successful treatment was made up to 2 months after discharge using a questionnaire. Recurrence of urethral obstruction occurred in 58% (7/12) of the case group and 57% (8/14) of the control group. The amelioration scores were similar between the groups.
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Keywords: idiopathic lower urinary tract disease, lidocaine, interstitial cystitis

INTRODUCTION

The term feline lower urinary tract disease (LUTD) has been used to describe clinical signs related to irritative voiding, but does not identify the underlying etiology (Hostutler et al., 2005; Forrester et al., 2007). The possible causes can include bacterial urinary tract infection, trauma, urolithiasis, urethral plugs, neoplasia, anatomic malformation, behavioral disorders and neurologic problems (Kruger et al., 2009; Hostutler et al., 2005). If no specific reason is found, the disease is called idiopathic (Westropp et al., 2004). Regardless of etiology, the resultant clinical signs are similar and include dysuria, stranguria, hematuria, pollakiuria and periuria (Forrester et al., 2007; Lekcharoensuk et al., 2001). The disorder can be obstructive, and urethral obstruction was reported to occur more commonly in young cats and almost exclusively in male cats due to their relatively long and narrow urethra (Hostutler et al., 2005).

Recurrence of obstruction is common. In 1 study, it was reported that 8 of 22 cats (36%) with idiopathic urethral obstruction re-obstructed after a median of 17 days (Gerber et al., 2008). In a more recent study, 11 of 55 cats (22%) with idiopathic obstructive LUTD experienced at least 1 recurrence in the 6 months after a previous episode (Segev et al., 2011). Currently, no treatment is known to decrease these high recurrence rates.

A syndrome in human beings, known as interstitial cystitis (IC), shares many features in common with cats that have idiopathic cystitis (Buffington, 2011). The cause of IC also is unknown, and treatment is mostly empirical and unsatisfactory (Moutzouris et al., 2009). In a recent manufacturer funded study, treatment with intravesical alkalinized lidocaine (PSD597) and sodium bicarbonate in patients with IC was reported to provide amelioration of symptoms beyond the acute treatment phase (Nickel et al., 2009). IC is thought, in part, to develop into a visceral allodynia, as a result of sensitized local bladder afferent nerves (Butrick 2003). Theoretically, intravesical administration of the local anesthetic lidocaine could help control the pain and inflammation associated with IC, returning the neuropathic bladder to a more normal state with time (Nickel et al., 2009).

Because of the positive effects of intravesical alkalinized lidocaine in affected humans, and the similarities reported between human IC and idiopathic LUTD in cats, we hypothesized that cats with LUTD might also benefit from intravesical lidocaine instillation. Because obstructive LUTD can become life threatening and urinary catheterization is necessary to relieve the obstruction, the study was only conducted on cats with urethral obstruction. The aim of this prospective study was to determine whether the intravesical instillation of lidocaine could effectively decrease the severity of clinical signs or the recurrence rate of urethral obstruction in cats with obstructive idiopathic LUTD.

MATERIALS AND METHODS

Case selection

Cats presented to the Clinic for Small Animal Internal Medicine, University of Zurich, between July 2010 and September 2011 showing ≥1 of the following clinical signs: pollakiuria, hematuria, dysuria, stranguria, inappropriate urination and with partial or complete urethral obstruction were considered for the study. A cat was regarded as obstructed if the bladder was distended and the cat was unable to void urine freely or only voided drops of urine.

Diagnostic investigation included history from the owner regarding previous episodes of LUTD and observed clinical abnormalities, a physical examination, urinalysis, urine culture, hematology, serum biochemistry profile, radiographs of the abdomen (care was taken to include the entire lower urinary tract to the tip of the penis) and ultrasound examination of the

urogenital tract. Urine was collected by cystocentesis or by catheterization. Qualitative urine culture was performed on sheep blood agar, Gassner agar and Clad agar[1]. If there was suspicion of urethral stricture or perforation of the lower urinary tract, contrast radiography (retrograde uretrography) also was performed.
Urolithiasis was diagnosed when calculi were seen on radiographs or during ultrasound examination of the urinary tract. Urinary tract infection was diagnosed when qualitative urine culture was positive. Urethral plug was diagnosed when a plug was identified during urethral catheterization. If the underlying cause of the obstruction could not be identified after appropriate evaluation, idiopathic LUTD was diagnosed. Only cats with the idiopathic LUTD were enrolled in the study. Owner consent was obtained before treatment with lidocaine. The government animal welfare authorities of the canton of Zurich, Switzerland approved the treatment protocol used in the study.

Procedure
After diagnostic investigation and confirmation of urethral obstruction, IV fluid therapy was started. Urethral obstruction was relieved in a standard manner. Cats were anesthetized with fentanyl[2] (5 μg/kg IV) and midazolam[3] (0.23 mg/kg IV) or ketamine[4] (10 mg/kg IV (for anesthetic induction) or IM (for deep sedation)) and midazolam (0.1 mg/kg IV or IM) and maintained under anesthesia with IV injection of propofol[5] or with inhalation anesthesia (isofloran[6]) until an indwelling urinary catheter[7] was placed and sutured to the prepuce. When feasible, the urinary catheter was kept in place for 3 days. The urinary catheter was connected to a sterile closed collection system[8] to keep the bladder empty and to quantify urine production. Cats were concurrently treated with an analgesic (buprenorphine[9] 0.006-0.014 mg/kg IV q6h) and fluid was administered IV (lactated Ringer's solution or 0.9% saline solution)[10]. The initial infusion rate was determined based on the hydration status and physical condition of the cat at presentation. The rate was adjusted daily based on urine production assessed during the day.
The first 12 cats were treated by intravesical lidocaine instillation[11], 0.1 mL/kg of a 2% lidocaine solution, a dosage reported to be safe after IV administration in a recent study (Ko JC et al., 2008). Sodium bicarbonate[12], 0.06 mL/kg of an 8.4% solution, was added immediately afterward. Because no adverse effects were seen and serum concentrations were low, we increased the amount of lidocaine in the solution. Subsequently, the next cats were randomly assigned to receive intravesical either 0.2 mL/kg of a 2% lidocaine solution or placebo (0.2 mL/kg of a 0.9% saline solution) and 0.06 mL/kg of an 8.4% sodium bicarbonate solution, respectively. If the owners declined to enroll their cats in the study or if the cats were too aggressive and uncooperative at the beginning of treatment, the cats were treated according to a standard procedure (3 days with an indwelling urinary catheter but without intravesical instillation).
The case group consisted of cats that received the intravesical medication of either 0.1 or 0.2 mL/kg of a 2% lidocaine solution and 0.06 mL/kg of an 8.4% sodium bicarbonate solution. The control group consisted of cats that either received intravesical instillation of 0.2 mL/kg placebo (equal to the volume of the instilled 2% lidocaine solution) and 0.06 mL/kg of an 8.4% sodium bicarbonate solution or those that underwent the standard treatment. Before instillation, the bladder was emptied and, after instillation, the urinary catheter was closed for 1 hour to allow the medication to remain in place. After 1 hour, the catheter was re-attached to the closed urine collection system and urine production was assessed. This procedure was performed once a day for a maximum of 3 consecutive days.
After removal of the urinary catheter, presence of spontaneous urination was assessed by monitoring the cats every 2 hours for up to 2 days. Antibacterial treatment with amoxicillin-clavulanic acid[13] (20 mg/kg PO q12h) or amoxicillin[14] (20 mg/kg PO q12h) was started

concurrently and continued in cats that did not re-obstruct immediately after removal of the urinary catheter.
Treatment success was defined as spontaneous urination (normal urine stream and empty bladder after voiding) and discharge from the hospital. Buprenorphine (0.006-0.014 mg/kg PO q8h) or meloxicam suspension[15] (0.025 mg/kg PO q24h) in cats with and without azotemia at presentation, respectively, was prescribed for 3 additional days after discharge. The antibacterial treatment was continued for 1 week. Follow-up of cats with successful treatment was made 2 weeks, 1 month and 2 months after discharge using a questionnaire to assess the severity of the clinical signs after therapy.
Treatment failure was defined as failure to have spontaneous urination (i.e., unable to urinate or only voiding drops of urine with a distended bladder). These cats were excluded from follow-up assessment. Their owners were asked to complete only the questionnaire for the clinical signs before treatment. A modification of a previously used questionnaire (Gunn-Moore et al., 2004) was used. All questionnaires were composed of 8 visual analogue scales, each 10 cm in length, with values ranging from 0 (normal cat) to 10 (very severe clinical signs). The 8 signs the owners were asked to record were: (1) increased frequency of urination, (2) straining while urinating, (3) crying out while urinating, (4) presence of blood in the urine (macroscopic hematuria), (5) urination outside the litter box, (6) increased grooming around the perineum, (7) altered behavior (increased aggression, fear, or nervousness) and (8) gastrointestinal symptoms (e.g., vomiting, or diarrhea).
The primary endpoint was the recurrence of urethral obstruction within 2 months after removal of the catheter. The recurrence rate between groups was assessed and compared.
A secondary endpoint included the assessment of changes in severity (amelioration) of clinical signs of LUTD from baseline (before treatment), 2 weeks, 1 month and 2 months after discharge in cats with successful treatment. Because of the subjectivity of the questionnaire, the median change from baseline (median amelioration scores) for individual clinical signs and the sum of the 8 scales were calculated at each time point. Differences between the groups were compared. The questionnaire for the time before treatment was performed before or at least on the same day of discharge.

Serum lidocaine concentrations and tolerability
Blood samples for the evaluation of plasma lidocaine concentrations were collected from 2 cats treated with 0.1 mL/kg of 2% lidocaine and 2 cats treated with 0.2 mL/kg of 2% lidocaine at time 0 h (immediately after instillation), 0.5 h, 1 h, 2 h and 3 h after treatment on 2 consecutive days of therapy. Plasma lidocaine concentrations were measured using high performance liquid chromatography-mass spectrometry. Any clinical signs of adverse effects related to lidocaine toxicity were monitored and recorded every 2 hours during hospitalization.

Statistical analysis
Results were analyzed using a commercial computer program (Statistical Package for Social Science 8.0; SPSS). Because of the small simple size, especially in the follow up assessment, comparisons of variables within and among groups were performed using a non-parametric test (the Mann-Whitney U test). Statistical analysis was not conducted if < 4 results were available to compare. Differences were considered significant at $p<0.05$.

RESULTS

Overall, 69 cats were presented to the Clinic for Small Animal Internal Medicine, University of Zurich between July 2010 and September 2011 because of lower urinary tract signs with

urethral obstruction. Thirty-four cats were excluded from the study because of urolithiasis (=13, 19%), urethral plugs (=5, 7%) and urinary tract infection (=14, 20 %). In 2 cats (3%), a definitive diagnosis was not possible because not all of the diagnostic investigations could be made. These 2 cats also were excluded from the study. In 35 cats (51%), no specific cause for the clinical signs could be identified. These cats were classified as having idiopathic obstructive LUTD. Of these 35 cats, 9 were excluded because of immediate surgery (perineal urethrostomy, 6 cats), urethral perforation after catheterization (1 cat) and euthanasia requested by the owner (2 cats). Twenty-six cats (38%) remained in the study.

The cats included in the study ranged in age from 1 to 9 years (median, 5 years) and weighed between 3.8 and 7.2 kg (median, 5.5 kg). There were 25 neutered males and 1 intact male. The breeds included 20 domestic cats, 2 Persians, 1 Main Coon, 1 Siamese and 2 Siberian Forest cats. Blood urea nitrogen (BUN) serum, creatinine and serum potassium concentration ranged between 5.5 and 138 mmol/L (median, 12.6 mmol/L), 70 and 1700 µmol/L (median, 150.5 µmol/L) and 2.8 and 8.6 mmol/L (median, 4.5 mmol/L), respectively. The present episode was the first known episode of LUTD for 21 cats whereas recurrent bouts were described for the 5 other cats. Twelve cats were treated with 2% lidocaine (4 cats with 0.1 mL/kg and 8 cats with 0.2 mL/kg). Fourteen cats were in the control group (8 cats were treated with placebo and 6 cats with standard therapy). There was no significant difference in age, breed, BUN serum, creatinine, serum potassium concentration, or number of LUTD episodes between groups. Body weight was significantly higher in the case group ($p=0.04$). Clinical signs scores available from 10 cats in the case group and 12 cats in the control group before treatment were not significantly different between the 2 groups (Table 1). In 3 cats treated with 0.2 mL/kg 2% lidocaine and in 1 cat treated with placebo, intravesical instillation was possible only for 2 days because of self-removal of the catheter after 2 days of therapy. In 1 cat treated with 0.2 mL/kg 2% lidocaine, intravesical treatment was possible only for 1 day because of the aggressive behavior of the cat after the first day of therapy. Median treatment duration in both groups was 3 days. All of the cats experienced post-obstructive diuresis after relief of obstruction. In 24 cats, the highest daily urine production was assessed, and ranged between 2.2 and 12.0 mL/kg/h (median, 6 mL/kg/h). Additionally, in 5 of the 26 cats, urine pH was measured at 1 hour immediately before re-attaching the urinary catheter to the collection system. Urine pH was 6, 7.5, 8.5 in 3 cats and 8 in other 2 cats.
Recurrence of urethral obstruction after removal of the urethral catheter was 58% (7/12) in the case group 50% (2/4) in cats that received 0.1 mL/kg 2% lidocaine, 63% (5/8) in cats that received 0.2 mL/kg 2% lidocaine within 1 to 14 days (median, 3 days) and 57% (8/14) in the control group (63% in 5/8 cats in the placebo group and 50% in 3/6 cats that received standard therapy) within 1 to 2 days (median, 1 day). Five cats in the case group and 6 cats in the control group had successful treatment for at least 2 months after discharge. These 11 cats were followed up for assessment of amelioration of clinical signs. Of all 11 questionnaires sent to the owners at each of 3 time points (2 weeks, 1 month and 2 months after discharge), 10 (4 of the case group and 6 of the control group), 10 (4 of the case group and 6 of the control group) and 9 (4 of the case group and 5 of the control group) were returned, respectively. The owners who did not return questionnaires were contacted by phone to assess recurrence. In the case group, the degree of severity in frequency of urination was not recorded in 1 questionnaire before treatment as well as in another cat 2 weeks and 2 months after treatment. For these clinical signs, 2 weeks and 2 months after treatment, the available results were insufficient to allow statistical analysis.
Cats treated with lidocaine showed significantly higher median amelioration score in straining 2 weeks after discharge compared to the cats in the control group ($p=0.01$). There were no

significant differences between groups in the other individual clinical signs as well as in the sum of the scores at any time point.

Serum lidocaine concentrations and tolerability

In all cats, lidocaine concentrations peaked within 60 minutes of instillation, ranging between 0.45 and 4.1 μmol/L (Table 2). In all 4 cats, blood sampling was not possible at all 5 time points. No severe adverse events were reported during intravesical therapy. One cat treated with 0.2 mL/kg 2% lidocaine experienced 1 episode of salivation on the third day of treatment.

DISCUSSION

The response of cats with idiopathic obstructive LUTD to lidocaine treatment with regard to recurrence and amelioration of clinical signs was poor. Within the 1-year trial period, recurrence of urethral obstruction was seen in 58% of the cats in the case group and in 57% of cats in the control group within 2 months. In a previous 1-year study, cats with idiopathic obstructive LUTD experienced a recurrence rate of only 22% within 6 months (Segev et al., 2010). It is unclear why the cats in the current study showed more recurrence of the disease, and may reflect the different definition used to describe the obstruction. In particular, in the current study a cat was defined as obstructed if it was unable to generate a normal stream of urine (i.e., only voided drops of urine) with a distended bladder. It also could be that the observation of the clinicians and the owners was closer because of the prospective study design and led to the recognition of even mild partial obstruction. Furthermore, idiopathic LUTD was diagnosed by exclusion of other possible causes and, as discussed in a previous study, a specific cause potentially could have been overlooked. For example, a plug may not have been seen and may have been retropulsed into the bladder after placement of the urinary catheter, leading to a misdiagnosis of idiopathic LUTD (Gerber et al., 2008). Furthermore, retrograde urethrography was only performed when leakage of the lower urinary tract was suspected. Anatomic malformations and strictures could not definitively be excluded in the cats in which urethrography was not performed.

A significant difference between groups in the follow-up assessment was only observed in amelioration of straining 2 weeks after discharge. This significance may only be the consequence of statistical analysis conducted for several clinical signs all reflecting the same disease (type I statistical error). However, it might also reflect a limited potential effect of lidocaine, inducing only relief from pain while urinating (stranguria) without inducing an adequate local anti-inflammatory effect. Lidocaine is primarily recognized as a neuronal sodium channel-blocking agent, but it also has proprieties capable of substantial antihistaminic effects. In an in vitro study, these effects were reported to be dose-dependent and at concentrations in the high micromolar range (234 to 2340 μg/mL or 1000 to 10000 μmol/L, respectively) (Yanagi et al., 1996). A low serum lidocaine concentration may be sufficient to generate a neuronal sodium-blocking effect (i.e., pain relief), whereas a very high tissue lidocaine concentration may be necessary to achieve antihistaminic effects (i.e., anti-inflammatory effect). The lack of a demonstrable relevant beneficial effect could be related to subtherapeutic treatment because of an inadequate dosage of lidocaine or sodium bicarbonate, inadequate duration of the treatment, or because of the small sample size and insufficient power.

It is well known that cats may be more sensitive than other species to the toxic effects of local anesthetics, in particular to central nervous system effects (Plumb 1999). However, the cumulative doses of lidocaine in healthy cats were reported to be 9.7 mg/kg at the stage of excitation and 22.3 – 27.3 mg/kg for the induction of convulsions (Seo et al., 1982). The

plasma lidocaine concentration associated with the onset of seizures was reported to be between 71.3 and 208.5 μg/mL (304.8 - 891.3 μmol/L) (Chadwick, 1985). Because adverse effects also have been observed after IV application of < 2 mg/kg lidocaine (Tilley et al., 1977) and because cats with cystitis have increased bladder permeability (Gao et al., 1994), the first cats of the current study were treated with a dose of 0.1 mL/kg of a 2% lidocaine solution. The serum lidocaine concentration was assessed in 2 of these cats. The concentration was well below to the plasma concentration reported to be associated with the onset of seizures, and the cats did not show any obvious adverse effects. Therefore, the next cats were treated with a higher dose (0.2 mL/kg of a 2% solution) and even with this dose a critical concentration was not reached. Only 1 cat showed 1 episode of salivation on the third day of the lidocaine treatment. This cat exhibited signs of stress, and the new environment may have contributed to the salivation. Previous studies conducted in humans demonstrated poor absorption of lidocaine from the bladder and poor local therapeutic effects if only applied intravesically (Pode et al., 1992; Birch et al., 1994). Enhanced absorption and therapeutic effects were reported after alkalinizing the injected solution with sodium bicarbonate (Henry et al., 2001; Parsons 2005). Therefore, a sequential instillation of 0.06 mL/kg sodium bicarbonate was added in all the cats receiving intravesical medication. However, voided bladder content pH 1 hour after application was not alkaline in all the 5 cats in which it was measured. Furthermore, the lidocaine concentration in serum differed considerably among cats. A possible explanation could be the phenomenon of post-obstructive diuresis (urine output > 2 mL/kg/h (Francis et al., 2010)). This pathophysiologic process could lead to dilution of urine, alteration of urine pH and reduction of the bladder lidocaine concentration within 1 hour after application. A longer duration of treatment also may have influenced the outcome. In studies of patients with IC, an immediate and sustained symptomatic relief beyond the treatment phase was reported after 5 consecutive days of lidocaine instillations (Nickel et al., 2008) as well as after 6 instillations over 2 weeks (Parsons, 2005). Because the risk of physical or chemical injury to the urinary tract and bacterial infections has been reported to increase with the duration of catheterization (Barsanti et al., 1985; Lees et al., 1984), therapy in the current study was limited to 3 days.

Important weaknesses of the study are the small sample size, in particular in the follow-up assessment. Furthermore, because of the uncooperative behavior of some cats, intravesical instillation was not always possible for 3 consecutive days. Moreover, only cooperative and non-aggressive cats as well as cats of owners who wanted to participate were randomly assigned to the study groups. Furthermore, because written consent by the owners of the cats treated with lidocaine was requested, we decided not to blind owners to the treatments used. These attendant circumstances could have biased our results.

In conclusion, the current study shows an alternative procedure for the treatment of idiopathic cystitis in cats with urethral obstruction. The results suggest that intravesical administration of lidocaine (0.1 or 0.2 mL/kg of a 2% solution) and sodium bicarbonate (0.06 mL/kg) for 3 consecutive days does not have apparent beneficial effects on decreasing the recurrence of obstruction as well as on clinical signs in cats with idiopathic obstructive LUTD.

TABLES

Table 1 - Median and range of the clinical signs score prior to treatment (baseline score) in the case (10 cats) and in the control group (12 cats)

Clinical signs	Group	Baseline
Increased frequency of urination	Case	5 (1 to 10)
	Control	8 (0 to 10)
Straining while urinating	Case	7.5 (1 to 10)
	Control	7 (1 to 10)
Crying out while urinating	Case	0 (0 to 8)
	Control	1 (0 to 10)
Presence of blood in the urine	Case	1 (0 to 10)
	Control	1 (0 to 10)
Urination outside the litter box	Case	8 (0 to 10)
	Control	7 (0 to 10)
Increased grooming around the perineum	Case	6 (2 to 10)
	Control	7 (0 to 10)
Altered behavior	Case	5.5 (0 to 10)
	Control	6.5 (0 to 10)
Gastrointestinal symptoms	Case	1.5 (0 to 10)
	Control	1 (0 to 10)
Sum	Case	39 (14 to 51)
	Control	43 (9 to 75)

Table 2 - Plasma lidocaine concentrations (µmol/L) and post-obstructive diuresis (mL/kg/h) at 2 consecutive days after intravesical lidocaine application in 4 cats.

	0.1 mL/kg 2% lidocaine				0.2 mL/kg 2% lidocaine			
	Cat I		Cat II		Cat III		Cat IV	
Hours (h)	Day 1	Day 2	Day 2	Day 3	Day 1	Day 2	Day 1	Day 2
0	-	<0.10	-	4.07	-	<0.10	-	-
0.5	-	1.57	2.48	2.71	0.48	0.45	0.96	1.64
1	1.34	1.45	1.36	-	0.51	-	0.93	2.46
2	-	-	0.79	1.20	-	0.35	0.42	0.92
3	0.65	0.87	0.64	0.79	0.24	-	0.30	0.30
POD	4.6	4.2	6.3	5.3	6.6	6.6	8.0	7.5

Highest serum lidocaine concentration of all collected blood samples per cat and day
POD, post-obstructive diuresis

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ENDNOTES

[1] Oxoid, Pratteln, Switzerland
[2] Sintenyl, Sintetica SA, Mendrisio, Switzerland
[3] Dormicum®, Roche Pharma (Switzerland) AG, Reinach, Switzerland
[4] Narketan®10, Vétoquinol AG, Ittingen, Switzerland.
[5] Propofol 1% MCT Fresenius, Fresenius Kabi (Switzerland) AG, Stans, Switzerland
[6] Abbott AG, Baar, Switzerland
[7] Portex®Jackson Cat Catheter, Smiths Medical International Ltd, UK / Slippery™Sam Tomcat Urethral Catheter, Smiths Medical PM Inc, Waukesha, Wisconsins.
[8] Urotube®20, B. Braun Medical Meslungen GA, Melsungen, Germany.
[9] Temgesic®, Reckitt Benckiser Healthcare Ltd, UK
[10] Fresenius Kabi GmbH, Hamburg, Germany
[11] Lidocain HCL 2%, Kantonapotheke Zurich, Switzerland
[12] B.Braun Medical AG, Sempach, Switzerland
[13] Clavubactin, Dr.E.Graeub AG, Bern, Switzerland
[14] Amoxicat40, Biokema SA, Crissier-Lausanne, Switzerland
[15] Metacam®, Boehringer Ingelheim (Switzerland) GmbH, Basel, Switzerland