Are glucocorticoids or NSAIDs effective in idiopathic feline urinary tract disease signs than no treatment or placebo?

A Knowledge Summary by

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KNOWLEDGE SUMMARY

PICO question

In cats with idiopathic feline urinary tract disease (FLUTD), are glucocorticoid or non-steroidal anti-inflammatory drugs more effective than placebo or no treatment in reducing clinical signs attributable to cystitis?

Clinical bottom line

Category of research question

Treatment

The number and type of study designs reviewed

Three randomised controlled trials have examined the efficacy of prednisolone or non-steroidal anti-inflammatory drugs (NSAIDs) in reducing the clinical signs of feline lower urinary tract disease compared to a placebo whilst one retrospective cohort study compared the reoccurrence of FLUTD in cats treated with meloxicam and without meloxicam

Strength of evidence

Weak

Outcomes reported

One small controlled trial compared prednisolone to a placebo and found no clinical differences in dysuria, microscopic haematuria, and occult blood for cats diagnosed with idiopathic non-obstructive feline lower urinary tract disease (FLUTD) hospitalised for 10 days. The study however had a very small sample size. Furthermore, the external validity of the study to similar patients discharged to their home environment is unclear.

The second small controlled trial compared meloxicam to a placebo in cats diagnosed with obstructive FLUTD. Statistical analysis was applied to determine if there were significant differences in voiding behaviour, general demeanour, haematuria, food intake and abdominal pain as assessed by the veterinarians in charge during hospitalisation and owners at discharge. No statistically significant differences ($P>0.05$) were calculated between the two treatment groups based on the owner questionnaire and veterinarian assessment but small samples in each treatment probably limited statistical power.

The third small controlled trial compared the reoccurrence of feline idiopathic cystitis (FIC), related clinical signs and recurrent urinary obstruction in cats at 10 days, 1, 2 and 6 months after discharge when treated with phenoxybenzamine and alprazolam, with or without the addition of meloxicam. No statistically significant differences were found in the reoccurrence of obstructed or non-obstructed FIC for cats treated with either meloxicam or no meloxicam. However, full details of each intervention group were not sufficient to assess for balance of prognostic factors, subjective scoring of clinical signs was not detailed, and the study was underpowered for the actual obstruction rates reported.

The fourth paper was a retrospective cohort study that examined the association of different treatment factors with 30 days reobstruction. The study found no significant association between the use of meloxicam and the rate of reobstruction but a number of confounders were present

Conclusion

Three small randomised controlled trials and a single retrospective cohort study failed to find a significant association between the use of glucocorticoids or NSAIDs with severity of FLUTD clinical signs or risk of reobstruction. Clinical outcome measures were heterogeneous and studies were significantly underpowered and/or at risk for bias and/or confounding. There is insufficient evidence to recommend the use of either drug category in decreasing time to resolution or severity of clinical signs in cases of idiopathic FLUTD or FIC

How to apply this evidence in practice

The application of evidence into practice should take into account multiple factors, not limited to: individual clinical expertise, patient's circumstances and owners' values, country, location or clinic where you work, the individual case in front of you, the availability of therapies and resources.

Knowledge Summaries are a resource to help reinforce or inform decision making. They do not override the responsibility or judgement of the practitioner to do what is best for the animal in their care.

Clinical Scenario

You are presented with a 2 year old, female spayed long hair Tortoiseshell with her third episode of frequent and painful urinations and gross haematuria. Her first episode occurred when the owners acquired a new puppy who she hides from. Prior ultrasound was negative for uroliths and her urine was culture negative. Haematology, serum biochemistry, and urinalysis are unremarkable aside from the finding of large numbers of red blood cells in her urine sediment. After explaining your suspicion for feline idiopathic lower urinary tract disease (FLUTD) (aka feline idiopathic cystitis (FIC)) and her probable bladder inflammation, her owners ask about the use of anti-inflammatory medications to alleviate her clinical signs. You discuss that both non-steroidal (NSAIDs) and steroidal anti-inflammatories (glucocorticoids) have been used in the past and the owners ask which, of any, you would recommend.

The evidence

There are four studies available that assesses the efficacy of prednisolone and/or non-steroidal anti-inflammatory meloxicam for FIC.

Summary of the evidence

Osborne et al. (1996)[1]	
Population:	**Criteria for eligibility and inclusion:** Felines diagnosed with idiopathic FLUTD. **Criteria for exclusion and rejection:** • Felines diagnosed with a major illness/illnesses of other body systems. • Obstructed felines requiring an indwelling catheter.
Sample size:	12 cats: • Eight males • Four females

Intervention details:	**Random allocation into two treatment groups:** • Prednisolone treatment group n=6 • Placebo treatment group n=6 **Dosage and administration of treatment:** • **Prednisolone treatment group:** Prednisolone was administered as a capsule by mouth twice daily at a dose rate of 1.0 mg/kg body weight. • **Placebo treatment group:** A capsule containing no prednisolone was administered by mouth twice daily. **Duration of therapeutic intervention:** 10 days treatment; all cats remained hospitalised during treatment. **Diet:** All cats were fed on Hills Science Diet Feline Maintenance throughout the duration of the study. **Collection of urine on days 0, 5, 10, 14, 28:** Urine was collected either via void or cystocentesis for assessment.
Study design:	Prospective double blinded and randomised clinical study

Outcome studied:	• Dysuria
	• Urinalysis during hospitalisation, 2 weeks, 4 weeks:
	  ○ Mean urine specific gravity
	  ○ Urine dipstick (Bayer Multistix®) pH and occult blood
	  ○ Struvite crystalluria
	  ○ Microscopic haematuria
	• Urine culture: baseline, 2 weeks, 4 weeks

Main findings: (relevant to PICO question):	• Dysuria reduced in an average of 1.5 days across both treatment groups. • Microscopic haematuria reduced in an average of 3.2 days in the prednisolone treatment group and 3.5 days in the placebo treatment group. • Trace to 1+ occult blood was detected across both groups during and after therapy. • Urine culture was negative in all cats. • No significant reduction in urine specific gravity was observed in the prednisolone group.
Limitations:	• No information about method, source, or time of patient recruitment. • No statement of ethical review. • Evaluative criteria for dysuria not stated. • Generalisability is unclear: hospitalisation and diet change represent significant potential stress triggers for FIC and results should be interpreted with caution for owned cats in their home environment. • Two differing methods of urine collection (cystocentesis and voided) likely confound comparison of haematuria between groups and over time points.

	• Small sample study size with no statistical analysis. Had authors performed statistical analysis, probable insufficient study power.

Dorsch et al. (2016)[2]	
Population:	**Criteria for eligibility and inclusion:** Cats with clinical signs of stranguria, haematuria, pollakiuria or painful voiding diagnosed with obstructive FIC. **Criteria for exclusion and rejection:** • Imaging evidence of urolithiasis or/and neoplasia. • Positive feline immunodeficiency virus (FIV) and/or feline leukaemia virus (FeLV) test. • Positive FIV. • Diabetes mellitus, hyperthyroidism. • Cats that had been treated with steroids, other NSAIDs or antimicrobial drugs within 2 weeks prior to presentation of the study. • Positive urine culture. **Recruitment and Treatment** All cats were treated at the Clinic of Small Animal Medicine, Ludwig-Maximilian Universität, Munich from November 2006 to August 2008.
Sample size:	37 cats
Intervention details:	**Random allocation into two treatment groups:** • Meloxicam treatment group n=18 • Placebo treatment group n=19 **Dosage and administration of treatment:** • **Meloxicam treatment group:** Meloxicam was administered orally (per os) at a dose rate of 0.1 mg/kg on day 1 and 0.05 mg/kg on days 2–5. • **Placebo treatment group:** A liquid formulation containing no meloxicam was administered per os for 5 consecutive days. **Duration of therapeutic intervention:** 5 days treatment. **Day 0 interventions:** • Subjects were administered an intravenous crystalloid fluid therapy (Lactated Ringer's solution). • Administered 0.01 mg/kg Buprenorphine and then every 8 hours subcutaneously for 2 days. • Under general anaesthesia, all cats were inserted an indwelling urinary catheter (silicon feeding tube – Charriere (CH) 4.5, 1.0 x 1.5mm, Braun). • Cats presented with post-renal azotaemia, metabolic acidosis or hyperkalaemia had repeated serum chemistry and blood gas analysis prior to starting treatment (day 0).

	Day 1 interventions: Meloxicam or placebo commenced 24 hours after presentation to ensure correction of hydration status and re-establishment of urine flow. **Day 2 interventions:** • Urinary catheter removed. • Urine sample via cystocentesis for aerobic bacterial culture. • Cats that were observed for having difficult voiding behaviour remained hospitalised until able to void spontaneously for 24 hours. **Day 2–5 interventions:** Upon discharge, owners were provided written instructions to complete the 5 days treatment course.
Study design:	Prospective double blinded and randomised clinical study
Outcome studied:	• Occurrence of recurrent urinary obstruction within the first 7 days. • Objective exam parameters during hospitalisation and 10–14 day post-discharge recheck (temperature, body weight, respiratory rate, heart rate, haematuria). • Subjective clinician scoring during hospitalisation and 10–14 day post-discharge recheck (general demeanour, pain on abdominal palpation, food intake). • Subjective owner scoring for 5 days post-discharge (general condition, voiding behaviour/pain, macroscopic haematuria, food intake). **Statistical analysis:** • Mann-Whitney U test to evaluate differences in age and body weight across treatment groups. • Kruskal-Wallis test and Dunn's multiple comparison tests to evaluate differences in continuous parameters between groups at different time points and within groups between different time points. • X^2 was used for all categorical parameters within and between groups (without correction for multiple comparisons). • Results were regarded as significant if $P<0.05$.
Main findings: (relevant to PICO question):	• 4/18 cats (22.2%) in the meloxicam group and 5/19 cats (26.3%) in the placebo group suffered from recurrent urinary obstruction within the first week. No statistical significance test is reported for this result and these cats were censored after day 2 from subsequent analysis. • No statistically significant differences between treatment groups on exam parameters during hospitalisation and 10–14 day post-discharge recheck (temperature, body weight, respiratory rate, heart rate, haematuria).

	• No statistically significant differences between groups on subjective clinician scoring during hospitalisation and 10–14 day post-discharge recheck (general demeanour, pain on abdominal palpation, food intake). • No significant differences between the two treatment groups at any time point based on the owner questionnaire.
Limitations:	• No explicit details on method of randomisation. • Unblinded mid-study. • Potential confounding by group imbalance for prior history of FIC: meloxicam group had statistically significantly higher (P=0.046) proportion of cats with ≥3 prior episodes (5/18) versus the placebo group (0/19). This may have obscured a positive effect in the meloxicam group if these cats had greater severity of FIC versus the placebo group. • Potential confounding by catheterisation: clinical signs attributable to FIC versus catheter-associated discomfort cannot be disentangled, at least for the initial 2–3 days of data collection. • Small sample size with probable low statistical power; no sample size or power calculation is presented. • Subjective clinician evaluation of abdominal pain, general demeanour, food intake did not use a validated instrument and was not assessed for inter-rater reliability; it is unclear how many clinicians contributed to data collection. • Owner questionnaire not validated. • Medication adherence not controlled for or assessed after discharge. • Unaccounted loss to follow-up.

Nivy et al. (2019)[3]	
Population:	**Recruitment and treatment:** The study was conducted in a referral teaching hospital between the years 2016 and 2018. **Criteria for eligibility and inclusion:** • Male cats admitted with obstructive FIC which had not received medication prior to admission. • Resolution of azotaemia during hospitalisation. • Ability to empty the urinary bladder before discharge. **Criteria for exclusion and rejection:** Not outlined in detail.
Sample size:	51 cats: • Seven intact males • 44 neutered males
Intervention details:	**Prior to urinary catheterisation to relieve urinary obstruction:** • All cats underwent blood sampling for serum chemistry and/or packed cell volume (PCV) /total solids/electrolytes, abdominal sonography, urinalysis and urine culture as part

	of their initial diagnostic evaluation; a subset (20/51) also underwent additional survey and contrast radiography where owner financial resources allowed. • All cats were medically stabilised and the obstruction relieved; IV fluid therapy, treatment of hyperkalemia, choice of urinary catheter and timing of removal were at the clinician's discretion. **Random allocation into two treatment groups:** • Cats were allocated to a treatment after discharge by draw from a sealed envelope for 14 days. • **Study group n=24:** Phenoxybenzamine (2 mg/kg PO q 12 hours) with alprazolam (0.125 mg/kg PO q 12 hours) and meloxicam (0.025 mg/kg PO q 24 hours). • **Control group n=27:** Phenoxybenzamine (2 mg/kg PO q 12 hours) with alprazolam (0.125 mg/kg PO q 12 hours) alone for 14 days. **Strict dietary intake:** Owners were instructed to feed a therapeutic urinary diet.
Study design:	Prospective randomised study
Outcome studied:	Reoccurrence of FIC related clinical signs and/or recurrent urinary obstruction were recorded at 10 days, 1, 2 and 6 months after discharge. **Statistical analysis:** • Primary hypothesis was that meloxicam would reduce the rate of reobstruction but many other associations were examined. • Fisher's exact test used to assess for association of categorical variables with recurrence. Logistic regression used to assess for association of continuous variables with recurrence. • Receiver operator characteristic (ROC) analysis was used to assess the predictive value of heart rate for presence of hyperkalaemia. • Results were regarded as significant if $P<0.05$; no mention of correction for multiple comparisons with the assumption that the control group has a 50% reoccurrence rate and that meloxicam reduces the risk by five fold. • Sample size calculated with G*Power 3.0.10 software; powered at 0.8 to detect a risk ratio of 0.2 in the study group assuming 50% recurrence in control group.
Main findings: (relevant to PICO question):	• Overall, recurrent FIC signs occurred in a total of 12 cats (6/24 (25%) cats from the study group and 6/27 cats (22%) from the control group) over 6 months after discharge. • No significant difference in obstructive or non-obstructive FIC signs between the study (meloxicam) and control groups (no meloxicam) at any time point in the 6 month period.

Limitations:	• Unclear how recurrent non-obstructed FIC signs were assessed; no mention of blinding of assessors. • Unclear whether groups balanced for potentially important measurable prognostic variables (no baseline table of groups characteristics). • Low statistical power; sample size not powered to detect relative risk reduction <80% assuming baseline risk for recurrence of 50% per the reported power calculation.

Hetrick & Davidow (2013)[4]	
Population:	**Recruitment and treatment:** Male cats diagnosed with urinary tract obstruction from January 2004 to December 2010 at private practice emergency referral hospital (Animal Critical Care and Emergency, Seattle, WA, USA). **Criteria for eligibility and inclusion:** Medical records of male cats treated as in-patients for uncomplicated urinary obstruction (UO) with an indwelling polyvinyl chloride catheter (infant feeding tube) and for which bladder imaging was available (ultrasound and/or radiography). Cases needed at least 1 day of follow-up information post-catheter removal for inclusion in the study. **Criteria for exclusion and rejection:** • Cats with UO secondary to urolithiasis or neoplasia or acetaminophen toxicosis. • Cats in which urethral catheterisation was attempted or accomplished prior to referral. • Prior urinary catheterisation within the last 7 days. • Cats transferred to the care of the referring veterinarian prior to urinary catheter removal. • Discharge from the hospital <24 hours after urinary catheter removal and without follow-up. • Ability to urinate within the first hour of administration of initial medications. • Urinary bladder rupture or urethral obstruction secondary to trauma or urethral tear. • Surgery after unsuccessful attempts to pass a urinary catheter. • Prior perineal urethrostomy.
Sample size:	192 cases
Intervention details:	• Records were reviewed for baseline characteristics (age, weight, body temperature, Blood Urea Nitrogen (BUN)/electrolytes) at admission and treatments administered in hospital. • 24 cases included cats treated with meloxicam and 27 cases cases included cats without meloxicam. • No details provided about stabilisation, that is the use of intravenous fluid therapy (IVF), repeat of hyperkalaemia, anesthesia/sedative use.

	• Primary aim of the study assessed the association of specific treatment factors with rate of reobstruction. **Treatment data extracted:** • Analgesia (buprenorphine or meloxicam). • Use of alpha-adrenergic antagonist (prazosin or phenoxybenzamine). • Antibiotic therapy after catheter removal • Duration of urinary catheterisation. • Size of indwelling urinary catheter. **Treatment details from included cases:** • Mean initial dose of meloxicam 0.09 mg/kg, mean of 3.7 doses administered to cats receiving meloxicam. • Mean dose of buprenorphine was 0.01 mg/kg twice a day (BID) or three times a day (TID) with mean duration of therapy 4.2 days. • Mean duration of therapy for cats receiving prazosin 7.8 days with most receiving 0.5 mg BID. • Mean duration of therapy for cats receiving phenoxybenzamine was 7.2 days. Most cats received 2.5 mg BID. Treatment protocol shifted over time: prior to 2006, meloxicam, phenoxybenzamine, and a 5 French catheter were more commonly used. Protocol changed after that time point with proportionately more cats treated with buprenorphine, prazosin, and a 3.5 French catheter from June 2006 to December 2010. **Statistical Analysis** • X^2 test (with Yates correction when indicated) was used to test for association of categorical treatment variables with recurrence of obstruction at 1 and 30 days. • Wilcoxson-rank sum or t-test for to assess for association of catheter duration with recurrence (unclear in methods which test was applied to this variable but appropriate test for normality and use of non-parametric and parametric testing is discussed). • Results considered significant at value of $P<0.05$.
Study design:	Retrospective cohort study
Outcome studied:	Recurrence of obstruction at 24 hours and 30 days.
Main findings: (relevant to PICO question):	There was no statistically significant difference between the reoccurrence of UO in cats administered meloxicam as compared to no meloxicam at 24 hours (5/46 versus 16/146) or 30 days (10/39 versus 27/118). This was due to loss or incomplete follow-up.
Limitations:	• High risk of confounding error by changing protocol which altered three variables (use of meloxicam, use of prazosin, catheter size) over the same time period; multivariable analysis would be required to assess for independent effects of each treatment. A graphical stratified analysis of the

	effects of catheter size and alpha antagonist is presented but no similar analysis is presented for analgesic agents. • Selection bias due to clinicians preferably selecting a treatment based on characteristics of a patient • Information bias with the selection of either choosing to report or not follow-up. • Temporal bias due to possibility of dietary or housing changes for cats from 2006 to 2010 affecting baseline risk of re-obstruction in cats.

Appraisal, application and reflection

Three studies examined whether clinical signs of FLUTD can be improved with glucocorticoids or NSAIDs whilst one study examined if the use of meloxicam significantly reduced the reoccurrence of FLUTD. None found a statistically significant difference of either drug class in reducing the clinical signs of idiopathic FLUTD/FIC. All had significant limitations in terms of statistical power and/or external validity and/or risk of bias.

External validity is defined as to whether casual relationships may be generalised and applicable to different measures5. Internal validity in contrast represents whether the variables operated adequately represent the theories and hypothesis proposed[5]. Whilst it is useful to know if there is a difference between glucocorticoid or NSAIDs versus no treatment at all for controlling the signs of FLUTD, the treatment options tested should be validated and applicable to the general FLUTD population. Clinical signs of feline cystitis may be elicited or exacerbated by stressful circumstances, which may include hospitalisation and/or diet change[6,7] thus the conditions for patients in the Osborne et al. (1996) paper may not be applicable to cats discharged from hospital to their home environment. There was no mention of whether there was a sudden food change for the hospitalised patients. Steckler & McLeroy (2008) emphasise the importance of knowing that a program is likely to be effective in other settings and populations. Through this, the results of not only Osborne et al. (1996) but also the others should be interpreted with caution as it is unclear how the risk of reoccurrence and the lack of resolution reported in any hospital setting may relate to the risk of reoccurrence and persistence in a home population.

Adequate sample size is essential in avoiding type II error (failure to detect a statistically significant effect when one exists)[8]. Osborne et al. (1996), Dorsch et al. (2016), and Hetrick & Davidow, (2013) did not provide details of sample size calculation nor did they present a power analysis but we can infer that statistical power was likely low. Nivy et al. (2019) and colleagues performed a sample size calculation assuming a population with a much higher risk for FIC recurrence actually occurred in their trial, thus high risk for type II error was also present.

Randomisation and blinding are key features of most controlled trials to balance groups for important prognostic variables and to minimise biased outcome ascertainment (e.g. randomisation to avoid selection bias and blinding to avoid information bias). In the paper by Dorsch et al. (2016) the study was unblinded midway, leading to risk of ascertainment bias. In the paper by Nivy et al. (2019) it is unclear whether group balance for prognostic variables was achieved.

Although cohort studies are often at higher risk for selection bias, this is less likely to be true of the study by Hetrick & Davidow (2013) since hospital protocol, rather than clinician choice, appeared to determine treatments for obstructed FLUTD. However, because three interventions in the hospital protocol were altered over the same time period and no adjusted analysis was reported for the effects of analgesic agent, results are at high risk for unmeasured confounding.

Finally, the heterogeneous outcomes reported limit evidence synthesis: each publication differed in methods of assessment of FIC. For Nivy et al. (2014) and Hetrick & Davidow (2013), recurrence of obstruction was a

primary and intuitively valid objective outcome. However, method of subjective scoring of non-obstructive cystitis signs was not transparent in two publications (Osborne et al., 1996; and Nivy et al., 2019); in the third publication (Dorsch et al., 2016), subjective scoring method was transparent but lacked detail on inter-rater reliability and validation; moreover, it is unclear how the raters were blinded.

Further study is needed to delineate what role, if any, glucocorticoids or NSAIDs have in the treatment of FLUTD/FIC. Adequately powered randomised controlled trials and/or meta-analysis are required; standardised and validated outcomes to assess bladder pain/dysuria are required.

In conclusion, there are no studies which appear to provide evidence for the use of steroidal or NSAIDs in decreasing symptoms or duration of clinical signs associated with FLUTD.

Glucocorticoids are not considered analgesics and there is insufficient evidence to suggest they provide a profound benefit in human interstitial cystitis. Glucocorticoids may elevate risk for diabetes mellitus in certain cats and carry some risk for secondary bacterial infection thus also cannot currently be recommended for FIC[10].

Although NSAIDs are considered a mainstay for management of chronic pain, they are not considered a first line treatment for the use in feline urinary cystitis-related cases[11]. The leading risk and adverse effects of NSAIDs includes nephrotoxicity, gastric ulcers, gastric perforations, and anorexia in cats[11]. Given the risk of adverse gastro-intestinal and renal side effects of NSAIDs in cats, the current evidence does not propose that the use of NSAIDs shortens the clinical signs of FIC and it is critical that veterinarians report and notify the risk factors if they choose to use NSAIDs as an adjunctive treatment to owners, colleagues and future proposing studies alike.

Opioids have been considered effective first-line analgesia for pain in cats[11] but currently in regards to the use of glucocorticoids and NSAIDs, pending higher quality studies with greater statistical power is required as there is no high-quality evidence for the use of glucocorticoid or NSAIDs in the treatment of FIC.

The plethora of emerging and numerous research on the aetiology of FIC has focused on multi-factorial factors including but not limited to behaviour, housing, environmental, dietary, litter type, cohabitation of with other cats or pets in the household, enrichment availability, anatomical formation, age, obesity, neuter states and even neurohormonal pathways[12,13,14]. The most effective treatment outcomes should be focusing on these factors as the foremost and then the use of pharmacological drugs as an additional secondary action if required.

Methodology Section

Search Strategy	
Databases searched and dates covered:	CAB Abstract database via Web of Science (1973–2021) PubMed database accessed via the NCBI platform (1910–2021)
Search terms:	((feline OR felines OR cat or cats) AND (idiopathic cystitis OR feline idiopathic cystitis OR feline lower urinary tract disease OR cystitis OR lower urinary tract disease OR urinary tract infection) AND (NSAID OR NSAIDS OR anti-inflammatories OR Meloxicam OR Metacam OR Loxicom OR non-steroidal anti-inflammatories OR Prednisolone OR Prednisone OR glucocorticoids OR glucocorticoid))
Dates searches performed:	8 Mar 2021

Exclusion / Inclusion Criteria	
Exclusion:	• Articles not written in English • Articles not associated with the efficacy of prednisolone or glucocorticoids or NSAID products for treating feline lower urinary tract disease • Case reports • Case studies • Book chapters • Conferences • Systematic reviews
Inclusion:	• Meta-analysis • Randomised controlled study • Clinical studies

Search Outcome

Database	Number of results	Excluded – Systematic reviews	Excluded – Did not relate directly to the factors of PICO	Excluded – Case reports and studies	Excluded – Book chapters	Excluded – Not written in English	Excluded – Conferences	Total relevant papers
CAB Abstracts	28	0	25	0	0	0	0	3
PubMed	37	1	31	1	0	0	0	4
Total relevant papers when duplicates removed								**4**

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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REFERENCES

1. Osborne, C.A., Kruger, J.M., Lulich, J.P., Johnston, G.R., Polzin, D.J., Ulrich, L.K. & Sanna, J. (1996). Prednisolone Therapy of Idiopathic Feline Lower Urinary Tract Disease. *Veterinary Clinics of North America: Small Animal Practice.* 26(3), 563–569. DOI: http://dx.doi.org/1016/s0195-5616(96)50085-9
2. Dorsch, R., Zellner, F., Schulz, B., Sauter-Louis, C. & Hartmann, K. (2016). Evaluation of meloxicam for the treatment of obstructive feline idiopathic cystitis. *Journal of Feline Medicine and Surgery*. 18(11), 925–933. DOI: https://doi.org/10.1177%2F1098612X15621603
3. Nivy, R., Segev, G., Rimer, D., Bruchim, Y., Aroch, I. & Mazaki-Tovi, M. (2019). A prospective randomized study of efficacy of 2 treatment protocols in preventing recurrence of clinical signs in 51 male cats with obstructive idiopathic cystitis. *Journal of Veterinary Internal Medicine*. 33(5), 2117–2123. DOI: http://doi.org/10.1111/jvim.15594
4. Hetrick, P. & Davidow, E.B. (2013). Initial treatment factors associated with feline urethral obstruction recurrence rate: 192 cases (2004–2021). *Journal of American Veterinary Medical Association*. 243(4), 512–519. DOI: http://dx.doi.org/2460/javma.243.4.512
5. Steckler, A. & McLeroy, K.R. (2008). The Importance of External Validity. *American Journal of Public Health*. 98(10), 09–10. DOI: http://dx.doi.org/10.2105/AJPH.2007.126847
6. Westropp, J.L., Kass, P.H. & Buffington, C.A.T. (2006). Evaluation of the effects of stress in cats with idiopathic cystitis. *American Journal of Veterinary Research*. 67(4), 731–736. DOI: http://dx.doi.org/ 2460/ajvr.67.4.731
7. McCobb, E.C., Patronek, G.J., Marder, A., Dinnage, J.D. & Stone, M.S. (2005). Assessment of stress levels among cats in four animal shelters. Journal of the American Veterinary Medical Association. 226(4), 548–555. DOI: http://dx.doi.org/ 2460/javma.2005.226.548
8. Jones, S.R., Carley, S. & Harrison, M. (2004). An introduction to power and sample size estimation. *Emergency Medicine Journal.* 20(5), 126. DOI: http://dx.doi.org/1136/emj.20.5.453
9. Banerjee, A., Chitnis, U.B., Jadhav, S.L., Bhawalkar, J.S. & Chaudhury, S. (2009). Hypothesis testing, type I and type II errors. *Indian Psychiatry Journal*. 18(2), 127–131. DOI: https://doi.org/10.4103/0972-6748.62274
10. Barasanti, J.A., Shotts, E.B., Crowell, W.A., Finco, D.R. & Brown, J. (1992). Effect of Therapy on Susceptibility to Urinary Tract Infection in Male Cats with Indwelling Urethral Catheters. *Journal of Veterinary Internal Medicine*. 6(2), 64–70. DOI: http://dx.doi.org/1111/j.1939-1676.1992.tb03153.x
11. Epstein, M.E., Rodanm, I., Griffenhagen, G., Kadrlik, J., Petty, M.C., Robertson, S.A. & Simpson, W. (2015). 2015 AAHA/AAFP Pain Management Guidelines for Dogs and Cats. *Journal of Feline Medicine and Surgery*. 17(3), 251–272. DOI: http://dx.doi.org/1177/1098612X15572062
12. Segev, G., Livne, H., Ranen, E. & Lavy, E. (2011). Urethral obstruction in cats: /predisposing factors, clinical, clinicopathological characteristics and prognosis. *Journal of Feline Medicine and Surgery*. 13(2), 101–108. DOI: http://dx.doi.org/1016/j.jfms.2010.10.006
13. Kim, Y., Kim, H., Pfeiffer, D. & Brodbelt, D. (2018). Epidemiological study of feline idiopathic cystitis in Seoul, South Korea. *Journal of Feline Medicine and Surgery*. 20(10), 913–921. DOI: http:/dx.doi.org/1177/1098612X17734067
14. Cameron, M.E., Casey, R.A., Bradshaw, J.W.S., Waran, N.K. & Gunn-Moore, D.A. (2004). A study of environmental and behavioural factors that may be associated with feline idiopathic cystitis. *Journal of Small Animal Practice*. 45(3), 144–47. DOI: http://dx.doi.org/10.1111/j.1748-5827.2004.tb00216.x