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2018
Antinol®

Cat Case
Study Contest

02



CLINICAL EFFECT OF
PCSO-524° ON 3 OSTEOARTHRITIC
CATS ASSOCIATED WITH
CHRONIC KIDNEY DISEASE

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Abstract

Three cats suffering from chronic kidney disease were admitted to animal hospital. The first cat showed sudden onset of right hindlimb pain without apparent cause. Bladder stone was found in the second cat while the third cat was admitted for nursing care. Caging was applied and fluid therapy were administered for the third cat. All 3 cats had never been diagnosed with arthritis prior to the admission. X-ray examination showed symptoms of arthritis at hip and stifle joints. PCSO-524® was then administered daily for 60 days. Pain evaluation using Feline Musculoskeletal Pain Index (FMPI), which is a reliable and effective method for pain evaluation in cats (Benito et al., 2013), showed that, after the treatment, chronic pain was decreased in all of the cats (Appendix 1). The cats' behavior was nearly normal compared with the behavior before the treatment. Interaction between the cats and owners was improved as well. By the end of the experiment, UP/C ratio was not altered and blood creatinine tended to decrease.

Keywords

Cats, Chronic kidney disease, Osteoarthritis, PCSO-524®

Introduction

Feline arthritis is often overlooked because cats tend to hide their pain due to their defensive instinct. This makes it difficult for the owners and attending veterinarians to observe clinical signs of diseases. During the past 10 years, study of feline arthritis has been more common. High prevalence was reported in feline population (Lascelles et al., 2010, Drensler, 2013, Tomas et al., 2015, Rodan, 2016). One of random studies conducted in cats of various ages found that 91% of cats were affected with arthritis as identified by radiographic examination. The disease can start since 6 months of age and the severity is increased over time (Lascelles et al, 2008).

Arthritis can cause chronic pain in cats similarly to what occurs in humans. The pain leads to peripheral and central sensitization of the nervous system, and eventually results in alteration of usual behavior. FMPI is a reliable and effective method for chronic pain evaluation in cats (Benito et al., 2013). Evaluation of behavior in daily life is included in the system in order to assess the pain and consequently prescribe appropriate pain control medication.

NSAIDs and long-term pain medication are usually drugs of choice for treatment of pain caused by either central or peripheral sensitization. Although NSAIDs are effective for controlling inflammation and pain, cats are at risk of the adverse effect. One of the most common adverse effects is renal disorder (Marcum and Hanlon, 2010). Therefore, restriction of NSAIDs use is concerned in patients with kidney disease. Arthritis may occur in as high as 44% of cats with chronic kidney disease, especially in senile cats (Lascelles et al., 2008).

Nutraceutical is one of alternative medicines to manage pain caused by arthritis (Ameye and Chee, 2006, Akhtar and Haqqi, 2012, Loseli et al., 2015). It is considered an appropriate choice when the effects of long-term use of NSAIDs need to be avoided (Akhtar and Haqqi, 2012). PCSO-524® (Antinol®, DKSH, Thailand), extracted from Green-lipped New Zealand mussel, was used in this study to observe improvement of clinical changes and quality of life in cats affected by arthritis and chronic kidney disease. There are several previous studies that also use PCSO-524 but the studies were conducted in dogs for observation of clinical changes and owner satisfaction (Mongkon and Soontornvipart, 2012, Soontornvipart et al., 2015, Kwananocha et al., 2016). There is no study of PCSO-524 that is related to this problem in cats to the present.

Patient History

Three cats were diagnosed with Chronic Kidney Disease (CKD). The first cat was a male, 4 years old Scottish fold with CKD that showed sudden onset of right hind leg pain without known cause. The cat was then submitted to surgical ward for further examination.

The second case was a female, 11 years old domestic shorthair cat that suffered from CKD for a long time without any complications. Prior to this admission, the cat was treated with PCSO-524® for one month in April and loss to follow-up until September. The cat returned due to increased creatinine and blood urea nitrogen, intermittent urination and bladder stone. Feline lower urinary tract disease; FLUTD, was diagnosed. The cat was submitted to surgical ward for cystectomy.

The third cat was a female 5 years old domestic shorthair cat also suffered from CKD without any complications. It was admitted for nursing care in a private animal hospital. Most of its activities were inside a cage, except for relaxation time outside the cage twice a day, half an hour each time.

Table 1. History of feline patients

	1 st Cat	2 nd Cat	3 rd Cat	
Age	4 years	11 years	5 years	
Gender	Male	Female	Female	
Breed	Scottish fold	DSH	DSH	
Underlying disease	CKD stage 2	CKD stage 2	CKD stage 2	
BCS	3.5/5	3.5/5	1.5/5	
CC	Lameness	CKD (follow up)	CKD (follow up)	

The three cats were monitored closely and followed-up for azotaemia and urinalysis. The cats were categorized as IRIS stage 2 (Figure 1). Diet specially formulated for cats with kidney disease and treatment for dehydration were given as appropriate.

Figure 1. IRIS staging of CKD (Source: International renal interest society http://www.iris-kidney.com/pdf/IRIS_2017_Staging_of_CKD_09May18.pdf)

Stage	Blood creatinine µmol/l mg/dl		Comments	
	Dogs	Cats		
At risk	<125 <1.4	<140 <1.6	History suggests the animal is at increased risk of developing CKD in the future because of a number of factors (such as, exposure to nephrotoxic drugs, breed, high prevalence of infectious disease in the area, or old age).	
1	<125 <1.4	<140 <1.6	Nonazotemic. Some other renal abnormality present (such as, inadequate urinary concentrating ability without identifiable nonrenal cause, abnormal renal palpation or renal imaging findings, proteinuria of renal origin, abnormal renal biopsy results, increasing blood creatinine concentrations in samples collected serially).	
2	125 - 180 1.4 - 2.0	140 - 250 1.6 - 2.8	Mild renal azotemia (lower end of the range lies within reference ranges for many laboratories, but the insensitivity of creatinine concentration as a screening test means that animals with creatinine values close to the upper reference limit often have excretory failure). Clinical signs usually mild or absent.	
3	181 - 440 2.1 - 5.0	251 -440 2.9 - 5.0	Moderate renal azotemia. Many extrarenal signs may b present, but their extent and severity may vary. If sign are absent, the case could be considered as early Stag 3, while presence of many or marked systemic signs might justify classification as late Stage 3.	
4	>440 >5.0	>440 >5.0	Increasing risk of systemic clinical signs and uraemic crises	

All of the cats had never been diagnosed with arthritis. During the past 3 months, they had not been treated with PCSO-524®, NSAIDs, calcium antagonist, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), any type of steroidal drugs, antibiotics, beta blockers, or omega-3 supplementation.

Physical examination and diagnosis plan

Table 2. Physical examination results

Day 0	1 st Cat	2 nd Cat	3 rd Cat			
X-rays	OA at both hip and stifle joints					
Lameness score	2/5	0/5	0/5			
Range of Motion	-	55-105 (hip)	55-105 (hip)			
(ROM)		45-110 (stifle)	45-110 (stifle)			
Quadriceps circumference measurement	16 cm	15 cm	11cm			
Hydration status	Well hydrated	<5% dehydrated	5-7% dehydrated			
Blood creatinine (mg/dl)	2.5	2.6	2.8			
Blood urea nitrogen	72	73	72			
RBC (×10°)	6.5	5.6	5.3			
HCT (%)	32	25	22			
Urine specific gravity	1.009	1.007	1.01			
UP/C ratio	< 0.2	< 0.2	< 0.2			
Urine sediment	Inactive sediments	Inactive sediments	Inactive sediments			
Blood pressure (mmHg)	< 180	< 180	< 180			

None of the cats showed any symptoms of disorder during the physical and orthopaedic examination, except the first cat that showed sign of lameness. After the consent was permitted by the owner, the cats were examined with X-ray imaging and all of them were diagnosed with arthritis at the hip and stifle joints.

Figure 1. X-ray image on day 0 of the first, second, and third cat, respectively



Limitation of NSAIDs use due to chronic kidney disease in all of the cats and senility in one cat was concerned. Continuous administration of PCSO-524® was prescribed as a substitute of NSAIDs for inflammation control. Follow-up was scheduled every 2 weeks. After the cats were familiarized with environments in the examination room, lameness score was evaluated according to criteria from Impellizeri, et al., 2000 (Table 3).

Table 3. Lameness scoring criteria (Impellizeri et al, 2000)

Lameness score	Walking	Running
0	Without lameness	Without lameness
1	Subtle lameness	Without lameness
2	Obvious lameness	Without lameness
3	Difficult walking	Lameness can be detected
4	Non-weight bearing	Lameness can be detected
5	Non-weight bearing	Non-weight bearing

Pain score was recorded using Colorado State University Feline Acute Pain Scale (CSU-FAPS) (Appendix 2) and Glasgow Feline CompositeMeasure PainScale (CMPS-Feline) (Appendix 3). The movement was video recorded when the cats jumped from 40 and 80 centimetres height (Jump test). The only evaluation done by the owner was evaluation of chronic pain using FMPI, except for the first evaluation that the attending veterinarian and the owner perform the evaluation together. The owners were assigned to be the same person every time the pain evaluation was performed in each cat.

Treatment plan

One capsule of PCSO-524® was administered daily for 60 days. Monitoring during the treatment on day 0, 14, 28, 42, and 60 included the followings;

- Blood profile consisting of creatinine and blood ureanitrogen
- Urinalysis
- Lameness score
- Jump test
- Blood pressure measurement

The monitor was done for the followings on day 0 and 60 during the treatment of PCSO-524;

- X-ray
- Range of motion (hip and stifle joints)
- Quadriceps circumference measurement
- Pain score assessment

Results

The monitoring in 3 cats (Appendix 4, 5, and 6) from day 0 to day 60 did not find any progression of arthritis as examined by radiographic image.



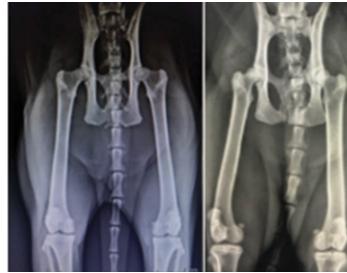


Figure 2. X-ray image in the first, second and third cat on day 60, respectively

On day 60 after starting daily treatment of PCSO-524®, blood profile and urinalysis, respectively, showed that creatinine was decreasing and UP/C remained normal throughout the treatment. The first cat showed improvement of lameness score after day 28. The jump test results in all cats were improved as compared with the performance prior to the treatment. Quadriceps circumference and range of motion of hip and stifle joint did not change.

Table 4. Pain score on day 0 and day 60

Day	Measurement	1st Cat	2nd Cat	3rd Cat
Day 0	CSU-FAPS	2	1	0
	CMPS-Feline	12	3	4
	FMPI	28	28	11
Day 60	CSU-FAPS	1	0	0
	CMPS-Feline	6	2	2
	FMPI	9	7	10

The data showed that pain scores as measured by 3 systems were decreased, especially the FMPI score, which indicated chronic pain. The owners of the 3 cats reported that the cats were more active and less aggressive, and the high jump performance the interaction with owners were also improved.

Discussion

All the 3 cats had never been diagnosed with arthritis and the owners also had never observed any sign of pain in the cats. This may due to the fact that cats tend to hide their pain, resulting in difficulty for clinical detection. Observation of changes in daily activity is crucial for the detection, for example, less playful, poor high jump, less grooming, and changes of litter box behavior (Bennett and Morton, 2009, Lascelles and Robertson, 2010). The FMPI is also useful for detection of chronic pain (Benito et al., 2013). In this study, daily treatment of PCSO-524® for 60 consecutive days was prescribed and the positive clinical outcome was observed in all of the cats.

Since arthritis and chronic kidney disease cause constant mild inflammation and PCSO-524® is effective for systematic control of inflammation, the cats showed recovery of normal activities. The owners were additionally educated for the adjustment and enrichment of environments for the cats during the study period. The owner of the second cat reported that after 1 month of the beginning of treatment, the cat's behavior changed from lethargy to performing low jump more often. However, the treatment was paused due to the owner's decision and the cat's performance remained unimproved. Later the cat showed signs of lower urinary tract infection and bladder stone was found and the cat was subsequently operated. After the operation, approximately 6 months of PCSO-524® discontinuation, PCSO-524® treatment was resumed again. The response was excellent as the cat showed increased appetite, less aggression, and performed higher jump.

Arthritis is a developmental disease so it is possible that central sensitization mechanism is stimulated. Long-term use of serotonin and norepinephrine re-uptake inhibitors or NMDA antagonists can be considered for reduction of neuropathic pain (Woolf, 2011, Nijs et al., 2014)

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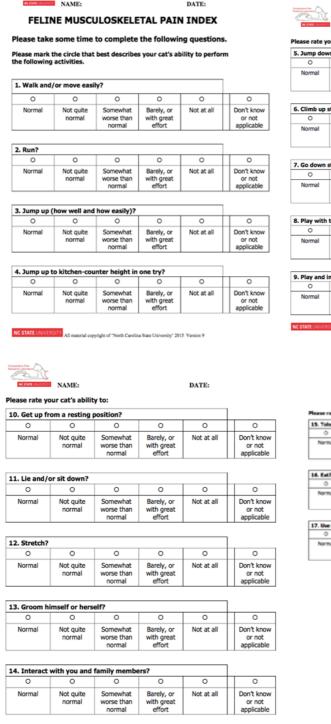
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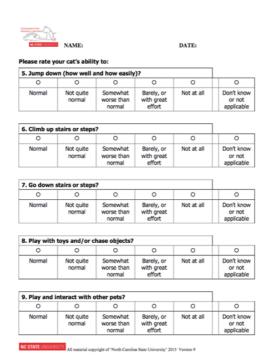
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Feline musculoskeletal pain index (FMPI) from North Carolina State University Source:https://journals.plos.org/plosone/article/file?type=supplementary&id=info:doi/10.1371/journal.pone.0131839.s001



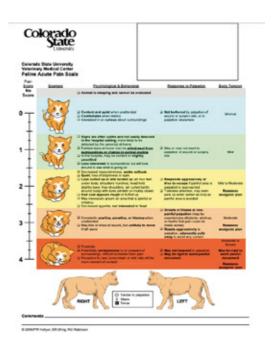


Appendix 2

Colorado State University Feline Acute Pain Scale (CSU-FAPS)

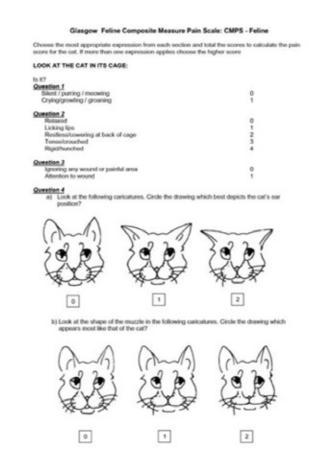
Source:

http://www.vasg.org/pdfs/CSU_Acute_Pain_Scale_Kitten.pdf



Appendix 3

Glasgow Feline Composite Measure PainScale (CMPS-Feline)
Source: http://www.aprvt.com/uploads/5/3/0/5/5305564/cmp_feline_eng.pdf





Results of examination in the first cat

	Blood work				UA		
	Blood	Bun	RBC	НСТ	SG	UP/C	Sediment
	Creatinine		(x10 ⁶)	(%)			
	(mg/dl)						
Day 14	2.6	67	6.6	34	1.009	<0.2	Inactive
Day 28	2.3	48	6.5	36	1.01	<0.2	Inactive
Day 42	2.2	31	6.4	36	1.01	<0.2	Inactive
Day 60	2	42	6.4	35	1.01	<0.2	Inactive

	Lameness	Blood pressure measurement	Quadriceps Circumference		Range of motion	
		(mmHg)	left	right	Нір	Stifle
Day 14	2	< 180				
Day 28	2	< 180				
Day 42	1	< 180				
Day 60	1	< 180	17	17	Х	X

Jump test

At 40 cm.	1	2	3	4	5
	not willing to jump	strong hesitation (take time and climbing)	hesitation (climbing)	mild hesitation (take time to look around)	Jumping without doubt
Day 0		2			
Day 14			3		
Day 28			3		
Day 42				4	
Day 60					5

At 80 cm.	1	2	3	4	5
	not willing to jump	strong hesitation (use steps or chair to help jumping)	hesitation (climbing> 2steps)	mild hesitation (climbing< 2steps)	Jumping without doubt
Day 0			3		
Day 14			3		
Day 28			3		
Day 42				4	
Day 60				4	

Results of examination in the second cat

	Blood work				UA		
	Blood	Bun	RBC	HCT	SG	UP/C	Sediment
	Creatinine		(x10 ⁶)	(%)			
	(mg/dl)						
Day 14	2.7	62	5.5	26	1.009	<0.2	Inactive
Day 28	2.2	44	4.8	23	1.008	<0.2	Inactive
Day 42	2.2	31	4.7	24	1.008	<0.2	Inactive
Day 60	1.9	32	4.8	24	1.009	<0.2	Inactive

	Lameness	Blood	Quadriceps Circumference		Range of motion	
	score	measurement (mmHg)	left	right	Нір	Stifle
Day 14	0	< 180				
Day 28	0	< 180				
Day 42	0	< 180				
Day 60	0	< 180	17	17	55-110	45-110

Jump test

1	2	3	4	5
not willing to jump	strong hesitation (take time and climbing)	hesitation (climbing)	mild hesitation (take time to look around)	Jumping without doubt
		3		
		3		
			4	
				5
				5
	not willing	not willing strong to jump hesitation (take time	not willing to jump strong hesitation (climbing) hesitation (climbing)	not willing to jump strong hesitation (climbing) hesitation (take time and climbing) hesitation (climbing) hesitation (take time to look around)

At 80 cm.	1	2	3	4	5
	not willing to jump	strong hesitation (use steps or chair to help jumping)	hesitation (climbing> 2steps)	mild hesitation (climbing< 2steps)	Jumping without doubt
Day 0			3		
Day 14			3		
Day 28				4	
Day 42				4	
Day 60				4	

Results of examination in the third cat

	Blood work				UA		
	Blood	Bun	RBC	НСТ	SG	UP/C	Sediment
	Creatinine		(x10 ⁶)	(%)			
	(mg/dl)						
Day 14	2.3	67	5.1	25	1.009	<0.2	Inactive
Day 28	1.8	48	5.1	22	1.009	<0.2	Inactive
Day 42	1.6	31	3.5	20	1.009	<0.2	Inactive
Day 60	1.2	42	3.8	20	1.01	<0.2	Inactive

	Lameness	Blood pressure	Quadriceps Circumference		Range of motion	
	score	measurement (mmHg)	left	right	Нір	Stifle
Day 14	0	< 180				
Day 28	0	< 180				
Day 42	0	< 180				
Day 60	0	< 180	11	11	55-110	45-110

Jump test

At 40 cm.	1	2	3	4	5
	not willing to jump	strong hesitation (take time and climbing)	hesitation (climbing)	mild hesitation (take time to look around)	Jumping without doubt
Day 0		2			
Day 14			3		
Day 28			3		
Day 42				4	
Day 60					5

At 80 cm.	1	2	3	4	5
	not willing to jump	strong hesitation (use steps or chair to help jumping)	hesitation (climbing> 2steps)	mild hesitation (climbing< 2steps)	Jumping without doubt
Day 0			3		
Day 14			3		
Day 28			3		
Day 42				4	
Day 60				4	



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Pharmalink and Vetz Petz® would like to thank everyone involved with the Antinol® research competition

At Pharmalink and Vetz Petz® we have a passion for Scientific Research and know that only this type of scientific proof is good enough to prove the benefits of ANTINOL® to the Veterinary community and owners alike. We also share the Vets passion for providing the best care for companion animals. This level of care and the credibility that goes with a Veterinarians recommendation cannot be achieved in good conscience if we do not have the participation and co-operation of the scientific community and Veterinarians alike. So we will continue to provide funding for projects that help companion animal owners and their Veterinarians to provide the best care for our beloved companion friends.

We would also like to offer a special thanks to ALL the committee members, Dr. Achinee and DKSH for their hard work organizing and hosting this very and unique event. You have graciously PROVIDED your time and vast experience and for that we thank you VERY much.

This project is the first of its kind for Pharmalink and Vetz Petz® and we are very excited about the research opportunities that have been shown as result of this competition. The future of Antinol® research is very bright and we are very thankful to everyone in loved.

John Dennis Waitzer Director

Pharmalink International Limited

Nathan Mclean
Director

Pharmalink International Limited

Kevin Cook President

Vetz Petz® group

Antinol® Contest has been organized successfully for 3 years since 2016 in Thailand. The key objective of this scientific contest is to encourage knowledges sharing amongst the Vet practitioners on how to treat the companion animals inflammatory cases safely & effectively by using Antinol® in conjunctive with others medicines especially the NSAIDs (Non Steroidal anti-inflammation drugs) which is the drug of choices of anti-inflammatory problems. However as we know apart from the high efficacy of NSAIDs it also can cause serious side effects such as renal or liver damage if it's used too long or no close monitoring when applied in animals.

Recently we have seen the increasing trend of cats populations adopted as the companions; Cat is the specie that has quite limited type of anti-inflammatory drug with safely applied. Therefore 2018 Antinol contest would like to promote the Vet practitioners to share their knowledges and experiences of using Antinol® as the drug of choices of anti-inflammatory cases in cats to demonstrate the option of safe and effective treatment which has been very successful applied as the combined therapy from different cases study in this contest resulted Antinol® is become commonly used as the safe choice of anti-inflammation in cats.

Dr. Achinee Runcharoen

DVM

CEO ASIA





