

**Clinical Results of Nineteen Dogs
with Tracheal Collapse
that received PCSO-524[®],
a Lipid Extract of the
New Zealand Green-Lipped Mussel
(Perna canaliculus)**

Koji Nishida

Medical Center NISHIDA Animal Hospital



Vol.25 No.163 2016

株式会社ファームプレス

Report

Clinical Results of Nineteen Dogs with Tracheal Collapse that received PCSO-524®, a Lipid Extract of the New Zealand Green-Lipped Mussel (*Perna canaliculus*)

Koji Nishida
Medical Center NISHIDA Animal Hospital

Introduction

Tracheal collapse is a respiratory disorder characterized by the decrease of supporting force of the tracheal cartilage which results in abnormal dilating and flattening of the trachea. It is common in small-breed dogs and brachycephalic dogs.

Tracheal collapse results from a number of causes including genetic factors, obesity, tracheal cartilage degeneration, chronic bronchitis, respiratory infection, and cardiovascular dysfunction. The combination with these causes worsens symptoms. Comprehensive management is required such as medical treatment as well as surgical treatment at the time of progression.

A study has reported that polysulfated glycosaminoglycan (Adequan®), which is used to treat articular cartilage disease, has been observed to apparently reduce clinical symptoms such as coughing associated with tracheal collapse, through its restoring effect on tracheal cartilage similar to that it has on articular cartilage. [1]

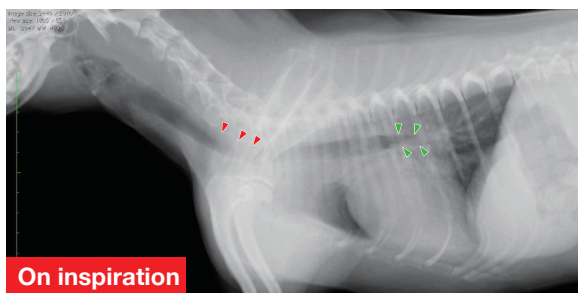
Based on this finding as well as the other report stating that fatty acids of green-lipped mussels (*Perna viridis*) have a pain-relief effect in New Zealand people with arthralgia, Adequan® was given to approximately 200 dogs with arthralgia at our hospital between 1987 and 1991. The effect in dogs was similar to that in human patients.

This report summarizes positive effects of PCSO-524® (Antinol®), a supplement product which includes anti-inflammatory fatty acids extracted from *Perna canaliculus*, another kind of green-lipped mussels, given to dogs with tracheal collapse.

Cases

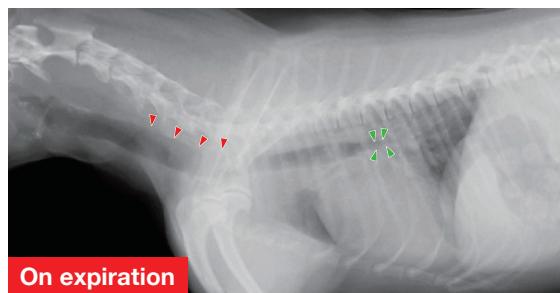
Nineteen dogs presented with cough and diagnosed with tracheal collapse based on inspiration / expiration chest radiography between December 2013 and April 2015.

Radiographic findings of tracheal collapse



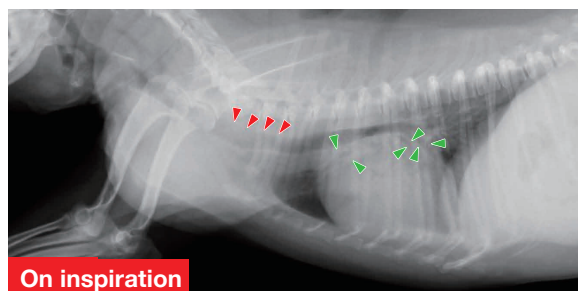
On inspiration

- Chihuahua A ▶ Flattening of the cervical trachea
▶ Dilating of the bifurcation of the trachea



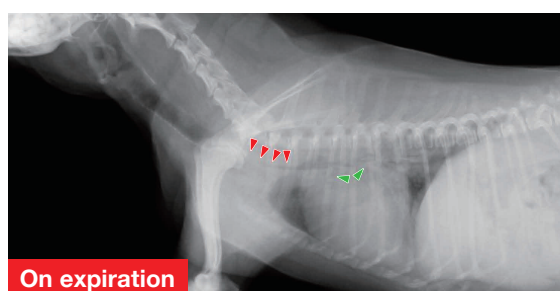
On expiration

- Chihuahua A ▶ Dilating of the cervical trachea
▶ Flattening of the bifurcation of the trachea



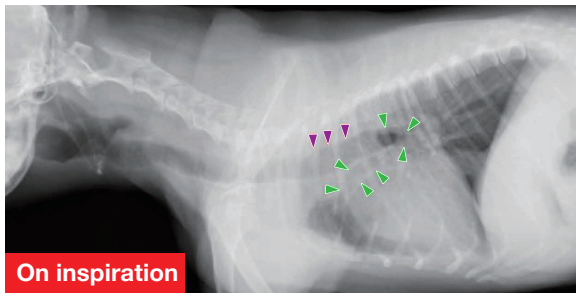
On inspiration

- Yorkshire terrier C ▶ Deformity of the cervical and thoracic trachea
▶ Dilating of the bifurcation of the trachea

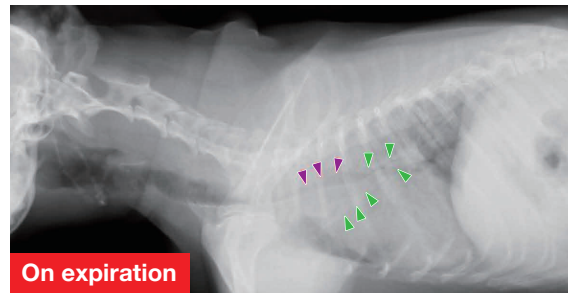


On expiration

- Yorkshire terrier C ▶ Deformity of the thoracic trachea
▶ Flattening of the bifurcation of the trachea



On inspiration
 Papillon A ▶ Dilating of the thoracic trachea
 ▶ Dilating of the bifurcation of the trachea



On expiration
 Papillon A ▶ Flattening of the thoracic trachea
 ▶ Flattening of the bifurcation of the trachea

Contents and Dosage of PCSO-524® used

- 100% natural oil (with olive oil and natural vitamin E) extracted from the New Zealand green-lipped mussel (*Perna canaliculus*) through the patented extraction process
- Granted a patent as anti-inflammatory lipids (including up to 91 different fatty acids)

Dosage

Body weight	In the first 2 weeks	After 3 weeks
10 kg	2 capsules/day	1 capsules/day
10-20 kg	2-4 capsules/day	1-2 capsules/day
> 20 kg	4 capsules/day (2 in the morning and 2 at night)	2 capsules/day

Fatty acids	Content (g/100 g)
Monounsaturated fatty acid	16.1
Polyunsaturated fatty acid	45.7
Omega-3 fatty acid	39.1
Omega-6 fatty acid	3.8
Omega-9 fatty acid	2

Typical fatty acids

Eicosapentaenoic acid	21.9	Stearic acid	4.3	Alpha-linolenic acid	1.4	Hexadecanoic acid	0.7
Palmitic acid	19	Vaccenic acid	3.6	Arachidonic acid	1.4	Eicosatetraenoic acid	0.5
Docosahexaenoic acid	11.1	Linoleic acid	2.1	Docosapentaenoic acid	1.1	Arachidic acid	0.4
Palmitoleic acid	10.6	Linolenic acid	2.1	Heptadecanoic acid	0.9		(g/100 g oil)
Myristic acid	8.3	Oleic acid	2	Pentadecanoic acid	0.8		

Summary of cases

Evaluation criteria: -, normal; O, abnormal

	Dogs	Male / Female	Cervical trachea	Thoracic trachea	Bifurcation of the trachea	Presence of valvular heart disease	Age at the first treatment
1	Chihuahua A	F / spayed	O	-	O	O	132
2	B	F / intact	O	-	-	O	108
3	C	M / castrated	O	-	-	O	18
4	D	M / intact	O	O	O	O	189
5	E	M / castrated	O	O	O	-	64
6	F	M / castrated	O	O	O	O	126
7	G	M / intact	O	-	O	O	154
8	Yorkshire terrier A	M / intact	O	O	O	O	195
9	B	M / intact	O	-	O	O	126
10	C	F / spayed	O	O	O	-	144
11	D	M / castrated	O	O	O	O	168
12	Pomeranian A	F / spayed	O	O	O	O	187
13	B	M / intact	O	O	O	O	105
14	C	F / spayed	O	-	-	O	102
15	D	M / castrated	O	O	-	O	148
16	Papillon A	F / spayed	-	O	O	-	197
17	B	F / spayed	O	-	-	O	199
18	Pug	M / castrated	O	O	O	-	167
19	Maltese	F / spayed	-	-	O	O	161

- A total of 19 dogs including 7 Chihuahuas, 4 Yorkshire terriers, 4 Pomeranians, 2 Papillons, 1 Pug, and 1 Maltese were included.
 - All were small-breed dogs.
 - Eleven male dogs (including 6 castrated) and 8 female dogs (including 7 spayed) were studied. This ratio was similar to the ratio in our clinical practice.
- No significant difference was found in the incidence rate of tracheal collapse between males and females.

- Tracheal collapse occurred the most frequently in the cervical trachea, and then in the thoracic trachea, and the least frequent in the bifurcation of the trachea. In nine dogs collapse was noted at all three sites. Valvular heart disease was noted in 15 dogs.
- The age of the dogs ranged from 63 months (5 years and 3 months) to 199 months (16 years and 7 months) (mean 150 months [12 years and 6 months]).
- Most of the dogs studied were in older age.

Changes in body weight from baseline to end of treatment (at 12 months)

Dogs	Weight at baseline (kg)	Target weight (kg)	Weight at 12 month: (kg)	Trigger of weight reduction
1 Chihuahua A	4.5	3.5	3.5	
2 B	5.5	5	5	
3 C	3.3	3.3	3.1	
4 D	3.4	3.2	–	Died of pulmonary edema at 10 months of treatment
5 E	2.6	3		
6 F	3.5	3.5	2.3	Renal failure following cardiovascular failure
7 G	3.7	4	–	Died of advanced valvular heart disease at 6 months of treatment
8 Yorkshire terrier A	3.5	3	3.2	
9 B	4.4	3.5	4	
10 C	3.1	2.5	–	Discontinuation of treatment due to dosing difficulty by the owner
11 D	4.2	3.7	3.9	
12 Pomeranian A	2.8	3.3	2.9	
13 B	3.6	3.4	3.2	Chronic pancreatitis
14 C	4.5	3.5	3.8	
15 D	6.9	4.5	6.4	
16 Papillon A	3.2	3	3.3	
17 B	2.5	2	2.1	
18 Pug	9.9	10.5	8.5	Anorexia associated with cardiovascular failure
19 Maltese	3.7	4.5	4.7	

- At baseline 12 dogs were obese, 5 dogs were lean, and 2 dogs were at normal weight.
- As we instructed the owners to follow our weight-control protocol, at 12 months of treatment 11 of 16 dogs showed improvements in body weight.
- Four dogs experiencing complications such as chronic gastrointestinal disorder, chronic pancreatitis, chronic renal failure, and cardiovascular failure had difficulty in weight control.
- Three dogs were excluded from the study: 1 died of pulmonary edema, 1 died of advanced valvular heart disease, and 1 discontinued PCSO-524® due to dosing difficulty by the owner.

Our weight-control protocol (instructions to pet owners)

- Set **target** body weight (human weight + animal weight) – human weight = **animal weight**
- Weigh once **daily**

Lower (or higher for lean dogs) than the weight of the previous day

Higher (or lower for lean dogs) than the weight of the previous day

Continue previous two steps.

Review the result of the previous day, determine cause of gain/loss of body weight, and change animal's **diet** or **daily-life activity**

Discuss progress and further instructions with veterinarian based on **weight record** of the past month.

- For animals with poor improvement in weight, the veterinarian should instruct owner on animal's diet and daily-life activity.
- It is important to control body weight for a month according to owner's individual concept of weight control. The veterinarian should correct the owner's concept or method of weight control as needed.

Evaluation of cough at home - Changes in the incidence rate of cough from baseline (first day of treatment with PCSO-524®) (%)

Dogs	baseline*	0.5 month	1 months	2 months	3 months	6 months	12 months
1 Chihuahua A	100	90	70	50	40	50	5
2 B	100	80	80	40	0	50	20
3 C	100	100	100	100	100	50	0
4 D	100	90	50	–	–	–	–
5 E	100	0	0	0	0	0	0
6 F	100	0	10	25	25	10	0
7 G	100	100	50	50	50	50	–
8 Yorkshire terrier A	100	0	0	0	10	0	0
9 B	100	0	10	0	10	10	0
10 C	100	95	10	10	10	10	–
11 D	100	50	60	60	100	0	50
12 Pomeranian A	100	40	80	80	80	30	50
13 B	100	15	40	30	40	40	20
14 C	100	50	10	10	20	10	0
15 D	100	0	0	0	0	0	0
16 Papillon A	100	0	0	0	0	0	0
17 B	100	50	50	40	20	10	10
18 Pug	100	70	50	40	40	50	50
19 Maltese	100	100	120	90	60	20	60

*Cough at baseline is assumed to be 100%.

- Cough was improved in all the 16 dogs that survived for 12 months. When worsening of cough associated with cardiovascular and inflammatory diseases occurred, concomitant supportive care was provided as needed.

■ Our supportive care for tracheal collapse

clinical signs	Drugs	Notes
Cough	Butorphanol (0.5 – 1.2 mg/kg, 2 – 4/day, PO)	<ul style="list-style-type: none"> Use only in severe cough Applicable case: short-term treatment in Chihuahua A and Pomeranian A
Dyspnea	<ul style="list-style-type: none"> 200 mL purified water 2 mL ALEVAIRE 2 mL DEXAMETHASONE Aqueous Solution for Injection A 1 mL GENTACIN 10 mg 	<ul style="list-style-type: none"> Local treatment by inhalation (not systemic treatment) can minimize adverse reactions No incidents encountered requiring treatment of this category for patients enrolled in this report
Infection	CONVENIA® (8 mg/kg, every 2 weeks, SC)	<ul style="list-style-type: none"> Immune compromise, periodontal disease, and susceptibility to infection in older dogs are considered as etiological factors

■ Summary of cases

- Nineteen dogs were all small-breed dogs.
- In 10 dogs tracheal collapse was noted at all three sites such as the cervical trachea, the thoracic trachea, and the bifurcation of the trachea.
- Valvular heart disease was noted in 14 dogs.
- At baseline 12 dogs were obese and 5 were lean.
- Weight control had beneficial effect on improvement of cough.
- The study mainly included older dogs; minimum, maximum, and mean ages at baseline were 63 months (5 years and 3 months), 199 months (16 years and 7 months), and 150 months (12 years and 6 months), respectively.

■ Summary of cases

Tracheal collapse is a progressive disease characterized by cough, and leads to dyspnea, syncope, and respiratory failure resulting in death.

After treatment with lipid extract of *Perna canaliculus* (PCSO-524®) in combination with medical therapy or weight-control interventions was provided for 12 months to dogs with cardiovascular disease, inflammation, cough, or exacerbation of dyspnea, conditions of the patients remained relatively stable.

It can be estimated that **Anti-inflammatory omega-3 polyunsaturated fatty acids** included in PCSO-524® are involved in the mechanism underlying this result. Stimuli by airflow in the flattened airway increase inflammatory secretion by the airway mucosa, which, in turn, blocks the airflow resulting in exacerbation of clinical signs. It can be estimated that anti-inflammatory fatty acids could stop this cycle. [2]

PCSO-524® might be recommended as a beneficial treatment option for both animals and their owners for the following reasons: first, PCSO-524® is an oral agent, whereas Adequan® is an injectable one. Second, unlike steroids and non-steroidal anti-inflammatory drugs, fatty acids as one of the nutrient components give little concern about adverse reaction related to long-term use.

It may be worthwhile to try PCSO-524® regardless of disease duration.

For the future, we are planning to give PCSO-524® to dogs undergoing surgery for severe tracheal collapse to evaluate its therapeutic efficacy.

I hope that this report will help in the treatment of tracheal collapse of older, small-breed dogs commonly kept in Japan. I wish to thank Dr. Michiro Fujita (Nippon Veterinary and Life Science University) and Dr. Hiromitsu Orima (ORM Corporation) for his guidance on radiographic interpretation, and V and P, Co., Ltd. for provision of the lipid extract of *Perna canaliculus* (PCSO-524®; trade name, Antinol®).

■ Summary of PCSO-524®

- No severe adverse reactions were noted during 12 months of treatment.
- Unlike surgery, no special technique or device was necessary.
- Except for 2 death cases and 1 case of dosing difficulty, all cases showed improvement of cough.

■ Key points of the treatment

- Tracheal collapse was not the only cause of cough.
- Combined therapy for cardiovascular disease or inflammation was necessary.
- One had difficulties to receive PCSO-524® orally.
- The total number of patients was relatively small.
- Patients with severe dyspnea and those with syncope were not included in the study.
- Evaluation of response to treatment required half a month or longer.

References

[1] Shun Y and Ryo N, et al. Results of clinical study of polysulfated glycosaminoglycan for tracheal collapse., Proceeding No. 14, the 85th Annual Meeting of the Azabu Veterinary Association, Journal of Azabu Univ. 2010;21/22:p.50.

[2] Maggiore AD, Tracheal and airway collapse in dogs., Vet Clin North Am Small Anim Pract. 2014 Jan;44(1):pp.117-127.