CAP Companion Animal Practice

JCVIM/JSVCP2009
Japanese College of Veterinary Internal Medicine
Japanese Society of Veterinary Clinical Pathology
2009 Convention

Effect of Pinfenon-S (containing Pycnogenol) on Mitral Regurgitation in Dogs

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Dog mitral regurgitation is characterized by the thickening/extension and divergence of the mitral valve, caused by myxomatous transformation. A regurgitation occurs due to the divergence of the mitral valve, and as the regurgitation volume increases, the conditions develops into congestive heart failure. Treatment for the condition usually consists of vasodilators (angiotensin converting enzyme inhibitor: ACEI, etc.) or other pharmaceutical-based solution. However, there are limits to the pharmaceuticals currently recommended. The variety and/or volume of medicines administered can be increased; however, this leads to other side effects.

We administered Pinfenon-S (Pycnogenol as a main ingredient) to study the clinical effects on dogs suffering from mitral regurgitation. Pycnogenol offers multiple effects such as antioxidant, vascular dilatation effect, and anti-platelet aggregation effect, and we expected it to be effective in myocardial protection. Our report follows below.

Key words : Pycnogenol, mitral regurgitation, Troponin I

Introduction

Pycnogenol manufacturer Horphag Research sponsors an academic symposium annually in May.

The latest symposium was held on May 10 in Malaysia, attended by nearly 100 individuals from seven countries including Japan, Korea, China, and Taiwan. Presentations included the following.

Raffaella Canali, PhD of the Italian National Research Institute on Food and Nutrition: Anti-inflammatory Properties of Pycnogenol® on Inflammatory Mediators COX-2 and 5-LOX

Frank Schönlau, PhD, Director of Scientific Communications, Horphag Research; Jeff Strong ND, Director of Scientific Communications, Horphag Asia: The Anti-Inflammatory Efficacy of Pycnogenol® in Joint Health; Pycnogenol® for Improving Cognitive Function

Gianni Belcaro MD, Chieti-Pescara University: The Effect of Pycnogenol on Diabetes Patients (capillary vessel and associated diseases); Performance Enhancement and Recovery using a Sports Drink Compound containing Pycnogenol

Yusuke Kasai, PhD, Kanagawa Dental College: The Effect of Pycnogenol on Bone Loss and Osteoporosis.

Materials and Methods

1. Target Case

We studied 12 dogs diagnosed with mitral regurgitation at the Veterinary Medical Teaching Hospital at Nippon Veterinary and Life Science University and Noya Animal Hospital. All dogs were diagnosed with thickening and divergence of mitral valve using echocardiography, and were confirmed to have mitral valve regurgitation. The ages of the subjects ranged from eight to 16 years (11.5 years average), and weights ranged from 2.75 to 8.7 kilograms (6.1 kilograms average). Ten dogs were male (four castrated male), two female (one infertile female). We categorized the subjects' cardiac disturbance level according to NYHA Functional Classification: NYHA I = three subjects; NYHA II = five subjects; NYHA III = four subjects.

Case	Breed of Dog	Sex	Age	Weight	NYHA Functional Classification	General Clinical Improvement Rate
NO 1	Pomeranian	Castrated male	10 yrs.	4.64 kg	II	No Change
NO 2	Shih Tzu	Male	12 yrs.	6.08 kg	III	No Change
NO 3	Shih Tzu	Male	15 yrs.	4.12 kg	II	No Change
NO 4	Pomeranian	Infertile female	13 yrs.	3.88 kg	III	Aggravation
NO 5	Hybrid	Castrated male	16 yrs.	8.50 kg	II	Clear Improvement
NO 6	Shih Tzu	Castrated male	13 yrs.	6.50 kg	I	No Change
NO 7	Shih Tzu	Male	9 yrs.	7.90 kg	I	No Change
NO 8	Shih Tzu	Castrated male	9 yrs.	8.70 kg	II	No Change
NO 9	Maltese	Male	8 yrs.	4.30 kg	III	Clear Improvement
NO 10	Shih Tzu	Male	9 yrs.	7.10 kg	I	Improvement
NO 11	Toy Poodle	Male	11 yrs.	2.70 kg	III	Improvement
NO 12	Cavalier King Charles Spaniel	Male	13 yrs.	8.50 kg	II	Improvement

2. Test Materials

For our tests, we used Pinfenon-S (Pycnogenol) 140mg tabs or Pinfenon-S (Pycnogenol) granule 600mg/ packet.

Pycnogenol is an extract from the bark of the maritime pine tree found exclusively in the south of France. The compound is a safe, water-soluble food supplement featuring extremely high bioactivity. The proanthocyanidin and over 40 other organic acids contained in Pycnogenol are low molecular antioxidants featuring special flavonoid characteristics. The compound is a strong activated carbon remover belonging to the polyphenol group.

3. Administration Method

We administered Pinfenon-S in four tabs per subject (560mg/ subject) or one packet per subject (600mg/ subject), in one or two doses per day, either mixed in with the subjects' food or given forcibly.

In conjunction with the cardiac insufficiency, we combined other generally used internal therapy: ACEI, furosemide, theophylline, digoxin, spironolactone, and pimobendan.

Studied Items

We performed a study of general clinical symptoms, physical examination, and blood chemical analysis. Our survey of general clinical symptoms included activity, appetite, changes in cough, and the Physical Activity Questionnaire from Oyama et. al. We also inquired the pet owners regarding their pets' physical activity. For the serum chemical analysis, we measured hepatic enzyme (AST, ALT, ALP), BUN, creatinine, and electrolyte. We also measured NT-proBNP and troponin I as heart biomarkers.

Fig. 1 NT-proBNO Concentration (pmol/l)

Case	Before administration	After administration
NO 1	2319	2032
NO 2	2180	2030
NO 3	1050	1473
NO 4	1776	1740
NO 5	1010	1216
NO 6	1450	2016
NO 7	388	320
NO 8	411	747
NO 9	1184	1377
NO10	617	317
NO11	2200	2324
N012	720	712

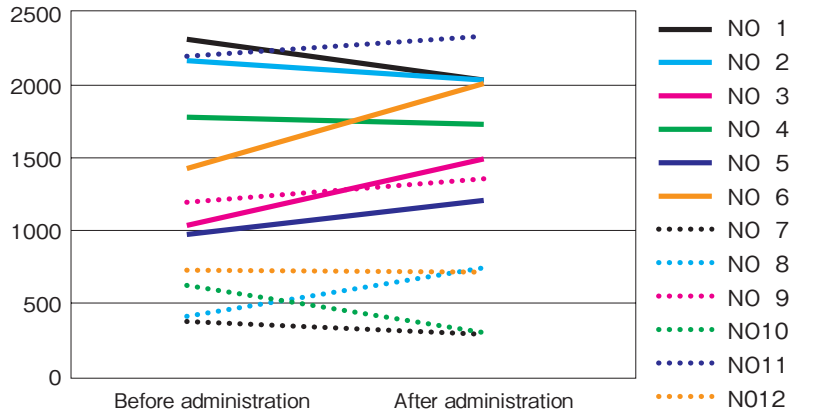
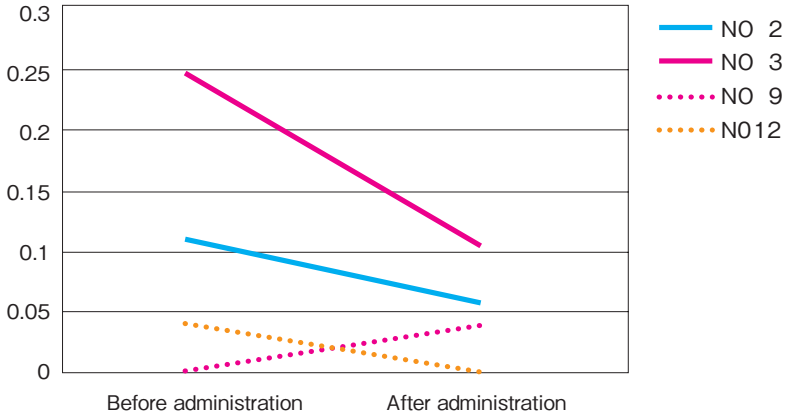


Fig. 2 Troponin I value before and after administration (μg/l)

Case	Before administration	After administration
NO 2	0.11	0.06
NO 3	025	0.11
NO 9	0	0.04
N012	0.04	0



We performed our study in monthly intervals, making a determination as to effectiveness at two months after administration as a rule. We performed blood chemical analysis prior to administration and at two months after administration at the time of our determination of effectiveness.

Results

The degree of improvement in subjects based on general clinical symptoms and the Physical Activity Questionnaire after administering Pinfenon-S are as follows: cases exhibiting clear improvement or improvement, 41.6% (5 of 12 cases); case exhibiting aggravation, 1 case. Subjects categorized under NYHA Functional Classification showing clear improvement or improvement in clinical symptoms are as follows: Class I, 33.3% (1 of 3 cases); Class II, 40% (2 of 5 cases), Class III, 50% (2 of 4 cases).

Fig. 1 shows the trend in NT-proBNP movement. Cases showing 40% change after administration were as follows: NYHA Class I, 1 case in 3 (No. 10) decreased from 617pmol/l before administration to 317pmol/l after. The other two cases experienced no notable changes. In Class II, 2 in 5 cases (No. 3, No. 8) experienced an increase from 1050pmol/l to 1473 pmol/l and an increase from 411pmol/l to 747pmol/l. There were no notable changes in the other three cases in Class II. None of the 4 Class III cases showed any clear changes.

There were numerous cases for which troponin I was below measurable levels; however, troponin I in the three measureable cases decreased after administration (Fig. 2). These were 1 case in 5 of the Class II subjects (No. 3), which decreased from 0.25μg/l to 0.11μg/l, and 2 cases in 4 of the Class III subjects (No. 2, No. 11), from 0.11μg/l to 0.06μg/l and 0.04μg/l to less than 0.01μg/l. However, 1 case under Class III (No. 9) changed from unmeasurable levels prior to administration to 0.04μg/l after. The clinical symptoms and physical activity of the three cases with measureable levels of troponin I prior to administration did not appreciably change in two subjects. The third subject (Class III) showed an improvement in clinical symptions.

We did not note any significant changes in blood chemical analysis, BUN, creatinine, or electrolyte during the administration period.

Observations

Myocardial troponin I is an acute and specific biomarker for myocardial damage, capable of detecting even minor myocardial lesion. It is used as a marker for myocardial infarction and myocarditis in humans. It has been reported that dogs with chronic mitral regurgitation experience ventricle remodeling and sclerotic change of the intramural coronary artery as the sickness progresses. This is believed to be one cause of myocardial insufficiency in the disease. We decided to measure troponin I as a myocardial biomarker to assess the extent of myocardial damage in our subjects. We discovered that the ratio of myocardial damage in the mitral regurgitation dogs was comparatively low, with most below the measurable limit. However, 20% of the subjects (1 in 5 cases) categorized as Class II under NYHA Functional Classification, 50% of Class III cases (2 in 4) experienced increases—albeit minor—to measurable levels after administration. We believe this suggests that dogs with slightly advanced mitral regurgitation had myocardial damage, though to a slight level.

In the three cases in which troponin I was measurable, all three experienced a decrease after Pinfenon-S administration. The principle ingredient of Pinfenon-S is Pycnogenol. Pinfenon-S is a strong active oxygen remover, and has been reported to reduce risk in human heart disease due to its vascular dilatation effect. Accordingly, the decrease in troponin I we noted during our study is possibly due to the myocardial protection effect of vascular dilatation and anti-platelet aggregation effect, stemming from the Pinfenon-S capacity for NO inactivation inhibition and production facilitation effect, endothelin-1 production inhibition effect and prostacyclin production facilitation effect. However, the trend in NT-proBNP showed one case of decrease, with almost no other instances of change. Conversely, we noted two cases exhibiting an increase. In other words, the administration of Pinfenon-S did not result in a clear improvement in left atrial pressure or myocardial load, nor in a direct measurable reduction in load on the heart. However, we do believe it is possible that there was a reduction in myocardial damage. In cases of chronic mitral regurgitation, the expression of myocardial failure in connection with the progress of the disease contributes significantly to the prognosis. This expression of myocardial failure entails myocardial damage associated with intramural coronary artery lesion and myocardial remodeling. Accordingly, the ability of Pinfenon-S in myocardial protection effect and prevention/ improvement of microthrombus may slow down the progress of disease.

We assessed general clinical symptoms of activity, appetite, and changes in cough, as well as using the Physical Activity Questionnaire developed by Oyama et. al. This Physical Activity Questionnaire was created for the purpose of allowing both pet owners and veterinarians to objectively and easily make a clear assessment. As a result, the administration of Pinfenon-S indicated general clinical symptom improvement (according to the Physical Activity Questionnaire) in 41.6% (5 of 12 cases) of our subjects. One in 3 cases of Class I subjects (NYHA Functional Classification), or 33.3%, 40% of Class II subjects (2 of 5 cases), and 50% of Class III subjects (2 of 4 cases) showed clear improvement or improvement. Given these results, we believe that administration of Pinfenon-S can lead to improvement in cases of advanced disease, and that this effectiveness is related to the multiple number of benefits attributable to Pinfenon-S, including antioxidant, vascular dilatation, and anti-platelet aggregation effects.

Our study covered a relatively small number of cases (12 cases). In the future, we believe there is a need to expand the number of test subjects and study the effects of long-term administration. We did not note any significant fluctuations in values of biochemical blood examination during Pinfenon-S administration. Accordingly, we believe Pinfenon-S can be safely administered to dogs experiencing mitral regurgitation.

Cited Texts

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