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Cardiac Drugs

for Treatment of Canine Heart Failure

Degenerative mitral valve disease (DMVD) and dilated cardiomyopathy (DCM) are common cardiac diseases in adult dogs. Both diseases can lead to heart failure and loss of quality and quantity of life.

Various cardiac drugs prolong survival and many others help alleviate clinical signs.

DIURETICS INDICATIONS

Diuretics are a mainstay of therapy in dogs with congestive heart failure (CHF) due to DMVD or DCM.

ADMINISTRATION

Bolus injections of furosemide (2–4 mg/kg Q 2 H) are used in dogs with respiratory distress secondary to acute heart failure until respiratory rate and effort begin to improve.

Alternatively, furosemide can be given as a constant rate infusion. Purported advantages of furosemide infusion over intermittent boluses include enhanced natriuresis and diuresis and less urinary potassium loss. I recommend using 0.66 to 1 mg/kg/H, monitoring respiratory rate every hour.

Once acute heart failure is resolved, chronic oral therapy with furosemide (1–2 mg/kg Q 12 H) is initiated. As

disease progresses, many dogs require escalating doses of furosemide to suppress signs of congestion and total doses of 6 to 8 mg/kg Q 24 H are not uncommon.

CONSIDERATIONS

In experimental studies, dogs have rapidly become resistant to chronic furosemide. In clinical patients, high doses of furosemide are often associated with diminishing polyuria and polydipsia and recurrent episodes of heart failure. In these cases, additional diuretics (hydrochlorothiazide or a hydrochlorothiazide–spironolactone combination, 0.5–1 mg/kg Q 24–48 H) help restore diuretic response. In most cases, the additional diuretics are added to the existing furosemide regimen.

In dogs with advanced disease, and particularly in cases of right heart failure, bioavailability of oral medications is likely reduced. Daily subcutaneous injections of furosemide can be used in place of oral administration and are often associated with restoration of copious diuresis.

MONITORING

In all instances of diuretic use, renal function should be closely monitored.

ACE INHIBITORS INDICATIONS

Severe heart disease is generally associated with activation of the renin–angiotensin–aldosterone system (RAAS), which promotes fluid retention, vasoconstriction, and myocardial and vascular remodeling. Use of ACE inhibitors in dogs with CHF is associated with improved quality of life and survival; however, data in support of this statement are less robust for dogs with DCM than for dogs with DMVD. When diuretics such as furosemide are administered, the reduction of plasma volume further stimulates RAAS activity and coadministration with an ACE inhibitor is generally recommended.

ADMINISTRATION

There are a variety of ACE inhibitors available, including enalapril, benazepril, ramapril, and lisinopril (**Table**). Differences are relatively minor, mainly involving route of metabolism/excretion and

ACE = angiotensin-converting enzyme; CHF = congestive heart failure; DMVD = degenerative mitral valve disease; DCM = dilated cardiomyopathy; RAAS = renin–angiotensin–aldosterone system

lipophilicity. From a clinical standpoint, many cardiologists consider them to be interchangeable. In the United States, the two most commonly used ACE inhibitors are enalapril and benazepril; both are associated with clinical benefit in dogs with signs of heart failure.

CONSIDERATIONS

In dogs with DMVD, the use of ACE inhibitors in those without clinical signs remains controversial. Two well-designed studies offer slightly different perspectives: One study in Cavalier King Charles spaniels with mild–moderate DMVD clearly indicated that enalapril did not delay onset of CHF. Another study involving dogs of many different breeds and more advanced DMVD also failed to show benefit with respect to the study’s primary endpoint; however, analysis of several secondary endpoints suggested that dogs that received enalapril avoided heart failure longer than dogs that did not.

In my opinion, if ACE inhibitors delay heart failure in dogs with DMVD that show no clinical signs, the effect is inconsistent from individual to individual, relatively small, and unlikely to dramatically change progression of disease. In dogs with severe heart enlargement and at high risk for CHF, I prefer to use an ACE inhibitor in tandem with low-dose diuretic therapy (furosemide, 1 mg/kg Q 24 H), as this more likely reduces plasma volume, intracardiac pressure, and risk of CHF than using an ACE inhibitor alone.

In human patients with asymptomatic DCM, early use of ACE inhibitors is widely recommended. In veterinary medicine, large-scale trials are lacking; however, a small study indicated that ACE inhibitors delayed onset of heart failure in Doberman pinschers with DCM. Thus, in dogs with DCM, I recommend use of ACE inhibitors prior to onset of clinical signs.

MONITORING

Adverse effects of ACE inhibitor treatment are relatively rare, but clinically significant renal dysfunction can occur. Less commonly, systemic hypotension or electrolyte imbalances are encountered. Renal function should be evaluated both before and after initiation of ACE inhibitors and at 3- to 6-month intervals thereafter.

PIMOBENDAN INDICATIONS

Both DMVD and DCM are associated with progressive loss of myocardial contractility. Poor contractility is much easier to detect in dogs with DCM as opposed to DMVD, where the presence of a large degree of mitral regurgitation often confounds routine echocardiographic evaluation of contractility.

Pimobendan is a positive inotrope and increases contractility through a mechanism different from that of traditional inotropes such as digoxin—the advantage of which is increased contractility without significant increases in myocardial oxygen demand. Pimobendan also relaxes vascular smooth muscle and elicits modest arterial vasodilation; this dual “inodilating” action is unique. Pimobendan improves survival and quality of life in dogs with DMVD, and very likely does the same in dogs with DCM.

ADMINISTRATION

The recommended dose is 0.5 mg/kg per day, divided into 2 doses that do not necessarily need to be equal.

CONSIDERATIONS

The benefits of pimobendan have been substantiated in dogs showing clinical signs associated with heart disease due to DMVD and DCM; treatment with this agent is recommended only if clinical signs are evident. Thus, in the majority of instances, pimobendan is prescribed only if and when dogs experience congestive heart failure and its attendant clinical manifestations (eg, cough, dyspnea, tachypnea).

Less commonly, dogs with exercise intolerance or syncope are also candidates for treatment. Currently, no evidence exists for the use of pimobendan in dogs with DMVD or DCM prior to the onset of clinical signs.

MONITORING

Pimobendan is generally well tolerated in dogs and no specific monitoring recommendations accompany its use.

continues

Table.
Commonly Used ACE Inhibitors in Dogs with DMVD & DCM

Drug	Dose	Tablet Sizes
Benazepril	0.25–0.5 mg/kg Q 24 H	5, 10, 20, 40 (mg)
Enalapril	0.5 mg/kg Q 12–24 H	2.5, 5, 10, 20 (mg)
Lisinopril	0.5 mg/kg Q 24 H	2, 5, 10, 20, 40 (mg)
Ramipril	0.125 mg/kg Q 24 H	1.25, 2.5, 5 (mg)

SPIRONOLACTONE

INDICATIONS

Spirolactone is a relatively weak potassium-sparing diuretic, and its potency prevents its use as the sole diuretic agent in dogs with CHF. The value of spironolactone most likely lies in its action as a specific aldosterone antagonist. Aldosterone is a part of the aforementioned RAAS and promotes fluid retention and vascular and myocardial remodeling. Interestingly, in both humans and dogs with heart disease, aldosterone can be elevated despite the use

of ACE inhibitors. Suppression of this “aldosterone escape” by spironolactone is associated with reduced morbidity and improved survival in dogs with DMVD.

ADMINISTRATION

In dogs with signs of heart failure, spironolactone (1–2 mg/kg Q 12 H) is recommended in addition to furosemide, ACE inhibitors, and pimobendan. In Europe, where spironolactone is specifically approved for use in dogs with DMVD, the recommended dose is 2 mg/kg Q 24 H. In

the United States, many cardiologists use a lower dose of spironolactone (0.5–1 mg/kg day) or spironolactone coupled with a thiazide diuretic such as hydrochlorothiazide.

MONITORING

Adverse effects can include hyperkalemia (especially in the face of concurrent ACE inhibitor) and azotemia, and routine renal and electrolyte monitoring is recommended.

**Treatment Schemes:
Degenerative Mitral Valve Disease & Dilated Cardiomyopathy**

	No Clinical Signs		Congestive Heart Failure	
	Mild → Severe		CHF	Refractory CHF
ACE Inhibitor				
Furosemide				
Pimobendan				
Spirolactone				
Hydrochlorothiazide				

Treatment scheme for dogs with DMVD as they progress from mild to severe disease (without clinical signs) to CHF and finally to advanced refractory disease. Recommendations in green are supported by veterinary trials; recommendations in orange are advocated by the author.

	No Clinical Signs		Congestive Heart Failure	
	Mild → Severe		CHF	Refractory CHF
ACE Inhibitor				
Furosemide				
Pimobendan				
Spirolactone				
Hydrochlorothiazide				
Beta-blockers				

Treatment scheme for dogs with DCM as they progress from mild to severe disease (without clinical signs) to CHF and finally to advanced refractory disease. Recommendations in green are supported by veterinary trials; recommendations in orange are advocated by the author.

Canine Cardiac Drugs Approved by the FDA

In the United States extralabel use of animal and human drugs is permitted in non-food-producing animal practice except when public health is threatened. However, it should be noted that products approved by the FDA for a particular species and use have gone through a rigorous review process.

Benazepril	Not in U.S.; approved in Europe & Canada
Enalapril	Enacard (merial.com)
Furosemide	Lasix (intervet.com); Disal (boehringer-ingenelheim.com)
Hydrochlorothiazide	Only approved for use in cattle (Hydrozide; merial.com)
Lisinopril	Not in U.S.
Pimobendan	Vetmedin (boehringer-ingenelheim.com)
Ramapril	Not in U.S.; approved in Europe
Spironolactone	Not in U.S.; approved in Europe

BETA-BLOCKERS INDICATIONS

Sympathetic tone is chronically elevated in dogs with DMVD and DCM and is thought to contribute to disease progression. In humans, plasma norepinephrine is a powerful predictor of morbidity and mortality. However, routine use of beta-blockers in veterinary medicine is hindered by lack of well-controlled clinical trials and risk for adverse events when initiating therapy, especially in dogs with advanced disease. In humans, beta-blockade is recommended in virtually all instances of reduced contractility, such as occurs in DCM. Thus, administration of beta-blockers is advocated by many cardiologists in dogs with DCM.

ADMINISTRATION

Because of the risk for acute slowing of heart rate and decreases in contractility, treatment with beta-blockers must be performed with caution. Typically, the dose is up-titrated over 4 to 6 weeks with close monitoring of heart rate, respiratory effort, and blood pressure. Titration is best tolerated in dogs with relatively early DCM.

CONSIDERATIONS

In dogs with DMVD, the use of beta-blockers is controversial and no consensus recommendations can be made.

Take Note

Drug doses listed in this article are guidelines for the "typical" dog with heart failure. They may need to be adjusted based on the patient's severity of signs, renal function, concurrent disease, and response to initial treatment. When prescribing medications to dogs with congestive heart failure due to DMVD or DCM, there is broad consensus that combination therapy with furosemide, an ACE inhibitor, and pimobendan is beneficial.

MONITORING

Practitioners who use beta-blockers must be prepared to monitor dogs closely and to deal with acute decompensation should it occur. Consultation with a cardiologist is recommended. ■

See Aids & Resources, back page, for references, contacts, and appendices.

Article archived on cliniciansbrief.com

ACE = angiotensin-converting enzyme; CHF = congestive heart failure; DMVD = degenerative mitral valve disease; DCM = dilated cardiomyopathy; RAAS = renin-angiotensin-aldosterone system

FELIMAZOLE™ (methimazole) Coated Tablets

2.5 mg and 5 mg strengths
For oral use in cats only

BRIEF SUMMARY (For Full Prescribing Information, see package insert.)

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: Methimazole is a thioureyne antithyroid drug, which inhibits the synthesis of thyroid hormones. Methimazole (1-methylimidazole-2-thiol) is a white, crystalline substance that is freely soluble in water. The chemical formula is C₄H₆N₂S. Molecular weight is 114.16.

INDICATIONS: FELIMAZOLE (methimazole) Coated Tablets are indicated for the treatment of hyperthyroidism in cats.

CONTRAINDICATIONS: Do not use in cats with hypersensitivity to methimazole, carbimazole or the excipient, polyethylene glycol. Do not use in cats with primary liver disease or renal failure, autoimmune disease, hematological disorders, or coagulopathies. Do not use in pregnant or lactating queens. Laboratory studies of methimazole in rats and mice have shown evidence of teratogenic and embryotoxic effects.

WARNINGS: Methimazole has anti-vitamin K activity and may induce bleeding diathesis without evidence of thrombocytopenia.

HUMAN WARNINGS: Not for use in humans. Keep out of reach of children. Methimazole is a human teratogen. Wash hands with soap and water after administration of methimazole or contact with the litter of treated cats. Do not break or crush tablets. Wear protective gloves to prevent direct contact with litter, feces, urine, or vomit of treated cats, and broken or moistened tablets. Methimazole may cause vomiting, gastric distress, headache, fever, arthralgia, pruritus, and pancytopenia. In the event of accidental ingestion/overdose, seek medical advice immediately and show the product label to the physician.

PRECAUTIONS: Use of FELIMAZOLE Coated Tablets in cats with renal dysfunction should be carefully evaluated. Reversal of hyperthyroidism may be associated with decreased glomerular filtration rate and a decline in renal function, unmasking the presence of underlying renal disease. Cats on methimazole therapy should be monitored closely for any sign of illness including fever, lymphadenopathy, or signs of anemia, as these may be associated with serious adverse reactions.

ADVERSE REACTIONS: The most common adverse reactions reported are lethargy, anorexia, vomiting, diarrhea/loose stool, abnormal vocalization, and self-induced excoriations of the head and neck. Serious, but less common, adverse reactions may include lymphadenopathy, hepatopathy, immune mediated anemia, thrombocytopenia, and agranulocytosis. Depression/withdrawn behavior, weight loss, hair coat abnormalities, increased blood urea nitrogen (BUN), weakness, and agitation have also been reported as associated with long-term use.


FELIMAZOLE™
(methimazole)

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