Proceedings of the
World Small Animal Veterinary Association
Sydney, Australia – 2007

Hosted by:

Australian Small Animal Veterinary Association (ASAVA)
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Next WSAVA Congress

33rd Annual
World Small Animal
Veterinary Association
14th FECAVA
Congress

DUBLIN, IRELAND
20th - 24th August 2008
AN APPROACH TO ASYMPTOMATIC ACQUIRED HEART DISEASE IN DOGS

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Cardiovascular diseases in dogs and cats produce devastating consequences in those severely affected. Newer diagnostic methods allow earlier and more comprehensive evaluations of patients with heart disease. Frequently the diagnosis is made before clinical signs are evident, obviously the best time for medical or surgical intervention, when possible. Acquired diseases for which early intervention has been proven or would seem likely to be beneficial include dirofilariasis, mitral regurgitation (endocardiosis; MR) dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), hypertension, endocarditis, and some cases of pericardial effusion. This brief manuscript will include a discussion of only the most commonly encountered canine diseases, MR and DCM.

This author does not generally employ diuretics and salt-restriction prior to the onset of (CHF). Potential exceptions to this stance might include diuretics in the management of coexistent hypertension and the use of spironolactone as an aldosterone receptor blocker. Similarly salt restriction, which is useful after the onset of CHF, is not employed prior to its appearance. Again, an exception is in the hypertensive patient. In addition, mild salt restriction, in the form of avoidance of salty treats is probably never contraindicated and the pet’s palate may likewise be retrained by mild restriction in anticipation of the need for future sodium restriction. With the exception of patients in atrial fibrillation, digoxin is likewise reserved for patients in heart failure. The role of exercise restriction is not well established. It is known that controlled exercise improves muscle strength and cardiac function in humans in CHF, but may also induce or aggravate arrhythmias. I do not restrict exercise in heart patients prior to the advent of CHF unless the precipitation of life-threatening arrhythmias or syncope are of concern.

Mitral Regurgitation

Mitral regurgitation, often recognized during mid-life, affords the veterinarian with the somewhat unique opportunity of a long symptom-free window for potential intervention. Since the ideal treatment, surgical correction, is available to a limited number of clients, medical intervention remains the only hope for most clients with dogs suffering from MR.

Potential and readily available interventions include angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, and afterload reducing agents. Each is aimed at blunting the remodeling that occurs with chronic volume loading and/or reduction in the regurgitant volume.

There are not data on beta-blockers in naturally-acquired canine MR, though there are data in experimental MR, indicating hemodynamic and remodeling benefit. Additionally, there are clear data indicating quality of life and survival benefit in humans with CHF, treated with beta-blockers. Unfortunately, dosing these agents is somewhat difficult in small dogs and this author has yet to routinely embrace this group of agents (carvedilol, atenolol, and metoprolol) in this setting, either before or after the onset of CHF.

ACE inhibitors have received the majority of attention in asymptomatic MR. There are studies which support and refute the activation of the RAAS prior to CHF in MR, leaving the
question to be answered by clinical trials. Two studies have prospectively evaluated enalapril in dogs with MR, prior to the onset of heart failure. The first (SVEP) was carried out in Northern Europe in cavalier king Charles spaniels. This well-designed double-blind, placebo-controlled (DBPC) study was unable to demonstrate a benefit in time to onset of CHF when the drug was compared to placebo in mildly to moderately affected Cavalier King Charles Spaniels. The second (VETPROOF), a DBPC trial carried out in the U.S., has recently been completed (to both CHF and death as end-points). This study showed benefits in time remaining in study, number of dogs CHF-free at 500 days and study termination. The Kaplan-Meier “Survival” Curves demonstrate a strong, but not statistically significant, trend toward a modest increase in time to onset of heart failure. Both studies demonstrated the safety of enalapril in aged dogs with compensated heart disease.

This author offers ACE-I therapy to dogs with asymptomatic MR and radiographic and/or echocardiographic evidence of remodeling (VHS > 11). Reasons for this approach include the proven hemodynamic improvement in human MR, the results of the VETPROOF, the strong safety record, and potential for benefit in reducing mitral regurgitation and in blunting remodeling initiated by the RAAS. Careful scrutiny of renal function, blood pressure, and serum potassium concentration is provided initially and periodically during therapy. In addition, the owner is advised as to cost, the potential for life-time administration, the risk of hypotension, and the varied results of clinical trials.

Aldosterone-receptor-blockers, such as spironolactone (0.5 mg/kg bid) or eplerenone have theoretical benefit in this setting as an adjunct to ACE inhibition as “aldosterone escape” has been recognized in humans receiving chronic ACE inhibition. Interestingly, 2 recent abstracts have failed to show diuretic efficacy with spironolactone alone and in conjunction with furosemide in normal dogs.

Conventional vasodilator therapy has been largely replaced with the advent of ACE inhibitors but venodilators play a role in emergency management of CHF and afterload-reducing arteriolar dilators agents are often employed to unload the heart, reducing mitral regurgitation. There is certainly evidence to show that arteriolar vasodilators, such as hydralazine and amlodipine, can reduce mitral regurgitation. Unfortunately, these drugs activate the RAAS and may increase resting heart rate as well. If used chronically prior to the onset of CHF, their use should be accompanied by concurrent ACE inhibition or angiotensin receptor blockade.

In summary, while each of these drug groups has theoretical utility in this setting, there is not strong evidence for any. While a combination of 2 or even 3 of these drugs has appeal, the risk is hypotension and its attendant undesirable sequelae. This author has employed the combination of enalapril and amlodipine in hypertensive dogs with severe MR, prior to the onset of CHF. In most cases, however, I begin an ACE-inhibitor after there is radiographic or echocardiographic evidence of remodeling. The owner is involved in the decision and are educated as to the limited proof of efficacy, cost, risks, and that the drugs will likely be given for life. Enalapril is initiated at .25-.5 mg/kg after renal function, blood pressure, and serum electrolytes are evaluated. In approximately one week the dosage is increased to the target dosage of .5-1 mg/kg either QD or divided BID. Renal parameters, serum electrolytes, and ideally systemic blood pressure are rechecked in 2-3 weeks and then as often as clinically indicated thereafter. For the motivated client, after the ACE-inhibitor is prescribed and tolerated, beta-blockade with carvedilol is instituted with up-titration to .8-1 mg/kg BID over 6 weeks. Ideally, serum carvedilol concentrations should be evaluated at this time, as there is marked individual to individual variation in bioavailability. If blood pressure allows, the off-loading agent, amlodipine is then added at .1 mg/kg daily.

**Dilated Cardiomyopathy**
DCM in dogs is a much more devastating disease than MR and is more often diagnosed after the onset of CHF. Nevertheless, DCM may be diagnosed prior to CHF, via echocardiography, after detection of a cardiac gallop or murmur or through routine screening in certain breeds. It seems clear that beta-blockers, administered early, are beneficial in this disease in humans; anecdotal reports suggest a similar benefit in dogs. ACE-inhibitors have been shown to provide benefit in humans with DCM or ischemic cardiomyopathy prior to heart failure. O’Grady, in a retrospective study, showed that Doberman pinschers with occult DCM lived longer (substantially so) when they received ACE-I, as compared to the control population which did not. Aldosterone-receptor-blockers, such as spironolactone (0.5 mg/kg bid) or eplerinone have the same theoretical benefit in DCM as in MR. Pimobendan, not yet available in this country, has improved survival and quality of life in Doberman pinschers with DCM and CHF and may have a future role prior to CHF. Carnitine and taurine have potential benefits in dogs deficient in these nutrients and may be instituted either alone or together, with or without having measured serum concentrations. Carnitine is provided as a treatment option for asymptomatic DCM, particularly in boxers, while taurine and carnitine are administered to all American cocker spaniels with DCM. Digoxin, in the author’s opinion, has no role in asymptomatic DCM unless atrial fibrillation is present. In this setting, digoxin is administered, with the addition of diltiazem or a beta-blocker, as needed to control the ventricular response.

In the clinic at NCSU, asymptomatic DCM would most typically be treated with avoidance of heavily-salted foods, possibly taurine and/or carnitine (depending on the breed and input from the owner), and an ACE-Inhibitor (Enalapril at .5-1 mg/kg daily, starting at .25-.5 and increasing to the target dosage in 1 week). If atrial fibrillation is present, digoxin (and diltiazem, if needed) are added, to control the ventricular response (<120 bpm, ideally) within 72-96 hours. After approximately 2 weeks carvedilol is added (for a large-breed dog, 3.125 mg QD x 2 weeks, then bid x 2 weeks, then 6.25/3.125 mg x 2 weeks, etc) until a full dose of 25-50 mg daily, divided BID, is achieved or the patient shows signs of intolerance. If intolerance develops (usually lassitude, inappetance, and hypotension), the dosage is dropped to the last tolerated dosage for 2-4 weeks and then an attempt is made to increase as previously described. If the patient cannot tolerate increases in carvedilol, the last tolerated dosage is accepted as maximum. Human studies indicate that, though lessened, sub-optimal dosages still provide benefit.
**Additional Reading**


