TREATING HEART FAILURE – KEEP IT SIMPLE

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from the Animal CardioPulmonary Consultancy (ACAPULCO), Belgium, discusses various approaches and shares her opinions on the treatment of heart failure in companian animals

HEART failure has always been defined as a state wherein the cardiac output is inadequate to meet the perfusion needs of the metabolising tissues.

However, it has become apparent that heart failure can no longer be named in simple haemodynamical terms and that the disease should be viewed as a progressive model of overexpression of biologically active molecules exerting toxic effects on the heart and circulation.

It is now well-established that the heart is more than a pump and that it is also a neuroendocrine organ. Hence a good understanding of the underlying pathophysiology is required to enable a sensible approach to the treatment of heart failure.

Arterial underfilling initiates a cascade

Arterial under-filling (decreased cardiac output and blood pressure) initiates a very complex neuro-humoral cascade, particularly the activation of the sympathetic nervous system (noradrenaline), the attenuation of vasodilator (nitrous oxide, prostaglandins and prostacyclins) and natriuretic systems (atrial natriuretic protein/brain natriuretic protein), the activation of the renin-angiotensin-aldosterone system (RAAS), the autocrine vasoconstrictory actions of endotheline (ET), the non-osmotic release of antidiuretic hormone (ADH), the increased activity of the hypertrophy/fibrosis signalling pathway (remodelling, RAAS), and the liberation of inflammatory mediators (TNF-α and interleukins). When these compensatory mechanisms become overwhelmed, clinical signs of heart failure become evident (**Table 1**).

Additionally, these neurohumoral reflexes may in the long-term have deleterious effects on the heart muscle and circulation.

Treatment consists of polypharmacotherapy

Considering the complexity of heart failure's pathophysiology it is understandable that its treatment warrants a staged polypharmacotherapeutical approach and that there is not now, and will never be, a miracle drug counteracting all the harmful effects of this neurohumoral cascade.

However, heart failure remains a clinical syndrome triggered by a specific cardiac disease, for example degenerative mitral valve disease, dilated cardiomyopathy, intra- or extracardiac shunt, etc. Hence every effort should be made to define the underlying aetiology in view of offering the most appropriate treatment on the basis of an accurate diagnosis.

Some treatments show rapid haemodynamical benefits, for example frusemide, nitrates, phosphodiesterase (PDE) III inhibitors: others are more long-term modulators, for example angiotensin converting enzyme inhibitors (ACEI), beta-blockers and spironolactone.

Many of the drugs providing acute symptomatic relief in heart failure do not lead to long-term benefits and may even lead to untoward long-term clinical outcomes: therefore, veterinarians should not formulate their treatment solely on the basis of haemodynamic improvement but should always incorporate antagonism of the neurohumoral cascade in their long-term treatment strategy.

The jury is still out on the ideal combination therapy, but multiple decades of research and clinical trials in human medicine: CONSENSUS (1987), SAVE (1992), SOLVD (1992), V-HeFT (1993), ATLAS (1999), HOPE (2002), EUROPA (2003); and veterinary medicine: IMPROVE (1995), COVE (1995), LIVE (1998) and BENCH (1999) have undoubtedly highlighted the importance of the RAAS in the clinical syndrome of heart failure.

Therefore, the use of ACEI should remain the mainstay treatment for every animal in heart failure whatever the underlying reason.

In this era of evidence-based medicine there is ample evidence, with multiple placebo-controlled studies enrolling many patients, for the benefits in survival and quality of life in dogs treated with ACEI (IMPROVE, 1995; COVE, 1995; LIVE, 1998; and BENCH, 1999).

The question should not be about which drug to use, but about when to use it. Two charts have been reproduced (**Figures 1 and 2**) to give some guidelines in the staged approach of treatment of chronic congestive heart failure in the most common causes of canine congestive heart failure: degenerative mitral valve disease and idiopathic dilated cardiomyopathy.

It should be emphasised that the efficacy of drugs used to treat heart failure depends very much

TABLE 1. International Small Animal Cardiac Health Council classification of heart failure

Class	*Criteria*
IA	Heart disease present. No clinical signs. No signs of compensation (no left ventricle volume overload)
IB	Heart disease present. No clinical signs. Signs of compensation on echocardiography or radiography (e.g. left ventricle volume overload or left atrial enlargement).
II	Heart disease present, with mild or moderate signs of heart failure. Clinical signs of backward failure on exertion or excitement. At rest, no clinical evidence of poor systolic function.
IIIA	Heart disease present, with clinical signs of advanced heart failure. Clinical signs even at rest. Cardiomegaly apparent on echocardiography or radiography. Death or severe debilitation likely without treatment.
IIIB	Heart disease present, with clinical signs of advanced heart failure. Clinical signs even at rest. Cardiomegaly apparent on echocardiography or radiography. Death or severe debilitation likely without treatment.

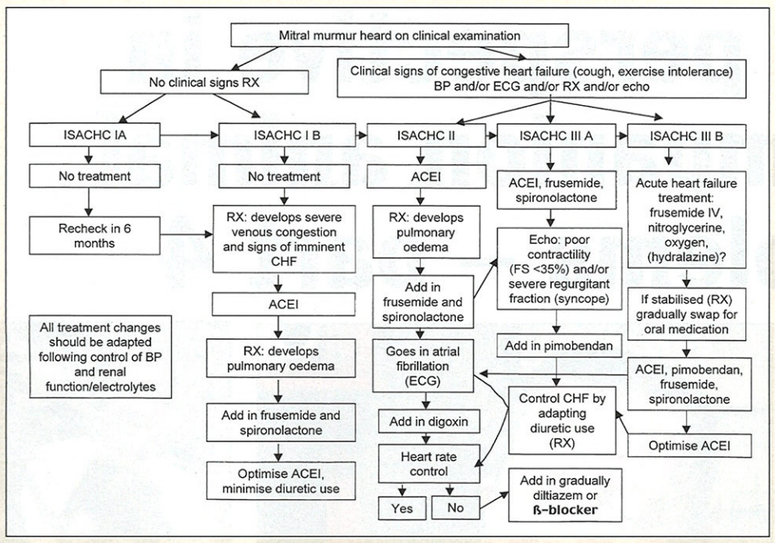

Figure 1. Degenerative mitral valve disease.

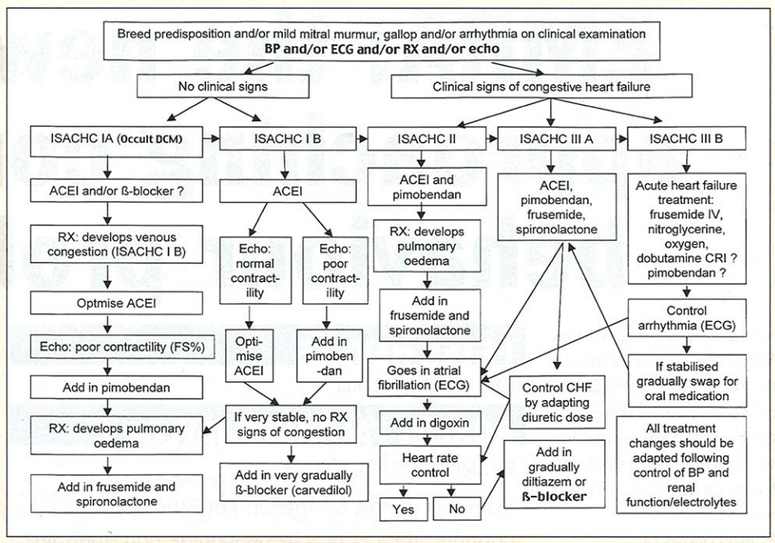

Figure 2. Idiopathic dilated cardiomyopathy.

on the drug type, underlying disease and individual patient response.

There are no set rules to refer to, and it is extremely important to regularly monitor a patient with heart failure (thorough clinical exam, blood pressure, ECG, radiographs, echocardiography, electrolytes and renal function). Treatment should be adapted, depending on the clinical evaluation of the individual patient.

Why keep it simple?

Trying to keep the treatment of heart failure simple by using monotherapy reflects poor understanding of heart failure's pathophysiology. The clinical syndrome of heart failure represents multiple anatomical, functional, biological and genetical alterations that interact together. It is this complex interaction that makes heart failure treatment an intellectual challenge tailored to the individual patient.

Good clinicians will distinguish themselves by using a combined approach. Trying to simplify the treatment just might not be in the animal's interest.

In human medicine, where polypharmacotherapy is standard, multiple trials have shown that repetitive monitoring by experienced individuals improved both the quality and duration of life. There is no reason to think that this should be different in veterinary medicine.

Why choose?

Currently there is a lot of debate about the use of pimobendan instead of an ACEI in heart failure patients and one of the most commonly-asked questions at current cardiology seminars is which one to use. My answer is that it is somewhat similar to asking a child to choose between his father and his mother. Both are essential, but perhaps one may be more important or useful at different times.

Why choose if we can benefit from both? Once again, the question is not what to use, but when to use it. I do understand that the evaluation of efficacy of polypharmacotherapy by a clinical trial is very complex and warrants high numbers of enrolled patients, and might be something unfeasible in veterinary medicine. As a clinician, I can only emphasise that we treat clinical patients with individual needs and responses.

Conclusion

Life might be full of choices, but heart failure treatment shouldn't be. Therapy should be tapered to the needs of the individual patient, based on an accurate diagnosis being carried out.

A staged polypharmacotherapeutical approach is the ideal way forward. It accentuates the understanding of heart failure's pathophysiology.

The application of this knowledge distinguishes the good veterinary clinician from the sales person.

And last, but not least, the animal will benefit from it.

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