Heart failure:

THE FUTURE

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In the last edition of HeartWise, I focused on present day management of heart failure. This second and final article on this syndrome will discuss three separate, though clearly related issues; namely, practical problems with the available pharmacological therapies, new therapeutic strategies and the development of an effective management structure for this condition.

Practical problems with available pharmacological strategies

The following comments will focus on heart failure associated with systolic dysfunction of the left ventricle. It is clear that real advances have been made in this area over the last 10 to 15 years. In addition to digoxin and diuretics, further symptomatic and prognostic benefits can be obtained from angiotensin converting enzyme inhibition, the combination of hydralazine and nitrate, beta adrenoreceptor antagonists and spironolactone. However, with this increasing array of effective therapies come certain problems, predominantly those of polypharmacy, and in the setting where one decides or needs to curtail the number of agents used which should be chosen first in which patient. Polypharmacy poses a real concern for what is, in general, an elderly population. Missed doses of medication, inadvertent misunderstanding of the prescription and drug interactions can all cause life-threatening sequelae and are felt to be responsible for many of the repeated admissions to hospital, so characteristic of this syndrome.

The question of which drug, beyond diuretic, should be used first in which person is also of real importance. This is in order to minimise polypharmacy and yet maintain pharmacological efficacy. There is little to guide clinicians in this regard at present. Agreed policy states that ACE inhibitor therapy should be used and titrated to proven doses, with the subsequent addition of beta blockade in stable patients for further prognostic benefit. However, we do not have data to completely support this policy and, in particular, to indicate that ACE inhibitors are more effective than beta blockers when used first in this setting. Indeed, which agent to use first may be dependent on certain features of the presentation, such as cause of the heart failure, the presence of a persistent tachycardia, or more specific indicators of activity of various neurohormonal systems. Furthermore, it may be more effective to use what is often limited blood pressure to titrate both ACE inhibitors and beta blockers in lower doses.

Therefore, while pharmacological advances continue, we are left with several practical problems outlined above. Until some answers are provided, I would recommend appropriate use of diuretic, immediate addition of ACE inhibition titrated to proven doses (Table 1), and in the setting of clinical stability consideration of beta blockade. Digoxin can be considered, especially if symptoms are problematic. Angiotensin receptor blockers and the combination of nitrate and hydralazine can be considered in patients intolerant of ACE inhibitors.

New therapeutic strategies

Over the next five to 10 years, several

further advances in pharmacological and device therapies for heart failure will undoubtedly be developed. Alternative means of modulating the neuroendocrine environment are presently being assessed. This remains the most attractive option in improving prognosis in this condition. The approaches presently being assessed include endothelin antagonists, antagonists of arginine vasopressin and vasopeptidase inhibitors. The last-named are an interesting family of compounds that combine ACE inhibition with inhibition of the neutral endopeptidase enzyme. The latter enzyme degrades the natriuretic peptides, which have important beneficial haemodynamic and anti-remodelling effects in heart failure. Preservation of these peptides by a compound that also modulates the renin-angiotensin-aldosterone system may exert a significant effect on symptoms and prognosis in this syndrome.

Recent clinical and experimental data have identified significant elevations in cytokine levels in heart failure. These inflammatory proteins have been associated with many of the manifestations of malignancy, especially cachexia. In heart failure, elevated levels of substances such as tumour necrosis factor may play a pathophysiological role in this syndrome. Inhibition of these cytokines at receptor level may improve haemodynamic function as well as well-being in this syndrome. Preliminary data from the initial clinical studies have been promising.

While the above will undoubtedly provide us with additional approaches with which to improve the lot of patients with heart failure, these developments will also further underline the growing concerns (mentioned above) of polypharmacy and drug interaction. The value of these proposed new therapies is being tested on top of standard therapy for this condition (i.e. diuretics, often digoxin, ACE inhibition and beta blockers), so that the demonstration of benefit of an additional drug expands the standard 'cocktail of therapy', almost to unmanageable proportions. This observation underlines the importance of seeking means of identifying which drug will be of most benefit to which patient.

Device strategies are also being assessed in heart failure. Implantable defibrillators with pacing capacity will likely be used more extensively to combat the problem of sudden cardiac death in this syndrome. It is likely that this event is due to a bradyarrhythmia or tachyarrhythmia. Ongoing studies are designed to assess which individuals with heart failure should receive these devices. At present they should be employed in patients who survive a life-threatening arrhythmia.

A potential further expansion of the role of pacing in heart failure may come with the investigation of the benefit of biventricular pacing in this condition. This concept has developed based on the observation that many patients with heart failure have interventricular conduction defects, which result in dysynchronous activation and relaxation of both ventricles. This would likely compromise systolic and diastolic function and may even contribute to some valvular regurgitation. Biventricular pacing from the right ventricle and the coronary sinus for the left ventricle certainly improves cardiac synchrony. Whether this will result in a meaningful improvement in systolic and/or diastolic function, and indeed in patients' symptoms, requires further study.

Effective structure for the management of heart failure

One of the critical deficiencies in our present approach to heart failure is the lack of an effective management structure for patients with this disease. Like many chronic diseases, such as diabetes mellitus, heart failure requires multidisciplinary care. Unfortunately this approach is not widely available in any jurisdiction and, to my knowledge, is not available at all in Ireland, outside of a pilot effort at St Vincent's University Hospital in Dublin. This approach emphasises patient and next of kin education, emphasising such issues as compliance with therapy, salt restriction, exercise and awareness of the early signs of decompensation. It also provides rapid assessment of patients when not doing well in an effort to avoid hospitalisation. These efforts are often nurse-led and require the development and training of nurse specialists to manage this effort. Other important contributors to this effort include dietitians, social workers, pharmacists, rehabilitation experts and counsellors. Results from centres assessing this approach have shown a reduction in hospitalisation and costs associated with the care of this patient group. Indeed, preliminary data from our centre has shown elimination of early hospital readmission as a result of this mulitidisciplinary approach.

In addition to these services, a multidisciplinary programme for heart failure should incorporate close monitoring of patients at risk for the development of heart failure, as prevention will always be the best approach to this syndrome. In this regard, focusing on survivors of myocardial infarction, people with long-standing hypertension and diabetes mellitus would likely be meaningful and cost-effective.

Summary

These two articles reviewing the subject of heart failure will hopefully provide some background on the present day investigation and management of this syndrome, as well as highlight potential future advances. While there is no doubt that significant advances have been made, it is also clear that many problems and deficiencies still exist. Hopefully, the next decade will bring further improvements to what remains a major cardiovascular and public health problem.

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