EDITORIAL

"THE FAILING HEART" - RECENT ADVANCES IN MEDICAL THERAPY

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Introduction

Congestive heart failure is a common final pathway of ischaemic, hypertensive, valvular and myocardial disease. In the United States of America alone, it has been estimated that about 400,000 people develop congestive heart failure every year. All practising cardiologists in Singapore recognise that heart failure (HF) is one of the most important cardiac problems in this country - a problem which will steadily increase with our rapidly ageing population.

Clinical Evaluation and Investigation

Heart failure may be acute (as in acute myocardial infarction and chordal rupture of the mitral valve) or chronic (as in dilated cardiomyopathy), left sided, right sided or combined and it may be due to systolic dysfunction or less commonly diastolic dysfunction. In every patient presenting with HF, a meticulous search for an underlying aetiology is essential. This is so because if an aetiology is found and particularly if it can be surgically treated (as in mitral stenosis), then the patient may be potentially cured of his HF - for many years at least. Unfortunately however, the great majority of patients presenting with refractory HF will have either end-stage ischaemic heart disease or idiopathic dilated cardiomyopathy, both of which can be surgically treated only with a cardiac transplantation.

As in all other cardiac problems, a 5-step approach is recommended in all patients with HF. Steps 1 to 4 represent history taking, physical examination, chest X-ray and electrocardiography respectively. All of these must be carried out routinely in every patient. Step 5 represents special investigations, which essentially consists of echocardiography, 24 hour ambulatory ECG monitoring when serious cardiac arrhythmias are suspected and exercise stress test/stress myocardial perfusion scintigraphy and coronary angiography when coronary artery disease is considered likely to be present. Of these, echocardiography is by far the single most important investigation and should be performed in almost every patient presenting with congestive heart failure. Two-dimensional echocardiography is an excellent technique for the evaluation of systolic function of the left ventricle. In addition, Doppler echocardiography is valuable for diagnosing left ventricular diastolic dysfunction. Although diastolic dysfunction is today a topical and fashionable subject, it is at present still quite controversial, largely because our knowledge is incomplete and many questions are as yet unanswered.

Pharmacological Therapy

The 4 major groups of drugs which are widely prescribed for congestive HF are (1) diuretics, (2) digitalis glycoside, (3) vasodilators, and (4) ACE inhibitors. When the HF is intractable, multiple drugs are frequently used in combination.

Diuretics are today still the cornerstone in the treatment of HF. They are extremely effective and often produce dramatic results in the improvement of symptoms and the elimination of peripheral oedema. There has so far been no study to determine whether diuretic therapy also reduces mortality. Nevertheless, most cardiologists believe that it is reasonable to assume that they do.

In 1985, the world celebrated the 200th anniversary of William Withering's first account of the successful use of the foxglove in the treatment of dropsy. The great value of digitalis in patients with rapid atrial fibrillation (with or without congestive HF) has never been in doubt. However, whether digitalis is useful or not in HF patients who are in sinus rhythm has been a source of continuing debate in the recent past. I still can remember vividly that in the 1970's, almost all patients with significant HF and in sinus rhythm were routinely given both diuretics and digoxin. To the surprise of everyone, studies in the early 1980's suggested that such patients actually derived no benefit from digitalis. However, more recent studies in the past 5-10 years have shown otherwise - ie digitalis indeed improves symptoms, exercise tolerance and haemodynamics and also reduces the frequency of hospitalisation in HF patients who are in sinus rhythm, especially if the HF is severe. The main issue today is not whether digitalis is effective or not, as it clearly is, but whether it should be used widely and routinely, given that: (1) the results of an ongoing mega study in the United States of America and Canada assessing its impact on mortality are as yet unavailable[1], and (2) that we have today, other excellent drugs like the ACE inhibitors. The other inotropic agents, such as the phosphodiesterase inhibitors, have not fulfilled their initial promise and have a very limited role in long term therapy. Currently, their main indication is for the acute treatment of patients who are awaiting cardiac transplantation or who have suffered temporarily post-operative left ventricular dysfunction after open-heart surgery.

With regard to the vasodilators, a combination of isosorbide and hydralazine was shown in the V-HeFT I (Veterans Heart Failure Trial) study to result in an improvement of symptoms and a slight reduction in mortality compared to placebo therapy. However, there was a high incidence of side effects resulting in a large drop-out of patients taking these two drugs. Furthermore, a subsequent V-HeFT II study comparing the combination of isosorbide and hydralazine vs enalapril found that the enalapril group of patients had a lower mortality[2].

Since time immemorial, it has always been taught to medical students and doctors that one of the major contraindications to the use of beta-blockers is congestive HF. It would therefore appear almost masochistic to even suggest that beta-blockers could be considered as an important form of drug therapy for such patients. And yet in 1975, Waagstein and his colleagues in Sweden showed in a small study that some of their patients with dilated cardiomyopathy and

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congestive HF actually improved with beta-blocker therapy. There is at present a large, ongoing multicentre trial (the Metoprolol Dilated Cardiomyopathy Trial), assessing the efficacy of metoprolol in reducing mortality and the need for cardiac transplantation in a group of patients with severe HF due to idiopathic dilated cardiomyopathy. The results of this trial are awaited with the greatest of interest. It is today generally accepted that some patients, especially those with manifestations of excessive sympathetic activity such as sinus tachycardia without an apparent cause, may indeed derive some benefit from beta-blockers. However, it is also well recognised that HF patients, especially those with severe HF, are a fragile, high risk group and some of them may unpredictably deteriorate catastrophically with the administration of beta-blockers. I have heard of isolated anedoctal accounts from my colleagues in Singapore regarding the beneficial effect of beta-blockers in a few of their patients, but I have never had the courage to try this form of therapy and probably never will.

Perhaps the greatest progress in the drug therapy of HF during the last few years has been with the ACE inhibitors. In 1987, the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS I) showed for the first time that the addition of an ACE inhibitor, enalapril, to pre-existing standard treatment in patients with severe class IV HF resulted in a 40% reduction in mortality at six months[3]. This decrease in mortality was due entirely to a decrease in deaths from progressive HF and not from sudden death. To date, no form of pharmacological therapy (including antiarrhythmic therapy) has been shown to reduce the incidence of sudden death, which accounts for about 40% of the total mortality. Very recently, the treatment arm of the SOLVD (Studies of Left Ventricular Dysfunction) trial showed that this ability to reduce total mortality with enalapril was also extended to patients with milder forms of HF (Class II and III)[4] . In addition, the prevention arm of the SOLVD trial showed that enalapril decreased the risk of developing HF and the need for hospitalization in patients who initially presented with left ventricular dysfunction (EF $\leq$35%) but no symptoms of HF. Most recently, the SAVE (Survival and Ventricular Enlargement) study showed that captopril when administered to patients whose left ventricular ejection fractions were <40%, 3-16 days post-myocardial infarction, reduced the total mortality, the recurrence of acute myocardial infarction and the risk of developing severe HF. Given all these very exciting developments, it is not surprising that many believe the 1990's will indeed belong to the ACE inhibitors, as far as medical therapy of HF is concerned.

Lastly, when the HF is refractory to all forms of medical and pharmacological treatment, cardiac transplantation should be considered as the final option. The results of cardiac transplantation in recent years have greatly improved largely because of the advent of better immunosuppressive drugs.

Conclusion

The last decade and the beginning of this new decade have seen tremendous progress in our understanding and management of HF. With the drugs that are currently available, it is possible not only to dramatically improve symptoms and quality of life, but also to retard the spiralling downward course and to reduce mortality in patients who are suffering from congestive heart failure.

References

1. Yusuf S, Garg R, Held P, Gorlin R. Need for a large randomised trial to evaluate the effects of digitalis on morbidity and mortality in congestive heart failure. J Am Coll Cardiol 1992; 69: 18: 64G-70G.
2. Cohn JN, Johnson G, Ziesche S et al. A comparison of enalapril with hydralazine-isosorbide dinitrate in the treatment of chronic congestive heart failure. N Engl J Med 1991; 325: 303-10.
3. The CONSENSUS Trial Study Group. Effects of enalapril on mortality in severe congestive heart failure: results of the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS). N Engl J Med 1987; 316: 1429-35.
4. Braunwald E. Ace inhibitors - a cornerstone of the treatment of heart failure. N Engl J Med 1991; 325 351-3.