receive treatment according to the standards of the individual health care system.

Clinical results of multicentre trials like PURSUIT help us to guide decisions on whether to institute a new treatment. Economic analysis, like the one presented in this issue, will help us to implement new therapies into our practice. Given the nature of multicentre trials, however, they will never match the real life scenario completely. The final decision on which patient to treat always remains a decision of the physician, based on his knowledge of the evidence, weighed against the specific details of the case, and with some consideration of the economic background.

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References


The value of diuretics in chronic heart failure demonstrated by an implanted haemodynamic monitor

See page 59, doi:10.1053/euhj.2001.2690 for the article to which this Editorial refers

Evidence-based medicine has clearly established that the combination of diuretics, digitalis, ACE inhibitors, and beta-blocking agents improves the prognosis of patients with chronic heart failure and increases their exercise capacity, at least to some extent. There is ample evidence in placebo-controlled double-blind studies that ACE inhibitors and beta-blocking agents are needed for a better life expectancy in mild, moderate and severe heart failure. This may not be true for diuretics, although all physicians when treating their patients are well aware of the great impact of diuresis on symptomatic efficacy in this syndrome. There are no randomized placebo-controlled trials, however, to support this everyday experience. Several studies indeed have shown that ACE inhibitors without diuretics fail to treat patients with congestion[1–3]. Because of this, most cardiologists include diuretics in their therapeutic regimen, even in the absence of oedema. Such colleagues are probably impressed by the haemodynamic effects of diuretics (see Table 1), which may result, because of decreased preload and
afterload, in an augmented cardiac index and other load-dependent indices of cardiac performance[4]. Recent investigations have shown that stroke volume may even increase despite a reduction in preload after chronic treatment with diuretics[4]. The all too simple explanation of Starling’s law, consistently demonstrating an increased cardiac output with higher left ventricular end-diastolic pressure, does not apply to the failing heart. Several investigators have convincingly shown that reduced wall stress, after diuretic-induced reduction of preload and afterload, may chronically lead to an increased stroke volume and probably also to decreased concentrations of circulating catecholamines and thereby to further reduction in vasoconstriction.

Effects and side effects of diuretics

It has recently been demonstrated that diuretics are very potent inhibitors of cardiac hypertrophy. They seem to be even more powerful than ACE inhibitors in this respect[5]. On the other hand, the danger of diuresis in non-congestive patients must also be emphasized: electrolyte disturbances with hypokalaemia and sudden death, hypotension and the possibility of thromboembolic events[6]. Therefore, we teach our medical students to test for the lowest effective diuretic dose in every patient. Some of us even treat patients with chronic heart failure in mild-to-moderate classes according to the New York Heart Association, only with ACE inhibitors and beta-blocking agents. In this respect, the paper by Braunschweig et al.[7] in this issue is of great importance for the evaluation of diuretic treatment. It shows that the withdrawal of loop diuretics in patients with stable chronic heart failure resulted in a deterioration of haemodynamic parameters, especially increased right ventricular pressures and heart rate. Body weight increased and heart failure worsened. After reinstitution of diuretics, patients improved. Similar findings have been reported with solely clinical methods in elderly stable heart failure patients in general practice[8].

This paper also clearly demonstrates what our teachers kept telling us 30 years ago about the most effective way of treating heart failure. By use of initially high doses of loop diuretics one should determine the optimal ‘dry weight’ of the patient and then tailor the diuretic dose according to the weight of the patient, which should be kept constant within narrow limits (∼ 1 kg). Make sure the patient weighs himself, takes his blood pressure and pulse rate daily, and make sure you see verification of this at every visit. After 30 years of treating chronic heart failure patients, I was very pleased to see that despite the sophisticated methods described in the paper by Braunschweig and colleagues, this old advice of my teacher is still very relevant, supported by new scientific methods. It may well be that for ethical reasons there will be no randomized placebo-controlled test with diuretics to find out whether they improve prognosis. I myself am certain that diuretics are the basis of heart failure therapy. Without diuretics, I would not want to be a cardiologist.

Future uses of an implanted haemodynamic monitor

The continuous recording of right heart pressure parameters and heart rate by an implanted haemodynamic monitor in CHF will probably be of great value in the future. Apart from the question about the proper use of diuretics in stable heart failure patients, it can be used to evaluate new drugs, physical exercise or bed rest and also may serve to optimize fluid intake. We all know that very often the acute positive effects of some agents (for incidence PDE-inhibitors) do not result in beneficial chronic effects in this malignant syndrome. The implantable haemodynamic monitor in the future might thus serve to answer at least some of our questions on the optimal long-term treatment of this severe disease. The authors should be congratulated for their careful clinical investigation, demonstrating the value of chronic diuretic treatment in stable heart failure.

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References

Interleukin-6: a neurohumoral predictor of prognosis in patients with heart failure: light and shadow

See page 70, doi:10.1053/euhj.2001.2780 for the article to which this Editorial refers

The pathophysiology and treatment of heart failure has changed in the last 50 years. Neurohormonal activation, for instance, is no longer considered to compensate for the failing heart; instead, it is supposed to contribute to the progression of the syndrome. Accordingly, beta-blockers, ACE inhibitors and antialdosterone compounds, all counteracting the effect of the various neurohormones, have substituted the classical treatment with positive inotropic agents, vasodilators and diuretics — that mimic or enhance the neurohormonal response.

Cardiologists have tried to gain prospective and diagnostic information by measuring the different hormones in the peripheral blood. Such a promising approach, particularly for brain and atrial natriuretic peptide, and chromogranin A[1,2], however, has not yet become daily routine, for a number of practical and cultural reasons. In practice, the majority of the assays are not available in every hospital, while for some hormones the proper handling of the sample is complex. Culturally, cardiologists are reluctant to rely on ‘a number’ obtained in ‘a laboratory’; they much prefer ‘the numbers’ such as ejection fraction (obtained with echocardiography or radionuclear ventriculography) or peak VO₂ (obtained with exercise testing). This attitude is understandable, but not necessarily correct. The two approaches, i.e. laboratory vs functional tests, are not mutually exclusive but do provide different information and might increase the cost/benefit ratio. Thus, the clinical diagnosis of heart failure could, in the not too distant future, be confirmed or denied by a simple and inexpensive neuroendocrine assay, while the more expensive cardiological tests could be reserved for patients who really need them. Equally, it may be possible to choose the most appropriate drug and dosing regime based on the reduction of serum levels of some neuroendocrine markers[3]. Also the correct timing for cardiac transplantation could be ‘driven’ by neuroendocrine parameters. This latter subject is addressed in depth in the excellent article by Kell et al, in the current issue[4].

There are several points raised in this work that merit comment and consideration.

1. The population studied. Correctly, only consecutive patients with heart failure in NYHA class III are included in the study: this is the population that needs to be stratified for short- and long-term life expectancy, in order to be considered for timely heart transplantation. The value of prognostic markers in patients with heart failure in NYHA I, II and IV classes is limited in terms of clinical decision-making as those patients are not candidates for heart transplantation (NYHA I and II) or should be transplanted (NYHA IV).

2. The markers considered. Emphasis has been given to neurohumoral vs neurohormonal activation. It...