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Severity of heart failure and dosage of angiotensin converting enzyme inhibitors

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Large studies have shown improved survival of patients with heart failure[1,2] and of those recovering from acute myocardial infarction[3,4] after treatment with high doses of angiotensin converting enzyme inhibitors. We studied the usage of angiotensin converting enzyme inhibitors for chronic heart failure in a tertiary referral centre to investigate the relation between the regimen used and patient variables and how this related to the dosages used in the published mortality trials.

Patients, methods, and results

We examined the drug regimens of 157 patients seen by two consultants in a specialist clinic for chronic heart failure. Chronic heart failure was diagnosed from the finding of impaired left ventricular function on echocardiography, radionuclide ventriculography, or cardiac catheterisation. All patients underwent exercise testing with metabolic gas exchange measurements. All had been reviewed at least once while taking their current angiotensin converting enzyme inhibitor and had had no change in drug treatment in the previous six weeks.

The dose of angiotensin converting enzyme inhibitor was standardised to the lowest target dose shown to improve mortality: captopril 25 mg twice daily,[2] enalapril 10 mg twice daily,[1] lisinopril 10 mg daily,[4] and ramipril 5 mg twice daily.[3] We also chose a clinical scale of equivalence based on drug datasheets: 12·5 mg captopril three times a day was assumed to be equivalent to 5 mg enalapril twice daily and to 5 mg lisinopril once daily.

Forty three patients were not taking any angiotensin converting enzyme inhibitor; 47 were taking captopril, 47 enalapril, 17 lisinopril, one ramipril, one fosinopril, and one perindopril (table). The diagnosis was dilated cardiomyopathy in 66 patients and ischaemic heart disease in 91. Diagnosis was not related to angiotensin converting enzyme inhibitor usage, and 85 patients were taking doses lower than the optimum suggested by the results of survival trials. Captopril was most likely to be given in dosages associated with improved mortality: 13 out of 47 were taking it twice daily and the remaining 34 three times daily. Thirty three of the 47 patients taking enalapril were taking the drug once daily.

There was no difference between the groups of patients in usage of alternative vasodilators. Patients taking an angiotensin converting enzyme inhibitor had more severe heart failure as judged by mean left ventricular ejection fraction (26·0% (SD 12·7%) *v* 34·6% (18·6%), 95% confidence interval for difference 5·84 to 11·46; P<0·01) and daily dosage of diuretic (85·6 (70·6) *v* 39·1 (36·2) mg frusemide equivalent, 41·4 to 51·7; P<0·001). Patients taking angiotensin converting enzyme inhibitor had lower mean serum sodium concentrations (138·2 (1·8) *v* 139·5 (2·7) mmol/l, −1·07 to −1·61; P=0·03) and higher mean concentrations of urea (8·35 (3·56) *v* 6·10 (1·91) mmol/l, 1·96 to 2·55; P<0·001) and creatine (121·06 (39·49) *v* 98·82 (17·39) μmol/l, 19·03 to 25·44; P<0·001). There was no correlation between

Dosage schedules for the three most commonly prescribed angiotensin converting enzyme inhibitors

Regimen	Dose (mg)	No of times daily	Daily dosage: Total (mg)	Daily dosage: % Of optimum*
Captopril 6·25-50 mg thrice daily	23·0 (13·1)	2·7 (0·45)	61·6 (35·3)	123·1 (70·7)
Enalapril 2·5 mg once daily-40 mg twice daily	10·5 (7·6)	1·3 (0·5)	13·2 (11·9)	66·2 (59·4)
Lisinopril 2·5-20 mg once daily	7·8 (4·4)	1	7·8 (4·4)	77·8 (43·9)

*To improve mortality.

the dosage of angiotensin converting enzyme inhibitor and ejection fraction, blood pressure, peak oxygen consumption, or serum concentrations of urea and electrolytes. There was a good correlation between the two scales of angiotensin converting enzyme inhibition (r=0·86, P<0·001).

Comment

Angiotensin converting enzyme inhibition improves survival of patients with chronic heart failure. As yet, a minority of patients are treated with angiotensin converting enzyme inhibitors.[5] Two trials to determine the relation between dose and benefit (NETWORK (studying enalapril) and assessment of treatment with lisinopril and survival (ATLAS)) are in progress. We found that even in hospital based care of chronic heart failure a wide range of different angiotensin converting enzyme inhibitor regimens is used. Clinical variables seem not to influence the dosage used. Only those patients taking captopril were likely to be receiving the drug in the range associated with a beneficial effect on mortality.

Until the results of studies comparing high and low doses of angiotensin converting enzyme inhibitors are known, the aim of treatment should be to reach a dosage associated with improved mortality.

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Improving notification rates for tuberculosis

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Notification of cases of tuberculosis is a legal requirement to permit calculation of accurate incidence figures and efficient contact tracing. We previously found considerable undernotification of cases at our hospitals.[1] To improve the percentage of cases notified several changes have been instigated. All consultants are encouraged to refer cases of tuberculosis to a chest physician; copies of reports of smears or cultures positive for *Mycobacterium tuberculosis* and histology suggestive of tuberculosis are sent to a consultant in communicable disease control (GD); and the pharmacy informs the consultant of patients prescribed isoniazid. When unnotified cases are identified during these procedures the consultant in communicable disease control contacts the consultant in charge of the patient as a reminder to notify.

We report an audit of the percentage notification rates of cases of tuberculosis diagnosed at our hospitals two years after making these changes.

Patients, methods, and results

As in our previous study,[1] we identified retrospectively all cases of tuberculosis diagnosed from 1 January 1992 to 31 December 1993 at the Royal London and London Chest Hospitals in patients aged 16 years or over. We identified cases from statutory notifications; microbiology reports of smears or cultures positive for *M tuberculosis*; histology reports suggestive of tuberculosis; hospital activity data; necropsy and coroners' reports; and pharmacy lists of patients prescribed antituberculous drugs. Notified cases were identified from the notification records kept by the consultant in communicable disease control. Tuberculosis was confirmed by review of notes in cases identified from histology reports, those with a clinical diagnosis alone, and those that had not been notified. We compared the data with those from our original study of notifications for 1985-9 using χ^2 tests for contingency tables and 95% confidence intervals.

During 1992-3, 252 new cases of adult tuberculosis were diagnosed. Of these, 235 (93%) were notified, an increase of 20% (95% confidence interval 15% to 25%) over the percentage notified in the 1985-9 study (73%). Only one case with a sputum smear positive for acid fast bacilli was not notified. The table shows the improvement in notification rates according to the specialty of the physician in charge of the case.

The mean age of patients was 46 years (range 16 to 96), and 149 were men. The proportion of African patients increased from 15 out of 580 (3%) in the original study to 29 out of 252 (12%), 18 of them being Somalis. Patients from the Indian subcontinent remained the commonest ethnic group affected (108/252 (43%)). Fourteen patients (5·5%) were positive for HIV infection in the 1992-3 cohort compared with four patients (0·7%) in our original study.

Notification rates according to specialty of consultant in charge of patients

	1985-9			1992-3		
Specialty	% Notified	No seen	No notified	% Notified	No seen	No notified
Chest medicine	82	377	308	95	177	168
Other medical specialty	60	112	67	91	46	42
Surgical specialty	62	39	24	88	24	21
Other/unknown	52	52	27	80	5	4

Comment

Tuberculosis is undernotified,[1,2] which may hinder disease control and makes accurate assessment of incidence difficult. Since the introduction of new mechanisms for notifying cases of tuberculosis we have found that a fifth more cases were notified from our hospitals, which are in an area of high incidence. Cases with positive sputum smears are the main risk to public health,[3,4] and in 1992-3 only one such case was not notified.

The local referral pattern of patients with tuberculosis has not changed enough to affect notification statistics. The recent resurgence of interest in tuberculosis may have independently made notification more likely. The large improvement in the percentage of cases notified suggests, however, that introducing systems of cross checking pathology reports, prescriptions for antituberculous drugs, and notifications by a consultant in communicable disease control is at least partially responsible. If accurate information on tuberculosis is to be available similar systems should be initiated nationally, especially for hospitals in areas where the incidence of the disease is high.

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