SCIENTIFIC LETTER

The impact of baseline left ventricular size and mitral regurgitation on reverse left ventricular remodelling in response to carvedilol: size doesn't matter

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β Blockers have been shown to reverse left ventricular remodelling (LVR) and to reduce the severity of functional mitral regurgitation (FMR) in patients with chronic systolic heart failure.^{1–4} It is unclear, however, to what extent the beneficial effects of β blockers on LVR or FMR are influenced by the severity of left ventricular dilatation or FMR at the time of commencement of β blocker treatment. We retrospectively analysed serial echocardiograms taken at baseline and two years after commencement of carvedilol in 257 patients with chronic heart failure caused by left ventricular systolic dysfunction.

PATIENTS AND METHODS

The study population was drawn from a total population of 476 consecutive patients who were treated with carvedilol for this indication. Patients were excluded from the echocardiographic analysis for the following reasons: death within two years of commencing the medication ($n = 35$); withdrawal from carvedilol because of non-fatal adverse events ($n = 63$); cardiac surgery (before or after commencement of carvedilol) that may have influenced the left ventricular dimensions and the degree of FMR ($n = 80$); technically unsatisfactory echocardiograms at baseline or follow up ($n = 41$).

Echocardiographic assessment of left ventricular function and FMR was performed with a Hewlett Packard Sonos 5500 ultrasound system with 2.5 and 3.5 MHz transducers. Left ventricular end diastolic and systolic dimensions (LVEDD and LVESD) were determined from standard M mode measurements. Left ventricular dimensions were normalised for body size by dividing the LVEDD and LVESD by the body surface area. Left ventricular fractional shortening (LVFS) was calculated according to the formula: $LVFS = (LVEDD - LVESD) / LVEDD$. Colour flow Doppler imaging was used to determine the presence and severity of FMR. The severity of FMR was graded semi-quantitatively as follows: 0–nil; 1–trivial; 2–mild; 3–mild to moderate; 4–moderate; 5–moderate to severe; and 6–severe. In order to simplify statistical analysis patients were then divided into three subgroups based on the grade of FMR at baseline: group A (FMR grades 0–1); group B (FMR grades 2–3); and group C (FMR grades 4–6). Unless otherwise stated data are presented as mean and standard error of the mean. A probability value of $p < 0.05$ was considered significant.

RESULTS

The average maintenance dose of carvedilol at two years was 42 (23) mg per day. After two years of treatment with carvedilol there were reductions in LVEDD/ m^2 and LVESD/ m^2 by 1.6 (0.3) mm and 2.6 (0.3) mm, respectively and an increase in LVFS by 3.8% (0.5%). All changes were highly significant compared with baseline ($p < 0.0001$, analysis of variance (ANOVA) analysis). Simple regression analyses

Figure 1 Regression plots of changes in LVEDD/ m^2 and LVFS after two years of treatment with carvedilol (dependent variables) against baseline LVEDD/ m^2 (independent variable).

showed highly significant relationships between the changes in LVEDD and LVESD and their baseline values (LVEDD/ m^2 ν baseline LVEDD/ m^2 , $p < 0.007$, and LVESD/ m^2 ν baseline LVESD/ m^2 , $p < 0.001$). A scatter plot of changes in LVEDD/ m^2 (dependent variable) against baseline LVEDD/ m^2 (independent variable) is shown in the upper panel of fig 1. The improvement in LVFS was independent of the baseline LVEDD/ m^2 ($p = 0.28$, lower panel of fig 1).

At baseline, 101 (39%) patients were in group A, 112 (44%) patients were in group B, and 44 (17%) patients were in group C. The extent of reverse LVR as reflected by changes in LVEDD/ m^2 , LVESD/ m^2 , and LVFS was not significantly affected by the grade of FMR at baseline. The mean reduction in LVEDD/ m^2 at two years was identical in all three subgroups (1.6 mm, $p = 0.99$). The mean reduction in LVESD/ m^2 was 2.2 (0.4) mm in group A, 2.9 (0.6) mm in

Abbreviations: FMR, functional mitral regurgitation; LVEDD, left ventricular end diastolic dimension; LVESD, left ventricular end systolic dimensions; LVFS, left ventricular fractional shortening; LVR, left ventricular remodelling

group B, and 2.7 (0.9) mm in group C ($p = 0.63$). Treatment with carvedilol was associated with a significant decrease in severity of FMR. After 24 months, the grade of FMR had decreased in 28% of patients, increased in 16%, and was unchanged in 56% of patients; 136 (52%) patients were in group A, 87 (35%) were in group B, and 34 (13%) were in group C ($p < 0.001$ v baseline).

DISCUSSION

Several investigators have reported that chronic treatment with β blockers results in reverse LVR in patients with chronic systolic heart failure.^{1,2} The results of the present study are highly consistent with these previous reports with regard to the magnitude of the changes in left ventricular dimensions and systolic function observed. The major findings of the present study were that the extent of reverse LVR and improvement in systolic function were not attenuated as the baseline left ventricular size increased. Indeed, the extent of LVR (as reflected by reductions in LVEDD/m² and LVESD/m²) was significantly related to the degree of left ventricular dilatation at baseline. Some caution is required in interpreting this finding however, as there is an inherent selection bias in the patients included in this analysis. Left ventricular enlargement is an independent risk factor for mortality in patients with systolic left ventricular dysfunction.⁵ Hence the exclusion of patients who died or did not tolerate carvedilol prior to the two year follow up would have been expected to bias the results towards those who responded favourably to carvedilol.

Another major finding of the present study was that reverse LVR in response to carvedilol occurred independently of the presence or severity of FMR at baseline. Importantly, the presence of moderate to severe baseline FMR did not limit reverse LVR. Indeed, the severity of FMR decreased in the study population over the two year observation period, with greatest extent of reverse LVR observed in patients

whose FMR became less severe (data not shown). The findings of the present study are consistent with those of others in relation to the effect of carvedilol on the severity of FMR,^{3,4} and demonstrate that the benefit of carvedilol on FMR is maintained for at least two years.

In conclusion, the extent of reverse LVR in patients with chronic systolic heart failure is inversely related to the degree of left ventricular dilatation and dysfunction at baseline and is independent of the presence or severity of FMR. In addition, chronic treatment with carvedilol is associated with a decrease in severity of FMR.

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REFERENCES

- 1 **Australia-New Zealand Heart Failure Research Collaborative Group.** Effects of carvedilol, a vasodilator-beta-blocker, in patients with congestive heart failure due to ischemic heart disease. *Circulation* 1995;**92**:212-8.
- 2 **Groening BA, Nilsson JC, Sondergaard L, et al.** Antiremodeling effects on the left ventricle during beta-blockade with metoprolol in the treatment of chronic heart failure. *J Am Coll Cardiol* 2000;**36**:2072-80.
- 3 **Lowes BD, Gill EA, Abraham WT, et al.** Effects of carvedilol on left ventricular mass, chamber geometry, and mitral regurgitation in chronic heart failure. *Am J Cardiol* 1999;**83**:1201-5.
- 4 **Capomolla S, Febo O, Gnemmi M, et al.** Beta-blockade therapy in chronic heart failure: diastolic function and mitral regurgitation improvement by carvedilol. *Am Heart J* 2000;**139**:596-608.
- 5 **White HD, Norris RM, Brown MA, et al.** Left ventricular end-systolic volume as the major determinant of survival after recovery from myocardial infarction. *Circulation* 1987;**76**:44-51.

IMAGES IN CARDIOLOGY

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Plastic bronchitis after Fontan operation: treatment with stent fenestration of the Fontan circuit

Plastic bronchitis is an extremely rare and potentially fatal complication after Fontan operation. It is characterised by expectoration of long, branching bronchial casts and can manifest with recurrent life threatening airway obstruction. The pathogenesis of this condition is not entirely clear. Contributing roles of elevated pulmonary venous pressure, increased central venous pressure, and endobronchial lymphatic leakage have been proposed. Various treatment modalities including thoracic duct ligation and cardiac transplantation have been proposed.

A 3.5 year old boy was admitted with acute respiratory distress, four weeks following Fontan operation for hypoplastic left heart syndrome. On admission he expectorated three large pearly white bronchial casts (left panel) with immediate symptomatic improvement. There was no history of atopy, allergy, or asthma. Total and differential white cell count was normal. Chest radiograph showed bilateral perihilar air space shadowing, no focal lung lesions, normal heart size, and no pleural effusion. Bronchial casts were composed of proteinaceous and mucoid material with a few lymphocytes. There was no evidence of bacterial viral or fungal infection, and sweat test was negative.

Treatment with inhaled salbutamol and steroids, nebulised N-acetylcysteine, and antibiotics had no beneficial effect. He needed two emergency readmissions with bronchoscopic removal of a cast. Cardiac catheter at this stage confirmed unobstructed Fontan pathways and raised central venous pressure (15 mm Hg) with an acceptable transpulmonary gradient (5 mm Hg). Percutaneous creation of a stent fenestration in the Fontan circuit resulted in full symptomatic recovery from plastic bronchitis. At three years follow up he has no recurrence of respiratory symptoms. He remains cyanosed due to a persistent right-to-left shunt via the stent fenestration.

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