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The efficacy and safety of chronic oral administration of xamoterol to patients with severe heart failure treated with ACE inhibitors

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Xamoterol 200 mg twice daily was given for 2 months to nine patients with severe heart failure already being treated with angiotensin converting enzyme (ACE) inhibitors. Left ventricular end-diastolic pressure fell from 28 to 13 mmHg and end-systolic volume fell from 115 to 106 ml m^{-2}; indices of contractility improved and ejection fraction rose from 33 to 38%. The time constant of ventricular relaxation, T_1, improved from 62 to 44 ms. Exercise tolerance improved. Thus, in this group of patients with severe heart failure, xamoterol produced benefits in systolic and diastolic function. There were no adverse effects.

Keywords xamoterol heart failure ACE inhibitors

Introduction

Administration of xamoterol has been shown to improve haemodynamics, effort tolerance and symptoms in patients with mild to moderate heart failure, whether or not they are concurrently receiving diuretics (The German and Austrian Xamoterol Study Group, 1988). Acute haemodynamic studies have indicated that in some patients with more severe heart failure, intravenous administration of xamoterol has produced negative inotropic and chronotropic effects, generally without clinical deterioration. This study investigates the effects of oral administration of xamoterol in patients with severe heart failure.

Methods

Patients

Seven male and two female patients of average age 58 years (range 48–68) with coronary artery disease and previous myocardial infarction were entered in the study. They were in New York Heart Association (NYHA) Class III heart failure and all had angina pectoris. Oedema was present in eight of the nine patients. Mean duration of heart failure was 11 months (s.d. ± 8). All other treatments were continued, and this included diuretics (four patients), calcium antagonists (five patients), and nitrates (nine patients). All patients remained in Class III heart failure despite administration of ACE inhibitors (captopril 75 mg, three patients; enalapril 10–20 mg, six patients).

Protocol

The trial was an open, non-randomised study with oral xamoterol 200 mg twice daily for a 2 month period. All other therapy, including ACE inhibitors, was continued throughout the study. Main assessments were performed at the beginning of the study and again at the end of the 2 month period. A symptom-limited bicycle exercise test was used to assess exercise capacity, and left ventricular catheterisation was employed for measurements of heart rate, aortic and left ventricular pressures and an angiogram performed in the right anterior oblique 30° position. Indices of the inotropic state used were (+) dP/dt_{max} and $(dP/dt)/DP_{40}$. The state of relaxation was assessed by the (−) dP/dt_{max} and T_1.

Table 1 Haemodynamics (mean ± s.e. mean, $n = 9$)

	Baseline therapy	*After 2 months on xamoterol*	P *value*
Heart rate (beats min^{-1})	83 ± 4	86 ± 4	NS
Mean aortic pressure (mmHg)	92 ± 5	90 ± 5	NS
Left ventricular end-diastolic pressure (mmHg)	28 ± 4	13 ± 2	$P < 0.002$
T_1 (ms)	62 ± 2	44 ± 2	$P < 0.001$
End-diastolic volume index (ml m^{-2})	167 ± 20	164 ± 21	NS
End-systolic volume index (ml m^{-2})	115 ± 19	106 ± 19	$P < 0.015$
Ejection fraction (%)	33 ± 3	38 ± 4	$P < 0.08$
dP/dt_{max} (mmHg s^{-1})	1221 ± 109	1377 ± 123	$P < 0.05$
$(dP/dt)/DP_{40}$ ($l\ s^{-1}$)	16.5 ± 1.9	24.1 ± 2.7	$P < 0.002$

Results

Table 1 shows the results obtained at baseline and after 2 months. Neither resting heart rate nor mean aortic pressure changed over the study period. Left ventricular end-diastolic pressure fell from 28 to 13 mmHg and T_1 was reduced from 62 to 44 ms. End-diastolic volume index was unchanged, but end-systolic volume index fell from 115 to 106 ml m^{-2}. Ejection fraction rose from 33 to 38% and the indices of contractility improved significantly on xamoterol treatment. Exercise capacity increased on xamoterol (Figure 1) and the heart rate at maximum capacity was lower than on placebo.

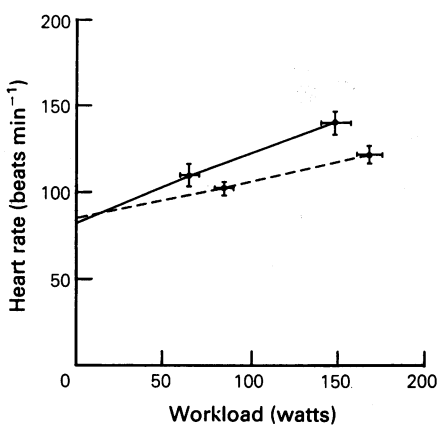

Figure 1 Exercise capacity (mean ± s.e. mean, $n = 8$). ●——● baseline therapy, ●-----● + xamoterol.

Conclusion

The study demonstrates that the chronic oral administration of xamoterol 200 mg twice daily in patients with severe heart failure due to ischaemic heart disease improves both systolic and diastolic function and exercise capacity. Because this study was not double-blind and placebo-controlled, the conclusions must therefore be viewed with this in mind. There were no adverse effects.

Reference

The German and Austrian Xamoterol Study Group. (1988). Double-blind placebo-controlled comparison of digoxin and xamoterol in chronic heart failure. *Lancet*, **i**, 489–493.