QUANTIFICATION OF EXERCISE TOLERANCE IN CONGESTIVE HEART FAILURE AND ROLE OF ACE INHIBITORS

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ABSTRACT

A prospective randomised controlled trial with captopril/enalapril was carried out on 25 patients with congestive heart failure (CHF) of various aetiologies in NYHA Class II & III to study the effect of Ace inhibitors on exercise tolerance. The control group (Gp-A) comprising of 12 patients received conventional treatment (digitalis and diuretics) and the test group (Gp-B) with 13 patients were in addition given captopril/enalapril as tolerated. They were followed up for a mean period of 101.6±50.6 days (approx 3 months). Ten patients from each group could complete the study. The exercise testing was done on treadmill using a suitable protocol and end-points, at the beginning and end of study. None of the clinical and noninvasive parameters showed significant difference, however the mean exercise duration in Group A improved from 7.84±3.34 to 9.2 ±3.16 minute ($P < 0.05$) and in Group B increased from 7.91±4.6 to 10. 92±4.66 minute ($p < 0.001$). On comparing the benefits of the two groups the difference was statistically significant ($P < 0.05$). It is concluded that Ace inhibitor improves the exercise tolerance in CHF and the benefit is evident despite any improvement in clinical and noninvasive indices of left ventricular function.

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KEY WORDS : Ace-inhibitor; Exercise capacity; Heart failure.

Introduction

Various attempts in the management of congestive heart failure (CHF) are aimed to improve the overall functional status with amelioration of signs and symptoms, removal of precipitating factors and treatment of underlying cause. For long digitalis and diuretics have been the mainstay of therapy. In recent years vasodilators have established an important place in the management. Ace-inhibitors are unique among the available vasodilators in having a salutary effect on both ventricular preload and afterload. They also improve renal blood flow which facilitates diuresis.

Quantification of effort tolerance by exercise testing in CHF has proved useful in evaluation of baseline status as well as the result of intervention [1]. Safety of graded symptom-limited exercise test in patients with stable CHF is established [2]. various trials on Ace-inhibitors intervention in CHF have shown improvement in exercise capacity [4,5]. However, studies done on Indian population are not only scant, the method of assessing efficacy is not exercise-based [7-9]. As the major aim of drug therapy for CHF is to improve patients's ability to withstand effort, an objective measure of exercise capacity would be more precise. This study is aimed to objectively assess the

benefit of Ace-inhibitor (captopril/enalapril in improving the functional capacity of patients with CHF in our population.

Material and Methods

The study was conducted on 25 patients of CHF of either sex being followed up in the out-patient department of cardiology. Patients of following categories were excluded: (i) Who are unable to perform exercise on treadmill-eg. motor weakness, peripheral vascular disease. (ii) Where it was considered unphysiological and unsafe-recent myocardial infarction within 6 months, frequent angina, recurrent ventricular tachycardia. (iii) With mechanical obstruction or restriction to blood flow-Valvular heart disease, Hypertrophic cardiomyopathy and Constrictive pericarditis. (iv) Where dyspnoea is not specific for cardiac limitation-primary lung disease, and (v) Patients on permanent pacemaker.

The diagnosis was established on the basis of clinical signs and symptoms. Echocardiography helped in confirming the aetiologies- ischaemic heart disease (IHD), hypertensive heart disease (HHD), dilated cardiomyopathy (DCM). They were stabilised on optimum doses of digitalis and diuretics along with treatment for underlying cause. A baseline record of NYHA class, clinical parameters (heart rate, blood pressure, jugular venous pressure, liver size), ECG, cardio-thoracic ratio (Xray chest) and echocardiographic measurements of ejection fraction (EF), left ventricular diameter (LVD), end-point septal separation (EPSS) were maintained.

After full familiarisation with the protocol (Manual (Table 1)), the treadmill exercise time was determined for each patient using the end-point of breathlessness and fatigue or inability to continue further. They were then randomly allocated in two groups - 'A' & 'B'. Patients of Group -A were used as control and Group-B were

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given Ace inhibitor (captopril/enalapril). They were given captopril in the doses of 6.25 mg TDS/Enalapril 2.5 mg BD to start with, and gradually built up to the maximum tolerated, not exceeding the maximum recommended doses. Background therapy with digoxin and diuretics were continued in both the groups and patients were followed up. At the end of study, repeat assessment of all the parameters was done including the exercise duration on treadmill. The initial and final observation data were compared statistically using Students T Test (paired).

TABLE 1
Treadmill exercise testing
Manual protocol

Stage	Duration	Speed	Grade
I	0-2 min	1 mph	0%
II	2 - 4 min	1.5 mph	0%
III	4 - 6 min	2.0 mph	0%
IV	6 - 8 min	2.5 mph	0%
V	8 - 10 min	2.5 mph	2.5%
VI	10 - 12 min	2.5 mph	5%
VII	12 - 14 min	2.5 mph	7.5%
VIII	14 - 16 min	2.5 mph	10%
IX	16 - 18 min	2.5 mph	12.5%

Results

The patients' characteristics in the two groups are summarised in Table-2. Follow up could be completed in 20 out of 25 patients. Of the 5 patients, 3 failed to report, one died of pulmonary thromboembolism (Gp-A), one patient suffered with intractable ventricular tachycardia and was excluded (Gp-B). The maximum tolerated dose of captopril was 25 mg TDS whereas for enalapril, it was 10mg BD. Other parameters were assessed as follows:

TABLE 2
Patients characteristics

	GP 'a'	GP 'B'
No of patients	10 (50%)	10 (50%)
Sex		
Male	7 (70%)	5 (50%)
Female	3 (30%)	5 (50%)
Age (years)		
Range	31 - 70	29 - 74
Mean $\pm$ SD	59.7 $\pm$ 11.7	50.1 $\pm$ 13.3
Causes of HF		
IHD	6 (60%)	6 (60%)
HTN	2 (20%)	2 (20%)
DCM	2 (20%)	2 (20%)
Duration of HF (months)		
Range	0.5 - 36	1 - 36
Mean $\pm$ SD	10.7 $\pm$ 11.7	10.7 $\pm$ 11.2
Period of follow up (days)		
Range	62 - 160	35 - 270
Mean $\pm$ SD	93.8 $\pm$ 31.8	109.4 $\pm$ 65.4

NYHA Class:-At the entry Gp-A had 7 patients in class II and 3 in class III (Mean 2.33 $\pm$ 0.48), at the end 1 attained class I, 2 improved to class II and 1 remained class III (Mean 1.9 $\pm$ 0.56). This improvement of 17.39% is not significant.

In Gp-B 4 were in class III, 6 in class II (Mean 2.4 $\pm$ 0.51) initially, later 3 improved from class III to II and 4 attained class I

(Mean 1.7 $\pm$ 0.67). This improvement of 25% is statistically significant ($p < 0.05$), but in comparison to Gp-A the benefit is not significant.

CLINICAL PARAMETERS : As shown in Table 3 the mean value of the clinical parameters-heart rate, blood pressure, pulse pressure, weight, JVP (height), and liver size between initial and final record do not show any benefit except for improvement in heart rate in both the groups.

CT RATIO, LVEF & LVID:-As shown in Table 3 these values did not show significant change improvement between initial and final observation in either group.

TABLE 3
Clinical and noninvasive lab parameters in the two groups of patients

	Group A		Group B	
	Initial	Later	Initial	Later
HR (bpm)				
Range	64-106	64-100	70-106	68-100
Mean $\pm$ SD	88.8 $\pm$ 16.38	81.8 $\pm$ 12.04	95.8 $\pm$ 9.68	87.2 $\pm$ 12.22
	(p < 0.05)		(p < 0.05)	
Sys BP (mmHg)				
Range	100-170	90 - 150	100 - 156	96 - 150
Mean $\pm$ SD	126 $\pm$ 24.12	128 $\pm$ 12.69	129 $\pm$ 17.55	127.6 $\pm$ 14.9
Dia BP (mmHg)				
Range	70 - 100	70 - 90	70 - 100	70 - 90
Mean $\pm$ SD	82.6 $\pm$ 9.7	83.2 $\pm$ 7.6	87.6 $\pm$ 10.94	83.4 $\pm$ 6.73
	NS		NS	
Pulse Pr (mmHg)				
Range	20 - 80	20 - 64	30 - 60	24 - 60
Mean $\pm$ SD	44.4 $\pm$ 18.41	40.6 $\pm$ 16.4	45.6 $\pm$ 12.21	45.2 $\pm$ 12.51
	NS		NS	
Wt. (kgs)				
Range	51 - 63	51 - 64	40 - 82	40 - 76
Mean $\pm$ SD	57.35 $\pm$ 5.14	56.95 $\pm$ 5.17	60.35 $\pm$ 14.8	59.1 $\pm$ 13.9
	NS		NS	
JVP (cm)				
Range	0 - 10	0 - 5	0 - 8	0 - 6
Mean $\pm$ SD	3.4 $\pm$ 3.5	1.25 $\pm$ 1.9	2.25 $\pm$ 2.26	1.3 $\pm$ 2.0
	NS		NS	
Liver size (cm)				
Range	0 - 5	0 - 5	0 - 5	0 - 5
Mean $\pm$ SD	2.6 $\pm$ 1.5	1.7 $\pm$ 1.56	2.2 $\pm$ 1.47	1.62 $\pm$ 1.5
	NS		NS	
CT ratio				
Range	0.48 - 0.7	0.47 - 0.68	0.42 - 0.68	0.43 - 0.64
Mean $\pm$ SD	0.54 $\pm$ 0.06	0.53 $\pm$ 0.06	0.55 $\pm$ 0.07	0.53 $\pm$ 0.06
	NS		NS	
LVID (cm)				
Range	4.7 - 7.4	4.8 - 7.25	5.42 - 7.64	5.4 - 7.32
Mean $\pm$ SD	5.99 $\pm$ 0.94	6.11 $\pm$ 0.88	6.27 $\pm$ 0.7	6.21 $\pm$ 0.62
	NS		NS	
LVEF (%)				
Range	24 - 46	26 - 50	21 - 43	24 - 49
Mean $\pm$ SD	35.4 $\pm$ 7.63	36 $\pm$ 8.43	30.9 $\pm$ 10.19	33.8 $\pm$ 8.95
	NS		NS	

NS - not significant

EXERCISE DURATION : In Gp-A, mean duration of exercise at the initial testing was 7.74 $\pm$ 2.4 (range 4.23-14.16) minutes, which improved to 9.2 $\pm$ 3.16 (range 6.03 -16.13) at the end of follow up. This Gp-B, mean duration of exercise at the initial testing was 7.959 $\pm$ 4.85 (range 2.51-15.3) minutes which improved to 10.929 $\pm$ 4.66 (range 5.446-17.14) minutes at the end of follow up. This improvement of 37.35% over the initial value is highly

Fig. 1 : Exercise duration on treadmill in two groups

significant ($P < 0.001$). When results of Gp-A were compared with Gp-B the difference in the benefits is also significant ($P < 0.01$) suggesting that addition of ACE inhibitor improves exercise performance.

OTHER PARAMETERS : Haematological parameters and serum biochemistry including electrolytes were within normal limits in the two groups initially and on follow up. No untoward effect of drug observed.

Discussion

Exercise quantification of functional capacity is an objective assessment of effort tolerance that is reproducible and is helpful in serial follow up. This measure is a better yard stick than any of the physical findings, chest films, echocardiography and resting haemodynamics for assessing cardiovascular status from time to time [1]. We followed up our patients in two groups A & B, for a mean period of 93.8 ± 31.8 days & 109.4 ± 65.4 days. All but one showed improvement in exercise duration in both the groups but the response was variable in individual patients. The improvements in NYHA class was not significant as compared to control group. The mean value of JVP, liver size, BP, pulse pressure, CT Ratio, LVID (in diastole), LVEF between initial and end of follow up do not show significant change except for improvement in heart rate ($P < 0.05$).

Similar observation was made by Engler et al in their 17 patients who were observed for a period of 24.8 ± 14.1 months.

There was no correlation between changes in exercise capacity and changes in ejection fraction, EPSS, CT Ratio, Pulmonary venous congestion or systolic time intervals [3]. Other studies have also shown that physical findings, Xray chest, echocardiogram and resting haemodynamics are inconsistently altered by therapeutic interventions which do increase exercise capacity [10].

The effect of Ace inhibitor in improving exercise capacity is established. Our study has demonstrated

Fig. 2 : Comparison of improvement in exercise duration

that there is an overall improvement in exercise duration as compared to the control group. Even the control group showed an improvement of 17.3% over the baseline value. This benefit is the result of progressive improvement of cardiac function being on digoxin and diuretics, and is partially attributable to better familiarisation with exercise protocol and conditioning effect due to peripheral factors on repeat performance. However with a relatively matched control, the add-on therapy with Ace inhibitors has shown an additional improvement of 20.68% over and above the control group which is attributable to this drug intervention perse.

Ace inhibitor are of proven value in CHF. Various small and large (multicentre) studies though differing in design, duration and drug preparation used, have convincingly established their benefit in improving the exercise duration [11-13]. The newer Ace inhibitors like lisinopril, quinapril, clizapril etc. and even Angiotensin II receptor inhibitor-losartan have shown comparable efficacy to captopril or enalapril [13-16]. Though wide range of drug doses have been tested, only one study establishes a convincing dose related benefit for quinapril [14]. Our results are consistent with those in the literature substantiating the beneficial role of Ace inhibitor in improving exercise capacity. Thus, it is concluded that Ace inhibitor improves exercise capacity despite no appreciable benefits in other clinical and noninvasive laboratory pa-

rameters.

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