HAEMODYNAMIC EFFECTS OF CAPTORIL IN CONGESTIVE CARDIAC FAILURE DUE TO RHEUMATIC HEART DISEASE

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SUMMARY

Rheumatic heart disease is a leading cause of congestive cardiac failure. Besides conventional therapy ACE Inhibitors have been found useful in patients with congestive cardiac failure. This study was conducted in 13 patients with CCF due to RHD to see the acute hemodynamic effects of an ACE inhibitor Captopril. Captopril 25mg was orally administered and haemodynamic changes were recorded at fixed intervals. The pulmonary wedge pressure dropped by 21% p <.001. Cardiac index improved by 8% p <.01 and the peripheral vascular resistance decreased by 19% p <.01. Captopril has a beneficial effect in patients with CCF because of lowering of preload and afterload with a little effect on cardiac output and heart rate.

INTRODUCTION

Congestive cardiac failure (CCF) is a major health problem claiming heavy toll both in mortality and morbidity all over the world.[1] The evidence of beneficial effects of vasodilator drugs to improve symptoms and mortality by favourable effects on circulation has led to the wide use of these drugs to supplement digitalis and diuretic in the treatment of symptomatic patients with congestive cardiac failure.[1]

Angiotension converting enzyme (ACE) inhibition offers a more physiologic approach to the management of congestive cardiac failure by not only decreasing ventricular preload and impedance but also depressing renin angiotensin aldosterone activity. Addition of ACE inhibitors to the conventional therapeutic regimen of digoxin and diuretic in congestive cardiac failure has been shown to improve hemodynamics and increase effort tolerance. Long term trials recruiting a large number of patients like VHeFT II,[3] CONSENSUS[4] and SOLVD[5] have conclusively shown the benefits in term of reduction in mortality and hospitalization in patients both with mild and severe congestive cardiac failure.

Rheumatic heart disease is still rampant in the developing countries. This presents a specific challenge as primary pathology affects the valves resulting in stenosis or regurgitation in various combinations. Left ventricular function is preserved in a majority of these patients in early course of the disease. Most of the studies have employed patients having congestive cardiac failure due to coronary artery disease or congestive cardiomyopathy. This study has been undertaken to evaluate the acute effects of an oral ACE inhibitor Captopril in patients with congestive cardiac failure exclusively due to rheumatic heart disease.

MATERIAL AND METHODS

Patient population this study was performed in thirteen patients, six men and seven women. The average age was 30.4 years (range 15-60 years) and average body surface area 1.4 m^2 (range 1.28-1.74). Five

patients had symptoms compatible with NEW York Heart Association (NYHA) functional class four and eight patients with class three. The etiology of CCF was Rheumatic heart disease in all.

Twelve patients had moderate to severe mitral stenosis where as one had re-stenosis following mitral commissurotomy. Mitral regurgitation was documented in seven patients. One patient had Aortic stenosis where as four patients had Aortic regurgitation concomitantly with mitral valve involvement. In six patients there were overt clinical signs suggestive of tricuspid regurgitation. Except for one all patients had at least two lesions. (Table 1)

M-Mode, 2 dimensional Echocardiography along with pulsed wave and continuous wave Doppler studies were performed in all patients documenting the lesions. Five patients demonstrated sinus rhythm and eight had atrial fibrillation. Four had electrocardiographic evidence of right ventricular hypertrophy where as two had left ventricular hypertrophy. All had radiological evidence of pulmonary edema, average CTR 2.62. Patients were admitted at least 48 hours before the start of study. Average intake of Fursemide was 108 mg daily, eight receiving parenterally and five orally. Twelve were taking cardiac glycoside. None of them received any vasodilator 72 hrs. prior to study. Morning doses of diuretics and digoxin were omitted on the day of study. Informed consent was obtained from all the patients.

Left Ventricular analysed by echocardiography showed preserved function with normal fraction shorting (>34%) and ejection fraction (>55%) in all the patients.

Right Heart Catheterization

A narrow bore (7F) double lumen Swan Ganz thermodilution catheter was introduced employing median basilic vein in ante cubital fossa and advanced into the pulmonary circuit under wave form monitoring control and fluoroscopy. Pressures were record using P 23 ID transducer in the supine position with the mid chest as zero reference. Cardiac out put measurement was performed in triplicate by thermodilution technique utilising a bed side computer model. Systemic arterial pressure was measured by standard cuff technique. Cardiac index, systemic vascular resistance and stroke volume index were derived from conventional formulae.

Study design

Patients were admitted at least 48 hours before baseline study. The measurement started 15 to 30 minutes after right heart catheterization to allow time for circulatory restabilisation. At least four sets of control observations at 20 minutes intervals were recorded over one hour period. After stabilisation as denoted by absence of any trend to change in any direction, Capropril 25 mg single tablet was administered orally. Haemodynamic variables were recorded at 30 minutes intervals for two hours and at hourly intervals for further two hours.

Statistical analysis

Statistical analysis was performed using paired students T test.

RESULTS

The study was completed without any adverse sequelae. No patient developed arrhythmia or systemic hypotension during the study period. There were no subjective adverse effects reported by patients. None of the patients required any supplementary therapy during the observation period.

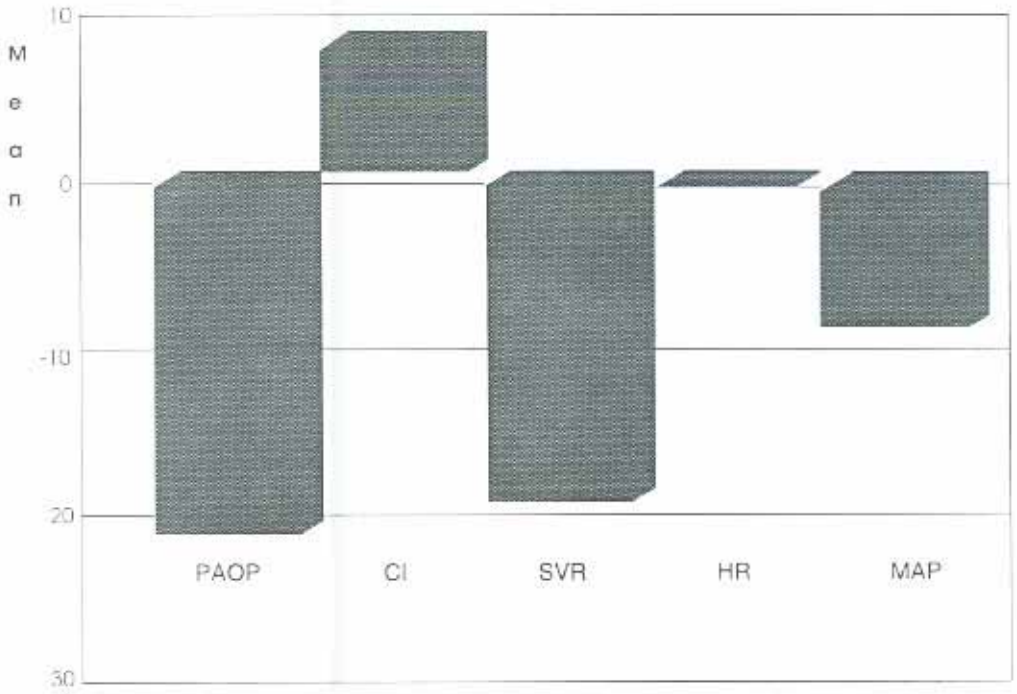
Control measurement

There was no trend of change in any variable over the control observation period, consequently these values were averaged for each subject. Pulmonary artery occluded pressure (PAOP) was increased in all patients to 23.9 ± 4.13 mmHg. Cardiac

TABLE – 1

EFFECTS OF CAPTOPRIL IN CCF

PERCENTAGE CHANGES FROM BASELINE



index (CI) averaged at 3.1 ± 0.96 l/min/m², where as mean pulmonary artery pressure (MPAP) was 41.72 mmHg. Mean arterial pressure (MAP) was 89.7 ± 8.2 mmHg and heart rate was 95.5 beats per minute. Systemic vascular resistance was increased to 1602 ± 511 dyne-s-cm^{-5}.

Response to Captopril

The haemodynamic changes produced by the 25 mg dosage of Captoril are shown in Table 1. The haemodynamic changes were apparent at 30 minutes, reaching a maximum at 90 minutes and persisting for a further 30 to 90 minutes.

No significant changes in heart rate was seen from the control value of 95 bpm during the observation period. Sixty minutes after Captopril administration, PAOP was significantly reduced from 23.9 ± 4.13 to 18,8 ± 5.4 and remained low till the end of study (-21.3% p<.001). Mean arterial pressure decreased from 89.72 ± 8.2 mmHg to 82.6 ± 10.43 at 120 min (-7.9% p < .01). Systolic arterial pressure demonstrated a modest fall at 180 min from 115 ± 8 mmHg to 106.7 ± 11.9 mmHg (-7.2% P < .01) where as diastolic arterial pressure fell at 120 min from 77.36 ± 10.9 mmHg to 69.9 ± 12.4 mmHg; (-9.6% P < .01).

SVR was significantly reduced from 1662 ± 511 dynes-s-cm^{-5} to 1338 ± 403 dynes-s-cm^{-5} at 180 min (-16.4%: p < .001); Cardiac index registered a little increase from 3.25 ± 0.96 l/min/m to 3.56 ± 0.88 at 90 minutes (+9.5% p < .05).

No statistically significant changes were seen in pulmonary artery pressure or stroke volume index. (Table – 1)

DISCUSSION

Congestive cardiac failure may be defined as decreased cardiac output relative to the needs of body. Regardless of etiology, CCF is characterised by certain pathophysiological features such as elevated pulmonary artery occluded pressure (PAOP), increased systemic vascular resistance (SVR), decreased cardiac index (CI) and decreased stroke volume index (SVI). Peripheral renin activity (PRA) is increased resulting in enhanced production of Angiotensin II which is a potent vasoconstrictor.[5,7]

ACE inhibitors have been extensively studied in patients with CCF due to cardiomyopathy and ischaemic heart disease. This study was undertaken to evaluate the effects of Captopril on haemodynamics in patients with congestive cardiac failure with valvular regurgitant or stenotic lesions exclusively due to rheumatic heart disease with preserved LV function. This drug has not been studied in this set up before.

Acute and chronic haemodynamic improvement in cardiocirculatory function following the administration of ACE inhibitors is well established.[8,9] ACE inhibitors owe their beneficial response in part to decreasing levels of Angiotensin II, as a result of interruption of renin angiotensin axis. As a consequence there is a fall in systemic vas-cular resistance. Metabolism of bradykinins is reduced hence enhance vasodilatory effect by accumulation of bradykinins.[4] The vasodilatory effect is more pronounced in renal vasculature, increasing renal blood flow and salt excretion.[10,11] By counteracting aldosterone, it averts the sodium retention seen with other vasodilators.[12]

Single oral dose of Captopril 25 mg was administered after haemodynamic stabilisation and the effects were studied for 4 hours. Clinical evidence suggest that maximal haemodynamic effects are produced by 25 mg dosage of Captopril, further increase in dosage only prolongs the effects without augmenting circulatory changes.[13]

Captopril is detectable in serum within twenty minutes of oral administration. Free Captopril reaches its peak in one hour where as total Captopril attains peak in two hours. Half life of free Captopril is one hour and is virtually undetectable after eight hours of administration.[16]

Our study in 13 patients with CCF due to rheumatic heart disease showed prompt vasodilatory effects of CPT as reported by others studies.[17-22] In patients with CCF due to cardiomyopathy or CAD. The abnormally elevated left heart filling pressure substantially declined in all patients and remained low throughout the study. Modest reduction of aortic outflow impedance and lowering of systemic blood pressure was observed. Baseline cardiac index was not abnormally depressed hence a little increase during the course of observation was demonstrated. It could also be because of fixed obstructive lesions present in all of our patients. Heart rate did not change significantly. No appreciable effects were seen on pulmonary artery pressures. The beneficial modulation of cardiocirculatory function as induced by CPT followed the same trend as in other studies though they were little less pronounced in our study.

To conclude, our study demonstrated that Captopril administered acutely is a useful therapeutic agent to be employed in CCF due to RHD as it reduces left heart filling pressures and decreases the after load with a little effect on cardiac output. Further long term studies are required to elucidate its role in chronic treatment of chronic CCF due to RHD.

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