ORIGINAL ARTICLE

Captopril Treatment in Rheumatic Heart Disease with Congestive Heart Failure
A Preliminary Report

by

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Abstract

A small scale controlled trial of captopril (ACE inhibitor) was conducted in 8 children with congestive heart failure due to rheumatic mitral regurgitation with or without mild mitral stenosis. The age of the patient ranged from 5.5 to 13 years (mean 9,3 years). Four children, served as control group, received digitalis and diuretics as standard treatment; while the other 4 children also received 2 × 12,5 mg of captopril in addition to standard treatment. The effect of both regimens were measured by using changes of left ventricular function as seen on the echocardiogram performed before treatment, and then 3, 7 and 14 days thereafter.

Definite conclusion cannot be made because of the small number of patients; but it is apparent that some improvements of left ventricular functions in the captopril group were more evident when compared with that of the control group of standard treatment.

Side effects of captopril were not found.

Introduction

Congestive heart failure (CHF) represents an abnormal condition in which the heart as a blood circulating pump is not able to fulfil the metabolic requirement of the systemic body tissue in rest as well as in exercise (Mason, 1976; Friedman and George, 1985). This may result from improper myocardial function, hemodynamic overload, or both.

Despite many criticisms about its efficacy, especially in the diseased myocardium, digitalis, in conjunction with diuretics is still widely used for standard treatment of congestive heart failure, including for those patients with congestive heart failure due to rheumatic heart disease.

The concept of preload and afterload manipulation offers a new method in managing congestive heart failure (Friedman and George, 1985). Captopril (Capoten-Squibb) belongs to vasodilators which influences the arteriolar blood vessels leading to dilatation of the arteriolar vessels, thus will improve the left ventricular performance by means of cardiac output improvement (Friedman, 1985; Squibb, 1986).

This small scale experimental study is conducted as a preliminary study to observe the clinical effect of captopril in children with congestive heart failure due to rheumatic heart disease.

Materials and Methods

This study was carried out at the Division of Pediatric Cardiology, Cardiology Unit, Dr. Kariadi Hospital Semarang. All paediatric patients with congestive heart failure due to rheumatic heart disease admitted to the Pediatric Cardiological Unit of the hospital from November 1986 to May 1987 were enrolled into this study.

Careful history was obtained in each patient, and thorough physical examination was performed. The diagnosis of rheumatic heart disease and congestive heart failure were based on the usual criteria. Electrocardiogram was obtained in every patient, as was the chest X-ray. Routine laboratory examinations were done according to the standard procedure of the hospital. Clinical assessment was performed daily.

All patients were given 5-10% of dextrose infusion. They all also received digitalization (Cedilanid) 0.01 mg/kg intravenously at 0-6-12 hours for the first 18 hours, followed by maintenane dose twice a day orally. The maintenance dose was in the average 0.01 mg/kg body weight daily, and was adjusted to the clinical condition. Furosemide (Lasix) was given 1-2 mg/kg body weight once or twice daily.

Four patients were treated with captopril 2 × 12.5 mg orally besides standard treatment, while the other 4 served as a control group.

Echocardiographic examinations were carried out in all 8 patients before starting treatment, and then 3 days, one week, and two weeks thereafter, using ALOKA SSd-720 with 5 Mhz transducer. Complete M-Mode measurement was done according to the standard procedure (Bjorkem, 1979), and calculations of the following were obtained: shortening fraction or delta left ventricular internal diameter (delta-LVID), mean velocity of circumferential fractional shortening (VCF), systolic time interval (STI) and left ventricular ejection time (LVET), using formulas recommended by several authors (Meyer at al., 1975; Feigenbaum, 1975 and 1981; Roelandt, 1977; Meyer, 1977)

Shortening fraction (SF) or delta LVID was calculated by formula :

$$SF = \frac{LVID_D - LVID_S}{LVID_D} \times 100\%$$

where $LVID_D$ denotes left ventricular internal diameter in end-diastole while $LVID_S$ denotes left ventricular internal diameter in end-systole. The result was depicted in figure, by comparing with normal value of SF (25-42%).

Mean velocity of circumferential fractional shortening (mean CVF) is calculated using formula :

$$\text{Mean VCF} = \frac{LVID_D - LVID_D}{LVID_D \times ET} \times 100\%$$

Systolic time interval (STI) was calculated as left ventricular pre-ejection period (LPEP)/left ventricular ejection time (LVET) ratio. Normal value for 2 weeks - 1 year old babies: 0,18 - 0,37; 1 year - 19 years: 0,27 ± 0,04 (Bjorkem, 1979).

Results

There were 8 patients fulfilling the criteria for inclusion in the study period, consisting of 4 males and 4 females, ranging in age from 5.5 - 13 years (mean 9,8 years). The sex distribution of patients was depicted in table 1. Table 2 shows the sex distribution and the anatomic diagnosis.

Table 1 : *Sex distribution of 8 treated and control groups*

Sex	Treatment	Control	Total
Male	2 (25,0%)	2 (25,0%)	4 (50,0%)
Female	2 (25,0%)	2 (25,0%)	4 (50,0%)
Total	4 (50,0%)	4 (50,0%)	8 (100,0%)

Table 2 : *Sex distribution and anatomical diagnosis*

Sex	M.I.	M.I. + Mild M.S.	Total
Male	3 (37,5%)	1 (12,5%)	4 (50,0%)
Female	1 (12,5%)	3 (37,5%)	4 (50,0%)
Total	4 (50,0%)	4 (50,0%)	8 (100,0%)

The mean LVID of both groups before treatment, 3 days, 1 week and 2 weeks after treatment are depicted in figure 1. Mean VCF in both treatment and control group is seen in fig. 2. The mean systolic time interval (STI) in treated and control group can be seen in fig. 3. Figure 4 shows graphic representative of comparison between LVET in % between treated and control group.

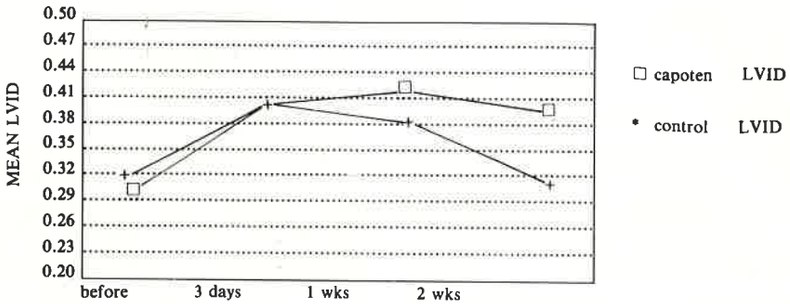

Fig. 1 : *Comparison between delta LVID in both treatment and control groups.*

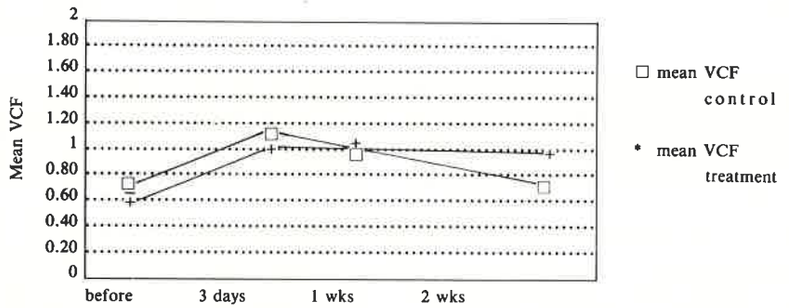

Fig. 2: *Comparison between mean VCF in both treatment and control groups.*

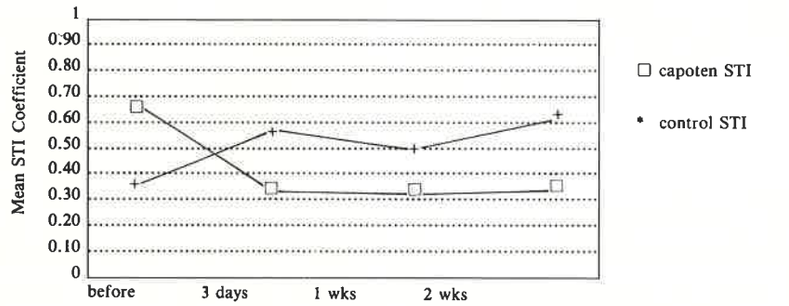

Fig. 3 : *Comparison between STI coefficient in both treatment and control groups.*

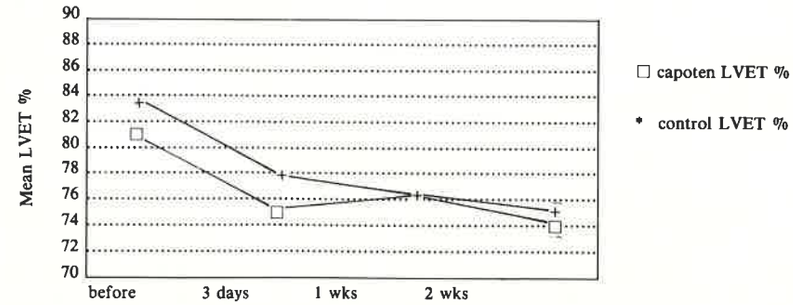

Fig. 4 : *Comparison between LVET % in both treatment and control groups.*

Discussion

Left ventricular internal dimension (LVID) can be measured non-invasively using echocardiography; shortening fraction can be calculated from LVID, and can be used as a parameter of LV function (Meyer et al. 1975, Feigenbaum, 1975). Study of Meyer (1975) revealed a strong correlation between LV minor dimension by echo measurement and lateral dimension in end diastole by cine-angiography (r = 0,889). A correlation of r = 0,753 was obtained between end systolic LV minor dimension measured by echocardiography and cine-angiography.

Captopril acts as angiotensin converting enzyme inhibitor (kininase II) or ACE inhibitor, improves left ventricular function. The action of captopril represents vasodilatation or lowering its afterload which followed by increase of stroke volume and cardiac output. It differs from digitalis and catecholamine which have myocardial inotropic action; calcium channel inhibitor are unusual for he treatment of congestive heart failure in children, except for conduction defect.

The aim of the vasodilator in the treatment of congestive heart failure is to improve the function of the heart, i.e. to increase the peripheral blood perfusion, and to omit the systemic and pulmonary venous congestion. Vasodilator is properly indicated in congestive heart failure with increased peripheral resistance (hypertension), left ventricular overload (mitral regurgitation) which increases the stroke volume and ejection fraction. However, administration of vasodilator in cases with inflow or outflow obstruction such as mitral stenosis, will alter the stroke volume and ejection fraction and poor peripheral perfusion will result (Feigenbaum, 1981).

In this study, left ventricular functions were measured noninvasively using echocardiography. The result shows that there is a tendency for the treated group to show improvement of left ventricular function, although definite conclusion cannot be made because of the small number of patients.

As seen in fig. 1 there was a low/subnormal shortening fraction (SF) prior to treatment in both group. Three days after treatment, the mean LVID of the treated group increased and then steadily maintained above the normal value until 2 weeks of treatment; while in the control group the LVID increased until the 3rd day of treatment, but then decreased reaching subnormal value after two weeks of treatment.

The mean velocity of circumferential fractional shortening (VCF) also showed similar tendency. As seen in fig. 2, the VCF in treated group increased from pre-treatment level in 3 days, and then maintained its level until the end of the study. The control group, in contrast, showed declining level after initial increase in the first 3 days, approximating the pre-treatment level by the end of the second week of treatment.

The systolic time interval (STI) is another parameter of LV function (Meyer, 1977). Simultaneous measurement of external carotid pulse and echocardiographic recording will obtain a more accurate result. The determinant factors of STI are (1) preload, (2) afterload, (3) myocardial contractility, and (4) ventricular conduction (Meyer, 1977).

We did not measure carotid pulse in this study. However, echocardiographic measurement of STI showed the benefit of the use of captopril, as seen in fig. 3. The STI coefficient before treatment of the treated group were higher than that of the control group. Following three-day treatment, STI coefficient of the treated group was lower than the control group, and further de-

crease of the treatment group was observed after 1 and 2 weeks after treatment. This phenomenon could be explained by the afterload- decreasing effect of the vasodilator (Meyer, 1977).

Left ventricular ejection time (LVET) denotes as systolic-electromechanical time measured from the point of opening to the point of clossure of the aortic semilunar valve on echocardiogram. Total electromechanical systole represents the interval between Q-wave seen on electrocardiogram which recorded simultaneously on the M-mode echocardiogram and the point of opening of the aortic semilunar valve (i.e. left ventricular preejection period = LPEP) (Feigenbaum, 1981; Meyer, 1977). LVET% should be calculated to determine LV function which be corrected to the frequency of the heart, i.e. :

$$\frac{\text{LVET calculated (actual)}}{372{,}52 - 1{,}19 \times \text{Freq. (expected)}} = \text{LVET\%}$$

The normal value for 2 weeks - 1 year old baby = 79 - 100%; up to 19 year old children = 100 ± 4%. Lowered LVET% with increased STI coefficient indicates cardiac failure.

Figure 4 represents normal average of LVET% as seen on both treated and control groups; after 3 days treatment both curves going downward until the lowest normal range then going up again, especially the treatment group; the control group did not show the increase of LVET%.

Taking into consideration the increase of STI coefficient and the decrease of LVET% as seen in figs. 3 and 4, it can be concluded that cardiac failure was still exist in the control group. On the other hand, increase of LVET% and decrease of mean STI in the treated group suggested the beneficial effect of vasodilator in the treatment of heart failure. This finding was in agreement with other reports in the literature (Meyer, 1977; Bjorkhem, 1979).

In summary, our observation on a small number of patients suggested that captopril might be of benefit if added to the standard treatment for congestive heart failure due to rheumatic valvular disease consisted of digitalis and diuretics. Further study is obviously indicated before more definite conclusion can be made.

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