

LEFT VENTRICULAR SYSTOLIC AND DIASTOLIC FUNCTIONS IN CHILDREN WITH RHEUMATIC MITRAL REGURGITATION

ROMATİZMAL MİTRAL YETMEZLİKLİ HASTALARIN SOL VENTRİKÜL SİSTOLİK VE DIASTOLİK FONKSİYONLARI

F. Sedef TUNAOĞLU, M.D., Deniz OĞUZ*, M.D., Serdar KULA, M.D.,
Rana OLGUNTÜRK, M.D.

Gazi University, Faculty of Medicine, Department of Pediatric Cardiology, Ankara-Turkey
Dr. Sami Ulus Children's Hospital, Department of Pediatric Cardiology*, Ankara-Turkey
Gazi Medical Journal 2002; 13: 35-39

ABSTRACT

Purpose: This study was performed to determine the left ventricular systolic and diastolic functions and assess the effects of short-term angiotensin converting inhibition by enalapril in children with rheumatic mitral regurgitation. **Methods:** Twelve patients (mean age: 14.0 ± 0.72 years) receiving digoxin were evaluated by echocardiography for left ventricular systolic and diastolic functions followed by enalapril treatment for 20 days. Echocardiography was repeated at the end of the treatment. **Results:** Left ventricular end-diastolic dimension (5.68 ± 1.19 vs 5.52 ± 1.02 cm), left ventricular end-systolic dimension (3.52 ± 0.98 vs 3.28 ± 1.04 cm), left ventricular end-diastolic volume (161.5 ± 63.2 vs 123.9 ± 37.5 ml), left ventricular end-systolic volume (58.8 ± 33.4 vs 41.9 ± 16.1 ml), and cardiac output (9.08 ± 1.18 vs 8.07 ± 0.87 L/min/m²) were reduced. Peak early filling velocity (1.49 ± 0.41 vs 1.45 ± 0.57 m/sec), and deceleration time (162.3 ± 72.6 vs 156.4 ± 63.1 sec) were decreased as well as isovolumic relaxation time (75.4 ± 20.2 vs 65.16 m/sec), and A duration. E duration and total diastolic time were prolonged. **Conclusion:** These data show that enalapril can normalize systolic and diastolic functions by altering loading conditions and be beneficial for children with mitral regurgitation.

Key Words: ACE Inhibition, Rheumatic Mitral Regurgitation, Children.

INTRODUCTION

Mitral regurgitation (MR) causes alterations in systolic and diastolic functions by producing volume overload to the left ventricle. Vasoactive drugs such as angiotensin converting enzyme inhibitors (ACEI) are increasingly used with or

ÖZET

Amaç: Bu çalışma romatizmal mitral yetmezliği olan hastaların sol ventrikül sistolik ve diastolik fonksiyonlarını değerlendirmek ve anjiotensin konverting enzim inhibitörü olan enalapril tedavisine verdikleri yanıtı değerlendirmek amacıyla planlanmıştır. **Yöntem:** GÜTF Çocuk Kardiyolojisi Bilim dalında romatizmal mitral yetmezliği nedeniyle digoksin tedavisi alan ve klinik olarak asemptomatik olan 20 hastanın (ort yaş: 14.0 ± 0.72 y) başlangıç ve enalapril tedavisinin 20.günündeki sol ventrikül sistolik ve diastolik fonksiyonları ekokardiyografik kayıtlardan retrospektif olarak değerlendirilmiştir. **Sonuçlar:** Enalapril tedavisinin ile sol ventrikül diastolik sonu (5.68 ± 1.19 vs 5.52 ± 1.02 cm), sol ventrikül sistol sonu çapı (3.52 ± 0.98 vs 3.28 ± 1.04 cm), sol ventrikül diastol sonu volüm (161.5 ± 63.2 vs 123.9 ± 37.5 ml), sol ventrikül sistol sonu volüm (58.8 ± 33.4 vs 41.9 ± 16.1 ml), kardiyak output (9.08 ± 1.18 vs 8.07 ± 0.87 L/min/m²) düşme saptandı. Erken dolun hızı tepe değeri (1.49 ± 0.41 vs 1.45 ± 0.57 m/sn), and deselerasyon zamanı (162.3 ± 72.6 vs 156.4 ± 63.1 sn) ve izovolemik relaksasyon zamanı (75.4 ± 20.2 vs 65.16 m/sn) tedavi ile azalırken; A ve E süresi ,total diastolik zamanda uzama saptandı. **Yorum:** Sonuçlar enalapril tedavisinin ventrikülün ön ve art yükünü etkileyerek sistolik ve diastolik fonksiyonları düzelttiğini ve mitral yetmezlikli hastalarda yararlı olabileceğini göstermiştir.

Anahtar Kelimeler: ACE İnhibisyonu, Romatizmal Mitral Yetmezliği, Çocuk.

without digoxin to decrease the effect of loading conditions. ACEI have been well documented to reduce left ventricular afterload, augment cardiac output (CO), and reduce left ventricular and right ventricular filling pressures in adult studies (1-3).

This study was designed to assess the short

term effect of ACEI therapy on left ventricular functions in children with mitral regurgitation by echocardiography.

MATERIAL AND METHOD

Twelve asymptomatic children with MR (10 females, 2 males) aged 10-18 years (mean: 14 ± 0.72), receiving digoxin for at least one year were included in the study (DG). Digoxin therapy had been started by different cardiology clinics because of documented heart failure symptoms like tachycardia and cardiomegaly. However, patients seemed asymptomatic at the time of study. Twelve also asymptomatic patients with MR (8 female, 4 male) aged 8-17 years (13.5 ± 0.91) who never had heart failure and were therefore not receiving digoxin, were enrolled in the study as the control group (CG). All patients were given an M-mode, 2-dimensional and pulsed wave Doppler echocardiographic baseline evaluation with General Electrics 6800 with 3.5 MHz transducer. Then ACEI therapy was begun in the digoxin group with Enalapril 0.5 mg/kg/day p.o b.i.d. under 30 kg and 10 mg/day p.o b.i.d. over 30 kg body weight. At the end of the 20th day of the therapy, the echocardiographic examination was repeated. Recordings were done with the subject in the supine position and breathing freely. M-mode tracings were obtained at the level of the tips of the mitral leaflets in the parasternal long axis position and measurements were performed according to the American Society of Echocardiography recommendations (4). After the two dimensional and M-mode examination, mitral flow was obtained from the cardiac apex in 4-chamber position using pulsed wave Doppler echocardiography. The sample volume was placed in the left ventricular inflow tract at the level of the mitral leaflet tips. Three consecutive measurements were averaged to avoid the differences due to respiration. Variables of diastolic function included; 1) Peak early (E) and peak atrial (A) filling velocity m/sec; 2) Ratio of E to A (E/A); 3) E acceleration time (Eat) msec; 4) E deceleration time (Edt) msec; 5) E wave velocity time integral (E VTI) cm; 6) A wave velocity time integral (A VTI) cm.; 7) E duration (Edur) msec; 8) A duration (A dur) msec 9) Total diastolic time (Tot.dur) msec; 10) Pulmonary vein systolic peak velocity (PVS) m/sec; 11) Pulmonary vein diastolic peak velocity (PVD)

m/sec; 12) Ratio of PVS to PVD (PVS/PVD); 13) Pulmonary vein retrograde flow velocity (PVa) 14) Isovolumic relaxation time (IRT) msec; this parameter was measured with the probe at the apical 5-chamber position while the sample volume was placed between the aorta and mitral valve where recordings of both valves were taken simultaneously.

All data were expressed as a mean \pm standard deviation. A two-tailed unpaired t-test was used for statistical comparisons between enalapril treated and not treated groups and the two-tailed paired t-test was used for comparing the effect of treatment on enalapril treated group by SPSS (The Statistical Package for the Social Science Program) and $p < 0.05$ indicated a significant difference between groups.

RESULTS

Enalapril treated group showed a decrease in left ventricular end diastolic dimension (LVEDD), left ventricular end systolic dimension (LVESD), left ventricular end diastolic volume (LVEDV), left ventricular end systolic volume (LVESV) and CO values. LVEDD, LVEDV and CO values were decreased significantly by the ACEI therapy. LVEDD and LVEDV were significantly larger when compared to the control group, decreased at the end of 20th day of therapy, and approached the values of control group. LVEDD values of the patients in two groups were also calculated according to body surface area in order to avoid the differences in body size and were significantly different also (108.3 ± 41.21 vs 81.98 ± 21.53 ml/m² respectively). Although the CO values of DG decreased significantly with the ACEI therapy, they were still high according to the CG's values. Left ventricular systolic function parameters are summarised in Table 1.

Among diastolic functions; E, EVTI, Edt, IRT, PVS, and PVD decreased whereas A, Adur, Eat, and PVa increased at the end of the 20th day. Left ventricular diastolic function parameters are summarized in Table 2.

Systolic and diastolic blood pressure values showed a non specific decrease at the end of the 20th day of enalapril therapy (114.17 ± 1.93 mmHg vs. 109.17 ± 2.37 mmHg and 63.75 ± 2.32 mmHg vs. 52.08 ± 5.17 mmHg respectively).

Left ventricular mass (LVM) also decreased

Table - 1: Systolic parameters measured by M-mode echocardiography.

Systolic Parameter	Base value	After therapy	Control group
LVEDD (cm)	5,68±1,19	5,52±1,02	4,84±0,69*
LVESD (cm)	3,52±0,89	3,28±1,04	3,14±0,41
EF (%)	64,45±8,51	66,74±7,30	64,50±5,34
FS (%)	36,87±8,09	37,44±5,69	34,33±4,75
LVEDV (ml)	161,5±63,2	123,9±37,5	111,3±38,6*
LVESV (ml)	58,8±33,4	41,9±16,1	39,7±14,1
CO (lt/min/m ²)	9,08±1,18	8,07±0,87	5,99±0,73**
Heart rate	85,25±9,52	88,8±13,4	85,4±11,3
Wall stress (g/cm ²)	84,66±31,74	85,86±29,62	85,40±31,74

* indicates p<0.05 between base value and control value

** indicates p<0.05 between the group with ACEI therapy and controls

EF : Ejection fraction

FS : Fractional shortening

Table - 2: Diastolic parameters measured by Doppler echocardiography.

Diastolic parameter	Base values	After therapy	Control
E m/sec	1,49±0,41	1,45±0,57	1,19±0,26*
A m/sec	1,00±0,46	1,14±0,60	0,71±0,23**
Acc time	86±24,7	93,5±22,2	93,1±14,4
Dec time	162,3±72,6	156,4±63,1	147,6±47,1
E dur msec	226,2±48,7	237,6±69,4	238,4±51,8
Tot. dur msec	398,6±52,4	404,8±91,4	397,8±81,6
PVa	0,34±0,14	0,36±0,13	0,26±0,12
PVS m/sec	0,74±0,55	0,61±0,22	0,51±0,19
PVD m/sec	0,6±0,31	0,54±0,23	0,42±0,17
IRT msec	75,4±20,2	65,3±16	58,4±18,1*
E VTI cm	22,31±9,66	19,32±7,42	16,23±6,1
A VTI cm	14,1±12	12,33±7,12	7,95±3,43

E: Peak early diastolic flow velocity

A: Peak late diastolic flow velocity

Acc time: E acceleration time

E VTI: E wave velocity time integral

A VTI: A wave velocity time integral

E dur: Early diastolic flow duration

PVD: Pulmonary vein diastolic flow velocity

Pva: Pulmonary vein retrograde flow velocity

Adt: Late diastolic flow deceleration time

Dec Time: E deceleration time

Aat: late diastolic flow acceleration time

EF slp: EF slope

Tot. Dur: Total diastolic flow duration

PVS: Pulmonary vein systolic flow velocity

IRT: Isovolumic relaxation time

* indicates p<0.05 between base value and control value

** indicates p<0.05 between the group with ACEI therapy and controls

at the end of the therapy but the difference was not significant either (219.92±116.1 vs. 208.69±116.9 g. respectively, control group: 127.80±49.07, p<0.05).

Wall stress values were 85.86±29.62 vs 84.66±31.74 g/cm² before and after ACEI therapy respectively (p>0.05), whereas control groups were 85.40±19.79 g/cm².

DISCUSSION

Mitral insufficiency due to rheumatic fever is still a major problem in developing countries where rheumatic fever is frequently seen (5). Children who show symptoms of heart failure are treated with digoxin. Also ACEI have been introduced in the treatment of congestive heart failure both for vasodilator and neurohormonal effects. ACEI show their effect on left ventricular performance by reducing both preload and

afterload and by remodelling. Konstam et al. (1) reported that chronic ACEI treatment slowed or reversed left ventricular dilatation in adults with asymptomatic systolic dysfunction. Levine et al. (2) showed that forward stroke volume increased and ejection fraction remained unchanged in patients with chronic mitral regurgitation treated with ACEI. Tischler et al. (3) studied patients with severe mitral regurgitation due to mitral valve prolapsus and reported that over a six month period ACEI therapy resulted in significant reductions in left ventricular volumes and mass in association with a minor reduction in regurgitant fraction. Shimoyama et al. (6) treated dogs with moderate heart failure and concluded that early long term therapy with enalapril prevents progressive worsening of functional mitral regurgitation and this beneficial effect is most likely achieved by prevention of progressive left ventricular dilation. Schon (7) also reported that long-term ACEI in patients with valvular regurgitation reverses left ventricular dilation and reduces left ventricular mass and hypertrophy thereby improving left ventricular function. Further he suggested that ACE inhibition may have the potential to delay aortic or mitral valve replacement (7).

There are few studies about the beneficial effects of enalapril in children with rheumatic mitral regurgitation (8). In this study digitalized children with mitral regurgitation seemed asymptomatic, however their LVEDD and LVEDV values were significantly larger and cardiac output values were significantly higher when compared to children not using digoxin. Enalapril treatment reduced these values even at the end of 20th day of therapy. There were also a slight decrease in systolic and diastolic blood pressure values which were not significant. Decreased preload indicated by reduced cardiac size and cardiac volume, and decreased afterload indicated by decreased systolic and diastolic blood pressure values caused by enalapril therapy also alters diastolic functional parameters. Our E and A values were significantly higher than patients not using digoxin at the beginning, indicating volume overload conditions. E was decreased at the end of 20 days of ACEI therapy. However, A was increased, indicating an increased atrial contraction role in diastolic filling. Duration of E, A and total diastolic time

were also increased after the treatment although the heart rate was unchanged. IRT, which were significantly prolonged before treatment, approached normal values by enalapril just as the deceleration time. These changes are probably partly due to altered loading conditions. The remodelling effects of enalapril on left ventricle is well known. However the duration of the study is not sufficient to debate the matter.

In conclusion, patients with MR have important hemodynamic abnormalities even though they have been using digoxin and showing no signs of congestive heart failure. Systolic functions as well as diastolic functions should be assessed to evaluate these hemodynamic abnormalities. Enalapril can alter these conditions and bring the values towards normal even with a short-term therapy. Addition of ACEI to the treatment of MR in the early stages can prevent the progression of latent systolic and diastolic dysfunction of the left ventricle and can delay the valve surgery or even render it unnecessary.

Correspondence to: F. Sedef TUNAOĞLU, M.D.
Gazi Üniversitesi Tıp Fakültesi
Çocuk Kardiyolojisi Bilim Dalı
06510 ANKARA - TÜRKİYE
Phone : 312 - 214 10 00 / 5626
E-mail :fst@med.gazi.edu.tr

REFERENCES

1. Konstam MA, Rousseau MF, Kronenberg MW, Udelson JE, Melin J, Stewart D, Dolan N, Edens TR, Ahn S, Kinan D. Effects of the angiotensin converting enzyme inhibitor enalapril on the long-term progression of left ventricular dysfunction in patients with heart failure. *Circulation* 1992; 86: 431-438.
2. Levine HJ, Gaasch WH. Vasoactive drugs in chronic regurgitant lesions of the mitral and aortic valves. *J Am Coll Cardiol* 1996; 28: 1083-1091.
3. Tischler MD, Rowan M, LeWinter MM. Effect of enalapril therapy on left ventricular mass and volumes in asymptomatic chronic, severe mitral regurgitation secondary to mitral valve prolapse. *Am J Cardiol* 1998; 82: 242-245.

4. Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: Results of a survey of echocardiographic measurements. *Circulation* 1978; 58: 1072-1083.
5. Olguntürk R, Aydın B, Tunaoglu FS, Akalin N. Rheumatic heart disease prevalence among schoolchildren in Ankara, Turkey. *Turk J Pediatr* 1999; 41: 201-206.
6. Shimoyama H, Sabbah HN, Rosman H, Kono T, Alam M, Goldstein S. Effects of long-term therapy with enalapril on severity of functional mitral regurgitation in dogs with moderate heart failure. *J Am Coll Cardiol* 1995; 25: 768-772.
7. Schon HR. Hemodynamic and morphologic changes after long-term angiotensin converting enzyme inhibition in patients with chronic valvular regurgitation. *J Hypertens Suppl* 1994; 12: S95-S104.
8. Calabro R, Pisacane C, Paciolo G, Russo MG. Hemodynamic effects of a single enalapril among children with asymptomatic chronic mitral regurgitation. *Am Heart J* 1999; 138: 955-961.