

허혈성 심부전증 환자에서 관상동맥 중재술후 Cilazapril의 좌심실 재구성에 대한 효과

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The Effects of Cilazapril on Left Ventricular Remodeling after Coronary Intervention in Patients with Ischemic Heart Failure

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ABSTRACT

Background and Objectives : Angiotensin converting enzyme inhibitor (ACEI) is known to be effective in the prevention of left ventricular failure (LVF) after acute myocardial infarction. The aim of this study was to investigate the efficacy of an ACEI, Cilazapril, on left ventricular remodeling in patients with ischemic LVF, who underwent coronary interventions. **Materials and Methods** : Cilazapril, 2.5 -5.0 mg per day was administered 12 weeks after coronary interventions in 25 patients (18 M, 7 F, 61.5 ±9 years) with impaired LV function (ejection fraction < 50%). Fifteen patients (9 M, 6 F, 59.4 ±7 years) without ACEI were compared by clinical examinations, blood chemistry, electrocardiogram and echocardiogram with Cilzapril group at 2, 4, 8 and 12 weeks after intervention. **Results** : Blood pressure and heart rate were not changed after Cilazapril. LV end-diastolic volume (LVEDV) decreased from 153.1 ±38.7 to 135.6 ±25.5 ml and end-systolic volume from 84.9 ±34.7 to 72.6 ±25.1 ml after 12-week Cilazapril p=0.003, p=0.001. Ejection fraction (EF) was increased from 44.4 ±3.2 to 52.4 ±2.8% after 12 weeks of Cilazapril p=0.034. In control group, LVEDV was changed from 152.7 ±44.6 to 143.6 ±28.7 ml, which failed to show significant reduction. Side effects of Cilazapril were 3 dry cough (3/25, 12%) and 1 facial edema, 1 hypotension and 1 dizziness. **Conclusion** : Cilazapril is a beneficial adjunctive therapeutic agent in patients with ischemic left ventricular failure for the prevention of ventricular dilatation, especially after coronary intervention. (**Korean Circulation J 1998;28(12):1964-1972**)

KEY WORDS : Ischemic left ventricular failure · Cilazapril · Ventricular remodeling.

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서 론

Cilazapril 2 (8%),
 17 (68%), 6 (2
 6%) , 19 (82.6%)
 가 3 (13%), 1 (4.4%)
 가 40
 1) 가 , 가 8 (32%)
 11 (44%)
 2) , 6 (24%)
 , 3 (13%), 6 (26%), 6 (26%)
 가 1 (4%)
 3)4) 1.5 mg/dl 가
 (Angiotensin Converting Enzyme Inhibitor, ACEI) angiotensin
 angiotensin 6 (40%),
 prostaglandin 4 (26.7%), 4 (33.3%)
 , 5 (55.6%),
 2 (22.2%)
 가 6 (40%), 2 (16%), 3
 Cilazapril sulf - hydryl 가 (20%) , 2
 (16%) . 5
 가 9)10) , 2 (16%), 3 (20%)
 가 가
 가 Cilazapril
 Cilazapril (p=0.
 027, Table 1 and 2).

대상 및 방법

연구대상 area - length
 method Teic -
 hholz method 50%
 Cilazapril
 50% , 2.5 mg 90
 mmHg
 5 mg 2
 Cilazapril
 12
 (Percutaneous Transluminal Cor -
 onary Angioplasty ; PTCA) 13
 61.5 ± 9) Cilazapril
 50% 15 (: = 9 : 6,
 59.4 ± 7) Cilazapril ACEI

Table 1. Baseline characteristics of patients

	Male (%)	Female (%)	Total (%)
Cilazapril group			
Age (years)			
41 - 50	5 (27.7)	0	5 (20)
51 - 60	3 (16.7)	0	3 (12)
61 - 70	7 (38.9)	6 (85.7)	13 (52)
71	3 (16.7)	1 (14.3)	4 (16)
Clinical diagnosis			
Acute myocardial infarction	12 (66.7)	5 (71.4)	17 (68)*
Old myocardial infarction	4 (22.2)	2 (28.6)	6 (24)
Unstable angina	2 (11.1)	0	2 (8)
Associated disease			
Hyperlipidemia	2 (11.1)	1 (14.3)	3 (12)
Diabetes	4 (22.2)	2 (28.6)	6 (24)
Hypertension	3 (16.7)	3 (42.8)	6 (24)
Control group			
Age (years)			
41 - 50	2 (13.3)	1 (6.7)	3 (20)
51 - 60	2 (13.3)	1 (6.7)	3 (20)
61 - 70	4 (26.7)	4 (26.7)	8 (53.4)
71	1 (6.6)	0	1 (6.6)
Clinical diagnosis			
Acute myocardial infarction	2 (13.3)	2 (13.3)	4 (26.7)*
Old myocardial infarction	3 (20)	2 (13.3)	5 (33.3)
Unstable angina	4 (26.7)	2 (13.3)	6 (40)
Associated disease			
Hyperlipidemia	2 (13.3)	1 (6.7)	3 (20)
Diabetes	4 (20)	2 (13.3)	6 (40)
Hypertension	3 (20)	3 (20)	6 (40)

*p=0.027 : Cilazapril vs. control group

9 PTCA package t - test
 , 6 p 0.05
 Cilazapril 2, 4,
 8, 12
 sodium, potassium creatinine
 4, 8, 12
결 과
 혈압 및 심박수에 대한 효과
 Cilazapril 128 ± 14/80 ± 10 mm
 Hg 12 118
 ± 10/80 ± 5 mmHg ,
 통계학적 분석 , 1 90 mmHg
 ± 8
 SPSSWIN(Window 98 release 8.0) 74 ± 8/min 12 71 ± 6/min

Table 2. Coronary angiographic findings and the site of coronary interventions

	PTCA (%)	Stent (%)	Total (%)
Cilazapril group			
Left anterior descending artery (LAD)	5 (41.7)	3 (23.1)	8 (32)
Left circumflex artery (LCX)	0	0	0
Right coronary artery (RCA)	0	0	0
Two vessel disease	5 (41.7)	6 (46.2)	11 (44)*
Left main + RCA	1 (Rt. 8.3)	0	1 (4)
LAD + LCX	2 (16.6)	2 (15.4)	4 (16)
LAD + RCA	2 (16.6)	2 (15.4)	4 (16)
LCX + RCA		2 (15.4)	2 (8)
Three vessel disease	2 (16.6)	4 (30.8)	6 (24)*
Total	12 (48)	13 (52)	25 (100)
Control group			
Left anterior descending artery (LAD)	4 (26.7)	2 (13.3)	6 (24)
Left circumflex artery (LCX)	1 (6.7)	1 (6.7)	2 (13.3)
Right coronary artery (RCA)	2 (13.3)	1 (6.7)	3 (20)
Two vessel disease	2 (13.3)	0	2 (13.3)*
Left main + RCA	0	0	0
LAD+LCX	1 (6.7)	0	1 (6.7)
LAD + RCA	0	0	0
LCX + RCA	1 (6.7)	0	1 (6.7)
Three vessel disease	0	2 (13.3)	2 (13.3)*
Total	9 (60)	6 (40)	15 (100)

*p=0.027 : Cilazapril vs. control group

Table 3. Changes of blood pressure and heart rate before and after Cilazapril

	Basal state	2 weeks	4 weeks	8 weeks	12 weeks
Systolic BP (mmHg)	128 ± 14	124 ± 30	124 ± 23	121 ± 13	118 ± 10
Diastolic BP (mmHg)	81 ± 10	83 ± 17	82 ± 14	81 ± 11	80 ± 5
Heart rate (/min)	74 ± 8	79 ± 12	72 ± 12	76 ± 10	71 ± 6

(Table 3).

44.4 ± 7% 12 50.2 ± 8%
가 (p=0.0034).

좌심실의 내경 및 용적, 좌심실 구혈률의 변화

Cilazapril 4.5 mm 12 52.4 ± 3.3 mm 55.3 ±
56.1 ± 6.5 mm 12 52.2 ± 4.5 mm 42.5 ± 4.9 mm 12 39.8 ±
41.9 ± 6.5 mm 7.7 mm
12 36.3 ± 7.3 mm 152.7 ± 44.6 ml
(p=0.034, p=0.025), 12 143.6 ± 28.7 ml
153.1 ± 38.7 ml 12 135.6 85.6 ± 32.3 ml 76.5 ± 37.8 ml
± 25.5 ml
84.9 ± 34.7 ml 12 72.6 ± 25.1 ml 42.5 ± 6% 12 48.5
(p=0.003, p=0.001). ± 5.8% 가 (p=0.0

39, Table 4).
 28.2 ± 3.4 wall motion score index 2.06 ± 0.18 1.76 ± 0.48 (Table 4).
 국소 벽운동 이상(Wall motion abnormality) 및 벽 운동 지수(Wall motion score)의 변화
 Cilazapril 좌심실 이완기능에 미치는 영향
 23 2
 23
 20 3 E wave/A wave 1
 3 2 (66.7%), 19 17 (89.5%), Cilazapril 16 (64%) 1
 Cilazapril 31.2 ± 3.4 8
 24.5 ± 2.3 wall motion 11 (73.3%)
 score index 1.95 ± 0.23 1.53 ± 0.21
 (p=0.022, p=0.012).
 심전도 변화
 10 6 23 ST , T
 4 5 2
 4 (80%), 1 (50%) 1 Cila-
 33.1 ± 1.5 zapril 2 ST

Table 4. Echocardiographic findings before and after Cilazapril administration compared with control group

	Basal state	2 weeks	4 weeks	8 weeks	12 weeks	p value
LVEDD (mm)						
- cilazapril	56.1 ± 6.5	56.3 ± 11.8	55.4 ± 7.8	53.7 ± 7.4	52.2 ± 4.5*	0.034
- control	55.3 ± 4.5		53.8 ± 6.4	53.3 ± 3.2	52.4 ± 3.3	0.069
LVESD (mm)						
- cilazapril	41.9 ± 6.5	42.1 ± 13.4	41.1 ± 8.5	39.4 ± 8.9	36.3 ± 7.3*	0.025
- control	42.5 ± 4.9		41.9 ± 7.1	40.2 ± 6.9	39.8 ± 7.7	0.129
LVEDV (ml)						
- cilazapril	153.1 ± 38.7	158.6 ± 42.7	157.6 ± 57.8	143.2 ± 38.1	135.6 ± 25.5*	0.003
- control	152.7 ± 44.6		154.5 ± 38.7	149.1 ± 51.2	143.6 ± 28.7	0.089
LVESV (ml)						
- cilazapril	84.9 ± 34.7	89.7 ± 43.8	80.2 ± 37.9	79.8 ± 35.7	72.6 ± 25.1*	0.001
- control	85.6 ± 32.3		81.4 ± 29.6	79.4 ± 39.1	76.5 ± 37.8	0.078
EF (%)						
- cilazapril	44.4 ± 3.2	48.1 ± 2.7	49.1 ± 4.2*	51.7 ± 3.5*	52.4 ± 2.8*	0.034
- control	42.5 ± 6.1		44.4 ± 6.4	45.6 ± 7.2	48.5 ± 5.8*	0.039
WMS						
- cilazapril	31.2 ± 3.4	28.8 ± 5.2	27.6 ± 5.4	25.6 ± 5.5*	24.5 ± 2.3*	0.022
- control	33.1 ± 1.5		31.2 ± 1.8	30.4 ± 2.5	28.2 ± 3.4	0.352
WMSI						
- cilazapril	1.95 ± 0.23	1.92 ± 0.36	1.64 ± 0.13	1.58 ± 0.33*	1.53 ± 0.21*	0.012
- control	2.06 ± 0.18		1.95 ± 0.19	1.91 ± 0.23	1.76 ± 0.48	0.065

WMS : wall motion score

WMSI : wall motion score index

* : Statistically significant

Table 5. Changes of serum creatinine, sodium and potassium before and after Cilazapril administration

	Basal state	2 weeks	4 weeks	8 weeks	12 weeks
Sodium (mEq/L)	140.6 ± 3.6	139.3 ± 3.7	142.9 ± 3.3	142.7 ± 2.4	141.5 ± 0.7
Potassium (mEq/L)	4.0 ± 0.5	4.4 ± 0.7	4.2 ± 0.2	4.4 ± 0.8*	4.5 ± 0.4*
Creatinine (mg/dl)	1.1 ± 0.3	1.2 ± 0.3	1.2 ± 0.4	1.2 ± 0.3	1.2 ± 0.2

*p<0.05

Table 6. Side effects of Cilazapril

Side effect	Number of patient (%)
Dry cough	3 (12%)
Facial edema	1 (4%)
Hypotension	1 (4%)
Dizziness	1 (4%)

검사실 소견에 미치는 영향
Cilazapril sodium creatinine
0.5 mEq/L, 12 potassium 4.0 ±
(p<0.05, Table 5).

증상의 개선 및 부작용

20 (80%) 가
3 (12%)
1 (4%)
1 (4%)

10 (40%) 가
20) 50%
1 (4%)

(Table 6).

고 안

가
11)12)
40%

13)

가
가
14)
(ventricular rem-
odeling)

15)
가
(reentry)가

16)
가

Kostuk 17) 4
4

가 가
가
18)19) White
20) 50%

renin - angiotensin system(RAS)

Angiotensin

21) Angiotensin
ACEI가

가 ACEI

10.3/85 ± 5.5 mmHg 12 115 ± 5.5/80 ± 6.3 mmHg . 12

가 ACEI
 , Raya ²²⁾

ACEI가 , 25

3 1

. Haber ²³⁾ ACEI , 1

가 creati - potassium

nine sodium 가

RAS 가

. ACEI angi -

otensin , bradykinin Cilazapril

endothelin 가

²⁴⁾

본 연구의 제한점

. ACEI 24 CO -
 NSENSUS - trial²⁵⁾ 가 12

trial²⁶⁾ 1 SMILE
 (placebo) Cilazapril

29%

ACEI 25
 , GI SSI - 3²⁷⁾ ISIS -
 4 trial²⁸⁾ 11% Cilazapril

6% 가 ,

ACE ACE Inhibitor My -
 ocardial Infarction Collaborative Group

가 가

. 75

가 Cilazapril 가

결론

²⁹⁾
 Cilazapril sulfhydryl 가 ACE 요 약

prilat 3 ACE cilaza -
³⁰⁾ 90% 연구배경과 목적 :

143.3 ±

azapril
 대상 및 방법 : Cil - 50%
 25 (: =18 : 7, 61.5±9) Cil -
 azapril 2.5 mg, 5 mg 12
 Cilazapril 15 (: =9 :
 6, 59.4±7) , , ,
 , , , 2, 4, 8, 12
 결 과 :
 Cilazapril
 56.1±6.5, 41.9±
 6.5 mm 12 52.2±4.5, 37.3±7.3 mm
 (p=0.034, p=0.025).
 Cilazapril 153.1±
 38.7, 84.9±34.7 ml 12 135.6±25.5
 72.6±25.1 ml (p=0.003, p=0.001).
 44.4±3.2 12 52.4±2.8%
 가 (p=0.034).
 55.3±4.5, 42.5±4.9 mm
 12 52.4±3.3 mm, 39.8±7.7 mm
 152.
 7±44.6, 85.6±32.3 ml 12 143.6±28.7
 76.5±37.8 ml ,
 , 42.5±6.1
 12 48.5±5.8% 가 (p=0.039).
 creatinine sodium
 가 potassium 8 가
 . 25 3 (12%) 가
 , , ,
 1
 결 론 :
 Cilazapril 가
 .
 중심 단어 : Cilazapril .

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