

중등도 심부전증 환자에서 Carvedilol의 치료 효과

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Clinical Efficacy of Carvedilol in Patients with Moderate to Severe Congestive Heart Failure

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ABSTRACT

Background : Clinical trials have shown that β -adrenergic blocking drugs are effective and well tolerated in patients with mild to moderate congestive heart failure. Carvedilol is a mild β_1 -selective adrenergic blocking agent with vasodilating properties due to β_2 blocker and antioxidant and anti-proliferative properties. This study assessed the efficacy and safety of carvedilol in patients with moderate to severe congestive heart failure caused by idiopathic dilated cardiomyopathy. **Methods :** We enrolled 27 patients with moderate to severe congestive heart failure with a left ventricular ejection fraction of 35% by MUGA scan. Each patient was randomly assigned to either control (n = 9) or carvedilol (n = 18, target dose 25 mg bid) for 6 months while background therapy with digoxin, diuretics, and ACE inhibitor remained constant. **Results :** Compared to the control group, patients in the carvedilol group showed significant increase of left ventricular ejection fraction ($p < 0.05$). In addition, patients in the carvedilol group had a tendency to show a decrease in left ventricular end-diastolic dimension and heart rate. Also, the carvedilol group had a greater frequency of symptomatic improvement than the control group. There was neither serious side effects nor hospitalization. **Conclusion :** These finding indicate that carvedilol produces important clinical benefits in patients with moderate to severe heart failure treated with digoxin, diuretics, and ACE inhibitor without serious side effects. (Korean Circulation J 1998;28(4):523-531)

KEY WORDS : Carvedilol · Congestive heart failure · beta-adrenergic blocker.

서 론

가

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, renin - angiotensin - aldosteron
1)
norepinephrine,²⁾³⁾ vasopressin, atrial na -

triuretic factor(ANF), endothelin 가
20

clinical trial 가 ACE 150 mmHg ,
95 mmHg , 2.0 mg/dl
hydralazine - isosorbide dinitrate,
가 27

9 carvedilol 18 ,
digoxin, , ACE
carvedilol ca -
metoprolol bisoprolol rvedilol(Dilatrend ,) 가
Carvedilol 6.25 mg, bid
2 25 mg, bid
Carvedilol 3 MU -
4) 가 GA(Multi - Gated Albumin) scan, , NYHA
(New York Heart Association) functional class
가 .

(Fig. 1). 2 , 4 , 6 , 12 , 16 , 20
carvedilol . Carvedilol 6
가 MUGA scan, , NYHA class 가

digoxin, Statistical Package for Social Science(SPSS) pro -
gram Student t - test chi - square test
, angiotensin converting enzyme(ACE) p 0.05
carvedilol 가 ± .

결 과

대상 및 방법
1996 6 1997 3
3
MUGA scan 35%
27 9 , carvedilol 18
, 5 : 4, carvedilol
14 : 4 carvedilol
68 ± 4.0 , 62 ± 2.5

(Table 1).
26.3 ± 2.1% Carvedilol
30.7 ± 2.6% ,
63.4 ± 2.1 mm Carvedilol
64.9 ± 2.0 mm
NYHA functional class class 가 27 18
(66.7%) 가 class 가 5
(18.5%), class 가 4 (14.8%) .

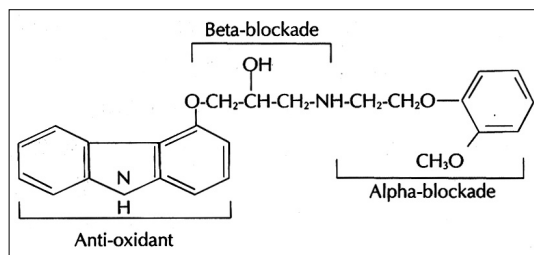


Fig. 1. The chemical structure of carvedilol.

2 digoxin , ACE
25 digoxin, , ACE
188 ± 9 carvedilol 191 ± 12
(Table 1).
6 MUGA scan
26 ± 2% 35 ± 3%
carvedilol 30 ± 3%
47 ± 3% carvedilol
(p<0.05)(Table 2,

Table 1. Pretreatment characteristics of patients in the study

	Control group (n = 9) Mean ± SD	Carvedilol group (n = 18) Mean ± SD	p value
Age (yrs)	68 ± 4	62 ± 3	
Sex (M/F)	5/4	14/4	
LVEF (%)	26.3 ± 2.1	30.7 ± 2.6	0.272
LVEDD (mm)	63.4 ± 2.1	64.9 ± 2.0	0.641
SBP (mmHg)	122 ± 7.6	132 ± 6.6	0.301
DBP (mmHg)	78 ± 4.0	87 ± 4.4	0.204
H.R. (/min)	100 ± 6.1	93 ± 4.6	0.375
NYHA class (cases)			
	3	1	
	4	14	
	2	3	
Concurrent medication			
Digoxin	8	17	
Diuretics	9	18	
ACEI	9	18	
Mean Duration of F/U (days)	188 ± 9	191 ± 12	

LVEF : Left ventricular ejection fraction
LVEDD : Left ventricular end-diastolic dimension
SPB : Systolic blood pressure
DBP : Diastolic blood pressure
H.R. : Heart rate
NYHA : New York Heart Association
ACEI : Angiotensin converting enzyme inhibitor
F/U : Follow up

Table 2. The changes of distribution of NYHA functional class between pre and post treatment state

	Control group (n = 9)		Carvedilol group (n = 18)		p value
	Before treatment	After treatment	Before treatment	After treatment	
LVEF (%)	26 ± 2	35 ± 3	30 ± 3	47 ± 3	0.04*
LVEDD (mm)	63.3 ± 2.1	60.4 ± 2.6	65.9 ± 2.0	60.5 ± 1.7	0.56
Heart rate (/min)	99 ± 6	81 ± 8	93 ± 5	69 ± 3	0.93

* : p<0.05

LVEF : Left ventricular ejection fraction
LVEDD : Left ventricular end-diastolic dimension

Fig. 2).

63.3 ± 2.1 mm 60.4 ± 2.6 mm
carvedilol 65.9 ± 2.0 mm
60.5 ± 1.6 carvedilol
(Table 2, Fig. 3).
99 ± 6 /min 81 ± 8
93 ± 5 /min 69
carvedilol
(Table 2, Fig. 4).

NYHA functional class class 가
3 (33.3%), class 가 4 (44.4%), class 가 2
(22.3%) class 2 (22.3%),
class 가 6 (66.6%), class 가 1 (11.1%)
2 NYHA functional class
Carvedilol NYHA functional class
class 1 (5.6%), class 가 14
(77.8%), class 가 3 (16.7%)
class 5 (27.8%), class 가 10 (55.6%),

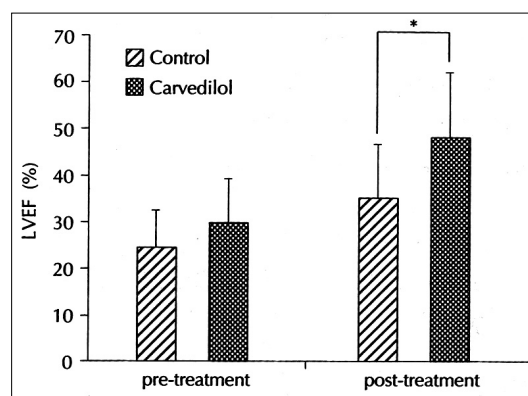


Fig. 2. Changes of left ventricular ejection fraction (LVEF) after treatment (* : p<0.05).

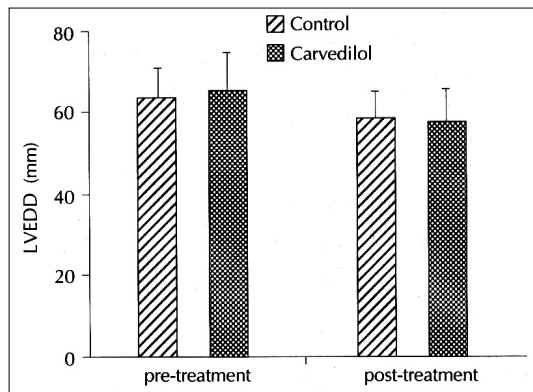


Fig. 3. Changes of left ventricular end-diastolic dimension (LVEDD) after treatment.

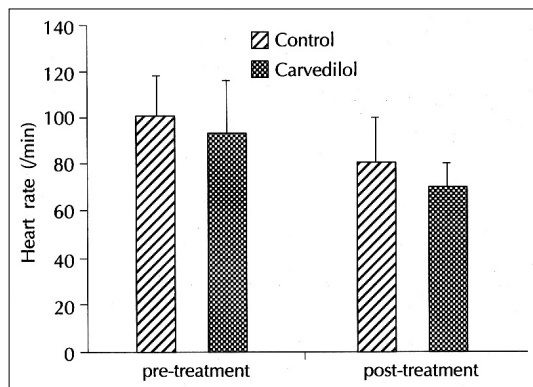


Fig. 4. Changes of heart rate after treatment.

Table 3. Response to carvedilol therapy

NYHA	Control group (n, %)		Carvedilol group (n, %)	
	Before treatment	After treatment	Before treatment	After treatment
Class I	0 (0)	2 (23)	0 (0)	5 (28)
Class II	3 (33)	6 (66)	1 (5)	10 (55)
Class III	4 (44)	1 (11)	14 (78)	3 (17)
Class IV	2 (23)	0 (0)	3 (17)	0 (0)

NYHA : New York Heart Association

class I 가 3 (16.7%) (Table 3, Fig. 5).

Carvedilol 2 (10.5%)

2 Carv - edilol 4

. Carvedilol 1

Carvedilol 1

carvedilol

carvedilol

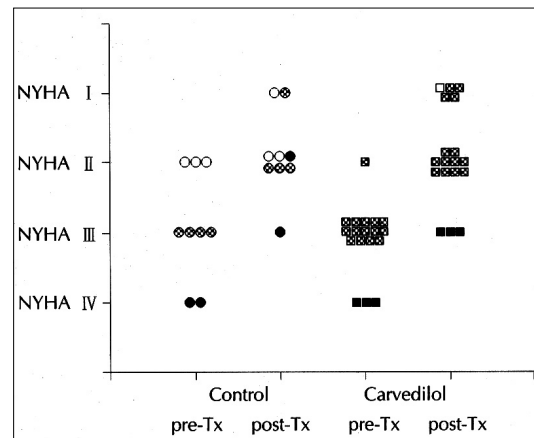


Fig. 5. Changes of NYHA (New York Heart Association) functional class after treatment.

고 안

, renin - angiotensin - aldosterone , vasopressin 가 가

4 40% 5)

20 가 clinical trial

ACE , hydralazine - isosorbide dinitrate metoprolol, bisoprolol, carvedilol .⁶⁾ dig - oxin⁷⁾ 8) 가 , Ca channel amlodipine⁹⁾ felodipine¹⁰⁾ nifedipine¹¹⁾ 가 , phosphodiesterase milrin - one¹²⁾

enoximone, B - agonist xamoterol,¹³⁾ HA class , metoprolol 12 가
 prostaglandin¹⁴⁾ flosequinan,¹⁵⁾ metoprolol 가
 inotropic agent pimobendan¹⁶⁾ 가 , CIBIS(Cardiac Insufficiency
 Bisoprolol Study)²³⁾ 320 NYHA class
 bisoprolol 가
 가
 가
 V - HeFT trial¹⁷⁾¹⁸⁾ hydralazine - iso - (survival benefit)
 sorbide dinitrate(HYD - ISDN) enalapril Carvedilol - 1(- 1)
 peak exercise oxygen consumption en - 가
 가 alapril 2 HYD - ISDN (Fig. 1)
 28% 40% . Packer
 가 80 Br -
 istow¹⁹⁾ “adrenergic hypo - 가 가
 thesis ” 가 signal tra - land Heart Failure Research Collaborative Group²⁵⁾
 nsduction 415 6
 가 carvedilol 가
 가 .²⁰⁾ 가
 V - HeFT trial norepinephrine , Doughty²⁶⁾
 (<600 ng/ml) norepinephrine 123 12 carvedilol
 (>900 ng/ml) norepinephrine 가 ation) remodeling (dil -
 Krum²⁷⁾ 56 6
 carvedilol carvedilol
 가
 nethidine iodine - 123 - metaiodobenzy -
 lguanidine(MIBG) Colucci²⁸⁾ US Carvedilol Heart Failure St -
 .²¹⁾ udy 366
 가 12 carvedilol
 가 . Waagstein MDC(Metoprolol in
 Dilated Cardiomyopathy) study²²⁾ 383 NY -
 . Olsen²⁹⁾ 60
 carvedilol

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연구의 제한점

. Carvedilol

- 1

가 가

carvedilol

1)

가(unchanged or mildly, moderately, markedly improved, worse), 2) NYHA functional class, 3) radionuclide ventriculography

대 상 :

MUGA scan 35%

(NYHA -) 27

carvedilol (n=18)

(Digoxin, , ACE) (n=9)

1) quality of life

score 2) (exercise tolerance)

6 - minute corridor walk

9 - minute self powered treadmill test가 . 1992

FDA 가

6 - minute corridor walk

9 - minute self powered treadmill test

가

scan, NYHA class, MUGA

2 6.25 mg bid 25 mg

bid 6 .

결 과 :

Carvedilol 30 ± 3% 47

± 3% 가 26 ± 2% 35 ± 3%

exercise capacity가

가 .

(p<

0.05). carvedilol 65.9

가 NYHA funct -

± 2.0 mm 60.5 ± 1.6 mm 63.3 ± 2.1

ionl class

mm 60.4 ± 2.6 mm

. Australia - New Zealand Heart

Failure Research Collaborate Group

NYHA functional class carvedilol

carv -

가 NYHA class가

edilol

2 (22.2%)

carvedilol 가

. NYHA functional

. Carvedilol 1

class 가 18 3 (16.7%)

2

carvedilol 가

carvedilol

가

결 론 :

carvedilol

가

randomized multicenter

carvedilol

가

가

중심 단어 : Carvedilol . ..

요 약

1997

연구배경 :

가

가

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