

1~2 기 본태성 고혈압 환자에서 Imidapril 대 Enalapril의 항고혈압 효과를 평가하기 위한 무작위, 이중맹검 임상시험

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A Randomized, Double-Blind Clinical Trial to Determine the Efficacy of Imidapril vs. Enalapril in Patients with Stage 1 to 2 Essential Hypertension

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ABSTRACT

Background : Imidapril is a long-acting angiotensin converting enzyme inhibitor, which has been demonstrated to be effective in reducing blood pressure. The purpose of this study is to compare the antihypertensive efficacy, safety and tolerability of imidapril and enalapril in patients with stage 1 to 2 essential hypertension. **Methods** : In this double-blind, double-dummy, randomized, parallel study, the efficacy, safety and tolerability of once-daily imidapril versus once-daily enalapril were evaluated in 84 patients with stage 1 - 2 hypertension during 8 weeks. If antihypertensive response was insufficient after 4 week treatment period, the dosage for both study drugs doubled until the end of study. **Results** : Data from 84 patients who completed the study were eligible for per-protocol analysis. An adequate antihypertensive effect was observed in 47.6% (20/42) in the imidapril group and in 23.8% (10/42) in enalapril group. There was statistically significant difference between the two treatments in the percentage of patients achieving a "reduced blood pressure". The pulse rate did not changed in both groups. Safety profiles were similar between treatments. **Conclusion** : In patients with mild to moderate hypertension, the imidapril group showed better response with regard to antihypertensive effect. Both imidapril and enalapril were well tolerated with similar safety profiles. (Korean Circulation J 1999;29(11):1234-1239)

KEY WORDS : Hypertension · Imidapril.

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서 론

Angiotensin Converting Enzyme inhibitor(ACEI)

1, 2 mmHg 109 mmHg

(JNC V)

5

(90

, 2 3

1)2)3)

가 방 법

.⁴⁾ Imidapril(Tanatriil,) Tanabe

ACEI

가 diacid imidaprilat 4

prodrug . Imidaprilat 90mmHg

ACE inhibitory activity enalapril en - (5 8)

alaprilat 2 , captopril 10 가 peak 90 mmHg

⁵⁾ , imidapril

imidapril 10 mg 1 1 1 1 5 mg 1 10 mg , en -

ACE 85 90% .⁶⁾ Imidapril alapril 1 1 5 mg

ACEI 가 0.9 3.7% 1 10 mg 가 .

1 2 imida -

pril enalapril 1 1 , 가 ,

(- 2 , 0 , 4 , 8)

대상 및 방법

계 획

1 1 imidapril(5 mg, 10 12 8

4 가 10 mg) , 5 2

enalapril(5 mg, 10 mg) 2

가 8 , 가 5 mmHg 가

1 2 1

(wash - out period) 2

(placebo period, 2

가) , , ,

대상환자의 선정

4 8

18

가 .

가 , 가

가

자료의 통계적 처리

Chi - Square

Fisher

(Table 1), 가

Chi - Square

Fisher

p 0.05

SAS Version 6.11

결 과

enalapril 49 , imidapril 63

enalapril 42 , imidapril 42

21 7 , 75%

가 (Table 2).

Table 1. Criteria for evaluation of changes (mmHg) in systolic (SBP), diastolic (DBP) and mean blood pressure (MBP)

	Reduced	Slightly reduced	No change	Increased
SBP	20	10 - 19	9	10
DBP	10	5 - 9	4	5
MBP	13	7 - 12	6	7

Efficacy

가 Table 1

8

imidapril

47.6%(20/42) , enalapril 23.8%(10/42)

imidapril (Ta -

ble 3).

imidapril 76.2%(32/42) , en -

alapril 52.4%(22/42)

. Fig. 1 0 8

(1 5 mg) imidapril

100%(6/6) , enalapril 33.4%(2/6) ,

(1 10 mg) imidapril 38.6%

(14/36) , enalapril 22.2%(8/36)

(Table 3).

Safety

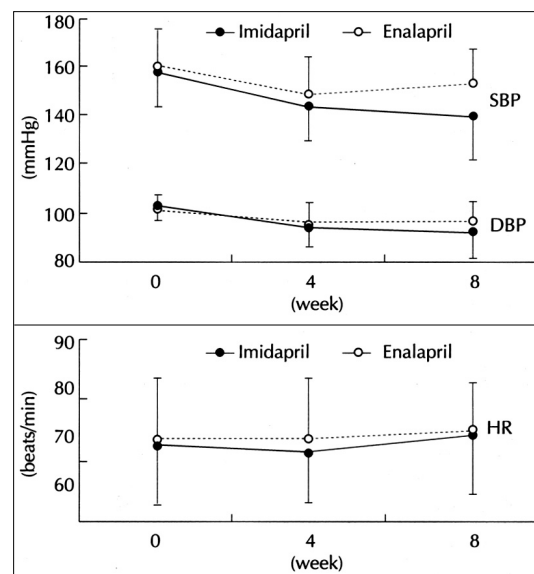


Fig. 1. Changes in blood pressure and heart rate during the study. Blood pressure decreased significantly compared with baseline in both treatment groups ($p < 0.05$, paired t-test).

가 imidapril 4.8%(2), enalapril 7.1%(3) .

perprotocol analysis imidapril 9(21.4%) enalapril 11(26.2.0%) (Table 4).

가

, ACEI 8)9)

가

Table 2. Demographic characteristics

	Imidapril group	Enalapril group
Sex (M/F)	16/26	22/20
Age (years)	52 ± 8.7	56 ± 8.9
Bwt (kg)	65 ± 7.9	65 ± 10.3
Hypertension severity		
Mild	14	16
Moderate	28	26
SBP (mmHg)	156 ± 12.4	159 ± 14.2
DBP (mmHg)	102 ± 5.5	101 ± 4.9
HR (beats/min)	73 ± 8.3	74 ± 10.1

Mean ± SD, Hypertension severity was graded according to The JNC V, All parameters were measured at the end of the Observation period, No significant differences were found Between groups

Table 3. Evaluation of changes in blood pressure

	Reduced	Slightly reduced	No change	Increased	Total	Overall response			
						Reduced (%)	POR	95% CI	p value
Imidapril group	20	12	10	0	42	47.6	2.91	1.04 - 8.26	0.04*
Enalapril group	10					23.8			
						0.06**			
5 mg									
Imidapril group	6	0	0	0	6	100	-	-	NS*
Enalapril group	2	3	1	0	6	33.4			
10 mg									
Imidapril group	14	12	10	0	36	38.8	2.23	0.71 - 7.13	NS*
Enalapril group	8	9	16	3	36	22.2			
Mild									
Imidapril group	6	4	4	0	14	42.9	3.25	0.50 - 23.4	NS**
Enalapril group	3	4	7	2	16	15.0			
Moderate									
Imidapril group	14	8	6	0	28	50.0	2.71	0.76 - 10.0	NS*
Enalapril group	7	8	10	1	26	26.9			

POR : prevalence odds ratio CI : confidence interval * : ² test

ACEI

가 CAPPP (Captopril Prevention Project) trial

.¹²⁾ Angiotensin AT1 receptor antagonist(AT1R blocker)가

RAS

가

** : Fisher's exact test

Table 4. Frequency of clinical adverse effects

	Imidapril (n = 42)	Enalapril (n = 42)
	2	3
	1	1
	1	0
	0	1
	2	1
	1	0
	1	0
	1	0
	2	3
Total	11 (26%)	9 (21%)

Angiotensin
tensin
prostaglandin

가
enalapril
nabe
ACEI
imidapril
Imidapril
Ta -
ACEI
imidapril
47.
6% , enalapril 23.8%
Saruta ¹¹⁾ 71.3%, 66.1%

Saruta 12
Imidapril
imida -
prilat가 enalapril
2 , captopril 10
ACE inhibitory activity ⁵⁾

가
enalapril
가
(1 5mg)
가 enalapril 33.4%(2/6
) imidapril 100%(6/6)
RAS activation

imidapril
ACE inhibitory action
가
가
Saruta ¹¹⁾ 0.9%
imidapril ACEI
imidapril 4.8%(2) ,
enalapril 7.1%(3)
Yoo imidapril ¹³⁾
Renin - angiotensin system

ATIIR1 blocker ACEI
Angiotensin
ATIIR1 blocker가
Park ¹⁴⁾
ATIIR1 blocker 4.3%
RAS
ATIIR1 blo -
cker가 ACEI
imidapril
ACEI
ATIIR blocker RAS가
ACEI potency가
가

가
imidapril
ACEI
ATIIR blocker RAS가
ACEI potency가
가

요 약
연구배경 :
1 2 imida -
pril enalapril 1 1 ,

방 법 :
, 1 1 imidapril(5 mg, 4

가 10 mg) enalapril(5 mg,
10 mg) 1 2
84 , 가
가 .
결 과 :
8 imidapril 47.6%
(20/42), enalapril 23.8%(10/42) imida -
pril .
imidapril 76.2%(32/42), enalapril 52.4%
(22/42) .
결 론 :
1 1 imid -
april enalapril
, imidapril
enalapril .
중심 단어 : . Imidapril · Enalapril.

REFERENCES

- 1) Hennekens CH, Albert CM, Godfried SL, Gaziano JM, Buring JE. *Adjunctive drug therapy of acute myocardial infarction evidence from clinical trials. N Engl J Med* 1996;335:1660-7.
- 2) Pfeffer MA, Braunwald E, Moye LA, et al., for the SAVE investigators. *Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction: Results of the Survival and Ventricular Enlargement Trials. N Engl J Med* 1992;327:669-77.
- 3) Grag R, Yusuf S, for the Collaborative Group on ACE Ingibitor Trials. *Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. JAMA* 1995;273:1450-6.
- 4) Lewis EJ, Hunsicker LG, Bain RP, Rohde RD, for the Collaborative Study Group. *The effect of angiotensin converting enzyme inhibiton on diabetic nephropathy: The Collaborative Stydy Group. N Engl J Med* 1993;329:1456-62.
- 5) Kubo M, Kato J, Ochiai T, Ishida R. *Pharmacological studies on (4s)-1-methyl-3- <(2s)-2- {N-[(1s)-1-ethoxycarbonyl-3-phenylpr-opyl]amino }propionyl >-2-oxo-imidazoline-4-carboxylic acid hydrochloride (TA-6366), a new inhibitor: . ACE inhibitory and antihypertensive activities. Jpn J Pharmacol* 1990;53:201-10.
- 6) Demolis P, Annane D, Duhaze P, Giudicelli JF. *Systemic, regional and cerebral hemodynamic effects of a new angiotensin converting enzyme inhibitor, imidapril, in healthy volunteers. Fundam Clin Pharmacol* 1994;8:80-9.
- 7) Pinto YM, vanVeldhuisen DJ, Tjon-Ka-Jie RT, Rooks G, Netzer T, Lie KI. *Dose-finding study of imidapril, a novel ACE-inhibitor, in patients with stable chronic heart failure. Eur J Clin Pharmacol* 1996;50:265-8.
- 8) Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure. *The sixth report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (JNC). Arch Inter Med* 1997;157:2413-46.
- 9) World Health Organization. *Hypertension control: Report of a WHO expert committee, Geneva. World Health Organization;1996.*
- 10) Saruta T, Omae T, Iimura O, Yoshinaga K, Abe K, Ishii M, et al. *Clinical evaluation of imidapril (ACE/TA-6366) against essential hypertension by administration with thiazide hypotensive diuretics: A collaborative multicenter study. J Clin Ther Med* 1991;7:2505-23.
- 11) Takao S, Teruo O, Morio K, Osamu I, Kaoru Y, Keishi A, et al. *Imidapril hydrochloride in essential hypertension: a double-blind comparative study using enalapril maleate as a control. J Hypertens* 1995;13(suppl 3):S23-S30.
- 12) Hansson L, Lindoholm LH, Niskanen L, Lanke J, Hedner T, Niklason A, et al. *Effect of angiotensin-converting enzyme inhibition compared with conventional therapy on cardiovascular morbidity and mortality in hypertension: The Captopril Prevention Project (CAPPP) randomized trial. Lancet* 1999;353:611-6.
- 13) Yoo WS, Choi JW, Yoo HJ, Choi SK, Ko HI. *Incidence of Dry Cough with Imidapril in Essential Hypertension. Circulation* 1997;3:47-52.
- 14) Park DG, Lee MM, Chai IH, Rhee MY, Lee HJ, Kim HS, et al. *The Antihypertensive Efficacy, Safety, and Tolerability of Losartan versus Fosinopril in Patients with Hypertension. Circulation* 1999;28:15-26.