

## 이미다프릴에 의한 마른 기침 발생율의 고찰

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### The Study of the Dry Cough Incidence Rate about Imidapril, the Angiotensin Converting Enzyme Inhibitor

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#### ABSTRACT

**Background and Objectives** : Imidapril, one of the ACE inhibitor, has been used to treat hypertension, congestive heart failure, diabetes mellitus and renal disease. ACE inhibitor, however often causes dry cough and this adverse effect affects the compliance rate negatively. This report aimed to examine the incidence rate of coughing caused by Imidapril treatment. And we compared the results with the incidence and tendency of dry cough caused by the other ACE inhibitors. **Materials and Method** : This study enrolled 38 patients who followed up at internal medicine and took Imidapril from the period of May 9, 1997 to December 17, 1997. We tested its effectiveness, safety and tolerance. The initial dosage of it was 5mg/day and the maximum dosage according to blood pressure was 10mg/day for 8 weeks. The tendency and the incidence of dry cough have been analyzed and compared with recently published Korean reports. **Results** : The 5 mg dosage of Imidapril showed 68.1% in lowering blood pressure rate and it went up to 81.8% during the 8 weeks treatment period. The blood pressure regularity rate was 36.3% after the 8 weeks treatment. The overall rate of adverse effect occurrence was 26.1% (6/23) and 8.7% of them were likely to cough. One of the patients who showed nausea stopped medication. The recent articles reported that the incidence of dry cough had been reduced : Enalapril (33.8%), Fosinopril (16%), Ramipril (15%), Imidapril (7.8 - 8.7%), Losartan (4.3%). **Conclusion** : Imidapril is as safe and effective as other ACE inhibitors. Various ACE inhibitors that were newly developed show their effectiveness in lessening incidence rate of dry cough, and Imidapril is thought to be an excellent drug for this matter. Even though Losartan shows the lowest incidence rate of dry cough, it needs to more regular usages since it is still on the stage of its medical adaptation. (**Korean Circulation J 1998;28(7):1154-1160**)

**KEY WORDS** : Imidapril · Angiotensin converting enzyme inhibitor · Dry cough.

#### 서 론

( ACE inhibitor)

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**Table 1.** Categories of antihypertensive response

|                        | Group 1      | Group 2   | Group 3 | Group 4      |
|------------------------|--------------|-----------|---------|--------------|
| Systolic pressure      | - 20 or more | - 19 - 10 | ± 9     | + 10 or more |
| Diastolic pressure     | - 10         | - 9 - 5   | ± 4     | + 5          |
| Mean arterial pressure | - 13         | - 12 - 7  | ± 6     | + 7          |

\*Group 1 : mean blood pressure reduced above 12 mmHg from baseline mean blood pressure

\*Group 2 : reduced blood pressure range (from 12 mmHg to 7 mmHg)

\*Group 3 : mean blood pressure reduced below 7 mmHg from baseline mean blood pressure

\*Group 4 : neither Group 1 nor Group 2 and Group 3

5)  
5  
6) 가 가  
ACE inhibitor Captopril Enalapril, Ra-  
mipril, Fosinopril, Lisinopril, Cilazapril  
가  
가  
가  
Imidapril(Tanat -  
ril®) ACE inhibitor  
(AT<sub>1</sub>)

**Table 2.** Characteristics of analyzed subjects(n = number)

|                             | Male<br>(n = 11) | Female<br>(n = 11) | Total<br>(n = 22) |
|-----------------------------|------------------|--------------------|-------------------|
| Age (yr)                    | 52.6 ± 11.2      | 53.8 ± 6.4         | 53.2 ± 8.9        |
| Height (cm)                 | 166.9 ± 5.7      | 155.3 ± 6.7        | 161.6 ± 8.4       |
| Weight (kg)                 | 69.6 ± 14.3      | 63.6 ± 11.0        | 66.6 ± 12.8       |
| Duration of<br>disease (yr) | 4.9              | 3.2                | 4.5               |
| Degree of<br>hypertension   |                  |                    |                   |
| mild                        | n = 1            | n = 0              | 4.5%<br>( 1/22)   |
| moderate                    | n = 2            | n = 3              | 22.7%<br>( 5/22)  |
| severe                      | n = 8            | n = 8              | 72.7%<br>(16/22)  |

Values of age, height and weight are mean ± standard deviation

대상 및 방법  
1997 5 9 1997 12 17  
(1  
) (3 ) (JNC V )  
38 가 23 ( 140/90 mmHg  
1 , 4  
(Table 1).  
8  
Imidapril 1 1 5 mg  
2 , 4 , 8  
( 13 mmHg  
)가 91 mmHg  
1 1 10 mg  
(p<0.05).  
paired t - test  
95%

**결 과**

연구대상자들의 특성

| 가       | 38           | 16         |
|---------|--------------|------------|
| 가       | 가            | 가 8        |
| 가       | 22           | 11         |
|         | 52.6         | 53.8       |
|         |              | 105.2 mmHg |
|         | 가 1 (4.5%)   | 가 5        |
| (22.7%) | 가 11 (72.7%) |            |

가 (Table 2).

혈압 강하 효과

|              | 90.6 mmHg        |
|--------------|------------------|
| 14.6 mmHg    | (Fig. 1).        |
| 18           |                  |
| 81.8%(18/22) | Imidapril        |
|              | (140/90)         |
| 8 (36.4%)    | (Table 3).       |
| 5 mg         | 68.1%            |
| (15/22)      | 가                |
|              | 91 mmHg          |
| 1 1 10 mg    | 10 mg            |
|              | 75.0%(9/12)      |
|              | 가                |
|              | 10               |
| 5 mg         |                  |
| mg           |                  |
|              | 9.3 mmHg, 9.58   |
| mmHg         | 가                |
|              | (Table 4 and 5). |

임상증상

가

12 (12/22 = 54.5%)

가

가 3 (13.6%)

Imidapril

#### 약물과 관련된 부작용

가

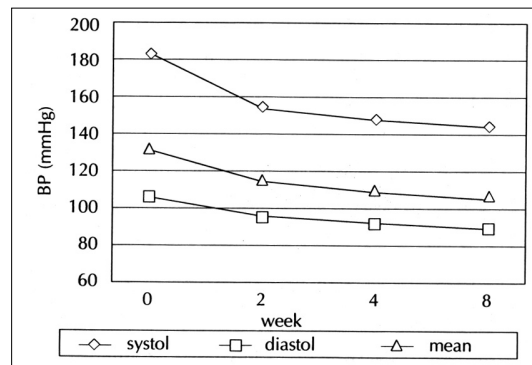
가 38

가 22

1

23

가



**Fig. 1.** Effects of imidapril monotherapy on systolic, diastolic and mean blood pressure.

**Table 3.** Blood pressure lowering effect with Imidapril monotherapy

| Effect              | Group 1       | Group 2 | Group 3 | Blood pressure regularity rate |
|---------------------|---------------|---------|---------|--------------------------------|
| Duration of therapy |               |         |         |                                |
| 2 Week              | 54.5% (15/22) | 2/22    | 5/22    | 4/22 (18.2%)                   |
| 4 Week              | 86.0% (19/22) | 1/22    | 2/22    | 7/22 (31.8%)                   |
| 8 Week              | 81.8% (18/22) | 3/22    | 1/22    | 8/22 (36.4%)                   |

\*Upper limit of blood pressure : systolic/distolic 139/89 mmHg

\*Group 1 : mean blood pressure reduced above 12 mmHg from baseline mean blood pressure

\*Group 2 : reduced blood pressure range (from 12 mmHg to 7 mmHg)

\*Group 3 : mean blood pressure reduced below 7 mmHg from baseline mean blood pressure

**Table 4.** Blood pressure lowering effect according to the dosage

| Dosage                       | Number | Group 1    | Group 2 | Group 3 |
|------------------------------|--------|------------|---------|---------|
| Effect after 5 mg medication | 22     | 15 (68.1%) | 1       | 6       |
| Effect after dose up 10 mg   | 12     | 9 (75.0%)  | 3       | 0       |

\*Group 1 : mean blood pressure reduced above 12 mmHg from baseline mean blood pressure

\*Group 2 : reduced blood pressure range (from 12 mmHg to 7 mmHg)

\*Group 3 : mean blood pressure reduced below 7 mmHg from baseline mean blood pressure

**Table 5.** Mean change in through sitting systolic, diastolic and mean blood pressure values are mean pressure

| Dosage                        | Number | Baseline (mmHg)          | Post-treatment (mmHg) | Change ( PmmHg) |
|-------------------------------|--------|--------------------------|-----------------------|-----------------|
| Effect after 5 mg medication  | 22     | syst. pressure<br>181.3  | 153.4                 | 27.9            |
|                               |        | diast. pressure<br>105.2 | 95.9                  | 9.3             |
|                               |        | mean pressure<br>130.8   | 115.2                 | 15.6            |
|                               |        |                          |                       |                 |
| Effect after 10 mg medication | 12     | syst. pressure<br>170.0  | 153.7                 | 16.3            |
|                               |        | diast. pressure<br>102.5 | 92.9                  | 9.6             |
|                               |        | mean pressure<br>125.1   | 113.1                 | 12.0            |
|                               |        |                          |                       |                 |

Values are mean pressure

**Table 6.** List of adverse effect induced by imidapril

| No | Sex | Age | Symptom    | Degree   | Time of onset                | Management         | Prognosis                      |
|----|-----|-----|------------|----------|------------------------------|--------------------|--------------------------------|
| 1  | M   | 60  | dry cough  | mild     | after 4 weeks medication     | observation        | spontaneous disappearance      |
| 2  | F   | 45  | dry cough  | mild     | after 3 weeks medicaton      | observation        | decreased frequency gradually  |
| 3  | F   | 46  | headache   | mild     | after 2 weeks medication     | observation        | pers istent for 6 weeks        |
| 4  | F   | 58  | nausea     | mild     | after 7 weeks medication     | observation        | persistent for 1 week          |
| 5  | F   | 57  | somnolence | mild     | for 3 days after medication  | observation        | spontaneous disappearance      |
| 6  | F   | 46  | nausea     | moderate | for 20 days after medication | Stopped medication | prompt recovery after stopping |

**Table 7.** Changing of the laboratory data according to medication

| Laboratory parameters | Baseline      | Post-medication | Significance |
|-----------------------|---------------|-----------------|--------------|
| White blood cell      | 7.24 ± 1.80   | 6.99 ± 1.95     | N.S.*        |
| Basophil              | 0.66 ± 0.52   | 0.46 ± 0.40     | p = 0.0157   |
| Eosinophil            | 2.73 ± 3.08   | 2.79 ± 2.71     | N.S.         |
| Neutrophil            | 53.30 ± 9.13  | 53.47 ± 10.07   | N.S.         |
| Lymphocyte            | 35.80 ± 8.70  | 33.26 ± 11.16   | N.S.         |
| Monocyte              | 6.82 ± 1.71   | 6.56 ± 2.58     | N.S.         |
| Glucose               | 108.2 ± 32.2  | 96.4 ± 39.9     | N.S.         |
| BUN                   | 13.5 ± 3.9    | 15.0 ± 4.3      | N.S.         |
| Total cholesterol     | 208.1 ± 52.9  | 195.7 ± 41.7    | N.S.         |
| Tryglyceride          | 187.7 ± 102.3 | 171.2 ± 103.8   | N.S.         |

\*N.S. : not significant

가 , , , 가  
6  
26.1%(6/23)  
2 (2/23=8.7%)  
2  
(Table 6).  
투약에 따른 임상 검사치의 변화  
1 22  
3 1 가

**Table 8.** Incidence of dry cough by various ACE inhibitor and AT 1 antagonist

| Drug       | Author | Rho <sup>11)</sup><br>1994 | Yoo <sup>12)</sup><br>1991, 1993,<br>1997 | Park <sup>8)</sup><br>1998 |
|------------|--------|----------------------------|---|----------------------------|
| Enalapril  |        | 33.8%<br>(23/68)           |   |                            |
| Fosinopril |        |                            |   | 16.3% (8/49)               |
| Ramipril   |        |                            | 15.2% (5/33)                              |                            |
| Delapril   |        |                            | 9.1% (3/33)                               |                            |
| Imidapril  |        |                            | 7.8% (16/204)                             |                            |
| Losartan   |        |                            |   | 4.3% (2/47)                |

가  
(p<0.05) (Table 7).

## 고 안

ACE inhibitor Imidapril (5 10  
mg 1 1 )

. ACE inhibitor  
, , , . bra -  
dykinin

가  
(5 30%)

. ACE inhibitor  
가  
Imidapril 81.8%  
(18/22) 36.4%(8/22)

Kim<sup>7)</sup>  
(87%20/23), (61%=14/  
23)

/ Kim<sup>7)</sup> 140/91  
mm Hg Kim

<sup>7)</sup> 14.6 mmHg, 15 mmHg Kim  
12 4

Losartan Fosinopril 가  
Park<sup>8)</sup>

pril Imidapril Losartan Fosino -  
69.4% 68.1%, 81.8%

4 5 mmHg

. ,  
가

. 5 mg 10 mg

68.1% 75.0% 10 mg

가 가 . 5 mg

10 mg

9.3 mmHg, 9.6 mmHg

10 mg 가

. Losartan Fosinopril 가

Park<sup>8)</sup>

. ACE inhibitor

가

Imidapril

5.5%(2/36)

8

8.7%(2/23)

. ACE inhibitor 1

14 9)

가

ACE inhibitor

Enalapril

<sup>10)11)</sup>

. 2

1

<sup>12)</sup>

8)11)

가

1

Yoo<sup>12)</sup> 3.9

4.5

3

50%

ACE inhibitor

2

Imidapril  
ACE inhibitor

가

Enalapril

재료 및 방법 :

Rho

<sup>11)</sup>

13.2%(9/68)

1997 5 9

1997 12 17

Yoo

<sup>12)</sup>

Imidapril

38

1.5%(3/204)

가

23

, 5

가 가

ACE inhibitor가

mg

가

1

1

10 mg

8

<sup>13)</sup><sup>14)</sup>

ACE inhibitor

substance P

결 과 :

Imidapril 5 mg

68.1%

, 8

81.8%,

<sup>15)</sup>

Table 8

36.3%

가

26.1%(6/23)

8.7%

Arakawa

ACE

inhibitor

Imidapril

Enalapril(33.8%) Fosinopril(16.3%) Ra-  
mipril(15.2%) Delapril(9.1%) Imidapril(7.8 8.7%)  
Losartan(4.3%)

ACE

2

(C N )가

가

, Imidapril C

N

결 론 :

ACE inhibitor Imidapril

(AT<sub>1</sub>)

가

8.7%

가

<sup>16)</sup><sup>17)</sup>

가 가

ACE inhibitor

가

가

Losartan 가

AT<sub>1</sub>

<sup>18)</sup><sup>19)</sup>

중심 단어 :

요 약

서 론 :

Imidapril ACE inhibitor

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