

## Consumption Time of Captopril Influenced the Outcomes of Patients with Stage 1 Hypertension

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### Abstract

Differences in drugs consumption time may affect its absorption and metabolism in the body which could lead to differences in its efficacy. For hypertension patients, one of the most frequently used drugs for lowering blood is captopril. However, information regarding the influence of consumption time on captopril efficacy was limited. Therefore, this study was conducted to compare the efficacy of captopril in lowering blood pressure when administered before and after meal. This was an experimental study with two treatment groups, conducted at Dr. Soedarso General Hospital, Pontianak, Indonesia, during April-June 2015. Statistical analysis was performed using Mann-Whitney, Exact-Fisher, and T-test. We found out that the reduction of systolic blood pressure in group who consumed captopril before and after meal was 30 mmHg and 25 mmHg, respectively ( $p < 0.05$ ). The similar reduction in diastolic blood pressure was observed in both groups (10 mmHg,  $p > 0.05$ ). In conclusion, it is recommended to take captopril on an empty stomach since it showed better efficacy when administered before meal compared to after meal consumption.

**Keywords:** hypertension, captopril, absorption

### Introduction

Stage 1 hypertension is a disease characterized by systolic blood pressure of 140-159 mmHg and diastolic blood pressure in the range of 90-99 mmHg. The recommended treatment for stage I hypertension include thiazide diuretic drugs, angiotensin converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), beta-blockers (BB), and calcium channel blockers (CCB). One of

the most frequently used anti-hypertensive agent is captopril.<sup>1,2</sup>

The timing of drug consumption could significantly affects effectiveness of the treatment. The presence or absence of food in the stomach could affect the absorption of drugs in the body which could lead to differences in its efficacy. The peak effect

of captopril is observed after 1-1.5 hours after drug administration and absorption is reduced by 30%-40% in the presence of food.<sup>4</sup>

In Indonesia, West Kalimantan was among in the top lists of provinces with the highest prevalence of hypertension.<sup>2</sup> Health Minister Decree HK.02.02/Menkes/390/2014 stated that one of the general hospital in Pontianak, Dr. Soedarso General Hospital, was referred as one of the national referral hospital for hypertension.<sup>5</sup> Based on the field observations conducted at this hospital, most nurses administered captopril after meal. The knowledge of medical staff responsible to administer drugs to patients was limited. Therefore, in this study we aimed to examine the effectiveness of captopril when taken on an empty stomach and after meals.

### Methods

This was an experimental study with two treatment groups, conducted at Dr. Soedarso General Hospital, Pontianak, Indonesia, during April-June 2015. The target population in this study was the stage 1 hypertensive patient who used a single captopril (10 mg) daily on inpatients at Dr. Soedarso General Hospital, Pontianak. This study was approved by ethical committee Universitas Padjadjaran.

Informed consent was obtained from each subject.

Inclusion criteria were:

- Patients with stage 1 hypertension (systolic blood pressure of 140-159 mmHg/diastolic was 90-99 mmHg).
- Patients aged  $\geq 18$  years old.
- Received single captopril therapy 12.5 mg during hospitalization.

We excluded patients who consumed drugs that might affect blood pressure (which interacts with captopril), *e.g.*, antacids (moderate), amifostine (moderate), aprotinin (major), and thiazide diuretics (moderate).

General characteristics of subjects, *i.e.*, age and sex were obtained from medical records. Blood pressure was measured before and after the treatment. Statistical analysis was performed using Mann-Whitney, Exact-Fisher, and T-test

### Results and Discussion

Thirty subjects were included in this study. The majority of the subjects aged more than 55 years old (73.33%) (Table 1). Older age is a risk factor for the progression of hypertension due to the increasing of peripheral resistance, sympathetic nerve activity, and decreased

**Table 1. Characteristics of participants**

Characteristics	Group	
	After meal consumption (n=15)	Before meal consumption (n=15)
1. Sex		
Male (%)	3 (20%)	4 (26%)
Female (%)	12 (80%)	11 (74%)
2. Age (years)		
Mean (SD)	56.3 (6.3)	59.3 (6.9)
Range	48-72	50-79

\* Exact-Fisher for sex and T-test for age

**Table 2. Systolic blood pressure on both groups**

Systolic Blood Pressure	Groups		P-value*
	Before meal consumption (n=15)	After meal consumption (n=15)	
Initial (mmHg)			
Mean (SD)	152.1 (3.2)	151.2 (4.2)	0.653
Median	150	150	
Range	150-158	145-158	
End (mmHg)			
Mean (SD)	127.3 (8)	118 (4.1)	0.003*
Median	130	120	
Range	120-140	110-120	
$\Delta$ (mmHg)	24.7 (7.3)	33.2 (6)	0.005*
Mean (SD)	25	30	
Median	10-35	25-45	
% reduction			
Mean (SD)	16.3 (4.8)	21.9 (3.6)	0.001*
Median	16.1	20	
Range	6.7-22.6	17.2-29	

\*) Mann-Whitney test

sensitivity of baroreceptor reflexes that are important in the regulation of blood pressure.<sup>6</sup>

Majority of the subjects (76.66%) were elderly women. The risk of hypertension in women would increase after menopause, indicating the major role of the presence of the estrogen hormone in blood pressure regulation. It can increase the level of high density lipoprotein which prevents the occurrence of the process of atherosclerosis which could lead to high blood pressure.<sup>7</sup>

Efficacy of drugs can be influenced by consumption time of drugs. Administration of drugs with food may reduce, delay, increase, or have no effect on drug absorption. Food can affect GI physiological factors such as gastric emptying time, acid secretion, blood flow, intestinal motility, bile and enzyme secretion.<sup>8-12</sup>

The effectiveness of captopril was assessed

by evaluating the difference ( $\Delta$ ) of systolic blood pressure (SBP) and diastolic blood pressure (DBP) in mmHg units seen from the median values. We found out that the reduction of SBP in group who consumed captopril on an empty stomach and after meal was 30 mmHg and 25 mmHg, respectively ( $p < 0.05$ ). The similar reduction in DBP was observed in both groups (10 mmHg,  $p > 0.05$ ).

In the group who took captopril on an empty stomach, the reduction of SBP and DBP were 30 mmHg (20% reduction) and 10 mmHg (11.1%), respectively. In the group who took captopril after meal, the reduction of SBP and DBP were 25 mmHg (16.1%) and 10 mmHg (11.1%), respectively (Table 2 and 3).

The target of SBP and DBP in uncomplicated hypertensive patients (without diabetes mellitus and chronic renal failure) aged  $\geq 60$  years are  $< 150/90$  mmHg. In hypertensive patients with diabetes and chronic kidney

**Table 3. Diastolic blood pressure on both groups**

Diastolic Blood Pressure	Groups		P-value*
	Before meal consumption (n=15)	After meal consumption (n=15)	
Initial (mmHg)			
Mean (SD)	94.7 (5.2)	92 (5.6)	0.285
Median	90	90	
Range	90-100	80-100	
End (mmHg)			
Mean (SD)	82 (4.1)	79.3 (2.6)	0.250
Median	80	80	
Range	80-90	70-80	
$\Delta$ (mmHg)			
Mean (SD)	12.7 (4.6)	12.7 (4.6)	1.000
Median	10	10	
Range	10-20	10-20	
% reduction			
Mean (SD)	13.3 (4.2)	13.6 (4)	0.412
Median	11.1	11.1	
Range	10-20	11.1-20	

\*) Mann-Whitney test

disease, blood pressure should be < 140/90 mmHg.<sup>1</sup> In this study, the target blood pressure was hardly achieved in group who took captopril after meal. In contrast, target blood pressure was achieved in several subjects from the group who took captopril on an empty stomach.

Previous study showed that the presence of food significantly affects the bioavailability of captopril until 40%. Current study determined whether the reduction in captopril bioavailability influence its clinical effect on lowering blood pressure. We found out that captopril time consumption significantly affect the blood pressure, particularly SBP. The roles of health care professionals, such as pharmacists, are crucial to ensure the appropriate method of drugs consumption was used to optimize therapeutic effect of the drugs.<sup>13</sup>

Limitation of this study included the absence

of the monitoring of dietary intake and level of stress which could influence blood pressure. However, in this study, we already excluded patients who had complications to reduce bias.

### Conclusion

The reduction of blood pressure was higher in subjects who took captopril on an empty stomach. Therefore, it is recommended to take captopril on an empty stomach since it showed better efficacy compared to after meal consumption.

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### Conflict of Interest

The authors declared no potential conflicts

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