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# Same effect of sublingual and oral Captopril in hypertensive crisis

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## **Abstract. – BACKGROUND AND OBJECTIVES:**

Hypertensive crisis is a condition characterized by rapid and inappropriate symptomatic elevation of blood pressure (BP) that is commonly seen in Emergency Departments. Oral or sublingual captopril is commonly used in the Emergency Departments. The unpleasant taste of the sublingual drugs causes uncomfortable condition to the patient. Studies showing no difference between oral and sublingual captopril has been ignored so far. Herein we compared the oral and sublingual captopril efficiency in the hypertensive urgencies.

**MATERIALS AND METHODS:** In this retrospective observational study, 71 patients admitted with hypertensive urgency to Emergency Departments of two hospitals in 2011 whose blood pressure were recorded before captopril administration and blood pressure were recorded after captopril administration at 0-5-15-30-45-60 minutes were included the study. The reductions of the blood pressure of oral and sublingual captopril groups were compared.

**RESULTS:** There were 28 patients at oral and 43 at sublingual captopril group. The mean age  $\pm$  SD was  $58.13 \pm 8.66$  years and 41 (57.7%) patients were female. The most common complaints were headache, nausea/vomiting and weakness. 65 (91.5%) patients were using anti-hypertensive drugs before admitted to hospital. The blood pressure at 0, 5, 15, 30, 45 and 60<sup>th</sup> minutes of therapy didn't show any difference between oral and sublingual captopril use.

**CONCLUSIONS:** There was any difference between oral and sublingual captopril efficiency to control of hypertension in patient with hypertensive urgency. For a more comfortable treatment, oral captopril may be a more convenient choice in the hypertensive urgencies.

## **Key Words:**

Captopril, Hypertensive urgency, Hypertensive emergency, Oral, Sublingual.

## **Introduction**

Hypertensive crisis is a risky condition that commonly seen in Emergency Departments and it is characterized by inappropriate symptomatic elevation of blood pressure. Elevated blood pressure with end-organ damage is called as hypertensive emergency and it is called hypertensive urgency if end-organ damage is absent. Cardiovascular, renal and central nervous system (CNS) are frequently affected<sup>1,2</sup>. The Joint National Committee suggests decreasing the blood pressure in cases of hypertensive urgency and emergency conditions in order to prevent end-organ damage<sup>3,4</sup>. Despite certain studies suggest fast and effective oral and sublingual agents in recent studies it is showed that the rapid and fast reduction of the blood pressure is dangerous<sup>4,5</sup>. Oral and sublingual usage of captopril is quite common in emergency services. There are many studies showing the sublingual captopril reduces the blood pressure effectively in hypertensive crises<sup>2,6</sup>. But the studies in the literature that showing no difference between oral and sublingual captopril have been neglected yet<sup>7</sup>.

Although sublingual route are preferred for some drugs, because of the unpleasant taste this route is an uncomfortable way of treatment for patients. Local hypersensitivity and chemical burns could be seen by the direct contact of the sublingual drugs with the oral mucosa. As a result, a burning sensation, metallic taste and ulcers could be seen in the mouth<sup>8</sup>. Additionally, in many studies the usage of cardiovascular drugs caused bad taste and the loss of sense of taste in the mouth<sup>9</sup>.

In this study we compared the efficiency of oral and sublingual captopril in patients admitted to the Emergency Department with hypertensive urgency.

**Table I.** The effect of oral and sublingual captopril on systolic, diastolic and mean arterial blood pressure in each group.

Oral Captopril n = 28				Sublingual Captopril n = 43		
Time (min)	SBP	DBP	MAP	SBP	DBP	MAP
0	182 ± 21	99 ± 14	126 ± 14	185 ± 21	99 ± 12	128 ± 15
5 min	172 ± 21	94 ± 13	120 ± 14	178 ± 23	98 ± 13	125 ± 15
15 min	165 ± 17	89 ± 9	115 ± 11	170 ± 23	93 ± 14	119 ± 15
30 min	158 ± 19	87 ± 8	111 ± 11	160 ± 20	91 ± 9	114 ± 11
45 min	152 ± 15	84 ± 8	107 ± 10	153 ± 17	86 ± 9	108 ± 13
60 min	147 ± 11	81 ± 6	103 ± 7	147 ± 13	83 ± 7	104 ± 10

\* SBP: Systolic Blood Pressure (mmHg), DBP: Diastolic Blood Pressure (mmHg), MAP: Mean Arterial Pressure (mmHg). The data are given as mean ± standard deviation

## Materials and Methods

In this retrospective study we searched hospitals records of patients admitted to Emergency Departments of Ankara Numune and Diskapi Yidirim Beyazit Training and Research Hospitals patients with diagnosis of hypertension according to the ICD 10 (International Classification of Diseases) between 01 January 2011 and 31 December 2011. Patients with stage 2 hypertension (systolic BP  $\geq 160$  mmHg or diastolic BP  $\geq 100$  mmHg) According to JNC-7 (Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure) were included the study. Patients with end-organ damage and clinical records of patients contain incomplete information or not accessible were excluded. A total of 2325 patients were evaluated as hypertension. 1214 of them were given only oral or sublingual 25 mg of captopril and whose data were recorded appropriately. Among those patients, the hospitals records including the blood pressure measurement of the patients at hospital admission, and at 0, 5, 15, 30, 45 and 60th minutes of captopril treatment, 71 patients were included in the study. The presence of a diagnosis of hypertension, previous medications, ages, gender, chief complaints of admission and blood pressures at 0, 5, 15, 30, 45 and 60<sup>th</sup> minutes were recorded.

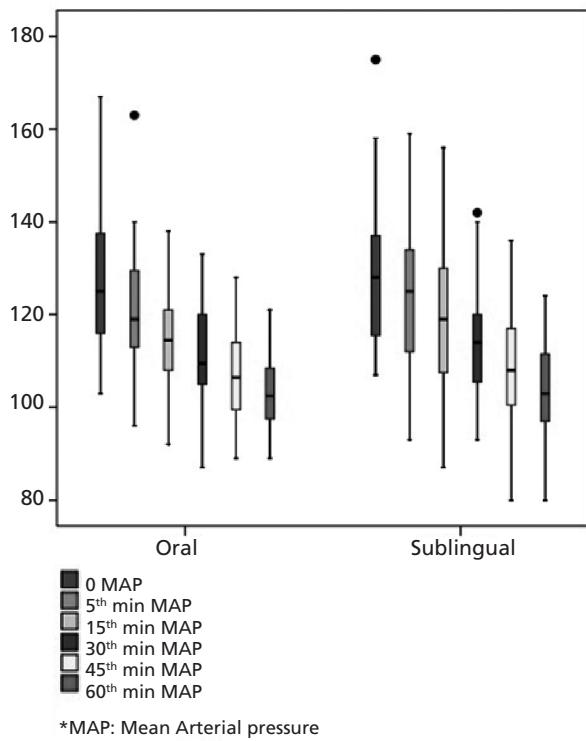
## Statistical Analysis

All statistical analyses were performed using SPSS 15.0 for windows (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed by mean ± SD (standard deviation) and frequent variables as percent. The distribution of continuous variables defined by histogram and One Sample Kolmogorov-Smirnov test. Difference between normally distributed variables were calculated by One Sample *t*-test; if the variables did

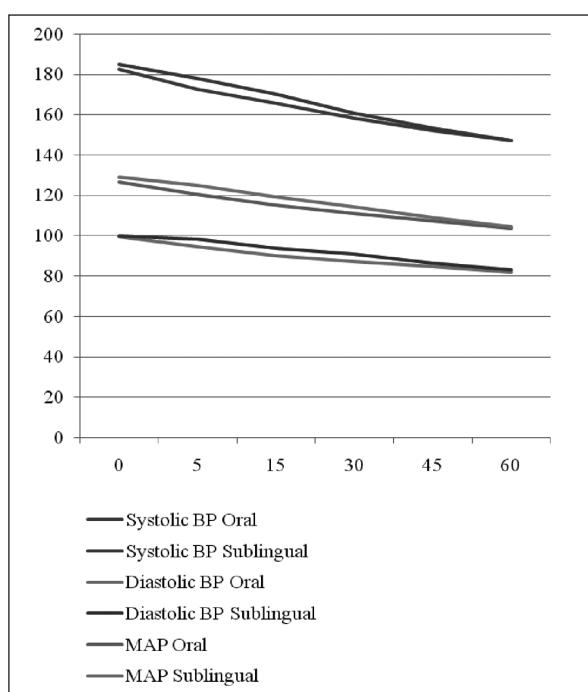
not normally distributed variables were calculated by Independent Samples *t*-test. Boxplot graph was performed for blood pressure values of oral and sublingual captopril usage. *p* < 0.05 was considered statistically significant.

## Results

A total of 71 patients were included in the study. The mean age ± SD was 58.13 ± 8.66 years and 41 (57.7%) patients were female. The most common complaints were headache (49 patients; 69.0%), fa-



**Figure 1.** The effect of oral and sublingual captopril on blood pressure.



**Figure 2.** The effect of oral and sublingual captopril on blood pressure.

tigue/weakness (27 patients; 38.0%) and nausea/vomiting (16 patients; 22.5%). 65 of the patients (91.5%) had a history of hypertension and receiving antihypertensive medication, other patients were not using any drug and didn't have any history of hypertension. Among drug using 65 patients, 41 of them (63.5%) were using ACE (angiotensin-converting-enzyme inhibitor) inhibitor. In the Emergency Department captopril were given to the 43 of the patients (60.6%) by oral route, and 28 of the patients (39.4%) by sublingual route. Mean  $\pm$  SD values of SBP, DBP and MAP were given in Table I for both oral and sublingual groups. Also boxplot graph of these values were given in Figure 1. In Figure 2, change in time (0, 5, 15, 30, 45 and 60<sup>th</sup> minutes) of SBP, DBP and MAP values were showed. At the admission SBP, DBP and MAPs were similar in both sublingual and oral captopril treatment groups ( $p > 0.05$ ) (Table II). BP measurement after oral and sublingual captopril were also similar at 5, 15, 30, 45 and 60<sup>th</sup> minutes after treatment ( $p > 0.05$ ) (Table II). Statistically significant BP decreases were observed in each group 15 minutes after the captopril treatment ( $p < 0.01$ ). There wasn't any difference between oral and sublingual group at any time.  $p$  values of the comparison of SBP, DBP and MAP between sublingual and oral captopril group were given in Table II.

## Discussion

Hypertensive urgencies are distinguished from hypertensive emergencies by the lack of acutely progressive target organ damage such as aortic dissection, acute myocardial infarction, acute pulmonary edema, intracerebral hemorrhage or hypertensive encephalopathy. There is no proven benefit from rapid reduction of the blood pressure in patients with hypertensive urgencies. In these patients, utilizing oral medications to lower the BP gradually over 24 to 48 h is the best approach to management<sup>10,11</sup>. Cerebral or myocardial ischemia or infarction can be induced by aggressive antihypertensive therapy if elevated blood pressure below the autoregulatory range of these vascular beds. On the other hand, drugs have rapid onset clinical effect such as sublingual nifedipine could be used in treatment of hypertensive emergency with end organ damage<sup>12</sup>.

Although many alternative antihypertensive drugs used in hypertensive urgencies, captopril have been used for more than 20 years at emergency services. As captopril could be used sublingually, it was compared with nifedipine in many studies and use of sublingual captopril was suggested in hypertensive crisis<sup>13,14</sup>. Medications could be applied by intravenous, oral or sublingual route as alternative methods in the Emergency Departments. If the patient is unconscious and the drug could be absorbed sublingually, rapid and safe treatment could be achieved by sublingual route.

Sublingual route is preferred because the oral mucosa is well vascularized, by-pass of the drug absorption at small intestines and the liver first pass absorption, rapid therapeutic effect could be provided<sup>15</sup>. But even in short term use, sublingual drugs gives bitter taste and bad effect on tongue, also

**Table II.** The comparison of oral and sublingual captopril on systolic, diastolic and mean arterial blood pressure in each group.

Time (min)	Systolic BP (p)	Diastolic BP (p)	MAP (p)
0	0.585	0.874	0.522
5 min	0.322	0.263	0.220
15 min	0.410	0.213	0.251
30 min	0.652	0.095	0.248
45 min	0.816	0.385	0.587
60 min	0.982	0.378	0.982

\* SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, MAP: Mean Arterial Pressure

causes undesirable effects because of hypersensitivity and chemical burns on oral mucosa<sup>8</sup>. As an alternative method oral route may be preferred frequently in the Emergency Departments because it is safe and easy. Thus drug remains in the mouth a short time compared to the sublingual way and it is tolerated better. In many studies it is reported that the sublingual captopril decreases the blood pressure better than the oral route<sup>16-18</sup>. However Dess-Fulgeri et al<sup>7</sup> reported there is no difference between oral and sublingual captopril to decrease the blood pressure and inhibition of plasma renin activity and angiotensin converting enzyme<sup>7</sup>. On the other hand Dali et al<sup>18</sup> reported that captopril absorption from the sublingual cavity of rabbits was low and did not agree with that observed in man<sup>19</sup>.

In our study, in the first hour there was no significant difference between sublingual and oral captopril to reduce the blood pressure. Also some studies showed this previously but they are neglected<sup>7,19</sup>. With these findings in case of hypertensive urgencies, oral captopril usage will be appropriate to control the blood pressure. But if the patient cannot tolerate the oral way, sublingual captopril is still effective despite its bad taste.

## Conclusions

Today, in the case of hypertensive urgencies, to research the end-organ damage is suggested. If end-organ damage is absent to reduce the blood pressure rapidly doesn't recommended. To reduce the blood pressure, captopril is still popular but the usage of sublingual captopril to reduce the blood pressure causes an uncomfortable treatment. For the management of hypertensive conditions, if end-organ damage is absent oral captopril will be a comfortable and safe management.

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