

## Sublingual Valsartan in Hypertensive Urgency

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**Abstract:** The objective of this study was to assess the effect of sublingual valsartan in a group of patients with hypertensive urgency. Forty-one patients with hypertensive urgency and systolic blood pressure >200 mmHg, diastolic blood pressure >100 mmHg were studied in an emergency room. Supine blood pressure readings were taken and the patients were given 80 mg of valsartan sublingually. Blood pressure and heart rate were recorded at 15 min intervals over a 90 min period. Systolic blood pressure decreased from 211.22±14.65 mmHg to 158.17±15.48 mmHg, diastolic blood pressure dropped from

120.12±13.44 mmHg to 93.05±6.01 mmHg. The differences were statistically significant. The heart rate decreased from 87.90±13.47 beats per minute to 82.59±10.84 beats per minute. The results of our study indicate that sublingual valsartan is an effective drug in patients with hypertensive urgency and it is easy to use sublingually because it is in a capsule form and it is side-effect free. Further work is required to assess the effect of sublingual valsartan in patients with hypertensive urgency.

**Key Words:** Hypertensive urgency, Valsartan

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### Introduction

Hypertensive crisis is defined as a severe elevation in blood pressure (BP) and is classified as either urgency or emergency. The presence of acute or ongoing end-organ damage, such as myocardial infarction, left ventricular insufficiency, acute renal insufficiency and hypertensive encephalopathy, constitutes a hypertensive emergency, where the absence of such complications is known as a hypertensive urgency (1-3). The goal of treatment in a hypertensive urgency is a gradual reduction of blood pressure. The appropriate medication for the treatment of hypertensive urgencies should have the following properties: availability for nonparenteral the ability to administration and decrease BP to a plateau (4,5). Several oral or intravenous drugs are available for the treatment of hypertensive crisis, such as captopril, enalapril, sodium nitroprusside and nitroglycerin (6,7). Recently, a review of multiple clinical trials has revealed that short-acting nifedipine may cause an increase in mortality. It is recommended that patients with acute coronary syndrome should not receive short-acting nifedipine (8). Several angiotensin II receptor blockers, including irbesartan, losartan, telmisartan, condesartan, cilexetil and valsartan, are used for the treatment of patients with hypertension. Valsartan blocks vasoconstriction caused by angiotensin II and is orally active. The onset of the hypotensive effect of angiotensin II receptor blockers appear to be more gradual than that

associated with angiotensin converting enzyme inhibitors, perhaps related to the lack of the bradykinin-potentiating capability of those agents (9,10).

The purpose of this study was to assess the effect of sublingual valsartan in patients with hypertensive urgency.

### Materials and Methods

Forty-one patients with hypertensive urgency who had discontinued antihypertensive drug or drugs by themselves 48 h prior were chosen for this study. On admission, all patients had documented hypertension and had been treated previously with various antihypertensive agents irregularly. Patients with systolic blood pressure (SBP) over 200 mmHg and diastolic blood pressure (DBP) over 100 mmHg were chosen for the study. Seventeen of these patients were men and the others were women. Their ages ranged from 29 to 68 years (mean 52.9±10.0 years). Twenty patients had associated ischemic heart disease with stable angina pectoris. Their resting electrocardiograms were normal. Ten patients had headache without neurologic signs and 11 patients had dizziness without neurologic signs. Fifteen patients had diabetes mellitus. Renal function was normal in all patients. Secondary forms of hypertension were ruled out after careful clinical and laboratory evaluations.

Three supine blood pressure readings using a standard sphygmomanometer were taken at 5 min intervals prior to the study. The DBP was recorded at the disappearance of Korofkoft sounds (phase V). The heart rate was also recorded. A valsartan capsule containing a dose of 80 mg was opened and given sublingually. The patients were asked to keep the drug in his/her mouth without swallowing. The valsartan capsules used were the standard peroral Diovan capsules manufactured by Novartis Pharma AG, Switzerland. Blood pressure was measured at 15, 30, 60, 90 min following valsartan administration. Statistical analysis, which consisted of comparing the onset blood pressure values with pressures at 15, 30, 60, 90 min was performed by the paired-t-test using SPSS for Windows Rel. 0.0.

Informed consent was obtained from the participants.

**Results**

Forty-one patients (17 men and 24 women, mean age 52.90 ±9.09 years) were included in the study. The SBP decreased from 211.22±14.65 mmHg to 158.17±15.48 mmHg at 90th min (p<0.01). In the same time interval, the DBP decreased from 120.12±13.44 mmHg to 93.05±6.01 mmHg (p<0.01). Hence, the SBP showed a

reduction of 33.5%, and the DBP of 29.0% by 90 min. The heart rate decreased from 87.90±13.47 beats/min to 82.59±10.84 beats/min. Hypotension did not develop in any patient.

In addition to the significant overall decreases in SBP and DBP readings during the 90 min period, the measured values for both these pressures declined significantly from the onset to each of the 15, 30, 60, 90 min measurements. The declines in SBP and DBP at these points of measurement is given in the Table. The Figure gives the graphical representation the mean values of SBP and DBP at each reading.

None of the patients showed any adverse reactions to valsartan during the study.

**Discussion**

The level to which blood pressure should be reduced in patients with hypertensive emergencies and urgencies is still unclear and controversial. The initial aims of therapy should be the reduction of blood pressure by one-third or 20 to 30 percent (11-13). Hypertensive urgency is between mild-moderate hypertension and hypertensive emergency from the point of view of severity. In hypertensive emergencies, blood pressure should be

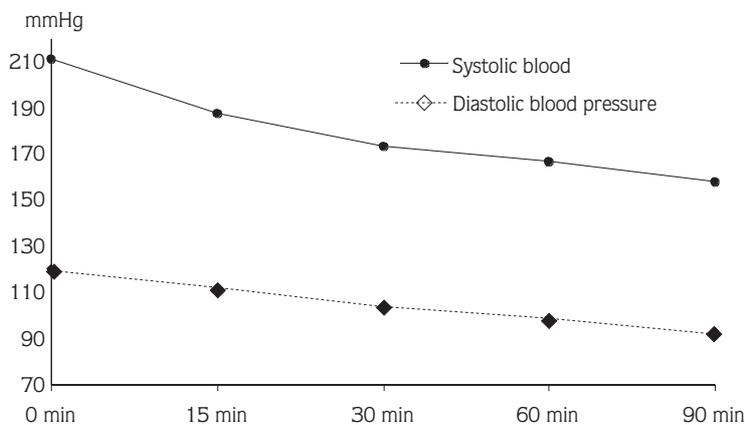


Figure. Mean effects of sublingual valsartan on blood pressure.

Table. The mean pre-and postdose SBP and DBP (mmHg) and % reduction.

	Onset	15 min	reduction %	30 min	reduction %	60 min	reduction %	90 min	reduction %
SBP	211.22±14.65	187.80±16.92	12.2	173.41±16.37	22	166.71±15.91	26.3	158.17±15.48	33.5
DBP	120.12±13.44	111.95±10.77	7.1	104.88±9.05	14.3	99.63±7.53	20.0	93.05±6.01	29

lowered within minutes with parenteral agents to prevent critical end-organ damage. But in hypertensive urgencies, blood pressure can be lowered more slowly over several hours, often with oral agents, to avoid a detrimental fall in blood pressure (5,13). No specific drug has been shown to be particularly efficacious in the treatment of hypertensive urgencies.

Angiotensin II receptor antagonists block a number of angiotensin II effects that are relevant to the pathophysiology of cardiovascular disease, including vasoconstriction, renal sodium reabsorption, aldosterone, vasopressin secretion and sympathetic activation. We did not find any reports in the literature about the effect of valsartan used sublingually for the treatment of hypertensive urgencies. Recently we reported on the comparison of the hypotensive effect of sublingual losartan with that of sublingual captopril and nifedipine in 1999. In this study, losartan, an Angiotensin II receptor antagonist, decreased the mean SBP from 190.50 mmHg to 146.25 mmHg, and mean DBP from 109.25 mmHg to 88.50 mmHg at 90 min (15).

In this study, forty-one patients were in hypertensive urgency and we used valsartan, a new angiotensin II receptor antagonist, in a dose of 80 mg sublingually. At 90 min a 33.5% reduction of SBP and a 29.0% reduction of DBP was achieved by sublingual valsartan.

We concluded that valsartan sublingually administered is an effective and safe alternative drug for managing hypertensive urgencies. Valsartan can be used as a first-line drug in emergency urgencies, since it is produced in capsule form and is easy to administer. Further studies are obviously necessary to compare valsartan to other antihypertensive regimens used for the treatment of hypertensive urgencies.

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