Turkish Journal of Medical Sciences

Volume 29 | Number 6 Article 11

1-1-1999

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Tr. J. of Medical Sciences
29 (1999) 655-660

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A Comparison of the Effectiveness of Sublingual Losartan, Sublingual Captopril and Sublingual Nifedipine in Hypertensive Urgency

Received: December 11,1998

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Abstract: The use of sublingual captopril and nifedipine has been indicated in hypertensive emergencies and in patients with essential hypertension, with the assumption that by this route, there would be a faster absorption and thus a more rapid effect on blood pressure (BP) than by the oral route.

A comparative study of the effects of Losartan, angiotensin II receptor antagonist, captopril and nifedipine on blood pressure was carried out in patients with hypertensive urgency.

Sixty patients with hypertensive urgency were subdivided into 3 groups of 20 patients each. The first group received sublingual captopril (25 mg), the second group received sublingual nifedipine (10 mg) and the third group received sublingual losartan (50 mg). In the captopril, nifedipine and losartan groups, the mean systolic pressures at the onset of hypertensive urgency were 188.00±23, 190.00±35 and 190.50±21 mmHg respectively. At 90 minutes, in the captopril, nifedipine and losartan groups, the mean systolic blood pressures were 138.50±18, 144.50±25 and 146.25±21 mmHg respectively. In the captopril, nifedipine and losartan groups, the mean diastolic blood pressures at the onset of hypertensive urgency were 116.00±15, 121.50±22 and 109.25±14 mmHg respectively. In the captopril, nifedipine and losartan groups, at 90 minutes, mean diastolic blood pressures were 84.75±10, 95.25±19 and 88.50±12 mmHg respectively. A significant ($P<0.05$) hypotensive effect of sublingual captopril, nifedipine and losartan therapy occurred at 90 minutes. The results of the study indicate that sublingual losartan is an effective drug in patients with hypertensive urgency

Key Words: Hypertensive Urgency, Losartan

Introduction

Hypertensive emergency is defined as severe elevation in blood pressure (BP) with signs or symptoms of acute, severe target organ damage that must be reduced within minutes (1, 2). Hypertensive urgency is defined as severe elevation in BP with mild or no acute target organ damage which must be reduced within hours[1,2]. The appropriate medication for the treatment of hypertensive emergencies and hypertensive urgencies should have the following properties: Availability for nonparenteral administiration, managing peripheral vascular vasodilatation and decrease BP to a plateau(3, 4).

Recent studies have demonstrated the effectiveness of sublingually administered nifedipine and captopril in rapidly reducing arterial pressure in hypertensive emergencies and in patients with essential hypertension(5, 6).

Losartan, angiotensin II receptor antagonist, blocks vasoconstriction caused by angiotensin II(7). Our study is a comparative evaluation of the effects of sublingually administered losartan, captopril and nifedipine on hypertensive urgency.

Patients and Method

The 60 patients who participated in this study were subdivided into three groups: 20 patients (12 female and 8 male, mean age 49.35±12.62 years) in the captopril group, 20 patients (9 female and 11 male, mean age 47.85±13.99 years) in the nifedipine group, and 20 patients (11 female and 9 male, mean age, 47.70±90.85 years) in the losartan group.

All patients had BP higher than 180/100 mmHg in three different measurements, 15 minutes apart. Patients who had no signs or history of cerebrovascular disease,

myocardial disease, diabetes mellitus, or renal disease, were included in this study. Secondary forms of hypertension were ruled out after careful clinical and laboratory evaluations. Patients who had a history of hypertension but had not taken an antihypertensive agent for at least 24 hours were chosen. The patients rested in the supine position for at least 20 minutes before the test began. BP measurements were made with a mercury sphygmomanometer. The values used were obtained from the average of three consecutive measurements. The diastolic arterial pressure was recorded at the disappearance of Korokoff sounds (phase V). Mean blood pressure (MBP) was measured by the following formula: 2 x Diastolic Blood Pressure (DBP) + Systolic Blood Pressure (SBP)/3. BP was measured before and 15, 30, 60 and 90 minutes after the administration of the drugs. The captopril group was treated with 25 mg captopril, the nifedipine group with 10 mg nifedipine, and the losartan group with 50 mg losartan. All drugs were administered sublingually. The patients were shown how to crush the captopril tablet and the losartan tablet and how to pierce the nifedipine capsule, and were told to wait for the drug to completely dissolve under the tongue. Statistical analysis of the results was carried out by BMDP2 V – analysis variance and covariance with repeated measures.

Results

There was no significant difference between the demographic data of the 3 treatment groups. In the captopril group, mean (±SD) SBP and DBP dropped from 188.00±23 to 138.50±18 mmHg and from 116.00±15 to 84.75±10 mmHg respectively at 90 minutes. In the nifedipine group, mean SBP and DBP dropped from 190.00±35 to 144.50±25 mmHg and from 121.50±22 to 95.25±19 mmHg respectively at 90 minutes. In the losartan group, mean SBP and DBP dropped from 190.50±21 to 146.25±21 mmHg and from 109.25±14 to 88.50±12 mmHg respectively at 90 minutes. The mean pre- and post-dose SBP and DBP in the 3 treatment groups are summarized in Table I. The mean SBP and DBP data before and up to 90 min after both sublingual doses are shown in Figures 1 and 2, respectively. No significant difference was observed in the magnitude of the SBP- or DBP- lowering effect between the captopril, nifedipine and losartan groups (P>0,05). The specified total of patients who had a 20% reduction in SBP and

Table 1. The mean pre-and postdose SBP, DBP in the three treatment groups (mm Hg).

	Captopril group	Nifedipine group	Losartan group
ONSET SBP	188.00±23.30	190.00±35.83	190.50±21.63
ONSET DBP	116.00±15.00	121.50±22.54	109.25±14.16
15 min SBP	162.75±29.97	164.50±35.90	168.25±24.02
15 min DBP	97.25±18.31	106.50±25.34	96.75±15.06
30 min SBP	152.75±30.23	162.50±31.60	157.00±22.44
30 min DBP	91.50±14.24	106.75±21.53	92.25±12.92
60 min SBP	144.50±25.65	150.25±29.22	144.00±24.36
60 min DBP	88.50±13.96	97.25±20.67	89.75±13.22
90 min SBP	138.50±18.14	144.50±25.49	146.25±21.69
90 min DBP	84.75±10.44	95.25±19.29	88.50±12.47

Table 2. Specified total of patients who had a 20% reduction in SBP, DBP and MAP at 15, 30, 60 and 90 min.

	Captopril group	Nifedipine group	Losartan group
15 min SBP	4	4	4
15 min DBP	6	6	5
15 min MAP	6	4	4
30 min SBP	8	5	9
30 min DBP	11	3	6
30 min MAP	11	4	5
60 min SBP	10	8	13
60 min DBP	12	9	9
60 min MAP	12	6	8
90 min SBP	13	13	14
90 min DBP	14	11	8
90 min MAP	15	11	8

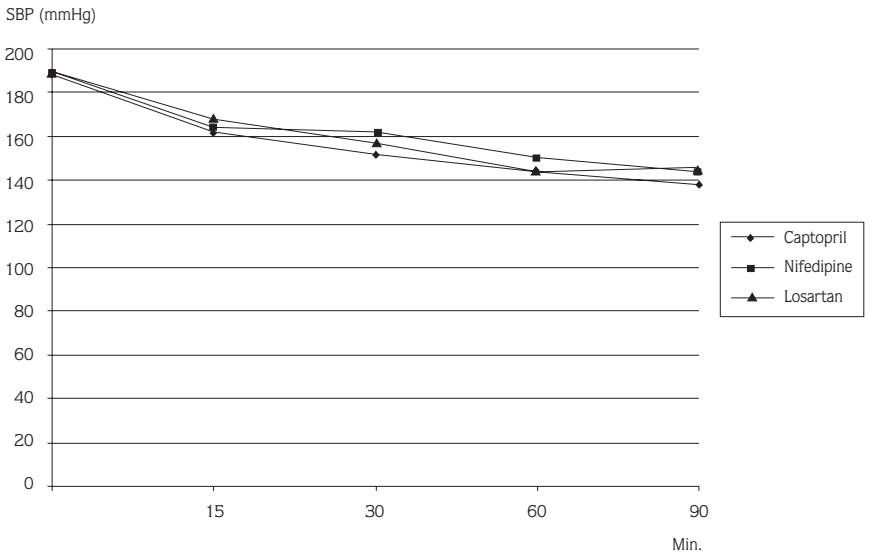

Figure 1. Mean SBP variability in 3 groups of patients at 0, 15, 30, 60 and 90 min

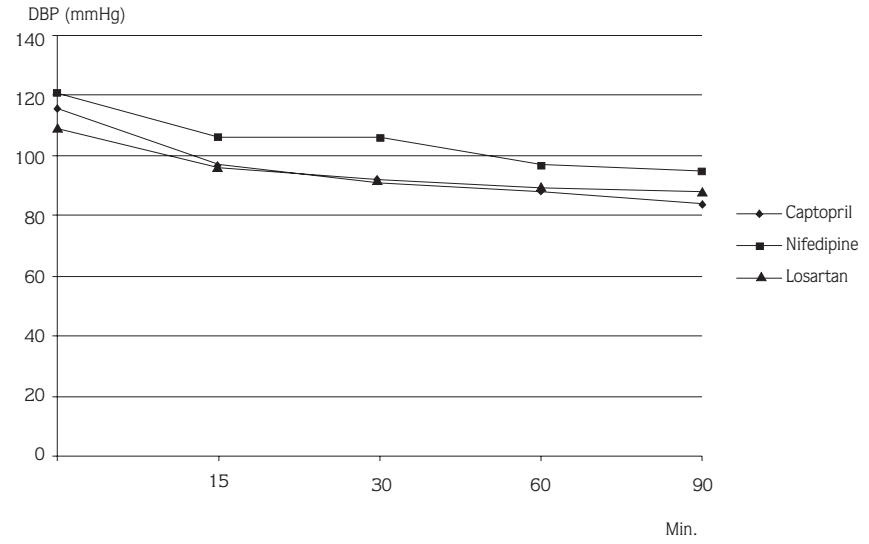

Figure 1. Mean SBP variability in 3 groups of patients at 0, 15, 30, 60 and 90 min

DBP and mean arterial pressure at 15, 30, 60 and 90 min are shown in Table II and Figures 3 and 4.

In the nifedipine group, a 20% reduction in DBP occurred in 6 patients at 15 min, but at 30 min this reduction occurred in 3 patients. This DBP increase in 3 patients did not occur in the other groups ($P<0.05$). Pre- and post-dose measurements of BUN, electrolytes, creatinine, LDH, SGOT, SGPT and glucose levels were all observed to be within the normal range in all patients. No abrupt decrease in BP occurred in the patients.

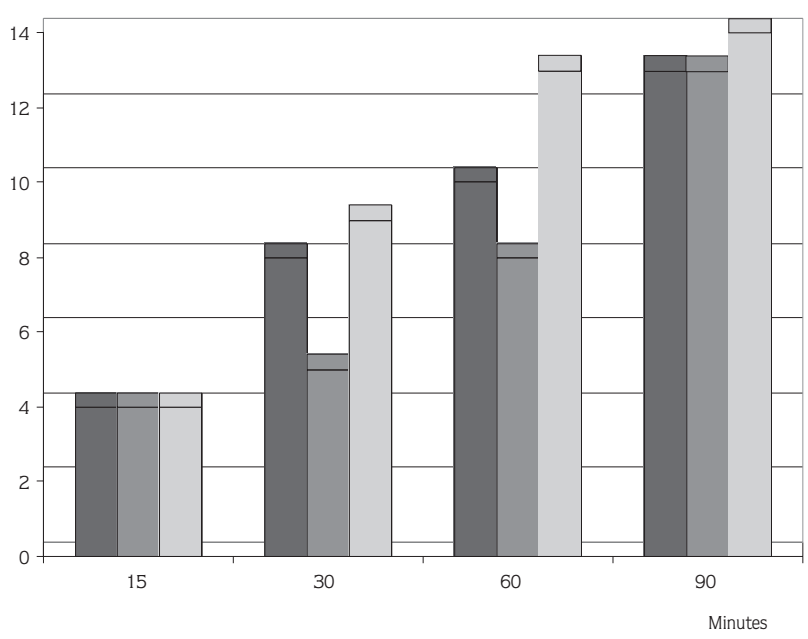

Figure 3. The specified total of patients who had a 20% reduction in SBP at 15, 30, 60 and 90 min when compared with initial blood pressures.

Losartan

Nifealipine

Captopril

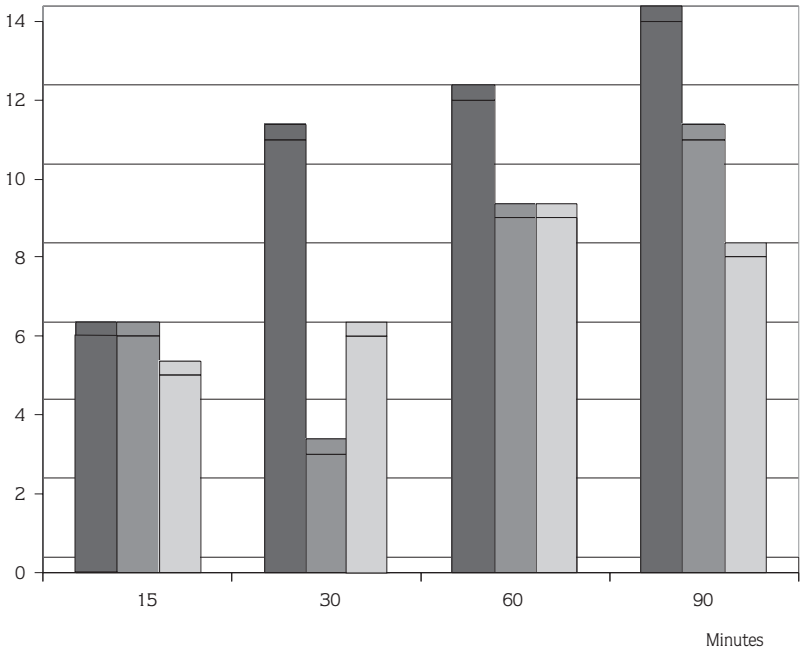

Figure 4. The specified total of patients who had 20% reduction in DBP at 15, 30, 60 and 90 min. compared with initial blood pressures.

Losartan

Nifealipine

Captopril

Discussion

Many antihypertensive agents such as captopril and nifedipine are used in hypertensive emergencies and hypertensive urgencies(3, 4, 8, 9). Some reports suggest the superiority of captopril to nifedipine, whereas others recommend nifedipine for hypertensive emergencies(6, 9, 10). Recently, a review of multiple clinical trials has revealed that short-acting nifedipine may cause an increase in mortality(11). It is recommended that patients with coronary artery disease (CAD), especially those with acute coronary syndromes, not receive short–acting nifedipine. Because of its potent vasodilatator effects, nifedipine is contraindicated in patients with unstable angina in whom reflex mediated increases in heart rate may be harmful(11, 12, 13).

The level to which blood pressure should be reduced in patients with hypertensive emergencies and hypertensive urgencies is still unclear and controversial. The initial aims of therapy should be reduction of blood pressure by one-third or 20 to 25 percent(14, 15, 16). The initial aims of the therapy in mild and moderate hypertension should be reduction of 5 to 10 mmHg in blood pressure at each step(17).

Our patients were in hypertensive urgency. Hypertensive urgency is between mild-moderate hypertension and hypertensive crisis from the point of view of severity. Because of this, a 20% decrease in arterial pressure was determined.

In our study in the nifedipine group, a 20% reduction of DBP occurred in 6 patients at 15 min, but at 30 min, a 20% reduction of DBP occurred in 3 patients. In three of these 6 patients, DBP was increased again, which obviously indicates a disadvantage of nifedipine.

We concluded that the hypotensive effects of sublingual captopril and losartan were more powerful than those of sublingual nifedipine. We also concluded that losartan sublingually administered is an effective and safe alternative drug for managing hypertensive urgency. It may be used as a first-line drug in the treatment of this condition, since it is easy to administer.

Thus sublingual losartan appears to be the most promising, while further studies are obviously necessary to compare it to other antihypertensive regimens used for the treatment of hypertensive urgencies.

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