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

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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 hours1.2. The appropriate medication for the treatment of hypertensive emergencies and hypertensive urgencies should have the following properties: Availability for nonparenteral administration, managing peripheral vascular vasodilation 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).

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 DBP at 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.
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 vasodilator 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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References
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