

Nifedipine, captopril or sublingual nitroglycerin, which can reduce blood pressure the most?

Ali Maleki⁽¹⁾, Masoumeh sadeghi⁽²⁾, Mahyar Zaman⁽³⁾
Mohammad Javad Tarrahi⁽⁴⁾, Behjat Nabatchi⁽⁵⁾

Abstract

BACKGROUND: Hypertension (HTN) is one of the most important problems in all parts of the world. Although the disease is usually asymptomatic, its diagnosis and treatment are easy. The aim of this study was to compare the effect of Nifedipine (Adalat®), Captopril and sublingual Nitroglycerin on reducing blood pressure (BP).

METHODS: This study was a parallel group randomized controlled trial. From the patients referred to our heart clinic, 120 patients with severe HTN were enrolled in the study. The patients were randomly allocated into 3 groups A, B, and C. The patients were advised to use 5 drops of Adalat in group A, Captopril 25 mg sublingually in group B, and 1 sublingual Nitroglycerin pearl in group C. The BP was measured every 20 minutes during one hour.

RESULTS: Systolic BP was reduced significantly by Adalat and Captopril compared with sublingual Nitroglycerin in the 20th, 40th and 60th minutes ($P = 0.001$), but there was no significant difference between Adalat and captopril in reducing systolic BP. In addition, the result of reducing diastolic BP was not significantly different among the three groups.

CONCLUSION: We saw the same effect on reducing BP by Captopril, Adalat, and sublingual Nitroglycerin. Among these three drugs, the side effects of Captopril were the least frequent. Adalat caused headache and flushing. Thus, it seems Captopril can be used instead of Adalat in medical centers.

Keywords: Adalat, Captopril, Nitroglycerin, Severe Hypertension.

ARYA Atherosclerosis Journal 2011, 7(3): 102-105

Date of submission: 14 May 2011, *Date of acceptance:* 20 Jul 2011

Introduction

Cardiovascular diseases are one of the most important causes of death in developed countries and Iran. Hypertension (HTN) plays the most important role in preventing these diseases. Controlling BP as a cost effective method has been encouraged by different references.

HTN crisis is a life threatening, preventable medical situation. It was previously divided into malignant and emergency HTN. Malignant HTN was defined as a condition in which BP rises to more than 180/120 mm Hg, and end organ damages happen. Emergency HTN is a condition in which BP rises to the same degree without end organ damages. In this condition, oral drugs should be administrated gradually within 24-48 hours. Also, malignant hypertension should be lowered during

the first 2-4 hours. It should be reduced to 15-25% of the initial BP, and in other words, not less than 100-110 mm Hg for diastolic PB.¹⁻⁵

According to the high prevalence of uncontrolled HTN among outpatient,⁵ we aimed to compare the effects of three drugs, Adalat®, Captopril and sublingual Nitroglycerin in patients with HTN crisis without end organ damages.

Materials and Methods

Ethical Approval

This study was conducted in Lorestan University of Medical Sciences (LUMS) in the autumn of 2009. The institutional review board of LUMS approved the protocol. Financial approval was signed by the institutional board and the costs were supported by the university. The aim of the study was explained to the

1- Assistant Professor, Department of Cardiology, Imam Khomeini Hospital of Lorestan University of Medical Sciences, Lorestan, Iran.

2- Associate Professor, Cardiac Rehabilitation Research Center, Isfahan Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran

3- General Practitioner, Imam Khomeini Hospital of Lorestan University of Medical Sciences, Lorestan, Iran.

4- Lecture, Department of Statistics, School of Health, Lorestan University of Medical Sciences, Lorestan, Iran.

5- BSc in Nursing, Imam Khomeini Hospital of Lorestan University of Medical Sciences, Lorestan, Iran.

Correspondence To: Ali Maleki, Email: sadeghimasoumeh@gmail.com

patients, and written consent was obtained. All authors respected the Helsinki declaration during the study.

Study Design

This study was a parallel group, randomized control trial. One hundred and twenty patients were randomly allocated to three groups (40 cases in each group). For randomization process, all the cases were enrolled in a randomizing table which minimizes the effects of bias and confounding factors on the results. Allocation concealment was accomplished by putting the names of the drugs in the numbered opaque sealed envelopes. A trained nurse who did not know the group of each patient, measured patients' BP by means of a standard sphygmomanometer first when the patient referred to the hospital (before taking the drugs) and then in the 20th, 40th and 60th minutes after drug administration. Also, the drugs were administered by a nurse who did not know the group of each patient. Five droplets of sublingual Nifedipine (Adalat®) were taken by group A. Captopril, 25 mg sublingually, was prescribed for group B and sublingual Nitroglycerin (glyceryl trinitrate) was prescribed for group C. Characteristic data and the BP were recorded in a checklist.

Participants

For our study, 120 patients with a systolic BP ranged from 180-210 mm Hg and a diastolic BP ranged from 110-120 mm Hg were enrolled. The inclusion criteria included severe HTN without cardiac symptoms and normal neurologic and fundoscopic examinations.

The exclusion criteria included the presence of chest pain, dyspnea, headache and decreased level of consciousness.

Data Analysis

We compared the frequency of reduced systolic and diastolic BP with each of the drugs, Adalat®, Captopril or sub lingual Nitroglycerin. For this purpose, we used Pearson X² test. For comparing the mean percentage of BP among the three groups, we used ANOVA test. A $P < 0.05$ was considered

significant. For statistical analysis, we used the SPSS software, version 16.

Results

The mean age was 61.2 years old in group A, 58.3 years old in group B and 63 years old in group C. From 40 patients in each group, 16 in group A, 18 in group B and 20 in group C were men.

We found that Adalat was effective on reducing systolic BP and the results were significantly different than those before using the drug ($P < 0.001$). Systolic BP was reduced by 16% in the 20th, by 24% in the 40th and by 28% in the 60th minutes by Adalat.

Captopril was significantly effective on reducing systolic BP ($P < 0.001$). Captopril reduced BP by 17% in the 20th, by 22.5% in the 40th, and by 27.6% in the 60th minutes (Table 1).

In the third group, sublingual Nitroglycerin was also significantly effective on reducing systolic BP ($P < 0.001$). The reduction rate by sublingual Nitroglycerin was 10.5 % in the 20th, 17% in the 40th, and 20% in the 60th minutes (Figure 1).

We used ANOVA test to compare reduction rate among three groups. Although, the results of systolic BP were significantly different among group A, B and C, the results were not significantly different for diastolic BP.

Comparing the reduced systolic BP after using Adalat in group A and C revealed a significant P value (0.001), but the comparison didn't reveal significant differences between the group who used Captopril with the one who used Adalat.

Discussion

By our investigation, there was a significant reduction of BP by Adalat, Captopril and Nitroglycerin, but the reduction rate was more remarkable by using Adalat® and Captopril.

Table 1. Comparing the differences between initial and secondary systolic BP after using each drug.

Time	Initial BP			In the 20 th minutes after using the drug			In the 40 th minutes after using the drug			In the 60 th minutes after using the drug		
	A*	C**	N***	A	C	N	A	C	N	A	C	N
The Mean Systolic BP (mm Hg)	200	198	190	167	163	170	152	153	156	143	142	150
Mean Percentage of Differences between before and after using the drug (%)	0	0	0	16	17	10.5	24	22.5	17	28	27.6	20

*Adalat

**Captopril

***Sublingual Nitroglycerin

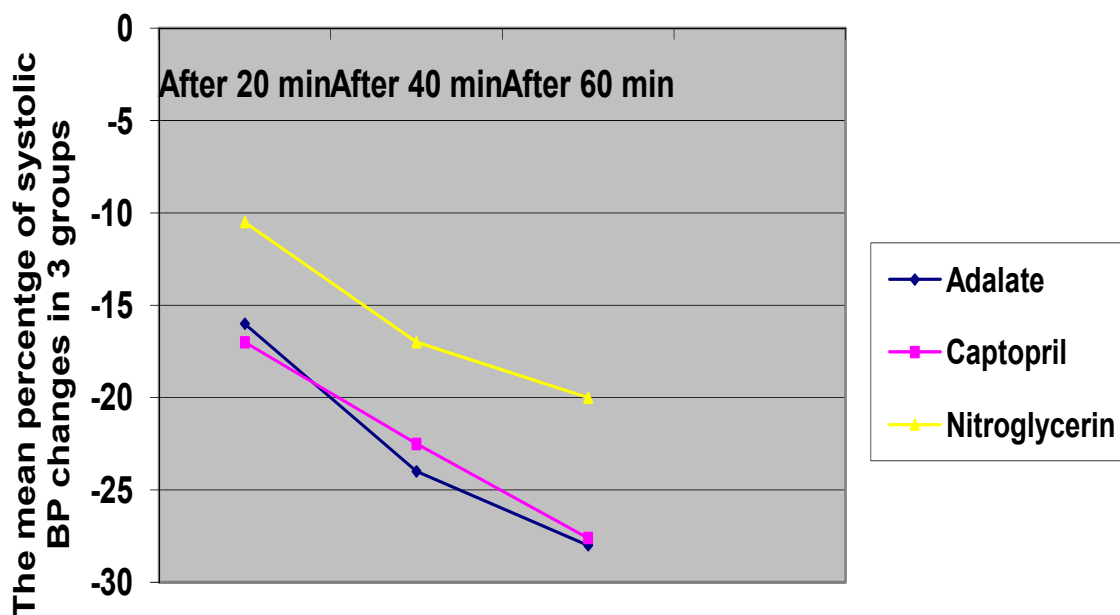


Figure 1. The comparison between the mean systolic BP variations in the 20th, 40th and 60th minutes of taking each of the drugs in group A, B and C.

Different protocols have been announced for management of HTN crisis by recent articles. Among them, intravenous therapy by sodium nitroprusside, Nitroglycerin or Labetalol after oral therapy was recommended by Ardigo S, et al. in 2008.⁶ In 2009, BP monitoring after intravenous therapy for emergent types and oral medications for urgent situations were recommended.⁵

Previous similar studies about the efficacies of oral drugs in patients with HTN crises were not paid attention in Iran. So, we designed our study to compare the effects of Adalat®, Captopril and Nitroglycerin on decreasing BP in patients with severe HTN.

In the last two decades, differences between Captopril and Nifedipine were frequently studied.

The results of the articles about reducing BP are almost the same; thus, the protocol should be suggested by considering the patients' conditions. For instance, Captopril should not be prescribed for patients with bilateral renal artery stenosis. In patients with ischemic heart diseases it is important to note that dihydropyridins such as Nifedipine increase the heart rate whereas clonidine, beta-blockers and labetalol decrease the heart rate. In patients with acute coronary attacks, (10 mg sublingually) are the two most efficient drugs for reducing BP in patients with severe HTN. With the purpose of finding the effect of these drugs, lots of studies have been designed Nitroglycerin is recommended.³

Captopril (25mg sublingually) and Nifedipine since 1990. Guerrero G, et al. showed a remarkable

decrease in BP after 10 minutes of using Captopril while the maximum efficacy was seen after 30 minutes. Although the effect of Nifedipine began within 5 minutes, the peak of effect appeared after 20 minutes. Except a delayed onset of effect by using Captopril in comparison with Nifedipine, they didn't find significant difference between the drugs in decreasing BP.⁷ In the next year, Schneider E, et al. compared the effect of Captopril and Nifedipine and their combination for emergent HTN. By their findings, BP was decreased more rapidly in the first 60 minutes by Nifedipine in comparison with other drugs, but the result was the same after 240 minutes. Using the two drugs, Nifedipine and Captopril, together reduced BP the most.⁸ In 1993, Dadkar VN et al. designed a study with the same dosages of Nifedipine and Captopril. Their result was approximately in accordance with Guerrero G, et al. in 1990 but they saw earlier onset of effect, more effective response and longer duration of response in patients who used Nifedipine in comparison with Captopril.⁹ In 1996 a study compared the efficacy of Nifedipine, Captopril and Nifedipine with Metoprolol in hypertensive crisis. By their results, the drugs affected within 5 minutes except Captopril which was effective after 15 minutes. In their studies, Nifedipine caused some side effects such as flushing and Captopril caused heaviness of head.¹⁰ In 1996, sublingual drugs were examined for rapid lowering BP and Captopril, Adalat® and Nitroglycerin were suggested.² In 1996, it was seen that the drugs were

more effective when used above the tongue than sublingual forms.^{2,11}

By considering previous studies and this trial, oral drugs are recommended to be used in patients with HTN crisis without any fears of undesirable side effects. It is noted that Captopril is completely forbidden during pregnancy. Regarding the Joseph Varon speech in 2009, due to the side effects of Nifedipine and Nitroglycerin, these drugs are not desirable choices for the first line therapy in patients with HTN crises.¹²

Conclusion

According to the previous studies and also our study, because of the same effect of Captopril and Adalat® on reducing BP and the side effects of Adalat®, Captopril is more recommended to be used in patients with HTN crisis without end organ damages.

Conflict of Interests

Authors have no conflict of interests.

References

1. Rhoney D, Peacock WF. Intravenous therapy for hypertensive emergencies, part 1. *Am J Health Syst Pharm* 2009; 66(15): 1343-52.
2. Nagy V, Zamolyi K, Szegedi N, Szekacs B. Emergency situations in hypertension. *Orv Hetil* 1996; 137(17): 913-21.
3. Grossman E, Ironi AN, Messerli FH. Comparative tolerability profile of hypertensive crisis treatments *Drug Saf* 1998; 19(2): 99-122.
4. Rhoney D, Peacock WF. Intravenous therapy for hypertensive emergencies, part 2. *Am J Health Syst Pharm* 2009; 66(16): 1448-57.
5. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 2003; 42(6): 1206-52.
6. Ardigo S, Rutschmann O, Waeber B, Pechere-Bertschi A. How urgent is it to decrease high blood pressure? *Praxis (Bern 1994)* 2008; 97(8): 431-6.
7. Guerrero G, Melina D, Capaldi L, Mauro R, Colivicchi F, Cardillo C, et al. Sublingually administered captopril versus nifedipine in hypertension emergencies. *Minerva Cardioangiol* 1990; 38(1-2): 37-44.
8. Schneider E, Jennings AA, Opie LH. Captopril, nifedipine and their combination for therapy of hypertensive urgencies. *S Afr Med J* 1991; 80(6): 265-70.
9. Dadkar VN, Karnik ND, Izar M, Sharma SR, Gandhi YP, Narawane NM, et al. Sublingual nifedipine and captopril in hypertensive urgencies and emergencies. *Indian Heart J* 1993; 45(3): 185-7.
10. Karnik ND, Bhatt AD, Trivedi TH, Dadkar VN, Kapadia NM, Vaidya AB, et al. Nifedipine, captopril, metoprolol and nifedipine with metoprolol in hypertensive crisis in non-intensive care setting. *J Assoc Physicians India* 1996; 44(7): 480-2.
11. Wolk R, Kulakowski P, Ceremuzynski L. Nifedipine and captopril exert divergent effects on heart rate variability in patients with acute episodes of hypertension. *J Hum Hypertens* 1996; 10(5): 327-32.
12. Varon J. The diagnosis and treatment of hypertensive crises. *Postgrad Med* 2009; 121(1): 5-13.