Clinical efficacy of sublingual captopril in the treatment of hypertensive urgency

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ABSTRACT

Introduction: This study aimed to evaluate the response rate, clinical efficacy and onset of action of sublingual captopril in patients diagnosed with hypertensive urgency.

Methods: In this cross-sectional study, 101 (67 female and 34 male) patients with a diagnosis of hypertensive urgency (systolic pressure greater than or equal to 180 mmHg and/or diastolic pressure greater than or equal to 110 mmHg, and no findings of target organ damage) were included. Sublingual captopril (25 mg) was administered and the blood pressure was measured during a follow-up period of 120 minutes.

Results: After 60 minutes, an ideal decrease (25 percent of the initial blood pressure) was detected in 54 patients (53.5 percent). An additional 25 mg of sublingual captopril was administered to the remaining 47 patients (46.5 percent). Of these, 19 (18.8 percent) did not respond even to the second dose of sublingual captopril. These non-responders consisted of patients who were taking multidrug antihypertensive regimens before presentation due to hypertensive urgency. No serious side effect was recorded during the study period.

Conclusion: Sublingual captopril can be used as an effective, easily applicable and safe treatment in the management of hypertensive urgency for 120 minutes for those who do not receive multidrug antihypertensive regimens.

Keywords: captopril, hypertension, hypertensive urgency, sublingual captopril

Singapore Med J 2009;50(4):400-402

INTRODUCTION

"Hypertensive crisis" is one of the most important clinical concerns in patients with hypertension. It is defined as an elevation in blood pressure in which diastolic blood pressure (BP) exceeds 120 mmHg and comprises a spectrum of conditions; hypertensive urgency is a sudden and severe increase in BP with mild or no acute damage to vital target organs including the heart, kidney, eye and brain.[1] If this critical increase in blood pressure is accompanied by damage to vital organs, characterised by symptoms such as headache, chest pain and shortness of breath, it is called a hypertensive emergency. The latter condition should be treated by intravenous medications and BP should be pushed down within an hour.[2,3] Hypertensive crisis has been lowered to less than 1% as a result of effective and appropriate treatment of chronic hypertension. In patients with hypertensive urgency, BP is lowered gradually over a period of 24–48 hours, usually with oral or sublingual medications that possess a rapid onset of action with few side effects.[4]

A growing list of medications (intravenous and oral) is available for controlling hypertensive crises. One of these products, captopril, is an angiotensin-converting enzyme (ACE) inhibitor, with acceptable antihypertensive properties and unremarkable side effects. Captopril inhibits enzymes that convert angiotensin I to angiotensin II, a potent vasoconstrictor. It also exerts its antihypertensive effect by decreasing the level of aldosterone and increasing bradykinin levels.[5] Due to the serious side effects of some antihypertensive agents, such as nifedipine (reflex tachycardia, hypertension, headache and flushing),[6,7] and difficult access to some newer and more expensive drugs (e.g. esmolol, fenoldopam), further evaluation of the clinical efficacy and action of accessible drugs is essential. This study aimed to evaluate the response rate, clinical efficacy and onset of action of sublingual captopril in a group of patients diagnosed with hypertensive urgency in our heart emergency unit.

METHODS

This cross-sectional study spanned from March 2004 to June 2005 in the heart emergency unit of our university hospital. The inclusion criteria was patients from both genders and all ages with a diagnosis of hypertensive urgency. Patients who had the following conditions were not included: vascular ischaemia, likelihood to suffer myocardial infarction with symptoms such as chest pain and abrupt variations in their electrocardiograms,

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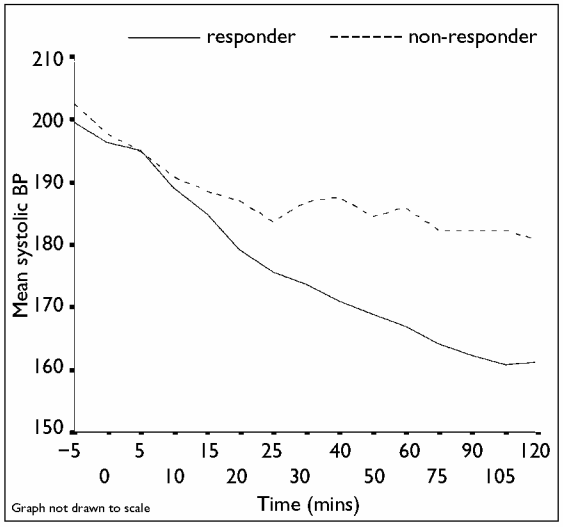

Fig. 1 Mean systolic blood pressure measured at different times for the patients' response to 25 mg sublingual captopril (responders vs. non-responders).

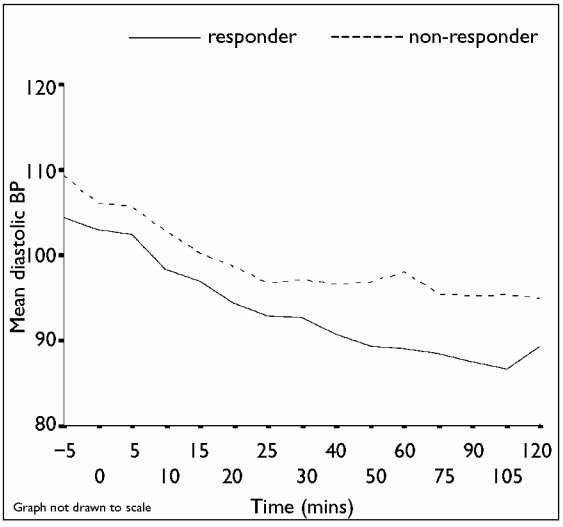

Fig. 2 Mean diastolic blood pressure measured at different times for the patients' response to 25 mg sublingual captopril (responders vs. non-responders).

severe cardiac deficiency or pulmonary oedema, cerebral symptoms (likelihood of hypertensive encephalopathy and stroke), renal artery stenosis (unilateral or bilateral), likelihood of aortic dissection, ocular conditions, allergy to captopril and pregnancy. Patients with hypertensive emergency who received treatment with intravenous nitrate were not included. Hypertensive urgency was defined as an increase in BP (systolic pressure ≥ 180 mmHg and/or diastolic pressure ≥ 110 mmHg) after two measurements, ten minutes apart in the supine position without any vital organ damage.

A total of 101 patients were identified as eligible to participate in this study. After taking the BP, 25 mg sublingual captopril was administered. The patients' BP was taken 13 times (at 5, 10, 15, 20, 25, 30, 40, 50, 60, 75, 90, 105 and 120 minutes) after the administration of captopril. BP measurements were made with a mercury sphygmomanometer (Riester Mercury Sphygmomanometer, Rudolf Riester GmbH, Riester Mercury Sphygmomanometer, Jungingen, Germany) by a general practitioner, who had received training in advance. Both systolic and diastolic BPs were measured and any reported complication was recorded in a checklist. An ideal and acceptable response to the administered captopril was defined as a 25% reduction in the BP. In the cases where the BP did not decrease after one hour, the same dose of sublingual captopril (25 mg) was administered again. When the BP dropped to an acceptable level, the patient would be given oral antihypertensive medications and discharged. The study protocol conformed with the ethical guidelines of the 1975 Declaration of Helsinki,[8] and informed consent was obtained from all patients prior to enrollment. For statistical analysis, descriptive indices such as frequency, mean and standard deviation (SD) were used. All analyses were performed using the Statistical Package for Social Sciences version 13.0 (SPSS Inc, Chicago, IL, USA).

RESULTS

67 patients (66.3%) were female and 34 (33.7%) were male. 42 patients (41.5%) were < 60 years of age, and 59 cases (58.5%) were ≥ 60 years of age. 14 patients (13.8%) had diabetes mellitus, 27 (26.7%) had hyperlipidaemia and 20 (19.8%) were current smokers.

The BP measured showed varying levels of decline throughout the follow-up period of 120 minutes. The average BP decline evidenced itself in the early minutes and reached its peak 25–30 minutes after the treatment had begun. The level of systolic and diastolic BP drop was almost equal. The greatest decline in BP levels registered was 30%, and no BP reduction of > 30% was recorded. 30 minutes after the initial dose of sublingual captopril, an ideal systolic and diastolic BP reduction (25% of the pre-treatment BP) was reported in 69 (68.4%) and 66 (65.3%) patients, respectively. 60 minutes after the initiation of treatment, the systolic and diastolic BP decline (> 10% of the pre-treatment BP) was detected in 58 (57.4%) cases and 60 (59.5%) patients, respectively. 47 patients (46.5%) did not respond effectively to the first dose of captopril, and did not have an ideal BP decline (i.e. 25% reduction of the initial BP) in 60 minutes. Therefore, an additional 25 mg of sublingual captopril was administered to these patients. Of these, 28 (59.6%) showed a 15% drop in their BP levels after one hour, while 19 (18.8%) did not respond even to the second dose of sublingual captopril, and so an intravenous agent was administered.

After 120 minutes, 30% of the patients showed only a 5% drop, while the remaining 70% registered a proper BP decline ranging from 5% to 25%. The response to captopril (i.e. a 25% reduction in BP) in the mean systolic and diastolic BPs at different times for responders and non-responders is shown in Figs. 1 and 2. The patients who were less responsive to sublingual captopril were actually known as treatment-resistant hypertensive patients who were taking multidrug antihypertensive regimens. 25 of them (53%) had previously used captopril. No serious side effects, such as headache, angina, reflex tachycardia or flushing, were reported by the patients enrolled in this study.

DISCUSSION

While the BP should be brought down as immediately as possible in hypertensive emergencies with intravenous agents, oral medications such as clonidine, captopril and labetalol are the first choice of treatment for cases of hypertensive urgency.[9] The results obtained indicated that patients who did not respond to the treatment, were those who did not use captopril previously and received multidrug hypertension treatment. Sublingual captopril was quite effective for those who used this treatment for their hypertension before participating in this study. The drop in the BP levels of responders started within ten minutes after the administration of captopril and gradually continued with a gentle decline. As it was not advisable to lower BP levels by more than 30% of the initial BP in a hypertensive crisis,[4] the results suggested that 25 mg sublingual captopril may be suitable treatment for a hypertensive urgency, especially in those who have used this treatment previously.

A gradual BP drop in the absence of serious side effects makes captopril an ideal antihypertensive agent. A rapid reduction in elevated BP is associated with severe complications such as coma, seizures, transient ischaemic attacks and blindness.[10,11] Captopril maintains a systemic supply of blood to the brain as it lowers blood pressure levels. In addition, it prevents a drop in the blood supply to the kidneys and a likely failure of these organs.

The current results are in agreement with previous clinical investigations in which 25 mg captopril has been used in hypertensive crises. In a study by Gemici et al to compare the safety and clinical efficacy of 25 mg sublingual captopril with sublingual nifedipine, sublingual captopril showed antihypertensive effects similar to 10 mg sublingual nifedipine. Furthermore, only three patients who received captopril had adverse effects (two individuals had headaches and one had weakness), while 23 patients who received sublingual nifedipine reported side effects including flushing, headache, palpitation, respiration, angina, nausea and reflex tachycardia. The authors suggested that captopril has suppressive effects on the sympathetic nervous system, and this was responsible for the fewer side effects of captopril.[10] Another randomised study by Addad et al, to compare the efficacy and safety of oral captopril (25 mg) vs. nicardipine (20 mg) in hypertensive crises, did not find any side effects in either group during a two-hour period of follow-up.[12] In another study, the effect of single doses of captopril and nifedipine on BP in black and white patients with hypertensive crisis was not much different after six hours, but nifedipine was more potent than captopril in black patients.[13] The reasons for not encountering any side effects in this study may be attributed either to the small sample size or the unacceptable reduction of BP in the non-responders group.

There were some limitations to this study and these included a small sample size, the absence of a control group and the usage of a manual sphygmomanometer instead of a properly-calibrated automatic BP measuring device. These limitations were unavoidable due to a lack of financial support for this study. In conclusion, sublingual captopril may be used as an effective, safe and easily applicable treatment during the first 120 minutes of hypertensive urgency for those who do not receive multidrug antihypertensive regimens.

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