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Original article

Evaluation of the clinical outcome of captopril use for hypertensive urgency in Khartoum State's emergency centres

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ABSTRACT

Background: Captopril is an important drug and is used to control hypertensive urgency world-wide. But there is very little data available regarding the evaluation of its outcomes in hypertensive urgency among African patients. This study aimed to evaluate the clinical outcomes of captopril use for hypertensive urgency at a selection of Sudanese emergency centres.

Methods: This was a cross-sectional study, conducted between 15 to 30 November 2015. A total of 50 patients, attending a selection of Khartoum State hospital emergency centres, with a clinical diagnosis of hypertensive urgency were approached by investigators for the study. Dose regimen, prognosis, and reduction in systolic and diastolic blood pressure were collected alongside a questionaire to patients regarding their care (compliance, etc.). Data were analysed using the Chi-square Test to compare the mean differences for various results. Differences were considered to be significant at $P < 0.05$.

Results: Around two-thirds (60%) of participants were female, and 28% were non-compliant with treatment. A 25mg dose of captopril was the most frequently used dose. Most of the patients (66%) did not have pre-existing disease. The majority of patients showed an improved blood pressure: both systolic and diastolic blood pressures were reduced by 16-25% and 5-15%, respectively.

Conclusion: The study concluded that the dose of 25 mg of captopril is effective in managing hypertensive urgency and controlling the blood pressure. We also recommend that patients receiving captopril must be observed in the emergency centre for further evaluation.

African relevance

- There is a paucity of data regarding the use of Captopril in hypertensive urgency within African emergency centres.
- A dose of 25 mg of captopril appears to be effective in managing hypertensive urgency and to control the blood pressure.

Introduction

Hypertensive urgency is a sudden and severe increase in blood pressure with mild or no acute damage to vital organs - including the heart, kidney, eye, and brain [1]. During the past decade, many drugs have been used in the management of hypertensive urgency, the most common being captopril, clonidine, and labetalol [2]. Recent studies have shown that rapid reduction of the blood pressure is dangerous and that caution should be taken to lower it by more than 10% to 25% within the first hour [3,4]. It is widely recognised that during the first hour of treatment, there is no significant difference between the sublingual and oral route for captopril to reduce blood pressure [5].

ACE inhibitors are classified into three groups according to the chemical structure of their active moiety [6]. Captopril is the prototype of the sulfhydryl-containing group. Captopril differs from other ACE inhibitors by its short half-life [7,8]. Whereas the majority of ACE inhibitors are administered as prodrugs, captopril is an active drug [9]. Captopril reduces peripheral vascular resistance without causing a compensatory increase in heart rate [10].

Although, captopril is considered a first-line therapy in controlling hypertensive urgency in emergency centres [2,11], in Sudan, it is rarely used for the management of hypertensive urgency. This appear to be due to a belief that it is not effective in Sudanese patients.

This study aimed to evaluate the clinical outcomes of captopril use for hypertensive urgency at local emergency centres among Sudanese

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patients.

Methods

Study design

For this cross-sectional study, data were collected using a custom-designed data collection form alongside baseline clinical and demographic data. The study was conducted at the emergency centres of three government hospitals in Khartoum state, Sudan. Data were collected between 15 and 30 November 2015, over three days per two weeks for each site.

Ethical considerations

The study was approved by the National Committee represented as the Research Department, Ministry of Health, Khartoum state. An Ethical Clarence certificate was obtained.

Data collection procedure

Clinical data were collected from the physician who directly supervised the patient within the emergency centre. Information included: captopril regimen used, prognosis, and response to treatment (pre- and post treatment systolic and diastolic blood pressure readings). Patients were also asked about their personal information.

Population criteria and sampling

The sample size was estimated by convenience; all patients attending the emergency centres at the selected hospitals during the study period with a diagnosis of hypertensive urgency were included.

Inclusion criteria

Inclusion criteria were: aged 18 years or over, clinical diagnosis of hypertensive urgency by the emergency centre physician, and have received captopril as treatment were enrolled.

Exclusion criteria

Exclusion criteria were: patients aged <18 years, clinically diagnosed with hypertensive urgency but attended to other hospital sites rather than the emergency centre, or clinically diagnosed with other emergency conditions. Patients who attended to the emergency centre with hypertension urgency but did not receive captopril, were also not recruited.

Data analysis

Statistical evaluation was performed using the Statistical Package for Social Science (SPSS) computer program version 16.0. Data were analyzed by through Chi-square Test to compare the mean differences for various results. Differences were considered to be significant at $P < 0.05$.

Results

Population characteristics

Representation at the selected hospitals were distributed as follow: Bahari represented 44%, followed by Khartoum 30%, and Omdurman 26%. The most common age group was 41–60 years and 60% of patients were female. The majority of cases were recent onset hypertension, and 28% were found to be non-compliant to their regular hypertension treatment.

The majority of patients (36%) were illiterate, with a sedentary lifestyle (44%). See Table 1.

Clinical and therapeutic aspects of captopril use at the emergency centre

Table 2 provides the clinical history as well as the medication prescription patterns.

The medications history reports that 80% of patients received captopril as a dosage of 25 mg, either on its own (36%) or with amlodipine (44%), either once or in repeated doses, mainly after 8 hs (22%) and for at least one day (84%). Moreover, past medications used for hypertension control were commonly missed (58%) as seen in Table 2.

Relationship between captopril dose and a reduction in blood pressure

As illustrated by Fig. 1A the systolic blood pressure reduced by 16–25% in response to captopril 25 mg in (32%) of hypertensive urgency patients.

The diastolic blood pressure reduced by 5-15% in 50% of hypertensive patients as shown in Fig. 1B.

Relationship between frequency of captopril dose and reduction in blood pressure

Captopril, when administered once, resulted in a 16-25% reduction in systolic blood pressure in 58% of patients, and 5-15% reduction in diastolic blood pressure in 62% of patients, as shown in Fig. 2.

Clinical decision making at the emergency centre

Most patients (68%) were discharged from the emergency centre, one hour after receiving captopril once, in a dose of 25 mg, as shown in Fig. 3.

Discussion

Captopril is considered a first-line therapy for controlling hypertensive urgency at emergency centres, but to date there is not enough data available regarding its clinical outcomes among African patients.

Most of the participants were female. Regretably, due to various local inequities related to education compared to male participants, the majority of female participants were non-compliant with advice provided

Table 1
Population characteristics, $n = 50$.

Variable	Variable breakdown	n (%) and p-value
1. Hospital		p=0.262
	Bahari	22 (44%)
	Khartoum	15 (30%)
	Omdurman	13 (26%)
2. Gender		p=0.157
	Male	20 (40%)
	Female	30 (60%)
3. Age		**p=0.019**
	18-40 years	11 (22%)
	41-60 years	26 (52%)
	> 60 years	13 (26%)
4. Educational level		p=0.079
	Illiterate	18 (36%)
	Primary	9 (18%)
	Secondary	16 (32%)
	Higher	7 (14%)
5. Occupation		**p=0.015**
	Inactive	22 (44%)
	Active	21 (42%)
	Very active	7 (14%)
6. Marital status		p<0.001
	Single	9 (18%)
	Married	41 (82%)

Table 2
Clinical history and medication prescription patterns, $n = 50$.

Pattern	Frequency/%	P-value
A. Clinical history		
Family history		
1° degree	34 (68)	p<0.001
2° degree	11 (22)	
3rd degree	1 (2)	
No family history	4 (8)	
Co-morbidity: presence of other conditions		
No	33 (66)	p<0.001
Diabetes -type I	2 (4)	
Diabetes -type II	10 (2)	
Asthma	1 (2.)	
Diabetes/Ischaemic heart disease	2 (4.)	
Diabetes/Asthma	1 (2.)	
End-Stage Renal Disease	1 (2.)	
Occurrence history		
1st event	24 (48)	p=0.002
2nd event	21 (42)	
3rd event	05 (10)	
Cause		
Newly discovered	17 (34)	p=0.022
Non-compliance	14 (28)	
Emotional stress	08 (16)	
Missed medications	7 (14)	
Other	4 (8)	
B. Medications		
Past medications for hypertension		
Amlodipine	10 (20)	p<0.001
Lisinopril	5 (10)	
Hydrochlorothiazide	2 (4)	
Combination	4 (8)	
Missed	29 (58)	
Current medications		
Captopril alone	18 (36)	p<0.001
With Amlodipine	22 (44)	
With furosemide	2 (4.0)	
Other medications	8 (16)	
Captopril dose		
12.5 mg	6 (12)	p<0.001
25 mg	40 (80)	
50 mg	4 (8)	
Dose regimen		
Once	24 (48)	p=0.777
Repeated	26 (52)	
Repeated after		
1 h	2 (4)	p=0.001
2 hs	2 (4)	
4 hs	1 (2)	
6 hs	8 (16)	
8 hs	11 (22)	
12 hs	2 (4)	
Missed	24 (48)	
Treatment duration		
1 day	42 (84)	p<0.001
2 days	6 (12)	
>3 days	2 (4.0)	

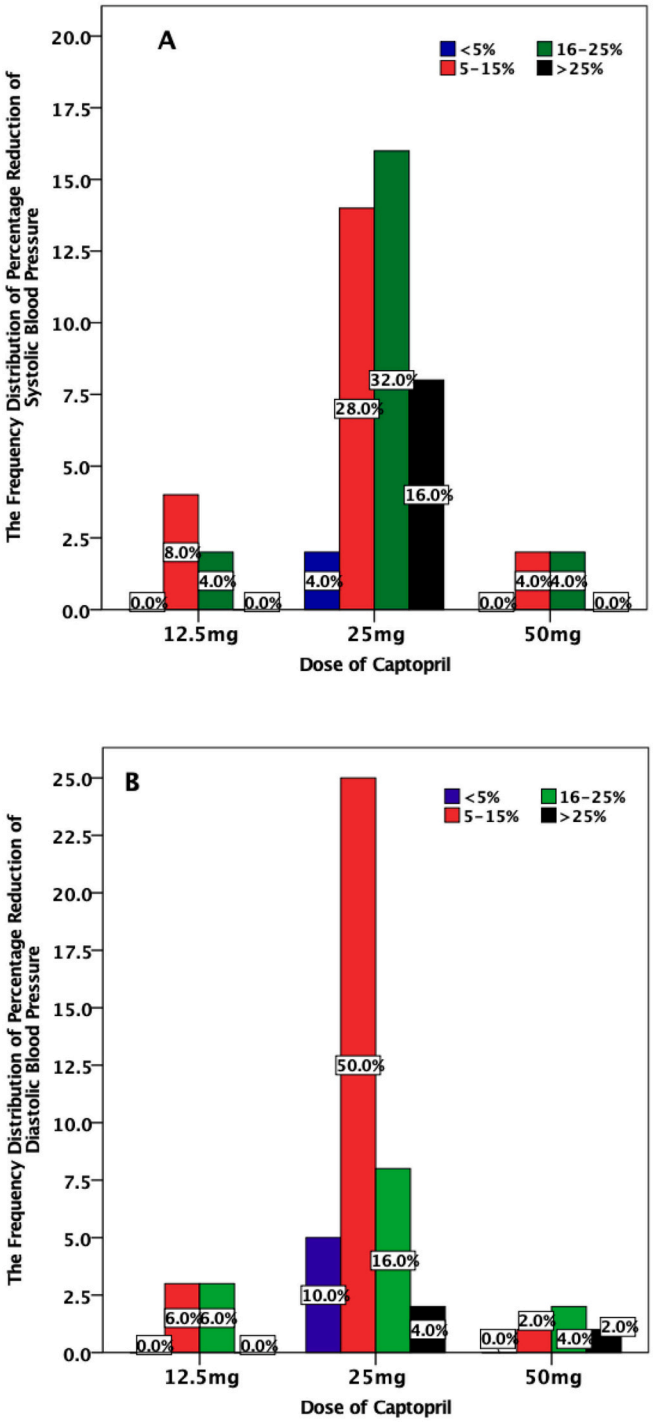

Fig. 1. Relationship between dose of captopril and percentage reduction in systolic (A) and diastolic (B) blood pressure among patients at emergency units of selected Khartoum state hospitals.

by health-care providers. This fits with previous work by Bilal et al. [12] Bilal found that most participants that did not adhere to their treatment were female; this was associated with lower education levels, being married and younger age (41-60 yrs). Reckelhoff et al suggested this may be linked to emotional stress and a hormonal effect [13]. Reckelhoff reported that loss of oestrogen in postmenopausal women play a role in increasing blood pressure and Salkic et. al [14] reported that hypertension is detected later in life due to its silent symptoms. Our findings also revealed that the majority of patients with hypertensive urgency attended Bahari hospital. This may be due to the lack of other emergency centres at Bahari district unlike other Khartoum state areas that has more.

The majority of participants were illiterate, which may explain why patients we mostly non-compliant. Miller et al [15], agrees that increased literacy, especially health literacy, is associated with better adherence to treatment.

The main cause of hypertension urgency among study participants appeared to be non-compliance. The majority of diagnoses were by chance. Bender et al [16], has also shown that the majority of hypertensive urgency patients were either newly diagnosed or not on antihypertensive.

The past medical history of the participants revealed that the majority had a first degree family history. Hopkins, et al. [17] reported that the risk of developing hypertension in persons under the age of 50 approximately doubled for each first degree relative that had

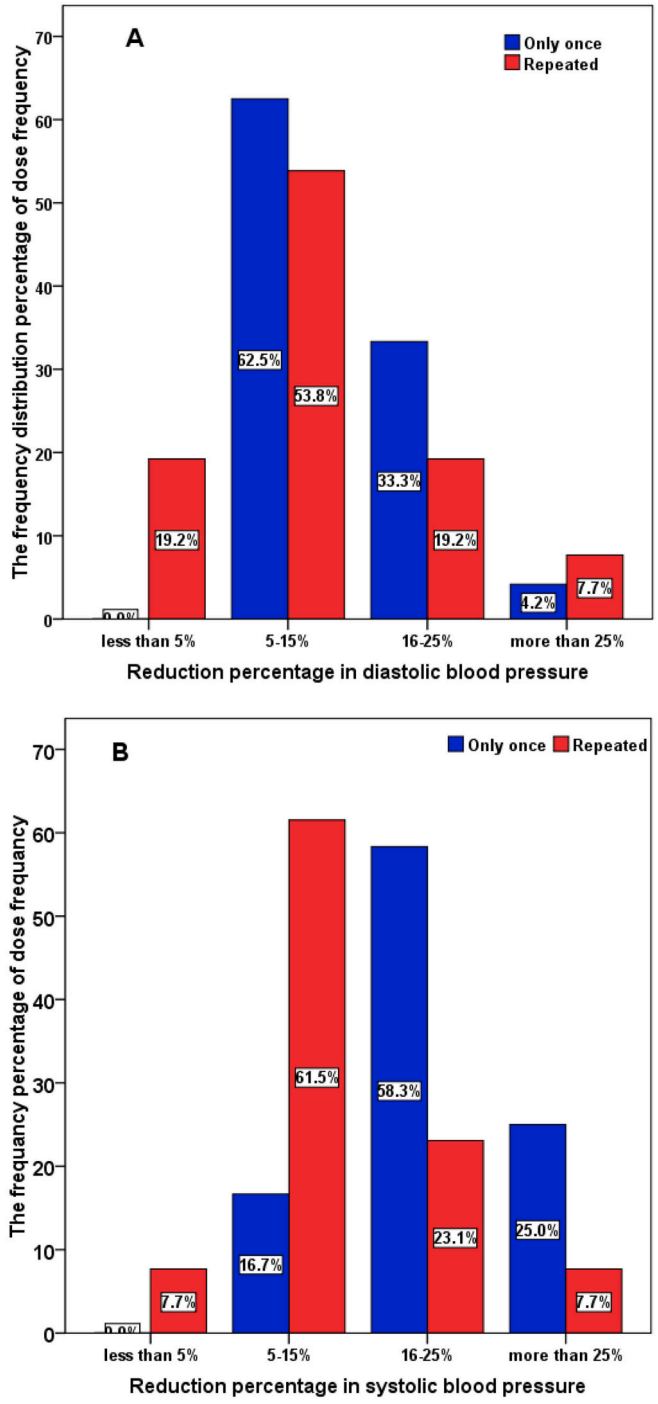

Fig. 2. Relationship between frequency distribution percentage of captopril dose and reduction in systolic (A) and diastolic (B) blood pressure among patients.

hypertension. This was also confirmed among Chinese patients where participants with a family history had a significantly higher prevalence of hypertension (Miao Liu et al. [18]). It is interesting to note though that Handler et al [19] reports that family history association for hypertension is conflicting in some studies.

From the medication history it is reported that most of the patients received captopril, either alone or with amlodipine. Kotruchin et al. [20] showed that there was no significant difference in efficacy and safety between captopril alone or combined with amlodipine. According to applied protocol, physicians tend to start with calcium channel blockers (amlodipine). This may be due to the common misbelieve that the

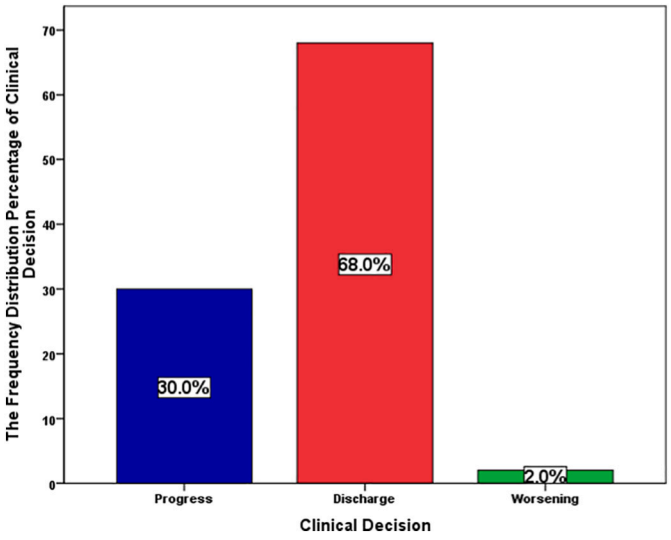

Fig. 3. The frequency distribution percentage of clinical decision taken by the physicians for patients received captopril at emergency units of Khartoum state hospitals.

efficacy of ACE inhibitors are questionable in African patients. Based on our study we observed that Captopril can be used alone to achieve the same therapeutic goal. This will likely reduce the expected side effects and cost of using two drugs.

The study stated that the dose of 25 mg of captopril given either once or repeatedly was more frequently used for hypertensive urgency. We have taken this as a reasonable guide that a dose regimen of 25 mg was effective among the Sudanese participants. Flack et al. [21], and Damasceno et al. [22] previously reported similar good blood pressure-lowering efficacy in this population with ACE inhibitors.

Our study showed that the majority of patients were discharged after 1 h. It is unlikely that this time was sufficient to reassure patients. Although it was possible to reduce the blood pressure to a safe level witin this time, it is would be better for a patient to remain longer for observation. Bender et al. [16] and Campos et al. [24] agree and confirm that observing a patient for 1 h in an emergency setting is not enough to assess for other morbidity and mortality variables. We believe that a longer period of observation is safer; such as the 5 hs average length of stay in the emergency centre for our cohort.

Conclusion

A 25 mg dose of captopril reduced blood pressure and was considered as effective to control hypertensive urgency in the emergency centre within a Sudanese population. Captopril can be used alone to achieve the same therapeutic goal as combination therapy, reducing side effects and cost. A common trend was discharge from the emergency centre within 1 h. Patients should be sufficiently observed at the emergency centre in case further control is required. This also allows further evaluation for other risk variables.

The findings of this study should be taken into considerations by the hospital committee to modify and develop their own safe-effective and affordable protocols. We recommend the establishment of more emergency centres in the Bahari area to better accommodate cases of hypertensive urgency as a life-threatening condition. Moreover, the level of health care and education must be improved especially for the elderly and females.

Dissemination of results

The results of this study were shared with staff members of the Pharmacology department, faculty of Pharmacy, OIU in Sudan through

an informal presentation. Results were also presented to Defending M. Pharm. in Clinical Pharmacology Committee, Pharmacy faculty at the University of OIU in a form of graduation project dissertation.

Authors' contribution

Authors contributed as follow to the conception or design of the work; the acquisition, analysis, or interpretation of data for the work; and drafting the work or revising it critically for important intellectual content: AHHO and AAEA contributed 50% each. All authors approved the version to be published and agreed to be accountable for all aspects of the work.

Declaration of competing interest

The authors report no conflicts of interest.

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