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Anti-hypertensive therapy for acute ischemic stroke survivors

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Summary
Background and objective: Anti-hypertensive medications are recommended for prevention of recurrent ischemic stroke in hypertensive and normotensive patients. The objective of this study was to analyze the use of anti-hypertensive therapy in acute ischemic stroke survivors.
Methods: All ischemic stroke survivors discharged from Al-watani governmental hospital in Palestine from August 2006 until September 2007 were investigated. Demographic data, clinical characteristics, and different classes of anti-hypertensive medications prescribed to stroke survivors were analyzed using SPSS 15.
Results: One hundred and twenty four ischemic stroke survivors were identified, of which 80 (64.5%) had a documented history of hypertension (HTN). Two thirds of the survivors ($n = 82$; 66.1%) were prescribed anti-hypertensive medications, mostly as mono-therapy, at discharge. Angiotensin-converting enzyme inhibitors (ACEI) 65 (45.6%), followed by diuretics 41 (34.5%) were the most common drug classes prescribed. ACEI were used in combination with diuretics in 29 (23.4%) survivors. Among survivors with a documented history of HTN, 70 (85.5%) were prescribed anti-hypertensive medications at discharge while 12 (8.5%) of survivors with no history of HTN were prescribed anti-hypertensive medications at discharge.
Conclusion: In this study, the use of anti-hypertensive medications as a mono-therapy was common among those with a history of hypertension but not among those without a history of hypertension.

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Introduction

Hypertension is one of the most important modifiable risk factors for stroke, and the use of anti-hypertensive medications is known to reduce this risk substantially [1,2]. In one study, a moderate reduction in blood pressure during the first week after acute ischemic stroke was associated with improved short-term functional outcome [3]. However, a meta-analytic study assessing the effect of altering blood pressure in people with acute stroke, and the effect of different vasoactive drugs on blood pressure in acute stroke concluded that there was insufficient evidence to associate altering blood pressure with outcome during the acute phase of a stroke [4]. This meta-analysis included 12 trials involving 1153 participants (603 participants were assigned active therapy and 550 participants received placebo/control). The trials tested angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, clonidine, glyceryl trinitrate, thiazide diuretic and mixed anti-hypertensive therapy. One trial tested phenylephrine. Functional outcome and death were not altered by any of the drugs [4]. Nevertheless, the new statement from the American Stroke association recommended the use of anti-hypertensive therapy for all hypertensive and normotensive ischemic stroke survivors [5]. Furthermore, the Joint National Committee on Prevention, Detection, Evaluation and Treatment of high blood pressure (JNC-7) suggested the use of angiotensin-converting enzyme inhibitors plus thiazide diuretics for blood pressure reduction in patients with recurrent stroke [6]. The LIFE study, a randomized, controlled trial showed that losartan was more effective than atenolol in reducing cardiovascular morbidity and mortality as well as mortality from all causes in patients with hypertension, diabetes, and LVH and that losartan appeared to have benefits beyond blood pressure reduction [7]. In the MOSES study group, eprosartan was compared with nitrendipine for secondary prevention after stroke. The result was an early comparable normotensive blood pressure. However, the combined primary end point of morbidity and mortality was significantly lower in the eprosartan group [8].

In the present study, we evaluated the frequency and pattern of anti-hypertensive therapy for acute ischemic stroke survivors at discharge in relation to recent recommendations and guidelines.

Methodology

Study population

This hospital-based study was conducted at Al-watani Governmental Hospital in Nablus, Palestine. Data were collected retrospectively from September 01, 2006 until August 31, 2007. All patients admitted to Al-watani hospital with an ischemic stroke and discharged alive were included in the study. The diagnosis of ischemic stroke was based on the World Health Organization definition of stroke and the computerized tomography (CT) scan results [9]. Patients with no definitive CT scan results or those suspected to have transient ischemic attacks were excluded.

Data collection

Data collection was authorized by the hospital administration. For each patient, demographic data, risk factors, and different classes of anti-hypertensive medications prescribed at discharge were obtained from patients' medical files. Demographic variables included age and sex. Risk factors consisted of a documented diagnosis of hypertension (HTN), ischemic heart disease (IHD), renal dysfunction, congestive heart failure (CHF), atrial fibrillation (AF), recurrent stroke, obesity, and age >65 years. Obesity was defined as a body mass index (BMI) > 30 for both males and females. Renal dysfunction was defined as a creatinine clearance <60 ml/min. Creatinine clearance (CrCl) was calculated for all patients using the Cockcroft–Gault formula with values for women obtained by multiplying the result by 0.85. A history of hypertension was based on a documented diagnosis of the disease in a patient's medical file.

We identified the prescribing rates of different anti-hypertensive drug classes, including angiotensin-converting enzyme inhibitors (ACE-I), angiotensin receptor blockers (ARB), b-adrenergic blocking agents (BB), calcium channel blockers (CCB), and diuretics. We then examined and analyzed the use of different classes of anti-hypertensive medications among patients with and without a documented diagnosis of hypertension. The number of prescriptions was documented for each class of anti-hypertensive drugs.

Statistical analysis

Analysis of data was carried out using the "Statistical Program for Social Sciences" (SPSS) for Windows

version 15.0 (SPSS Inc., Chicago, IL). Descriptive analysis included mean ± SD and frequency. Univariate analysis for each variable in relation to differences in the frequency of demographic characteristics, and risk factors among ischemic stroke patients with and without anti-hypertensive drug utilization at discharge were assessed with the Pearson chi-square test (X^2).

Results

During the study period, 153 ischemic stroke patients were admitted to the hospital. Three patients were discharged against medical advice and 26 died during hospitalization. One hundred and twenty four ischemic stroke patients were discharged alive and were included in the analysis. The average age of the stroke survivors was 68.3 ± 11 years. The majority of survivors were females (56.5%). Forty three (43.7%) survivors had recurrent stroke attacks while 81 (65.3%) had a first-ever stroke. Among stroke survivors, 80 (64.5%) had a documented history of hypertension while 44 (35.5%) had no diagnosis of hypertension in their clinical history. In the present study, patients with and without hypertension had comparable demographic and clinical characteristics (Table 1).

In patients with a history of hypertension, 70 (85.5%) survivors received anti-hypertensive

Table 1 Univariate analysis of stroke survivors by anti-hypertensive pharmacotherapy status at discharge.

Variable	Total	Anti-hypertensive therapy at discharge		*p* value
	n (%) *N* = 124	Yes *n* = 82	No *n* = 42	
Age				
<65	83 (66.9)	51 (62.2)	32 (76.2)	0.08
⩾65	41 (33.1)	31 (37.8)	10 (23.8)	
Gender				
Male	54 (43.5)	36 (43.9)	18 (42.9)	0.53
Female	70 (56.5)	46 (56.1)	24 (57.1)	
Hypertension				
Present	80 (64.5)	70 (85.4)	10 (23.8)	**0.0001**
Absent	44 (35.5)	12 (14.6)	32 (76.2)	
History of DM				
Present	54 (43.5)	32 (39)	22 (52.4)	0.11
Absent	70 (56.5)	50 (61)	20 (47.6)	
Renal dysfunction				
Present	38 (30.6)	24 (29.3)	14 (33.3)	0.39
Absent	86 (69.4)	58 (70.7)	28 (66.7)	
History of CHF				
Present	17 (13.7)	14 (17.1)	3 (7.1)	0.10
Absent	107 (86.3)	68 (82.9)	39 (92.9)	
History of AF				
Present	20 (16.1)	13 (15.9)	7 (16.7)	0.54
Absent	104 (83.9)	69 (84.1)	35 (83.3)	
History of IHD				
Present	8 (6.5)	5 (6.1)	3 (7.1)	0.54
Absent	116 (93.5)	77 (93.9)	39 (92.9)	
Recurrent stroke				
Present	43 (34.7)	29 (35.4)	14 (33.3)	0.49
Absent	81 (65.3)	53 (64.6)	28 (66.7)	
BMI				
Present	20 (16.1)	13 (15.9)	7 (16.7)	0.54
Absent	104 (83.6)	69 (84.1)	35 (83.3)	

DM: diabetes mellitus; CHF: congestive heart failure; AF: atrial fibrillation; IHD: ischemic heart disease and BMI: body mass index.

Table 2 Anti-hypertensive drug prescriptions in ischemic stroke survivors.

Drug classes	Total number of prescriptions $n = 119$ for 82 stroke survivors	Most commonly prescribed anti-hypertensive drug n (% of drug class)	Stroke patients with HTN $n = 80$	Stroke patients without HTN $n = 44$	Mono-therapy $n = 48$	$\geqslant 2$ drug prescriptions for 34 patients $n = 71$
Drug therapy						
ACE-I	65 (54.6)	Enalapril 55, (84.6%)	60 (75)	5 (11.4)	34	31
Diuretics	41 (34.5)	Furosemide 41, (100%)	33 (41.3)	8 (18.2)	9	32
BB	8 (6.7)	Atenolol 8, (100%)	8 (10)	0 (0)	3	5
CCB	5 (4.2)	Dilitiazem 5, (100%)	5 (6.3)	0 (0)	2	3

HTN: hypertension.

therapy at discharge while only 12 (8%) patients without a prior diagnosis of hypertension were treated at discharge. Most of the tested factors, notably DM ($p = 0.11$) and a history of recurrent ischemic attacks ($p = 0.49$), were not significantly associated with the prescribing of anti-hypertensive medications at discharge. The only significant factor was the presence of a history of hypertension ($p = 0.001$) (Table 1).

Overall, approximately two thirds ($n = 82$; 66.1%) of ischemic stroke survivors received anti-hypertensive therapy at discharge. Of those, 48 (58.5%) received one anti-hypertensive medication while 34 (41.5%) received $\geqslant 2$ anti-hypertensive medications. Foremost patients ($n = 65$; 45.6%) were prescribed an ACE-I, followed by a diuretic ($n = 41$; 34.5%, CCB ($n = 5$, 4.2%), and BB ($n = 8$; 6.7%) (Table 2). Within the ACE-I drug class, enalapril (84.5%) was most commonly prescribed. Of the diuretic class, only furosemide, a loop diuretic (100%) was prescribed. The most common combination regimen prescribed at discharge was an ACE-I with a loop diuretic, which was used in 29 (23.4%) survivors. The average number of anti-hypertensive drug classes at discharge was 0.96 ± 0.8 per patient.

Discussions

This study showed that one out of every three stroke survivors was discharged on no anti-hypertensive therapy. Furthermore, the study showed that among those who were prescribed anti-hypertensive medications, the majority were on monotherapy. There is strong and widely accepted evidence that lowering blood pressure (BP) reduces the risk of primary and secondary stroke attacks in patients with hypertension and in those whose BP is considered normal but who are at high risk for stroke [10,11].

In this study, neither a history of recurrent stroke nor the presence of DM was significantly associated with anti-hypertensive prescription at discharge despite the fact that DM is a strong risk factor for recurrent stroke [12—14]. Among diabetic stroke patients, thiazide diuretics, BB and ACE-I are beneficial in reducing stroke incidence and cardiovascular events [15—17].

Recent American guidelines call for anti-hypertensive combination therapy in stroke survivors [6,18]. However, only 27.4% of the survivors were discharged on combination anti-hypertensive regimens. In this study, a thiazide was not prescribed at discharge, although guidelines recommend thiazide diuretics for treatment of most hypertensive patients either alone or combined with drugs from other classes [6]. Thiazide diuretics are of proven benefit in the primary [19] and secondary prevention [19] of stroke, particularly when used in combination with an ACE-I [6,15].

Our findings regarding the prescribing of anti-hypertensive medication for patients without a history of hypertension may not actually reflect the adherence of physicians to the results of clinical trials and guidelines. It is possible that these medications were prescribed for other therapeutic reasons such as a b-blocker for cardiac rate control or ACE-I or loop diuretics for heart failure rather than for prevention of recurrent strokes. Our study has several limitations: (1) we did not collect data on the potential contraindications that might have prevented the use of certain anti-hypertensive medications; and (2) we had no information on actual blood pressure measurements during hospitalization which might have influenced anti-hypertensive treatment decisions.

Conclusion

In this study, the use of anti-hypertensive medications while common, was mostly not in compliance with recent recommendations regarding the number or type of drug classes. Since hypertension is

one of the important risk factors for stroke, better control of blood pressure is needed to minimize the risk of stroke. Furthermore, screening stroke survivors for blood pressure control and initiating appropriate anti-hypertensive medications should help reduce the risk of recurrent strokes and increase survival. Finally, continuing medication education and increased awareness among health practitioners regarding the latest guidelines, including recommended therapeutic choices for the control of high blood pressure among stroke patients, is required.

Conflict of interest

None declared.

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