

Discharge Medications Among Ischemic Stroke Survivors

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Background: The aim of this study was to analyze the types and cost of medications prescribed at discharge for ischemic stroke survivors. *Methods:* This is a descriptive study of medications prescribed for ischemic stroke survivors admitted to Al-watani hospital during a 6-month period. *Results:* A total of 95 consecutive stroke patients were included in the study period; 78 (82.1%) survivors were having ischemic stroke subtype and were designated the study group. The average age of the survivors was 66.9 ± 12.7 years. Survivors had prevalent risk factors such as diabetes mellitus (70%), hypertension (68%), and ischemic heart disease (34.6%). On average, survivors experienced a minimum of 0.73 complications (range 0-3) with the most common being infections ($n = 35$, 44.8%). Forty-two per cent of the ischemic stroke survivors were taking antiplatelet drugs prior to the current attack. At discharge, ischemic stroke survivors were prescribed an average of 4.9 medications from 4.3 different drug classes. All ischemic stroke survivors were prescribed antiplatelet therapy at discharge. Aspirin monotherapy was prescribed for 61 survivors while the combination of aspirin/clopidogrel antiplatelet therapy was prescribed for 17 survivors. The average monthly cost for prophylactic therapy and for medications used to treat post-stroke complication was approximately 52 USD per survivor. *Conclusion:* Most of the patients in the study group were having the traditional risk factors for ischemic stroke and were suffering from typical post-stroke complications. Lack of medical insurance will impose a heavy financial burden on stroke survivors in Palestine. **Key Words:** Medications—ischemic—stroke—cost—Palestine.

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Stroke or cerebrovascular accident (CVA) refers to an acute onset of neurological deficit lasting more than 24 hours or culminating in death caused by sudden impairment of cerebral circulation.¹ Stroke is one of the most common causes of disabilities and death among the elderly in most countries worldwide.²⁻⁴ Stroke can be transient (TIA) or complete attacks. The complete stroke attacks could be due to either ischemia or hemorrhage.⁵

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There are many identified risk factors for stroke. Modifiable risk factors include hypertension, myocardial infarction, atrial fibrillation, congestive heart failure, diabetes mellitus, carotid artery stenosis, and hypercholesterolemia. Nonmodifiable risk factors include advanced age, hereditary hyper-coagulable states, and male gender.⁶⁻⁹

Patients who have had an acute stroke are at risk of developing a wide range of complications, such as complications are important because they may cause death or delay successful rehabilitation.¹⁰⁻¹⁷ Depression, urinary tract infection, and limb pain are the most common complications experienced among stroke survivors.^{18,19} The medications to be prescribed and the medical complications occurring after stroke are considered important challenges for the medical team and families of the patients, and illustrate the need for careful supervision of the patients and their health related issues.^{20,21}

Many stroke survivors are started on new medications, such as antihypertensive, anticoagulants, and antiplatelets,

during their hospitalization and after discharge, in an attempt to control risk factors and prevent recurrent strokes. Prophylactic antiplatelet therapy such as aspirin, clopidogrel, and the combination of aspirin with extended release dipyridamole, all have been proven effective in patients with ischemic stroke subtype.²²⁻²⁴ Several recommendations about the choice of antiplatelet drugs in patients with stroke have been published.²⁵⁻²⁹ Recommendations for clopidogrel are usually restricted to patients who are intolerant to aspirin, or who have had a recurrent ischemic event while on aspirin. Aspirin is the best studied antiplatelet agent and its clinical efficacy in secondary prevention and cardiac protection has been demonstrated in numerous large clinical trials.^{30,31} Many stroke survivors are also prescribed other additional medications such as antihypertensive or anticoagulants in an attempt to control risk factors and prevent recurrent strokes.

In Palestine, the Ministry of Health (MOH) is the major provider of medical services for a total population of 4,151,668 inhabitants. In the northern part of Palestine, Nablus district is a well-defined area with a total population of 362,159 native Palestinian inhabitants. Al-watani hospital is the only governmental hospital in Nablus district that offers medical services to patients with acute stroke. Acute stroke cases are admitted to the emergency department of Al-watani hospital and treated as inpatients. The hospital is located in the center of the district and offers 24-hour emergency services for acute stroke cases. The purpose of this study is to (1) explore stroke-related risk factors and post-stroke medical complications, (2) identify the types and cost of medications prescribed for ischemic stroke survivors, and finally (3) investigate the prescribing pattern of anti-platelet drugs.

Methods

This observational descriptive study was performed in the internal medicine department of Al-Watani governmental hospital, Nablus, Palestine. The study was conducted for a period of 5 consecutive months starting in October 2005 and ending in March, 2006. Stroke survivors diagnosed with ischemic stroke subtype were included in the study and designated as stroke group. On the other hand, patients diagnosed with hemorrhagic stroke were excluded from the study. Diagnosis was confirmed by computerized tomography scan. The data for the study were obtained from the patients' medical files. Data obtained included demographic characteristics, medications prior to admission and upon discharge, risk factors, and post-stroke medical complications. Risk factors that were considered in this study were hypertension (HTN), diabetes mellitus (DM), congestive heart failure (CHF), atrial fibrillation (AF), ischemic heart disease (IHD), smoking, and recurrent stroke attack. A post-stroke complication was defined as any health complaint

post the attack such as constipation, seizures, anxiety/depression, infection, limb pain, and gastrointestinal upset. The number of risk factors and number of post-stroke complications for each patient were counted and included in the analysis.

Medications prescribed to stroke survivors at discharge were classified based on their therapeutic class. Regarding calculation of medication cost imposed on stroke survivors at discharge, the price of medications used for either prophylaxis or management of main complications were considered. The price of medications was obtained from the updated price list available at drug stores. For cost calculations, the full retail price was considered.

Statistical Analysis

Analysis of data was carried out using the Statistical Program for Social Sciences (SPSS) for windows version 10.0 (SPSS Inc., Chicago, Ill). Categorical variables were expressed as frequency and percentage while continuous variables were expressed as mean \pm standard deviation (SD). Pearson χ^2 and independent Student's *t*-test were used in univariate analysis. Pearson correlation was used to test for correlation. *P* value $<$.05 was used as a significance level.

Results

A total of 95 stroke survivors were identified during the study period, 78 (82.1%) of them had ischemic stroke subtype and were designated as the study group. The excluded patients ($n = 17$) were those having hemorrhagic stroke or those who died during hospitalization. Of the 78 ischemic stroke survivors, 23 (29.5%) had recurrent stroke attacks while the remaining had a first-ever stroke. The average age of the patients in the study group was 66.9 years (SD = 12.7, range 25-90) and 32 (41%) were males. Stroke survivors experienced an average of 1.6 stroke-related risk factor (SD = 0.96, range 0-3). The most common stroke-related risk factors were diabetes mellitus (70%), hypertension (68%), and ischemic heart disease (34.6%). On average, ischemic stroke survivors experienced a minimum of 0.73 complications (SD = 0.71; range 0-3) with the most common being infections, especially urinary tract infections ($n = 35$, 44.8%). Other post-stroke complications were seizure, vertigo, and psychiatric problems.

Prior to the current stroke attack, 55% of the patients were not on antiplatelet therapy, while the remaining 45% had been taking antiplatelet agent as aspirin monotherapy (94%), or aspirin/clopidogrel combination (3%), or aspirin/dipyridamole combination (3%). Prior antiplatelet therapy was significantly associated recurrent stroke but not with gender, diabetes mellitus, or ischemic heart disease (Table 1). Stroke survivors were discharged with an average of 4.9 medications (SD = 1.9, range 1-12) per patient from 4.3 different drug classes (SD = 1.5, range

Table 1. Utilization of antiplatelet agents before and after the current attack

Variable	Anti-platelet therapy before the current attack			Anti-platelet therapy at discharge		
	Yes n = 35	No n = 43	P value	Anti-platelet monotherapy n = 61	Anti-platelet Combination n = 17	P value
Gender						
Male	11 (31.4)	21 (48.8)	0.12	22 (36.1)	10 (58.8)	.09
Female	24 (68.6)	22 (51.2)		39 (63.9)	7 (41.2)	
Diabetes mellitus	20 (57.1)	16 (37.2)	0.079	28 (45.9)	8 (47.1)	.9
Ischemic heart disease	11 (31.4)	6 (14)	0.063	11 (18)	6 (35.3)	.12
Recurrent stroke	12 (34.3)	2 (4.7)	0.001	11 (18)	3 (17.6)	.9

= 1-8). The number of medications prescribed at discharge was positively correlated with the number of stroke-related risk factors ($r = 0.39$, $P = .01$) and negatively correlated with age ($r = -0.19$, $P = .038$). The types of medications prescribed at discharge were consistent with the stroke-related risk factors and post-stroke medical complications identified in the patients' medical files. Forty-nine (92.5%) ischemic stroke survivors with a diagnosis of hypertension were discharged on antihypertensive medications. Angiotensin converting enzyme inhibitors (ACE-I) were the most ($n = 25$, 51%) prescribed class of antihypertensive among the 78 ischemic stroke survivors. Oral antidiabetic medications were prescribed for 64.8% of those with a diagnosis of diabetes mellitus. The most common therapeutic classes of discharge medications can be seen in Table 2. Analysis of discharge medications in the study group indicated that anti-platelet and gastro-protective agents were the most commonly prescribed medications followed by the antihypertensive agents and antibiotics. Drug classes such as laxatives, anti-emetics, nonsteroidal anti-inflammatory drugs (NSAIDs) were also prescribed but to a lesser extent. All stroke survivors were prescribed antiplatelet agents at discharge. Aspirin mono-therapy and aspirin/clopidogrel combination were prescribed for 78% and 22% patients, respectively. The choice of antiplatelet mono-therapy *v* combination therapy was not significantly associated with gender ($P = .09$), DM ($P = 0.9$), IHD ($P = .12$), or recurrent stroke ($P = .9$) Table 2. Aspirin mono-therapy at 100 mg daily dose was prescribed for 62% patients, aspirin mono-therapy at 250-325 mg/daily dose was prescribed for 16.5% of the patients and finally, 21.5% of the patients were prescribed a low-dose aspirin/clopidogrel combination.

The monthly cost of medications used to treat post-stroke complications or used as a prophylactic measure can be overwhelming especially for patients with lower economic income. The monthly average wholesale prices of medications used by ischemic stroke survivors are shown in Table 3. Stroke survivors with no governmental insurance incur a total monthly cost of approximately 52 USD. This accounts for more than 25% of the monthly income of an ordinary Palestinian person, given that the

average reported monthly income in Palestine is less than 200 USD. In case of medical insurance, the government covers all the expenses during hospitalization, at discharge, and during rehabilitation. This should raise the issue of primary prevention and modification of existing modifiable risk factors to minimize governmental financial expenses.

Discussion

In this study, ischemic stroke survivors were prescribed a wide range of medications that were consistent with the reported health conditions of the patients. Diabetes mellitus, hypertension, and ischemic heart diseases were the most common risk factors present among the patients in this study. Modification and screening for such existing risk factors, especially among the elderly patients, should be the primary prevention strategy in treating stroke. Hypertension is also considered a potent modifiable risk

Table 2. The most common classification of medications taken by stroke survivors

Classification (common example)	Frequency
Antiplatelet (aspirin)	78 (100)
Anti-Ulcer (ranitidine)	69 (88.5)
Antihypertensives (enalapril)	46 (59)
Antibiotics (cefuroxime)	35 (44.9)
Antidiabetics (glibenclamide)	36 (46.2)
Cardiotonic (digoxin)	11 (14.1)
Antiseizure (phenytoin)	10 (12.82)
Antianginal (isosorbide dinitrate)	9 (11.54)
Antihyperlipidemic	6 (7.7)
Antihistamines	5 (6.4)
Anticoagulant	4 (5.1)
Bronchodilator	3 (3.8)
Antiemetics	3 (3.8)
Antipsychotic	2 (2.6)
Laxatives	2 (2.6)
Sedatives	2 (2.6)
NSAIDs	1 (1.3)
Antiarrhythmics	1 (1.3)
Steroids	1 (1.3)

Table 3. Monthly average wholesale price of medications prescribed for treatment of stroke complications and for secondary prevention after discharge

Medication	Frequency (n)	~Price per pack (USD)	Packs per month	Total cost per month (USD)
Aspirin 100 mg	78	3	1	78X3X1 = 234
Clopidogrel	17	100	1	17X100X1 = 1700
Ranitidine	69	5	2	69X5X2 = 690
Antibiotics	42	20	1	41X20X1 = 820
Phenytoin or Carbamazepine	12	40	1	12X40X1 = 480
Betahistine	5	10	2	5X10X2 = 100
Total monthly cost imposed on the 78 survivors				4024 USD
Total monthly cost imposed on each survivor				~ 52 USD

factor for recurrent stroke, and the use of antihypertensive treatment has been shown to reduce risk of recurrent stroke substantially.³²⁻³⁵

In the current study, stroke survivors were suffering from a wide range of post-stroke complications. It has even been suggested that the effectiveness of organized stroke care in reducing mortality may be attributable to improvements in the prevention, identification, and treatment of secondary complications.²⁰ Several studies have shown that although deaths within a few days of stroke are usually the direct consequence of brain damage, those occurring over the following weeks are mainly due to potentially preventable problems.¹³⁻¹⁷ Many of the complications described in this study are potentially preventable or treatable if recognized. In several studies, the complication rates after a stroke vary from 48% to 96%.³⁶ It has been suggested that better stroke care does not only depend on diagnosis and treatment but also on improved treatment of post-stroke complications. In our study, the most common complication was infection, and was mainly treated with second generation cephalosporins or fluoroquinolones, suggesting that these infections were mainly in the urinary tract. Urinary tract infections (UTI) caused by extensive use of catheters could also be managed by discontinuation of catheters. Few patients in this study were suffering from constipation, which is expected due to prolonged bed rest. Constipation among stroke survivors is usually managed with laxatives as well as by encouraging ambulation to assist with intestinal motility.³⁷ Seizure and anti-seizure medications were fairly common among the patients. It is known that stroke leads to neuronal damage, which can disturb neuronal function. Ten percent of stroke victims may experience seizures that can be controlled with anti-convulsants.³⁸ Few patients in our study were treated for depression. This is contrary to other studies in which large number (50%) of patients experienced post-stroke depression. In our study, depression was either not screened for or under-estimated.

Among patients with no previous stroke, antiplatelet therapy was not commonly used despite the fact that most of those patients were having risk factors for stroke.

The role of antiplatelet drugs, including aspirin, in the prevention of a first stroke is controversial.³⁹ Nevertheless, administration of antiplatelet or anticoagulation agents is a potential strategy for the prevention of cardio-embolic stroke.^{40,41} In this study, all stroke survivors were discharged with antiplatelet therapy and few were discharged with anticoagulants. Our study found that among stroke survivors, the majority was treated with aspirin, and only a small number of patients were treated with aspirin/clopidogrel and none were treated with dipyridamole. The pattern of use of antiplatelet in this study was different from studies conducted in other countries in which significant proportion of patients was prescribed aspirin/dipyridamole.^{42,43} The ESPS-2 trial found that dipyridamole plus aspirin to be twice as effective for stroke prevention as either drug alone.^{44,45} However, the Antithrombotic Trialist's meta-analysis found no benefit of adding dip to aspirin.³⁰ Furthermore, studies have shown that extended release dipyridamole is more effective than the immediate release formulation. All above mentioned reasons seem to discourage physicians from prescribing dipyridamole, especially since only immediate release formulation of dipyridamole is available at the hospital.³⁰ In our study, the most frequently prescribed dose was 100 mg daily, which is consistent with the current evidence showing that the most appropriate daily doses of aspirin for the long-term prevention of serious vascular events in high risk patients is 75 to 100 mg.³⁰ Higher doses of aspirin are no more effective than low or medium doses but only more gastrotoxic. The clopidogrel antiplatelet therapy was less prescribed than aspirin. This antiplatelet drug is very expensive and not available at the pharmacy unit in the hospital. Patients prescribed clopidogrel need to purchase the medication from community pharmacies.

Families of stroke survivors bear an economic burden after discharge. The cost of medications used in prophylaxis and in treating complications and co-morbid conditions is an important issue. Given the low personal income in Palestine, insurance coverage for stroke survivors is very important to make medications and medical care affordable for those patients. Cost of medications is

an important factor in a patient's compliance and thus in therapeutic outcome. In this study, the total costs of antiplatelet therapy and treatment medications of some post-stroke complications for 1 month were estimated to be \$4024. Of course this estimation does not include institutional costs and medical service during hospitalization. This cost estimation is different from that found by other studies conducted in European countries.⁴⁶⁻⁵⁰ This is expected because medical service and medication types are assumed to be lacking here compared with other countries. Taking into consideration the tremendous economic burden of stroke medications, it is highly recommended to implement antiplatelet therapy as a primary prevention among patients with high risk factors. Doing so will reduce the incidence of stroke and thus will relieve the health system and the families of the patients from a lot of economic and emotional burden.

This study also should emphasize the role of clinical pharmacists, if present in the hospital, in medication selection and patient education. It is known that stroke survivors have a lot of neurological disabilities and many newly prescribed medications, and thus close communication and education regarding medication is required to avoid possible mistakes. Also, pharmacists are knowledgeable of current therapeutic recommendations and various drug alternatives with their prices. Thus, pharmacist can help cut cost by providing physicians with therapeutically equivalent choices that are less expensive. Pharmacists can also help in preparing patients for discharge with emphasis on medications with potential side effects (eg, antidiabetic medications), those that may have interactions with foods or other drugs (eg, anticoagulants), and those that need regular follow-up (eg, antihypertensive medications).

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