



Pharmacotherapeutical Study of Stroke Patients: A Hospital Based Survey

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Abstract

Stroke is an acute vascular event occurs within the brain, one of the frequent cause of disability and leading cause of mortality around the world. Stroke incidence declines in West population while continuously increasing in South Asia. The present study was conducted in Saidu Teaching Hospital (STH), Saidu Sharif Swat, Khyber Pakhtunkhwa, Pakistan. The purpose of the study was to determine the risk factors, epidemiology, prevalence and evaluation of medication trends and drug-drug interactions prescribed to stroke patients on a specially designed questionnaire. Determination of risk factors is important in understanding treatment and pathogenesis of stroke. Data was collected from 15 October 2011 to 15 January 2012. Twenty seven patients were included in the study. Out of 27 patients, there were 17 (62.96%) male and 10 (37.03%) were female. Age range of the patients was 52-80 years (mean \pm SD 64.51 \pm 6.74), and the most predominant age range was 60-70 years. The risk factors identified were hypertension 77.77%, recurrent stroke 77.66%, smoking 29%, diabetes mellitus 22.22%, past smoking history 22.22%, ischemic heart disease 11.11%, atrial fibrillation 3.7%, obesity 7.4% and use of warfarin or heparin 3.7%. The therapy was satisfactory at ward level, but in some cases drug-drug interactions were observed. Our finding shows that there is little knowledge regarding stroke-related risk factors; Hypertension, smoking and diabetes. Special management is needed at the time of discharge of patients about the therapy and related risk factors and prescription errors should be minimized by involvement of clinical pharmacist at ward level.

Keywords: Cerebrovascular accident; Drug-drug interaction; Hypertension; Prevalence; Rational pharmaco-therapy; Transient ischemic attack

Introduction

According to World Health Organization (WHO) stroke is “a clinical syndrome consisting of rapidly developing clinical signs of focal disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin” [1]. Stroke is considered as one of the leading causes of mortality and morbidity all around the world [2]. The incidence of stroke is higher in blacks 0.233 % followed by Hispanics 0.196 % and whites 0.193% [3]. The incidence is going to decrease in Western population while a continuously increase is observed in South Asian countries, including Pakistan, India, Bangladesh and Sri Lanka and expected to rise [4].

The incidence of ischemic stroke is higher in men than in women in age <80 years but after the age of 80, women have higher incidence [5,6]. According to WHO 15.5 million individuals suffer from stroke each year. Among these 5 million patients died and 5 million are completely disabled [7]. Throughout the world 75-89% of strokes occur in age of above 65 years [8,9]. The rate of stroke is doubled after age of 55 years in each decade of life in men and women [10]. People who have a previous stroke episode are more susceptible to subsequent episodes of stroke [11]. It has been reported that stroke is the second common cause of epilepsy in aged people, a joint cause of dementia and the most frequent cause of depression [12,13].

A reversible ischemic neurological deficit which remains more than 24 hours and reverses within three weeks is also reported by some clinicians as a Transient ischemic attack (TIA). In stroke condition, the signs and symptoms suggest a focal lesion near a major artery that gradually extends with time to involve nearest motor and sensory zones [14]. The distinctive feature of stroke is the sudden break in the continuity of the blood flow to a specialized region within the brain that results in neurologic deficits [15].

There are two principal mechanisms of stroke pathogenesis, ischemia and hemorrhage. Ischemic strokes represent about 80% of all stroke cases. Low or absence of blood supply deprives neurons

of necessary substrates. Ischemia rapidly affects the brain because of absence of glucose stores in the brain and the brain's incapability of anaerobic metabolism [16]. Lacunar Infarcts (thrombotic occlusion of small vessels) and ruptured microaneurysms cause ischemia and hemorrhage, respectively [17]. Intracerebral hemorrhage of non-traumatic origin represents nearly 10-15% of all strokes and produced from deeply penetrated vessels, causing injury to brain tissue by disrupting connecting pathways and localized pressure injury. Destructive biochemical substances which release from various sources are mainly responsible for tissue damage in either case [18].

The risk factors for stroke can be divided into modifiable and non-modifiable. Modifiable risk factors include hypertension, smoking, diabetes mellitus, hyperlipidemia, heart failure, atrial fibrillation, alcohol consumption, positive family history, oral contraceptives and polycythemia. Non-modifiable risk factors include age, gender (Males more than females), hereditary, predisposition to vascular events such as myocardial infarction, stroke or peripheral embolism [17,19]. The consequences of stroke are same in both younger and elderly survivors, including hemiparesis, spasticity, hemiplegia, hemispatial neglect, balance issues, cognitive deficits, pain, dysphagia, emotional liability, fatigue and depression [20].

The present study was aimed to determine patient's age distribution, risk factors, drug-drug interaction, case mortality, incidence in these particular patients and to elaborate the role of clinical pharmacists in the management of stroke by educating the patients and by using professional skills and knowledge for improving health outcomes.

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Received February 20, 2015; **Accepted** March 25, 2015; **Published** April 02, 2015

Citation: Ullah S, Khan I (2015) Pharmacotherapeutical Study of Stroke Patients: A Hospital Based Survey. Primary Health Care 5: 184. doi:10.4172/2167-1079.1000184

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Materials and Method

The present study was conducted in STH, Saidu Sharif Swat, Khyber Pakhtunkhwa, Pakistan for three months from 15 October 2011 to 15 January 2012. The hospital has a capacity of 800 beds at a time.

A standard questionnaire was designed and issued to each student from Department of Pharmacy, University of Malakand Khyber Pakhtunkhwa Pakistan to record the patient medication history which contains age, sex, present and past history, chief complaints, biochemical tests, diagnosis, treatment, drug-drug interaction and other relevant information. Data was obtained from the medication record of the patients in hospital and other necessary informations were obtained from the patient's attendant. The data was collected from all population groups of hospitalized patients both male and female having a cerebrovascular accident in Medical A and B ward. Ethical committee of Saidu Teaching Hospital approved and recommended conduction of research with keeping names of the patients' secret and prior approval from the patient attendant. Afterwards, the data was screened for drug-drug interaction and related problems. The data was statistically analyzed by using SPSS Ver. 19.

Results

Data of all hospitalized patients (total of 27 patients) were selected

Risk Factors	Patients %
Diabetes mellitus	22.22
Hypertension	77.77
Smoking	29.62
Past smoking history	22.22
Ischemic Heart Diseases	11.11
Arterial fibrillation	3.7
Obesity	7.4
Recurrent stroke	77.66
Warfarin or heparin	3.7
Diabetes + Hypertension	25.92

Table 1: Risk factor distribution.

Main drug	Interacting drug	Effects	% Occurrence Total history 27
Antibiotic (Ceftriaxone)	Alone or in combination with anti-coagulants.	N-methylthiotetrazole side-chain can cause bleeding alone or more severely in the presence of an anticoagulant [34a].	85.1
Piracetam		Piracetam is contra indicated in cerebral hemorrhage [35a].	48.1
Calcium channel blockers	Miconazole	Miconazole (azoles) increases the Nimodipine level [34b].	7.4
	Nimodipine	If Nimodipine is used with another calcium-channel blocker, monitoring and a possible dose reduction or discontinuation of the other calcium-channel blocker is recommended [35b].	18.5
	ACE-inhibitors	Enhanced hypotensive effect when given with ACE inhibitors [35c].	25.9
	Beta-blockers	Enhanced hypotensive effect when given with beta-blockers [35d].	33.3
Corticosteroids (dexamethasone)	Aspirin	Increased risk of gastro-intestinal bleeding and ulceration when corticosteroids given with aspirin also corticosteroids reduce plasma concentration of salicylate [35e]	88.8
	Ramipril	Corticosteroids antagonize hypotensive effect of ACE inhibitors [35e].	48.1
	Amlodipine	Corticosteroids antagonize hypotensive effect of calcium-channel blockers [35e].	62.9
	Furosemide	Increased risk of hypokalemia when corticosteroids given with loop diuretics [35e].	29.6
Aspirin	Clopidogrel	Increased risk of bleeding when aspirin given with clopidogrel [35f].	74
	ACE inhibitors	Aspirin antagonize antihypertensive effects [35g].	40.2
	β-blockers	Decreased antihypertensive effect [35h].	11.1
	Corticosteroids	Increases the risk of gastrointestinal bleeding and ulceration [35f].	88.8
Rosuvastatin	Antacids	Absorption of rosuvastatin reduced by antacids [35i].	14.8
	Warfarin.	Increase the anticoagulant effects of warfarin [35i].	7.4

Table 2: Drug-drug interaction in prescribed medication.

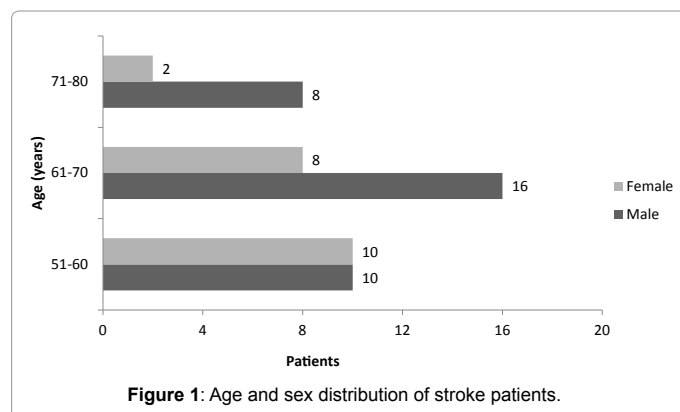


Figure 1: Age and sex distribution of stroke patients.

in this study. The age range was from 52 years to 80 years (64.51 ± 6.74). There were 17 (62.92%) male patients and 10 (37.02%) female patients (Figure 1). The male patients having a mean age of 65.64 (SD:5.72) and feminine 62.2 (SD:8.16).

Based on risk factors the distribution was as follows: Diabetes mellitus 22.22% (n=6), hypertension 77.77% (n=21), smoking 29.62% (n=8), past smoking history 22.22% (n=6), ischemic heart diseases 11.11% (n=3), arterial fibrillation 3.7% (n=1), obesity 7.4% (n=2), recurrent stroke 77.66% (n=21), use of warfarin or heparin 3.7% (n=1) (Table 1).

The risk of drug-drug interaction in the prescribed medication was summarized in Table 2. The highest interaction between drugs was observed in Corticosteroids and Aspirin that are 88.8% followed by antibiotics-anticoagulants 85.1%, Aspirin-Clopidogrel 74%, Corticosteroids-Amlodipine 62.9%, Corticosteroids-Ramipril 48.1%, Aspirin-ACE inhibitors 40.2%, Calcium channel blockers-Beta-blockers 33.3%, Corticosteroids- Furosemide 29.6%, Calcium-channel blockers-ACE-inhibitors 25.9%, Calcium-channel blockers-Nimodipine 18.5%, Rosuvastatin- Antacids 14.8%, Aspirin β-blockers 11.1%, Rosuvastatin-Warfarin 7.4%, Calcium-channel blockers-Miconazole 7.4% and Piracetam is contraindicated in cerebral hemorrhage was observed in 48.1%.

Discussion

Stroke is considered a major health burden and leading cause of death throughout the world [21]. The present study was focused to analyze stroke characteristics in patients in STH and aimed to evaluate and assess the risk factors and drug-drug interactions in drugs prescribed to these patients. This study was the part of partial fulfillment of obtaining Pharm-D degree with necessary three month Hospital clerkship. Moreover, after discharge of the patients their follow-up was difficult because they were from very remote areas. Pharmacotherapy of this disease i.e. stroke was selected because its occurrence increases in winter season and there was no such study carried out in our country. reviewed a total of 98 articles and found that male stroke incidence rate is 33% higher than female, with huge variation between age bands and population [22]. In Qatar, a hospital-based study showed the onset of stroke in 57 years of age, which is comparable to our study where the onset was observed in 60-70 years range. Our Study is agreed with the findings [23]. In our study, the mean age was 64.51 ± 6.74 and shows age risk factors for stroke and 100% stroke patients having age higher than 55 years. Matchar and Samsa reported that stroke was strongly age-linked [24].

Smoking is a major risk factor for both hemorrhagic and ischemic stroke. The smokers have two-fold high risk of stroke when compared to nonsmokers [25]. In our study, the 29% (n=8) smokers were observed and 22.22% (n=6) having past history of smoking, which revealed a robust relation of stroke with smoking. Found a strong relationship between stroke and cigarettes in young and older age [26].

Stroke is more common in our region because of hypertension. In the present study majority of the stroke patients (77.77%) had hypertension. There are many reports, which reveal that usual high blood pressure continuously and directly links with the initial occurrence of stroke. As we did not have pre-morbid blood pressure values and could not evaluate further. However, in a randomized trial of Perindopril-based pressure, lowering regimen revealed a continuous reduction in risk of stroke in both hypertension and non-hypertension patients by lowering blood pressure [27]. In a study, Jafar et al. concluded that 70% people are unaware of their hypertension condition and less than 3% strongly controlled their blood pressure [28]. Khealani, reported that ischemic stroke was independent of predictors of diabetes mellitus and ischemic heart disease in hypertensive patients [29].

Diabetes mellitus is another serious cause of stroke. In the present study, the results show that 23% patients have diabetes mellitus. In a study, it has been documented that for stroke recovery, diabetes mellitus is a bad prognostic factor [30]. It was also found that 25.92% patients have both diabetes mellitus and hypertension complaints. Saif reported that 44% of hyperglycemic and 20% of normoglycemic were died within one month of stroke attack [31].

The prevalence of ischemic stroke was high (70%) as compared to hemorrhagic stroke (30%). A number of studies have reported, which predicts about the ischemic versus hemorrhagic stroke [32]. The ischemic stroke patients have high prevalence of heart disease, diabetes mellitus, history of TIA and family history when compared to hemorrhagic stroke [5].

The interaction between drugs is the most serious risk factor. The highest interaction was observed in Corticosteroids and Aspirin, which are 88.8%. These interactions have different effect upon the patients it either increase the therapeutics effects which are may cause toxicity or antagonize the potentials of other drugs, which directly lead to therapeutic failure [33]. The ultimate consequences of these interactions

may increase the cost and decrease patients' compliance to therapy; it may also increase the incidence of mortality and morbidity.

Case mortality rate from 15 Oct, 2011 to 15 Jan, 2012 was 11.11% (n=3), including 3.7% (n=1) male and 7.4% (n=2) female. As the incidence of stroke in male was more than female, but females were more severely affected. The Recurrent stroke attack was also observed in 77% patients, which reveals that the patients were non-compliant to therapy.

Conclusion

It was concluded that with increase in age, the chances of stroke increases and the consequences become worst. This might be related to certain risk factors (atrial fibrillation, carotid artery stenosis, and congestive heart disease) and changes within central nervous system due to aging that increase the incidence of stroke. To achieve rational therapy for the management of stroke patients on realistic grounds, one should follow the standard procedures mentioned in literature such as British National Formulary and/or Stockley's Drug Interactions Pocket Companion and should also overcome those problems which are common among ward level, like drug-drug interactions, side effects, adverse drug reactions, compliance rate and poor patient education.

Recommendations

1. It is recommended to commence educational programmes to promote awareness about stroke in people and among professionals, i.e. paramedics and emergency physicians.
2. Immediate emergency-room triage, laboratory, clinical, imaging evaluation, therapeutic decision, accurate diagnosis and proper treatment are recommended.
3. Suspected stroke or TIA patients should have an easy access to brain Computed tomography scan or magnetic resonance imaging is recommended.
4. Stroke units should be reserved for stroke patients in each hospital are recommended.
5. Pharmacoeconomic factor for the patient should be considered.
6. Patients should be educated regarding drug therapy to achieve compliance.
7. Apart from the Chief pharmacist in hospital, each ward should be provided with the service of Clinical pharmacist to evaluate each and every prescription for drug-drug interaction and to suggest therapeutic alternatives for pharmacoeconomic considerations.

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