Research Article



Utilization Pattern of Different Drugs in Different Types of Stroke in A Tertiary Care Teaching Hospital

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Received: 08-03-2018; Revised: 02-04-2018; Accepted: 13-04-2018.

ABSTRACT

Now – a – days, increasing incidence of stroke becomes a major public health problem dealt by the neurologists and neuroprotective drugs have become the mainstay of treatment. Due to lack of well-defined research in India regarding its clinical symptomatology medications for stroke, more research in this field is required. Our study has aimed to focus on the pattern of prescription of drugs in the management and prevention of stroke. The study was a cross-sectional observational study of stroke admitted to neurology departments of IMS & SUM Hospital, Bhubaneswar over 2 years. Clinico-epidemiological data were obtained from patients and from records using standard case-report form. A total of 1224 patient were studied during a period of two year. Out of 1224 patients, 60.6% were males and 39.4% were females. The incidence of stroke was maximum in the age group 40-59 years. 65.9% patients were diagnosed as Ischemic Stroke and 31.4% as hemorrhagic stroke amongst the study population at a ratio of 2.09. The most common risk factors associated with the stroke was hypertension (65.7%)] followed by dyslipidemia (52.6%), diabetes (50.1%). Most common drug prescribed in hospitalized stoke patients was antihypertensive followed by hypolipidemic agents and antiplatelet drugs. Further large clinical as well as epidemiological studies must be conducted in our country to confirm and further enlighten our observations.

Keywords: Stroke, dyslipidemia, hemorrhagic shock, hypertension, Antiplatelet drugs, hypolipidemic agents.

INTRODUCTION

troke or cerebrovascular accident (CVA) is a condition that is developed due to poor blood flow to the brain-ultimately leading to death if not diagnosed earlier and treated properly. It is a major cause of morbidity leading to long-term disability affecting the socioeconomic status of patients & their family. ¹ It is the major cause of death worldwide, most commonly in elderly individuals.² It is also the third commonest cause of death in developed countries³ due to raised intracranial pressure (ICP) and its consequences in the acute stage.⁴⁻⁶ The mortality rate due to stroke in India is 22 times more common than that of malaria and 1.4 times than tuberculosis. ⁷ Stroke leads to premature death and disability due to increasing prevalence of common modifiable risk factors and also due to unaffordable financial status of patients to the high price management strategy.³ Increase in age is one of the important risk factor for increasing incidence of stroke in which 75% of stroke affects the elderly. 8,9 Another problem associated with stroke is recurrence, seen most commonly in ischemic stroke or with recent history of transient ischemic attack (TIA).¹⁰ Recurrence of stroke is again associated with increase in mortality, morbidity, hospitalization rate and also leads to cognitive impairment and dementia. $^{\mbox{\tiny 11}}$

History of hypertension, diabetes, smoking and obesity are other major risk factors related to stroke in Indian

population ¹² and proper management can reduce the risk. ¹³ Stroke becomes a major public health problem dealt by the neurologists ¹⁴ and mostly managed in stroke unit in acute setting. The medical and surgical interventions come into play for raised ICP. ^{6, 15} Several clinical trials proved the efficacy of antiplatelet and oral anticoagulants in stroke prevention. ^{16, 17}

The management of stroke should be individualized. As proper drug utilization is a concern for various diseases, the same is also important for stroke management. The drug utilization in stroke care is very much concern in developing countries, as healthcare infrastructure is inadequate ¹⁸, government has insufficient control on the system of drug supply 19 and also d/t free availability of drugs on prescription $^{20, 21}$ often illegally. 22 The drug treatment strategy is involved with proper selection of drugs like thrombolytics, anticoagulants, antihypertensives (angiotensin converting enzymeinhibitors, angiotensin II receptor blockers, diuretics), blood lipid lowering agents (statins), antiplatelet drugs (aspirin and clopidogrel), and neuro protectors. WHO addressed drug utilization as a marketing distribution, prescription as use of drug in a society considering its constituents medical, social and economic.²³

It is also recommended to select, a route, and dosage form of drugs to have optimal therapeutic effects to manage cerebrovascular accident. $^{\rm 24,\,25}$



MATERIALS AND METHODS

This study was carried out on a patient pool of 1224 over two-year period (from October 2014 to September 2016) in the department of Neurology and Medicine in collaboration with the department of Pharmacology, IMS & SUM HOSPITAL, & AIIMS, BBSR. This was a retrospective hospital-based study. All the medicines prescribed by the neurologists during this period were recorded on case record forms. Diagnosis will be made on the basis of medical history, physical examination and neuro–imaging. The study was approved by the institutional ethics committee and informed consent was obtained from all the study subjects. The data were collected from 1224 cases of stroke patients on the basis of demographic data, clinical features and prescription pattern.

In this study, all the patients were of either sex of age 20 vears and above, diagnosed with different types of stroke (Ischemic stroke, hemorrhagic stroke, sub arachnoid hemorrhage), who had radio-logically confirmed diagnosis of stroke using CT/MRI scan admitted in the Neurology/Medicine departments inpatient for minimum of 7 days duration. Only definite symptoms were taken into accounts not the suspected or attainable ones. Most of the patients' data were collected from case sheets and laboratory reports of patients. Risk factors and associated co-morbidities associated were analyzed. Patients are diagnosed as hypertensive with systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg and as Diabetic having fast blood sugar level was ≥126 mg/dl. On admission, we have considered only those individuals that presently smoked cigarettes (ten cigarettes per day for over 6 months), alcoholic (consumed alcohol at-least once each day for a minimum period of 6 months), obese only when waist hip ratio was ≥ 0.9 cm in males and ≥ 0.8 cm in females and if participants had serum cholesterol ≥ 220 mg/dl, were considered to have hypercholesterolemia. Transient ischemic attack was defined as the abrupt onset of focal neurological deficit lasting for less than 24 hours. Those patients were excluded from the study if that they had history of the other CNS disorder or infections, hepatic encephalopathy, liver disorder patients, HIV infected patients.

Prescribing pattern of various drugs in patients was noted in terms of demographic profile of the patient (age and gender), type and etiology of stroke, drug data (group of the drug, name of the drug, mono or polytherapy, number of drugs per prescription, formulation) and associated adverse drug reactions with the prescribed group of drugs were recorded during this study period. The prescriptions which include neuro-protective drugs, antibiotics, diuretics, lipid lowering drugs and antacids were audited and analyzed category wise.

OBSERVATIONS AND RESULTS

In this study, a total of 1224 patient were studied during a period of two year. Out of 1224 patients, 742(60.6%) were males and 482(39.4%) were females. The age range was from 20 years to 86 years with mean age of $56.72(\pm 12.6)$ years. The incidence of stroke was maximum in the age group 40-59 years which comprised of 702(57.3%) patients followed by the age group of 60-79 years which comprised of 402(32.9%) of entire study population (Table 1).

Age in years	Male (%) 742(60.6%)	Female (%) 482(39.4%)	Total (%) 1224
20 – 39	68(9.2)	32(6.6)	100(8.2)
40 – 59	391(52.7)	311(64.5)	702(57.3)
60 – 79	270(36.4)	132(27.5)	402(32.9)
≥ 80	13(1.7)	7(1.4)	20(1.6)

 Table 1: Demographic profile analysis of the study population: n= 1224

Out of the total study population, 65.9% patients were diagnosed as Ischemic Stroke and 31.4% as hemorrhagic stroke (Table 2). The ratio of Ischemic stroke to Hemorrhagic stroke was 2.09.

Table 2: Type of stroke: n=1224

Type of Stroke	Number of patients with %
Ischemic Stroke	807(65.9%)
Hemorrhagic Stroke	385(31.4)
Sub arachnoid Hemorrhagic stroke	32(2.7%)

Table 3: Various risk factors & co morbidities associatedwith the stoke patients: n = 1224

Risk Factors	Number of patients with %)	
High blood pressure	805(65.7)	
Deranged lipid profile	644(52.6)	
Diabetes Mellitus	614(50.1)	
Smoking history	390(31.8)	
Associated cardiac problems	347(28.3)	
Alcohol	318(25.9)	
Obesity	302(24.6)	



Table 4: Groups of drugs prescribed in stroke populations:n= 1224

Groups of drugs	Number of patients with %
Antihypertensives	856(69.9)
Lipid lowering agents	819(66.9)
Antiplatelet agents	805(65.7)
Cerebral activators/ Neuroprotective	412(33.6)
Anticoagulants	314(25.6)
Thrombolytic	23(1.8)

Table 3 shows, the most common risk factors associated with the stroke was hypertension 805(65.7%) followed by dyslipidemia 644(52.6%), diabetes (50.1%). Other conditions associated were obesity, history of smoking, alcohol and heart diseases.

Most common drug prescribed in hospitalized stoke patients was antihypertensive followed by hypolipidemic agents and antiplatelet drugs. (Table 4)

Table 5: Individual agents in each category of drugsprescribed in our set up: (n=1224)

Types of drugs		No of patients with %
Thrombolytic: Tissue plasminogen activator t-PA: alteplase		23(1.8)
Anticoagulants:		314(25.6%)
•	Enoxaparin,	143(45.5)
•	Heparin,	93(29.6)
•	Dalteparin	47(14.9)
•	Fondaparinux	21(6.6)
Oral anticoagulant-Dabigatran		10(3.1)
Antiplatelet drugs		n=805(65.7)
•	Aspirin	380(47.2)
•	Clopidogrel	241(29.9)
•	Aspirin+Clopidogrel	162(20.1)
•	Aspirin+ Dipyridamole	22(2.7)
Ant	tihypertensives [*] :	n=856(69.9%)
•	Beta blockers (Metoprolol, Atenolol, Propranolol, Nebivolol)	108(12.6)
•	$\alpha 2$ adrenergic agonist (Clonidine)	72(8.4)
•	Alpha-adrenergic blocker (Prazosin)	45(5.2)
•	Mixed Alpha + Beta blockers (carvedilol, labetalol)	70(8.1)
•	Calcium channel blockers (Nifedipine, Amlodipine, Cilnidipine, Nicardipine, Nimodipine, Verapamil, Diltiazem)	443(51.7)
•	Angiotensin converting enzyme Inhibitor (Ramipril, Enalapril, Perindopril, Lisinopril)	290(33.8)

 Angiotensin receptor antagonist (Losartan, Telmisartan, Olmesartan, Valsartan) 	212(24.7)
 Diuretics (Furosemide, Torsemide, Spironolactone, Hydrochlorothiazide, chlorthalidone) 	126(14.7)
Lipid lowering agents	819(66.9)
Atorvastatin	513(62.6)
Rosuvastatin	302(36.8)
Fenofibrate	63(7.6)
• Ezetimibe	21(2.5)
Cerebral activators:	412(33.6)
• Citicholine,	354(85.9)
• Piracetam,	105(25.4)
• Edaravone,	34(8.2)
Cerebroprotein hydrolysate	11(2.6)
 Antibiotics: Amoxicillin+ Clavulanic acid, Clindamycin, Ceftriaxone, Amikacin, Levofloxacin, Piperacillin + Tazobactum, Metronidazole, Vancomycin, Meropenem 	380(31.04)
Antiepileptics	422(34.4)
• Phenytoin	338(80.09)
• Valproate,	92(21.8)
Levetiracetam	61(14.4)
Osmotic Diuretics	811(66.2)
Mannitol	682(84.09)
• 3% Normal saline	82(10.1)
• Glycerol	137(16.8)
Antipsychotics / Sedatives: Quetiapine, Haloperidol, Midazolam	138 (11.2)
Laxatives(Lactulose)	331(27.04)
Anti-acidmedications(Omeprazole,Esomeprazole,Pantoprazole,Rabeprazole,Domperidone,Ranitidine)	942(76.9)

A surgical intervention (Decompressive craniectomy, Ventriculostomy) was done in 95(7.7%) patients.

DISCUSSION

Stroke is a leading cause of death or disability worldwide.²⁶ Therefore stroke prevention is of great importance for public health. Several epidemiological studies have investigated risk factors for stroke $^{27 - 30}$ Therefore drug utilization studies which evaluated, analyzed the medical, social and economic outcomes of the drug therapy observe the prescribing attitude of physician in stroke patients.

The raised intracranial pressure (ICP) in ischemic stroke is due to vasogenic edema and in hemorrhagic stroke is due to mass effect and surrounding vasogenic edema.³¹ Factors that are responsible for the increase in ICP are the



size of infarct or the hematoma, associated edema, and brain compliance.

There are two types of prevention of stroke based on etiology. One is primary prevention of stroke that mainly antiplatelet therapy like aspirin, statin therapy and blood pressure management. Carotid endarterectomy, carotid angioplasty, warfarin and heparin are listed under secondary prevention and management. Calcium antagonists like oral nimodipine is useful in sub arachnoid hemorrhagic stroke. ³² One of the major complications and troublesome for the physician in the acute phase of stroke is infection that should be managed promptly and with ease. One of the major criteria for treatment failure and poor outcome is post stoke infection. So, for better outcome by reducing infection it is important to treat the acute phase of stroke with preventive antibiotic therapy. Effective prevention and treatment of infections becomes an important strategy aiming to reduce the impact of stroke. 34

Stroke symptoms without a history of TIA or previous history of stroke is a predictor of clinically unrecognized stroke, and important indicators increased risk of future stroke events ^{35 - 39} which is beneficial in terms of clinical effectiveness and cost effectiveness on prevention of stroke. Early diagnosis and treatment of a stroke enhance patient outcomes and decrease danger of recurrence. ⁴⁰ It is seen that awareness about stroke symptoms is low among the overall population. ⁴¹

Common risk factors for stroke are diabetes, hypertension, smoking, and obesity. ⁴² Here the statement 'prevention is better than cure' comes true for hypertensive and diabetes mellitus patients to avoid any stroke in the future as they are at a larger risk of future stroke events than the general population.⁴³

In the present study, we have assessed the prescribing patterns of neurologists to identify the selection of a drug over another and what changes are made once a stroke happens in these patients. The rationality is of utmost importance because the irrational use will cause misuse, underuse or overuse of medicines. ⁴⁴ The drug treatment strategy involved with choosing medication like thrombolytics, anticoagulants, antihypertensive (angiotensin changing enzyme-inhibitors, angiotensin II receptor blockers, and diuretics), blood lipid lowering agents (statins), antiplatelet medication (aspirin and clopidogrel), and cerebral activators. It's also suggested to select a route and dosage form of medication to own the best therapeutic effects to manage stoke.^{45,46} In rapid increase in burden of stroke in coming years and restricted accessibility of stroke care in India, it might be better to review stroke preventive ways. The present study aims to provide a comprehensive review on sex differences in stroke, with specific stress on the demographics, clinical presentation and medical aid. The objective of this study was to work out the prevalence of stroke symptoms, risk factors, clinical parameters and medicines prescription pattern in stroke occurred patients.

In our study population of 1224 patients during a period of two year. 60.6% were males and 39.4% were females in comparison to a study by Vurumadla et al. where it was 69.33% & 30.66% male and female respectively. ⁴⁷ The incidence of stroke was maximum in the age group 40-59 (57.3%) patients followed by the age group of 60-79 (32.9%) comparable to the study of Chachu Kuriakose et al. ⁴⁸ According to the study the prevalence of ischemic stroke was higher65.9% as compared to hemorrhagic stroke31.4% which is in accordance with the study of Chachu Kuriakose et al. ⁴⁸ Most common condition associated with the stroke was Thrombotic stroke (43.3) followed by intracerebral hemorrhage (31.4%)Hemiplegia around 56% of total study population is the major and most frequently seen symptoms associated with stroke which is followed by altered sensorium and abnormal speech. Among 1224 patients, the most common risk factors associated with the stroke was hypertension (65.7%)] followed by dyslipidemia (52.6%), diabetes (50.1%) which is almost everywhere comparable to various studies. ^{48, 49} Other conditions associated were obesity, history of smoking, alcohol and heart diseases. Most common drug prescribed in hospitalized stoke patients in our study was antihypertensive followed by hypolipidemic agents and antiplatelet drugs where as in the study of Spurthiet al ⁴⁹ patients are treated with a different class of drugs among which anti-platelets 88 (91.16%) accounts the highest percentage and nitrates 6 (0.62%) is the least prescribed. Surgical interventions (Decompressive craniectomy, Ventriculostomy) was done in 95(7.7%) patients.

CONCLUSION

Despite recent advances in the treatment of acute ischemic stroke, the number of effective and feasible treatments remains limited. For this reason, prevention of ischemic stroke, particularly secondary prevention, is a major clinical and public health issue. Proper management reduces the incidence and progression of the disease. Drug utilization pattern provides the rationality in drug prescribing and analysis. The study could not assess the complications and their therapy as, follow-up was not there. Finally, we conclude that proper risk factor management and following the guidelines in the treatment reduces the severity, thereby the prognostic factors will be good. Early identification of risk factors and pattern of therapy plays a crucial role in qualitative patient care.

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Source of Support: Nil, Conflict of Interest: None.

