

Abstract

Stroke is a clinical syndrome characterized by rapidly developing clinical symptoms of focal (or global, in the case of coma) brain dysfunction lasting more than 24 hours or causing death with no apparent cause other than vascular. Stroke is broadly divided into subarachnoid hemorrhage, ischemic stroke, and hemorrhagic stroke. Stroke is the second leading cause of death and the third leading cause of disability worldwide. Stroke is the most common non-communicable disease (NCD) in India, accounting for 3.5 percent of Disability-Adjusted Life Years (DALY). According to studies, the prevalence of strokes in India is 116-163 strokes per 100,000 people. Recently, the ICMR published a report titled "India: According to the National Health Service, stroke was the fourth leading cause of death and the fifth leading cause of Disability-Adjusted Life Years (DALYs) in 2016". All the literature evaluating pharmacy interventions in stroke patients and the role of the clinical pharmacist in the evidence supporting stroke care are well established. This review aims to provide a comprehensive explanation of pharmacist interventions for stroke patients. Outcomes can be improved by clinical pharmacist involvement in the prescribing process, computerized entry of medication orders, pre-administration monitoring of drug interactions, and patient counseling.

Keywords: Stroke, Clinical Pharmacists, Pharmaceutical Care Plan, Drug Related Problems.

Introduction:

“The World Health Organization defines stroke as a clinical syndrome characterized by rapidly developing clinical signs of focal (or global, in the case of coma) disturbance of cerebral function lasting more than 24 hours or resulting in death with no apparent cause other than a vascular origin”.¹ “Stroke is broadly divided into subarachnoid hemorrhage, ischemic stroke, and hemorrhagic stroke. Ischemic stroke happens because of a blockage of the vein, which restricts the blood supply to the mind, while hemorrhagic stroke happens because of a breakage of a vein driving spillage of blood in the intracranial cavity”.² “Worldwide, stroke is the second-leading cause of death and the third-leading cause of disability”.³ “Globally, 68% of all strokes are ischemic, while 32% are hemorrhagic.”³ The numbers in the United States are slightly different, with 87% being ischemic, 10% being hemorrhagic, and about 3% being subarachnoid hemorrhage”.^{4,5} In India, stroke, a major non-communicable disease (NCD), accounts for 3.5 percent of Disability-Adjusted Life Years (DALY).

According to studies, the prevalence of strokes in India is 116-163 strokes per 100,000 people. Recently, the ICMR published a report titled "India: Stroke was the fourth leading cause of death and the fifth leading cause of Disability-Adjusted Life Years (DALYs) in 2016, according to National Health Data". “There is a wealth of literature evaluating pharmacist interventions for stroke patients, and the role of the clinical pharmacist in stroke support is well established. Proven, the purpose of this review is to provide a comprehensive overview of pharmacist interventions with stroke patients. The pharmacist needs a better

understanding of drugs and their therapeutic effects because drug regimen development is an ever-evolving process. A treatment plan improves both the patient's health and the ability of healthcare professionals to prevent disease. The stroke medication plan plays a vital role in differentiating drug problems (DRPs) and investigating the nature and recurrence of DRPs, including untreated symptoms, under-corrected measurements, inappropriate dosing, overt drug use, failure to obtain medications, inappropriate drug prescription, drug interactions and side effects. According to the multicentre Trial of Acute Stroke Treatment (TOAST), there are three kinds of ischemic stroke":⁶

1. Large vessel stroke
2. Small vessel stroke or Lacunar stroke
3. Cardioembolic stroke

Thrombotic or embolic occlusion of the major arteries of the brain, such as the internal carotid artery, middle cerebral artery, anterior cerebral artery, or vertebrobasilar system, may result in large artery strokes. The involvement of smaller or perforating blood vessels that supply the brain's deeper structures is the primary cause of lacunar strokes.

“Time is the most crucial factor in treating an acute ischemic stroke. When an ischemic stroke occurs, the patient loses 190,000 brain cells every minute, approximately 14,000,000 nerve connections every minute, and 12 kilometers (7.5 miles) of nerve fibers every minute. For every hour that the brain is without blood, it ages by 3.6 years”.⁷ Acute ischemic stroke can be treated with one of two methods: Mechanical thrombectomy and intravenous thrombolysis

The next steps must be taken once an acute stroke clinical diagnosis has been made.

- Verify the patient's medical stability.
- Look for neurological symptoms that can be fixed.
- Determine the type of stroke ischemic or hemorrhagic and how to treat it.
- Find out what causes stroke (which goes beyond the scope of this chapter).

Pharmaceutical interventions were defined as medication optimization, where medication management included medication evaluation, medication coordination, medication problem identification, and resolution. Findings are divided into primary and secondary prevention optimization to enable comparison of similar results across different treatment programs.

A person's risk of having a stroke can be assessed using the acronym **FAST**

Face: invite the person to smile; this helps distinguish dead or missing part of the face.
Hands: Ask the person to raise both hands. Check if one arm has fallen lower than the other.
Speaking: Ask the person to repeat a short sentence.

Care provided at different levels of healthcare

The Primary Health Center's (PHC) role is limited to risk assessment, prompt recognition of symptoms, stabilization, and referral to higher centers with management facilities due to the complexity of stroke treatment.

- Primary health care: primary prevention, early recognition and referral, rehabilitation.
- Secondary health care: acute stroke management, secondary prevention and follow-up, rehabilitation.

- Tertiary health care: complex and higher-level management of acute cases, follow-up of stroke for enablement and support services and rehabilitation of residual impairment.

Pharmacological Treatment of Stroke

“Whether the stroke is ischemic or hemorrhagic, stroke treatment can be divided into two categories: stroke-specific treatment and prevention of stroke”.⁹ Tissue plasminogen activator (tPA) and antiplatelet agents are pharmacotherapeutic options for primary ischemic stroke under certain conditions. The goal of pharmacotherapeutic treatment of hemorrhagic stroke is to control the patient's blood pressure and intracranial pressure. Acute ischemic stroke (AIS) is usually treated with alteplasin intravenous thrombolysis. Antiplatelet therapy with aspirin (acetylsalicylic acid) has been shown to reduce the risk of early recurrent stroke when started within 48 hours of an ischemic stroke, but it does not treat a stroke that has already occurred. Aspirin and newer antiplatelet drugs have shown promising results in preventing early recurrence, and clinical trials are ongoing. Patients receiving acute therapeutic anticoagulation with unfractionated heparin (UFH) or low molecular weight heparin (LMWH) have shown no clinical benefit compared with antiplatelet agents in acute ischemic stroke. The role of acute anticoagulation in certain situations with a high risk of early stroke requires further investigation.

Table 1. **The indicative List of Drugs under NPCDCS for emergency care is as follows:**¹⁶

ACE Inhibitors	Enalapril, Ramipril, Lisinopril, Captopril
Calcium channel blocker	Amlodipine
Diuretics	Indapamide, Chlorthalidone, Frusemide, Hydrochlorothiazide
Aldosterone antagonist Beta blocker	Atenolol, Metoprolol, Labetalol
Oral Hypoglycemic	Metformin, Gliclazide, Glibenclamide
Insulin	Short, Intermediate, Long-acting
Fibrinolytics	Streptokinase, rTPA (alteplase and Tenecteplase)
Anti-platelet	Clopidogrel
Lipid-lowering	Statins

“Tissue plasminogen activator (tPA): Alteplase is the only IV Tissue plasminogen activator (tPA) agent approved by the FDA for the treatment of ischemic stroke. This indication was approved once the drug's effectiveness in the NINDS rt-PA Stroke Study was established. The International Stroke Registry's Safe Implementation of Thrombolysis in Stroke (SITS-ISTR) A 3-to-4.5-hour research found no differences in mortality, a modified Rankin Scale score of 0 to 2, or symptomatic intracerebral hemorrhage between individuals treated within 3 hours and those treated within 3-to-4.5 hours”.^{13,14} “Despite the fact that stroke patients who qualify for IV Tissue Plasminogen Activator (tPA) should be treated within 3 hours, the established guidelines for stroke treatment Seizures, new ischemic strokes, cerebral oedema, and brain herniation have all been associated with the use of alteplase for ischemic stroke”.¹⁵

Medicines Optimisation for Primary Prevention of Stroke

“Three main prevention studies looked at the safety and effectiveness of adjusting anticoagulant and antithrombotic drugs for people at risk of stroke”.^{8,9,10} A pharmacist intervention identified 78 of 218 (35.6%) needed adjustments to optimize the current antithrombotic medication for patients hospitalized at risk of stroke (e.g., with AF), in accordance with locally developed evidence-based guidelines. To reduce the risk of stroke, prophylactic medications¹¹ that may be less effective but safer had to be prescribed in 60 (76.9%) of the instances. Similar to this, a hospital's 134 patients with AF participated in a pharmacist-led stroke risk assessment program that increased warfarin use from 74% at admission to 98% at discharge. “Of the 50 recommendations for medication change, 44 (80%) were accepted and put into practice. More effective therapy was needed in 30 out of 44 instances (or 68%)”.¹² “According to the clinical audit, 382 anticoagulant and antithrombotic optimization suggestions for patients with AF received approval by general practitioners in 77% of cases”.¹⁰

Men whose risk is sufficiently high (10-year risk > 10%) for the benefits to outweigh the risks associated with treatment can use aspirin daily (50-100 mg) for cardiovascular events, including stroke prophylaxis. The 10-year risk can be calculated using a cardiovascular risk calculator; however, there is no calculator designed specifically for India. Utilizing clinical judgment and the WHO calculator, risk can be assessed

Because aspirin has been associated with an increased risk of bleeding, it should only be taken when absolutely required. Utilizing clinical judgment and the WHO calculator, risk can be assessed. Through ongoing Indian studies, risk calculators customized for Indians will be created in the upcoming years.

Post-menopausal women, including those with diabetes mellitus, whose risk¹¹ is sufficiently high for the benefits to outweigh the risk associated with treatment can benefit from taking aspirin (50 mg to 100 mg daily). Its use should be clinically examined for draining potential.

Table 2. **Adverse Drug Reactions to Drugs**¹⁶

Drugs	Adverse drug reaction
Aspirin plus dipyridamole, Cilostazol	Headache, Palpitation, Tachycardia
Nicardipine	Phlebitis
Warfarin	Upper gastrointestinal bleeding
Hydralazine, Carvedilol	Hypotension

The therapeutic outcome will be improved by clinical pharmacist involvement in the discharge process, computerized drug order entry, monitoring drug-drug interactions prior to administration, and patient counseling.¹⁶

Various studies have shown that pharmaceutical interventions improve patient outcomes. Patients with dual antiplatelet therapy and a high bleeding risk may benefit from drugs such as the addition of omeprazole, a reduction in the dose of piperacillin or tazobactam from 4.5 g IV 6 h to 2.25 g IV 6 h in patients with creatinine clearance less than 20 ml/min. increasing the dose of atorvastatin from 20 mg to 40 mg for better LDL cholesterol reduction Physicians agreed with 84% of the top clinical pharmacists.¹⁷

Table 3. **Different Drug-Related Problems**

Drug use without indication	Domperidone, Piperacillin+tazobactam, Ondansetron, Paracetamol, Pantoprazole, Tramadol
Drug Duplication	Clopidogrel, Pantoprazole
Subtherapeutic Dose	Amlodipine, Telmisartan, Metoprolol, Nimodipine
Overdose	Ranitidine, Rabeprazole
Adverse Drug Reactions	Amlodipine-induced constipation, atorvastatin-induced myopathy, insulin-induced hypoglycemia
Improper drug selection	Rabeprazole, Ramipril, Ondansetron
Failure to Receive drugs	LMWH Multivitamins
Medication errors	Clopidogrel, Aspirin, Atorvastatin, Mannitol Pantoprazole

Most of the side effects were in the WHO "probable" category. None of the side effects identified were "probably preventable" or "eventual" and most were "mild" in severity. Involving the pharmacist in the evaluation of medication-related issues improves the patient's quality of life, especially for elderly multi-pharmacy patients. "The primary goal of the pharmacy should be to locate potential drug-related problems. In the majority of cases, the drug therapy is being altered, and these recommendations were widely accepted. Polypharmacy was found to be a potential risk factor for drug-related issues. The therapeutic outcomes are enhanced by involving pharmaceutical care for the early detection of drug-related issues".¹⁸

Conclusion

Patients' health-related quality of life (HRQoL) has been shown to improve as a result of hospital care, as shown by various studies. Research also shows that men are more likely to have a stroke because of their social habits and that those aged 41-70 are at the highest risk. The most important drug interactions observed in this study increased both the likelihood of hospitalization and healthcare costs. Antiplatelet agents, anticoagulants, and antihypertensive medications were the most common interacting medications. The use of antihypertensive drugs significantly increases the probability of side effects. Most drug-related problems occur during the prescribing process and DRP due to the wrong indication and dosage of the drug. Age, aphasia, high comorbidity, polytherapy, and the intravenous (IV) route of administration are additional factors that increase the risk of medication errors due to impaired oral administration. A patient receiving a combination of heparin, warfarin, blood pressure medication, and platelets is at high risk for drug interactions and prescribing errors. Therapeutic outcomes are improved through clinical pharmacist participation in the prescribing process, computerized entry of medication orders, monitoring of drug interactions prior to administration, and patient counseling. Patients who do not receive intensified drug therapy are more likely to experience a decline in health-related quality of life (HRQoL). Drug treatment has clear benefits and positive effects on patient HRQoL.

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