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Original Article

An outlook study on the combination of pharmacotherapy and physical rehabilitation for clinically significant acute ischemic stroke patients

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ABSTRACT

The occurrence of an ischemic stroke arises from the unfortunate circumstance in which a blood vessel becomes impeded or obstructed, resulting from the presence of a clot, atherosclerosis, or the narrowing of arteries. The neurology department of a 300-bed, multi-specialty tertiary teaching hospital was the site of this six-month observational study. Prescriptions for both inpatients and outpatients in the neurology unit, totalling 90, are considered according to the inclusion criteria. Patient case sheets, questionnaires, interviews, biomedical and radiological reports, and drug regimen charts are the main data sources. Acute ischemic stroke (AIS) patients are more prevalent in the over-60 age group than in the 20–35 age group. The information obtained indicates that male patients have greater effects than female ones. Furthermore, our research indicates that AIS is more common in obese and overweight people. One of the main risk factors for developing AIS is alcohol drinking, tobacco chewing, and smoking, which affect most AIS patients. Treatment options for acute ischemic stroke (AIS) include intravenous thrombolytic therapy (IVT), anti-platelet therapy, anticoagulant therapy, and adjuvant therapies using statins and drugs based on the comorbidities of the patients. This research highlights that individuals with AIS have shown higher progress when physical rehabilitation is combined with intravenous thrombolytic treatment (IVT) for patients with comorbidities. It has been found that the individuals who continued taking their medicine and therapy after their discharge from the hospital had better motor strength than those who stopped. Our study concludes that the integration of pharmacotherapy with physical rehabilitation yielded significant enhancements in the functional capacity of individuals affected by stroke.

1. Introduction

Stroke, is also known as a cerebrovascular accident, is a widely seen condition across various patient groups and may have a substantial impact on both death and disability rates. Strokes are classified as ischemic and haemorrhagic. Ischemic stroke may be attributed to many aetiologies, including cardio-embolism, small-vessel blockage, and large-artery atherosclerosis [1].

A haemorrhagic stroke occurs when a blood vessel ruptures and causes bleeding

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into the brain [2].

The aetiology of ischemic stroke may be attributed to either a thrombotic or embolic event, resulting in a reduction in cerebral blood flow. During a thrombotic event, cerebral blood flow is impeded inside the blood vessel because of intrinsic vascular malfunction, often caused by atherosclerotic disease, arterial dissection, fibromuscular dysplasia, or an inflammatory illness. During an embolic event, the circulation of blood through the affected channel is obstructed by debris originating from other regions of the body. The aetiology of stroke has a significant impact on both prognosis and outcomes [3].

Stroke is a leading cause of death and disability in both high-income and, more and more, middle-income nations throughout the world. The disease burden from strokes is higher in low- and middle-income countries (LMICs) than in high-income nations. In India, stroke is in the top five for both death and disability [4].

Age-related, non-communicable diseases like stroke have become more common as the average life expectancy in India has increased to above 60 years old in recent years [5]. Stroke frequency ranged from 26 to 757 per 100,000 people, and case fatality rates in one month ranged from 18% to 42% [6]. The annual incidence of stroke ranged from 108 to 172/100,000.

A total of 11–29% of AIS is caused by large vascular occlusions (LVO). These can be in the internal carotid artery (ICA), the M1 or M2 section of the middle cerebral artery (MCA), or the vertebrobasilar arteries. When blood flow is cut off to part of the brain, as happens when an LVO cause's hypoperfusion, brain tissue dies irreversibly. Immediately restoring blood flow to the brain's centre may rescue hypoperfused tissue around the core [7]. For recanalization in LVO, endovascular therapy (EVT) has shown effectiveness [8, 9].

The most typical symptoms of a stroke are facial numbness and paralysis, decreased vision, weakness in one or both arms or legs, difficulty walking, dizziness, nausea, vomiting, a sudden, intense headache for no apparent reason, and difficulty communicating [7]. Women are more likely than men to appear with non-traditional stroke symptoms such as light-headedness and loss of consciousness [10], although men and women report an equal prevalence of typical stroke symptoms. Different stroke field triage assessments have been created to aid in quick diagnosis and patient prioritisation. These ratings have been clinically verified, so they may be used to quickly determine whether a patient is suffering from an acute ischemic stroke. The patient's diagnosis is made based on the clinical examination using stroke scales. When a National Institute of Health Stroke Scale (NIHSS) score of 11 or less was used to make a diagnosis, the greatest rate of accuracy was 79% [11]. Stroke therapy options, such as intravenous tissue plasminogen activator (IV tPA) and endovascular mechanical thrombectomy, must be chosen quickly once a diagnosis is made.

2. Materials and Methods

2.1. Study sites, design, and period

The research is a six-month prospective observational study carried out in the department of neurology of a 300-bed multi-specialty teaching hospital. In the study, 90 prescriptions altogether were analysed. The hospital's institutional ethics committee gave its approval to the research protocol and the written informed consent to consider both inpatients and outpatients from the SVS and Sri Krishna hospitals' neurology departments.

2.2. Inclusion Criteria

- ✓ Ischemic stroke patients, both hospitalised and otherwise, who are willing to participate and provide informed consent.
- ✓ A clinical diagnosis of an ischemic stroke with observable neurological impairment.
- ✓ The onset of symptoms is 4.5 hours before the start of therapy; if the precise time of stroke onset is unknown, it is determined by the most recent instance in which the patient was known to be normal or at neurologic baseline.
- ✓ A minimum of 18 years old.

2.3. Exclusion Criteria

- ✓ An ischemic stroke along with a serious head injury in the last three months.
- ✓ A past intracranial haemorrhage
- ✓ An intraaxial intracranial tumour or aneurysm
- ✓ Tumours of the gastrointestinal tract
- ✓ Bleeding in the intestines in the most recent month
- ✓ A recent three-month period of intracranial or spinal surgery.
- ✓ People who have had multiple ischemic strokes
- ✓ Nursing or pregnant mothers.

2.4. Method of data collection

- ✓ Case Report Forms.
- ✓ Patient Questionnaire/Interview.
- ✓ Radiology and biomedical parameters
- ✓ Physical examination

2.5. Tools of the study

- ✓ Blood Pressure & GRBS Monitoring
- ✓ CT-Brain and MRI
- ✓ Lipid profile
- ✓ National Institutes of Health Stroke Scale (NIHSS) & Glasgow Coma Scale (GCS)

2.6. Study procedure

A prospective observational study was conducted at SVS Medical College Hospital and Sri Krishna Super speciality Hospital, Mahbubnagar, Telangana, India. Screened 90 patients visiting the hospital with ischemic stroke and were enrolled in the study according to the inclusion criteria after obtaining informed consent. Data collection forms consisting of demographic details of the patients were prepared and used for the study. Patients are interviewed for the improvement and recovery of the disease. Currently, drugs of various classes and rehabilitation details are analysed for the assessment of treatment regimen. All information relevant to the study was collected at the time of admission till the date of recovery. Treatment outcome was assessed based on NIHSS and GCS and scores. The data was analysed using suitable methods.

3. Results

3.1. Prevalence of acute ischemic stroke with respect to age, gender, and body mass index (BMI)

There are 46 patients (51.1%) above the age of 60, 22 patients (24.4%) between the ages of 46 and 60, 18 patients (20%) between the ages of 36 and 45, and 4 patients (0.4%) between the ages of 20 and 35 (Table 1). Patients with acute ischemic stroke (AIS) are more common in those over 60 than in people between 20 and 35 years. According to the data gathered, it is shown that male patients, who are 52 (58%) compared to female patients, who are 38 (42%), have a higher prevalence of AIS.

The BMI of patients with AIS was assessed, and it was shown that 72 patients (80%) were overweight or obese, with just 18 patients (20%) being normal weight or underweight. It suggests that AIS affects obese and overweight individuals more often.

Table 1. Prevalence of acute ischemic stroke with respect to age

Age	Total No of Patients	Percentage
20-35	4	4.44
36-45	18	20.01
46-60	22	24.44
>60	46	51.11

3.2. Prevalence of acute ischemic stroke depending on addiction

According to the collected data, out of a total of 90 patients, 22 % of patients are addicted to alcohol, 07 % of patients are addicted to tobacco chewing, and 10 % of patients are addicted to smoking. It has been shown that most patients 61% are addicted to more than one kind of addiction (Figure 1).

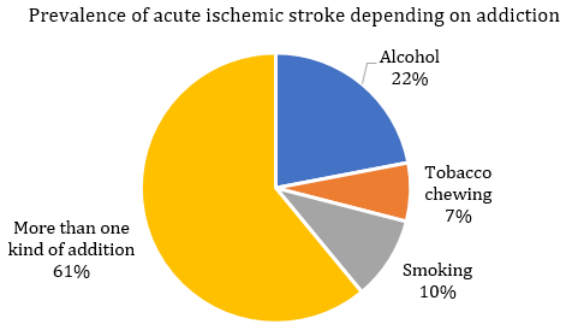

Fig. 1. Prevalence of acute ischemic stroke depending on addiction

3.3. Co-morbidities in acute ischemic stroke

Throughout the course of this research, it has been clear that the most prevalent comorbidities are hypertension, diabetes mellitus, dyslipidaemias, and renal illnesses. It was also shown that some individuals had more than one comorbid condition, such as diabetes, hypertension, dyslipidaemia, and/or renal disease.

3.4. Severity of acute ischemic stroke (NIHSS and GCS Scale) and motor strength grading

After utilising the GCS and NIHSS Scales to determine the severity of AIS, we found that out of 90 patients with acute ischemic stroke, 25 patients had a minor stroke (where the NIHSS score ranges from 1–40), and 65 patients had a moderate stroke (where the NIHSS score ranges from 5–15). According to the Motor Strength Grading, the majority of patients were found to have fair to poor strength, which is equivalent to a score of 2–3 out of 5, while very few patients had high motor strength.

3.5. Treatment choice in acute ischemic stroke

The goal of treating an AIS is to preserve tissue in areas where blood flow is inadequate to cause an infarction. The first step in treating a stroke is to ensure the patient's medical stability. As with any medical emergency, the patient's airway, breathing, and circulation have been checked. Preserving oligemia-affected tissue requires keeping its blood and collateral vessels open. Recombinant tissue plasminogen activator (rtPA), such as alteplase, has been widely regarded as the standard therapeutic approach for managing acute ischemic stroke over a long period of time. IV alteplase is given to patients who match the inclusion criteria and whose symptoms began or returned to their baseline within three hours. Administered intravenous alteplase at a dosage of 0.9 mg/kg not exceeding a maximum dose of 90 mg. A bolus of 10% is administered within the initial minute, followed by the administration of the remaining 90% over the subsequent 60 minutes. There were a few patients who were granted extensions of up to 4.5 hours.

Oral anticoagulant medication treatment with IV alteplase produces orolingual angioedema in patients aged 60 and above whose NIHSS score is classified as significant or moderate. Emergency treatment of the airway has been administered in the event of an angioedema reaction. Diphenhydramine, methylprednisolone, and endotracheal intubation are used to stabilise the airway. Alternate fibrinolytic medications, such as Tenecteplase 20 mg, are substituted with alteplase in some situations. Patients who have had fibrinolytic therapy are not excluded from consideration for mechanical thrombectomy. Endovascular thrombectomy during the first six hours was shown to be more effective than standard medical treatment for significant arterial blockage in the arteries of the proximal anterior circulation.

Comorbid hypertensive patients received intravenous labetalol (10–20 mg) if their blood pressure was 180/200 mm Hg or higher. 5mg of amlodipine and 40mg of telmisartan is another choice of treatment. Amlodipine 5 mg, Telmisartan 40 mg, and Hydrochlorthiazide 12.5mg are administered to people with hypertension and renal disorders. When ICP increases after an ischemic event, cerebral perfusion pressure, which is dependent on MAP, is monitored to prevent hypotension and hypovolemia.

Maintaining healthy blood glucose levels is a crucial consideration. The target range for glucose in the first 24 hours is between 140 and 180 mg/dL. Dextrose solutions of 5% are used to normalise glucose levels in those whose blood sugar is below 60 mg/dL. Since

the brain has a high metabolic demand and relies on glucose for its oxidative processes, hypoglycemia inhibits brain repair. Reductions in reperfusion caused by hyperglycemia are related to the decrease of vascular tone and oxidation of nitric oxide-dependent pathways. Damage to the lactic acid-sensing channels results in increased acidity. Human insulin (40 IU) and glimiperide (1 mg) with metformin (500 mg) are used to treat hyperglycemia in these individuals.

In patients presenting with a minor ischemic stroke, it is recommended to administer Aspirin 75 mg and Clopidogrel 75 mg within 48 hours of the event. This combination therapy has been shown to effectively reduce the incidence of recurrent strokes within the initial 3-month period following a minor ischemic stroke. In certain cases, the administration of either 40 mg or 60 mg of the antithrombotic medication enoxaparin is also advised, depending upon the severity of the stroke. Patients with clinical atherosclerotic cardiovascular disease were given high-intensity statins (either atorvastatin 80 mg or rosuvastatin 20 mg) to treat their dyslipidaemia. The people who had been taking statins before the ischemic stroke kept taking them. In the range of 7–14 days after a mild to severe stroke, anticoagulation treatment may begin.

Anticoagulation was held off for two weeks for those who had a modest haemorrhagic change after an acute stroke. This delay has no negative effects on stroke recurrence. Mannitol 100 mL, an osmotic diuretic, is often recommended for patients with renal problems. Supplements that boost cognitive function, such as Citacoline 250 mg and Piracetam 200 mg, are also administered as adjuvant therapy. Patients are also given proton pump inhibitors like pantoprazole 40mg to reduce their risk of gastrointestinal bleeding (Table 2).

Ischemic cerebellar infarctions get worse with cerebellar swelling and get better quickly. Cerebellar swelling results from cytotoxic and vasogenic oedema. The development of hydrocephalus obstructing the fourth ventricle, herniation of the trans tentorial superior vermis, and herniation of the cerebellar tonsils posteriorly are all possible outcomes of elevated intracranial pressure. Mental impairment, limited awareness, breathing difficulties, dilated pupils, abnormal posture, and death may all be indicators. After cerebellar infarction, early neurosurgical consultation is necessary because obstructive hydrocephalus necessitates a ventriculostomy. Mass-effect cerebral oedema is treated by decompressive suboccipital craniectomy.

Table 2. Drugs used in the treatment of acute ischemic stroke

Category Of Drugs	Majorly Used Drugs
First Choice Of Drugs	
Anti-Platelets	T. Preva-As 75 (Aspirin 75 Mg + Clopidogrel 75 Mg)
Anti-Coagulants	Inj. Enoxarin (Enoxaparin 40 Mg Or 60 Mg Based On Severity Of Stroke)
Thrombolysis	
Tissue Plasminogen Activator (Tpa)	Inj.Tenectase (Tenecteplase 20 Mg, Changes Based On Weight Of The Patient)
Adjuvant Therapy	
Nootrpics	Inj. Ceham + Flocetam (Citacoline 250 Mg + Piracetam 200 Mg)
Osmotic Diuretics	Mannitol (100 Ml)
Statins	T. Lipitas (Rosuvastatin 40 Mg)
Proton Pump Inhibitors	Pantoprazole (40 Mg)
Category Of Drugs	Majorly Used Drugs
Hypertension	
Alpha + Beta Blockers	Inj. Labetalol (If Bp Is >|=180|200 Mm Hg
Calcium Channel Blockers + Angiotensin Receptor Blockers	T. Telvas Am (Amlodipine 5mg + Telmisartan 40 Mg)
Calcium Channel Blockers + Angiotensin Receptor Blockers + Thiazide Diuretics	T. Telzox Trio (Amlodipine 5 Mg + Telmisartan 40 Mg+ Hydrochlorthiazide 12.5 Mg)
Type-2 Diabetes	
Insulin Hormone	Inj. Insulin (Human Insulin 40 Iu) Based On Blood Sugar Levels
Sulfonylureas + Biguanides	T. Metsmall G (Glimiperide 1 Mg+ Metformin 500 Mg)

3.7. Pharmacotherapy and rehabilitation in AIS patients

Rehabilitation after a stroke should begin quickly, but not within the first 24 hours. Physical activities are an important part of rehabilitation plans, and they may range from motor skill exercises to boost overall muscular strength and coordination to mobility training to assist with the use of assistive devices like walkers, canes, wheelchairs, and ankle braces. Ankle bracing,

also known as a constraint-induced treatment, may improve limb functionality and range of motion by stabilising and strengthening the ankle. Treatment is intended to reduce stress on muscles and restore mobility. One example of technologically aided physical activities is functional electrical stimulation, in which electricity is used to contract weak muscles. Repetitive actions performed by robots on behalf of disabled users may help such users' limbs recover strength and function. Using a wireless activity monitor, virtual reality video games, or other forms of computer-based therapy may help stroke survivors become more active again. Examples of mental and emotional labour include treatment for cognitive problems and cognitive functions such as memory, problem-solving, processing speed, judgement, social skills, and safety awareness may be reestablished via occupational therapy and speech therapy. Treatment for speech and language problems psychological examination and therapy may include testing one's level of emotional adjustment and offering counselling on how to exercise emotional self-control, while speech therapy may help one restore lost skills in those areas as well as in writing, reading comprehension, and speaking.

The results of treatment were evaluated using the NIHSS and the Glasgow Coma Scale. Functional improvement was greater in individuals with acute ischemia who maintained rehabilitation and medication after discharge than in those who did not. The rate of recovery is higher in the absence of co-morbidities than in their presence. In 61 patients with comorbidities, the duration of treatment was more than 6 months, whereas in 29 patients without comorbidities, it was between 3 and 6 months.

4. Discussion

The World Health Organisation defines a stroke as a clinical illness characterised by the sudden onset of symptoms indicative of a focal (or global in the case of coma) impairment of brain function that persists for more than 24 hours and can lead to death and has no obvious cause other than a vascular one. Similar to Mohammed Yousufuddin's [12] research, we find that the majority of strokes affect those over the age of 60. While Kathyrn M.'s [13] research revealed that women were more likely to suffer from an acute ischemic stroke, ours found the opposite. AIS is most often associated with obesity, cigarette smoking, and heavy alcohol use [14, 15]. Comorbidities, including renal disorders, hypertension, diabetes, and dyslipidemia, are common in stroke patients [16]. IV Alteplase is administered as an initial treatment option, and it must be administered within three hours after the onset of neurologic deficits. Alternatives to alteplase include the fibrinolytic drug tenecteplase. The effectiveness and safety of tenecteplase in treating a mild stroke were found to be comparable in an earlier study [17].

Medications such as labetalol, amlodipine, telmisartan, and hydrochlorothiazide are used to treat hypertension [18]. Treatment options like metformin and glimepiride are advised as first-line therapy for these individuals with diabetic comorbidities. Metformin may have neuroprotective characteristics that lessen the severity of stroke if taken prior to the onset of symptoms [19].

Aspirin and clopidogrel, two drugs used in antiplatelet therapy, are often taken during the first two days after the onset of symptoms. Because it reduces the risk of future ischemic strokes and increases the survival rate. The severity of a stroke determines whether or not the anticoagulant enoxaparin is recommended. High-intensity statin therapy was recommended for individuals with clinical atherosclerotic cardiovascular disease and dyslipidemia. People who were previously taking statins at the time of their ischemic stroke kept doing so. For mild to severe strokes, anticoagulation should begin within 7–14 days [20, 21].

Rehab for stroke victims should begin quickly, but not within the first 24 hours after the event. The A Very Early Rehabilitation Trial for Stroke (AVERT) study compared standard stroke-unit treatment versus very early rehabilitation after 24 hours following stroke and found that early mobility resulted in lower modified Rankin ratings, which supports our study. A quicker rate of recovery is seen in cases where co-morbidities are absent [22].

5. Conclusion

The demographics of our ageing population and improved acute stroke treatment choices, which will raise stroke patient survival rates, are anticipated to cause an increase in the absolute number of people with stroke-related disabilities over the next decades. Thus, it becomes imperative to explore novel therapeutic approaches in the aftermath of a stroke, to mitigate the adverse effects on the patient's well-being and enhance the overall quality of life for both the individual and their dedicated carer.

The remarkable progress in our comprehension of stroke-induced reorganisation of brain networks has been propelled by notable advancements in functional neuroimaging and non-invasive brain stimulation techniques. Mounting evidence suggests that network effects distant from the injury considerably contribute to motor deficit and recovery. The temporal and geographical variability of these effects poses a significant challenge for future endeavours aimed at influencing network reorganisation using brain stimulation techniques. Individual network readouts and/or multivariate decoding methods are necessary for stratifying patients to attain the best treatment response due to the high degree of diversity in network responses after a stroke.

Abbreviations

AIS: Acute ischemic stroke
AVERT: A very early rehabilitation trial for stroke
BMI: Body mass index
CT: Computerised tomography
EVT: Endovascular therapy
GCS: Glasgow coma scale
ICA: Internal carotid artery
ICP: Intracranial pressure
IVT: Intravenous thrombolytic therapy
IVtPA: Intravenous tissue plasminogen activator
LMICS: Low- and middle-income countries
LVO: Large vascular occlusion
MCA: Middle cerebral artery
MPA: Microscopic polyangiitis
MRI: Magnetic resonance imaging
NIHSS: National institute of health stroke scale
rt-PA: Recombinant tissue plasminogen activators
SVS: Sri venkata sai

Conflict of Interest

The authors confirm they have no conflicts of interest.

Consent for publications

All authors read and approved the final manuscript for publication.

Informed Consent

The authors declare not used any patients in this research.

Availability of data and material

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Author's contributions

All authors contributed equally to the study as well as the analysis and interpretation of the data. All authors read the final manuscript and gave their approval.

Ethics approval and consent to participate

The ethical committee clearance was obtained from the Institutional Ethical Committee of SVS MEDICAL COLLEGE HOSPITAL before initiating the study. Reference number:

IEC/DHR-014/2022/155(4)

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