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MANAGEMENT OF ISCHAEMIC STROKE – RECENT ADVANCES

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ABSTRACT

There is a better understanding of the natural course of stroke as well as its pathogenesis. This has led to the philosophy of "watch and intervene as appropriate" in the management of stroke. Treatment efforts attempt early intervention to restore blood flow and protect neurones from ischaemic damage. Thrombolytic therapy given within 3 hours of ictus has been effective but this is not feasible in Africa because of time delay and lack of neuro-imaging facilities in most centers. Contemporary management of stroke is divided into 4 phases: acute, early subacute , late subacute and long term.

Acute phase involves early assessment and supportive care from the onset of stroke to the 7th day. These include adequate fluid therapy (not haemodilution) of isotonic or hypertonic infusion to improve cerebral blood flow and reduce cerebral oedema; insulin therapy for hyperglycaemia as well as use of free radical scavengers. Hypertension is the commonest predisposing factor for stroke, but the weight of available evidence does not support its treatment in the first 10 days of stroke onset.

However, for extra cerebral complications with blood pressure above 220 / 120, oral antihypertensive agents could be beneficial. Combination of thrombolytics, agents to protect against the effects of ischaemia and anti-oedema measures are likely to be required. Possible agents that might halt the ischaemic process before infarction becomes inevitable include NMDA receptor blockers, ion channel blockers, free radical scavengers, caspace and xanthine oxidase inhibitors.

During the early subacute phase, from the 2nd to the 4th week, prevention of pulmonary embolism with subcutaneous heparin, treatment of pneumonia with antibiotics and early physiotherapy are important. During the late phase, physical and psychological rehabilitation and prevention of stroke recurrence by modifying the risk factors are essential.

For effective management of stroke ("brain attack"), stroke units are now in vogue in developed nations. Stroke management in our nation should be reprioritised as a time dependent urgent medical emergency just as is currently stressed for major trauma and acute myocardial infarction (heart attack). Efforts should equally be made to set up stroke units and strengthen primary prevention.

KEYWORD: ***stroke: management.***

INTRODUCTION

Stroke is a common and serious neurological problem. It is a major cause of morbidity and mortality all over the world and efforts should be directed at reducing the mortality and improving the quality of life in survivors. No longer can we stand by, while stroke threatened brain undergoes irreversible injury.

With the better understanding of stroke pathogenesis, its natural course and the recent recognition of the potential for reversing or ameliorating acute stroke through early intervention[1-6], patients with acute neurological dysfunction (brain attack) have now joined the ranks of acute myocardial infarction (heart attack) and major trauma[7]. There is therefore the need for rapid identification of patients and provision of definitive intervention.

Pathophysiological basis of Management

The specific treatment approach in stroke is clearer if we consider this simplified pathogenesis. In cerebral infarction, there is occlusion of a vessel due to a thrombus, embolus or vasospasm[8]. This results in reduced perfusion in the absence of adequate collateral circulation and generates a central area of infarction (umbra) and a subjacent surrounding area of reversible ischaemia with potentially salvageable neurone (penumbra)[9]. In the umbra region, the morphological threshold of less than 10mls/100g/min of cerebral tissue has been exceeded and cell death ensues. In the penumbra region, the functional threshold of less than 15mls/100g/min has been exceeded and neural tissue would cease function without loss of morphology. Necrosis predominates in the umbra while apoptosis predominates in the penumbra[10] with the possibility of recovery after blood flow is restored within a limited time frame – the therapeutic time window. The duration of the time window is 2 – 3 hours in experimental animals and 5 – 6 hours in primates[9]. Time window in man is variable and dependent on the status of the collateral circulation, age, coexisting metabolic abnormalities (e.g. hyperglycaemia) premorbid medication and other confounding factor[1].

Cerebral oedema is a significant cause of morbidity and mortality in stroke and it is predominantly cytotoxic and intracellular. It occurs as a result of failure of the energy dependent mechanisms, such as $Na\text{-}K^+$ ATpase, consequent on the reduced blood flow and nutrient supply. Sodium influx accompanied with water is therefore unchecked and intracellular oedema ensues. Pari-pasu with this, there is also calcium influx, which would activate the proteases, lipases and endonucleases (calcium

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dyshomeostasis). This sets in motion series of intracellular destructive catabolic processes and creates a new osmol which further worsens the intracellular oedema already engendered by the influx of sodium and water.

Management of stroke

The management of stroke has been divided into phases: acute, subacute (early and late) and chronic care (Table 1)[3, 12, 13].

[a] Acute phase:

The acute assesment of patients with suspected stroke include detailed clinical evaluation and investigations which aims to

a) confirm clinical diagnosis if in doubt,
b) establish any treatable cause,
c) establish baseline data to assess improvement or deterioration,
d) determine any risk factors with might be manipulated to prevent recurrence,
e) predict the likelihood of immediate complications, and
f) exclude other possibilities[14].

However, the age of the patient, the potential for recovery or recurrence, and the clinical suspicion as regards the aetiology would guide the clinicians about the extent or choice of investigations (Tables 2 and 3).

ECG would exclude arrhythmia as a cause of cardioembolic stroke. Moreover, there could be coexistence of cerebral and coronary arteriosclerosis with evidence of myocardial ischaemia in the same patient since they have similar predisposing factors. Elderly female diabetics are prone to silent myocardial infarction and ECG may provide the only pointer. Chest X-ray would reveal aspiration pneumonitis complicating stroke as well as the end–organ effect of long-standing hypertension. Haemoglobin genotype is mandatory in young stroke patients. (Sicklers are prone to cerebral infarction below the age of 10 years and sub-arachnoid haemorrhage in the teen ages. Occlusion of the vasa vasorum of the vessels of the circle of Willis renders these vessels fragile thus predisposing to the development of aneurysmal dilatation and subsequent rupture into the sub-arachnoid space[15].

CT scan should be done in all patients with acute neurological dysfunction especially when considering treatment with aspirin, anticoagulant or surgery[16]. CT scan is positive in 54% and 90% of cases of cerebral infarction by the 2nd and 4th day respectively and could miss early lesions. It is not useful in brainstem stroke. However, unlike in cerebral infarction, CT scan can confirm intracranial haemorrhage within minutes of onset if the intracerebral collection is more than 0.5 cm in diameter[16]. Although, an isodense haemorrhagic lesion in patients with severe anaemia and haemoglobin below 10g/dl may be missed, since the increased density of blood on CT is a function of the haemoglobin concentration[17]. MRI is superior to CT for posterior fossa lesions and detects infarction as early as 45 minutes[18] but it is expensive and causes claustrophobia.

Supportive care aims to

a) treat the underlying disease process if possible, as factors such as old age and haemoglobinopathy are not readily treatable.
b) protect ischaemic brain tissue from necrosis while attempting to reverse or limit the degree of brain dysfunction,

Furthermore, pari-pasu with subacute care, it aims to

c) prevent and treat complications,

rehabilitate the disabled patient - physiotherapy, occupational and speech therapy and
prevent recurrence[8,9].

Table 1: **Phases of Contemporary Management of Stroke**

PHASES	Period from onset	Activities	Preferred Location
1. Acute (Emergency) Care	1st-7th day	a) Assessment b) Early Supportive Care	Hospital
2. Early Sub-acute (Supportive) Care	2nd-4th week	Prevention and Treatment of complications Early rehabilitation	Hospital
3. Late Sub-acute (maintenance) Care	2nd-6th month	Rehabilitation Psychological support Prevent recurrence	Hospital/ Community
4. Long-term (Chronic) Care	7th month onwards	Rehabilitation Psychological Support Social support Prevent recurrence	Community

Table 2: **Acute emergency care**

Activities	Complications	Investigations	Treatment
a) assessment		1) Full blood count; ESR; 2) Clotting profile; 3) Blood glucose; cholesterol 4) Electrolytes and urea. 5) ECG 6) Chest X-ray 7) CT scan without contrast 8) Echocardiography 9) Blood cultures (in infective endocarditis) 10) Genotype in children	1) Intravenous infusion 3litres /day; 2) Thrombolytics rTPA (alteplase) 3) free radical scavengers 4) Do not treat hypertension except B.P > 220/120. If at all, use oral agents: Beta and Ca2+ blockers; ACE inhibitors
b)Early supportive care	Neurological 1) Cerebral oedema		1) head-up tilt; (15-30°) Dexamethasone Mannitol Glycerol Do not give hypotonic infusion
	2) Increased ICP		2) monitor level of consciousness + neurologic deficit
	3) Haemorrhagic transformation		3) withhold anticoagulant
	4) Seizures		4) anticonvulsants
	Systemic		
	5) Hypoxia		5) clear airway + good ventilation + intra nasal O_2
	6) Hyperglycaemia		6) insulin
	7) Aspiration pnemonitis		7) do not feed orally; ± if unconscious ±NG – tube, antibiotics, suction +Chest physioRx
	8) Cardiac arrhythmias (lone/non valvular A/F)	8) continuous cardiac monitoring	
	9) SIADH	9) monitor serum Na+	9) fluid restriction; domeocycline

Prior to 1995, most medical community considered management of stroke to be largely supportive care and this led to the Traditional "wait and see" approach. The evolving designation of stroke as a brain attack[7], in terms of its analogy to a heart attack, suggests the need for immediate intervention. The cardiologists' mantra that ''time is muscle'' (regarding the salvage of myocardium in acute myocardial infarction) might then be expanded to ''time is neurons'' for the stroke patients[19]. Perhaps, the ''golden hour ''for achieving definitive trauma care should be more aptly applied to stroke management[1]. This philosophy has led to the concept of "watch and intervene as appropriate'' and the advent of stroke team in stroke units[20,21].

Stroke unit is a multidisciplinary team of committed professional staff – Physician, neurosurgeon, endovascular neuroradiologist, physiotherapist, occupational therapist, speech therapist, nursing staff and social worker. It has been the proven singular therapeutic measure in reducing stroke mortality and morbidity[21]. This team is made available within 15 minutes, 24 hours a day and 7 days a week. There is therefore the need for improved case identification, immediate transfer of patients, and rapid mobilisation of health personnel. The organisation of stroke units for all communities would provide the hope for better outcome in developing countries of Africa[22].

Once a case is identified, there is need for cardiopulmonary

resuscitation with maintenance of adequate airway and administration of oxygen at low flow rate (1 –2 L/ min) except for patients in respiratory distress when assisted ventilation may be required. Attempts are further made to protect ischaemic brain tissue from necrosis and reverse or limit the degree of brain dysfunction. This could be achieved by a) restoring blood flow and nutrients (especially glucose and oxygen) before ischaemia causes irreversible infarction, and b) protecting the neurones from the adverse milieu created by the biochemical changes triggered by ischaemia, thus lengthening the therapeutic time window[9].

Restoration of blood flow could be medical (thrombolysis) or surgical (embolectomy, vascular reconstruction or thromboendarterectomy). There are promising results that recombinant tissue plasminogen activator (rtPA)[4, 6, 12, 13] and streptokinase[21] may be effective in lysing the clot and restore blood supply to infrarcted region. This benefit is seen if given less than three hours or preferably within 90 minutes of the onset of symptoms (Table 3). The later it was in the time course of the stroke, the higher the risk of bleeding complications following thrombolytic therapy[6]. The door to needle time (from onset of symptoms to commencement of treatment) in the developed nations is about 60 minutes. Majority of our stroke patients do not present within this time frame and the reality of thrombolysis in the developing world is questionable, more so, in the absence of neurosurgical and neuroimaging facilities in most centres.

Thrombolytic therapy is predicated on appropriate clinical evaluation and a negative test such as the absence of abnormality on the CT scan. It is also recommended that strict monitoring and regulation of blood pressure below defined upper limits should be maintained with hourly assessment of neurological status for 24 hours after treatment.

Thrombolysis should exclude patients with

a) CT signs of haemorrhagic stroke; sub-arachnoid haemorrhage; intracerebral haemorrhage; subdural and epidural haemorrhage,
b) focal neurological deficit with stroke-like presentation,
c) rapidly resolving neurological deficit,
d) in whom the time of onset is difficult to establish (patient with stepwise progression of deficit brought to hospital because of the last of multiple events)
e) in whom CT scan shows massive infarction[6].

The American Heart Association recommends that thrombolytic therapy should not be used unless facilities that can handle bleeding complications are readily available (Table 5). This should also apply to the use of thrombolytics in thrombotic stroke. Facilities for neurosurgical intervention, neuroimaging, administration of cryoprecipitate and platelet should also be readily available[6].

Hemodilution[23], induced hypertension and hyperbaric oxygen[24] have been tried to reverse or limit the degree of brain dysfunction with minimal success. Haemodilution focuses on the haemorrheology of blood and reduces the haemoglobin to 10 – 11g/dl to improve collateral blood flow and overcome the yield shear stress that resists restarting of stopped capillary blood

Table 3: **Early sub acute (supportive care) 2nd to 4th week.**

Activities	Complications	Investigations	Treatment
Prevention/Rx	Neurological 1) Seizures 2) depression	1)EEG	1) anticonvulsant 2) antidepressant(amitryptilline)
	Systemic 3) DVT / Pulm. Embolism	3)Doppler ultrasonography	3) anticoagulant (sc heparin 5000 units q 8/12 hrs (>48hrs of ictus)
	4) Bronchopneumonia	4) CXR	4) appropriate antibiotics
	5) UTI	5) Urinalysis + m/c/s	5) minimise/avoid catheterisation (use paul's tubing/condom) + appropriate antibiotics
	6) Septicaemia	6) Blood culture	6) antipyretics/antibiotics
	7) Decubitus ulcers	7) Lesion swab m/c/s	7) change position q 2-4 hours
	8) Joint stiffness		8) early physioRx
Early rehabilitation	Chronic illness		Psychological support Social support PhysioRX

flow. However, it places an extra load on the diseased myocardium in cardioembolic stroke. The increased cerebral blood flow that follows haemodilution requires substantial increase in cardiac output that may aggravate ischaemic heart disease. The reduced oxygen carrying capacity of blood could further aggravate the cerebral ischaemia, thus widening the umbra at the expense of the penumbra. The increased cerebral blood flow also increases the tendency to hydrostatic cerebral oedema[23].

Encephabol (piritinol) causes "cerebral steal" and its use should be discouraged. It causes vasodilatation of the normal vessel and increases blood flow to the normal side at the expense of the abnormal side. The vessel on the ischaemic side having been maximally vasodilated physiologically and compensatorily, can no longer be dilated even to potent cerebral vasodilator like carbon monoxide or nitric oxide[5].

Several neuro protective agents to lengthen the therapeutic window have been tried[13]. They would increase the ability of the neuron to withstand ischaemia. Lactic acid, free radicals and disruption of neurotransmitters are products of ischaemia and have been implicated in neuronal death. These agents include:

a) free radical (singlet oxygen, hydroxyl ion, hydrogen peroxide) scavengers such as 21- Aminosteroid, Ascorbate and alpha-tocopherol (Vit C and E)[25].

b) inhibitors of excitatory amino acid (NMDA receptor blockers – MK- 801, D-CPP-ene, CGS19755). Glutamate is released in very high concentration during ischaemia and causes neuroexcitotoxicity. Its inhibition would therefore protect the neuron.
Futhermore, putative inhibitory transmitter and neuromodulators such as noradrenaline and adenosine are neuroprotective. Adenosine level rises in ischaemic/hypoxic brain and reduces the release of excitatotry neurotransmitters[26]. Upregulation of several proteins that participate in apoptosis (such as Caspase – 3) has been detected in stroke damaged brain tissues. Animals that have been treated with caspase inhibitors show less damaged tissue after experimentally induced stroke[10].

c) barbiturates, hypothermia and steroids reduce metabolic demand and are neuroprotective but are not practical measures to lengthen the therapeutic window.

d. Naftidrofuryl improves neuronal efficiency because metabolic needs are more easily met and metabolic demand reduced. It reduces the level of lactate and increases the supply of ATP as well as efficiency of substrate use[27].

e. Nitric oxide (NO) synthase inhibitors reduce the level of neuronal and inducible nitric oxide which are cytotoxic[9].

f. Calcium antagonist[11] – nimodipine reduces infarct volume in animal models in middle cerebral artery occlusion. The same effect was found in man but the initial enthusiasm has not been sustained.

g. *Antihypertensives*: Hypertension accounts for 80% of the predisposing factors in our environment[15]. However, the weight of available evidence does not support its treatment in the first 10 days of stroke onset except if there are extracerebral complications such as dissecting aortic aneurysm, ischaemic heart disease / myocardial infarction, acute pulmonary oedema and rapid decline in renal function[3,9]. These complications are usually found if the mean arterial pressure (MAP) is greater than 145 (SBP >220, DBP >120). MAP of 130, (SBP 185 / DBP105) is the goal of such gradual reduction by oral agents. Hypertension is not a risk factor for haemorrhagic transformation in cerebral infarction[28]. In fact, high admission blood pressure is associated with low frequency of progression of neurologic deficit[29].

In the immediate post-CVA period and up to three weeks thereafter, there is loss of cerebral autoregulation[30]. The cerebral perfusion pressure is therefore dependent on the mean arterial pressure, which must be high to sustain cerebral perfusion and keep the collateral circulation open (yield shear stress). This would ensure reversal of the area of ischaemia and possibly reduces infarct size if this is achieved within the therapeutic time window. Furthermore, the increased intracranial pressure due to the space occupying effect of cerebral hematoma and / or cerebral oedema accompanying cerebral ischaemia, suggest the need for increase blood pressure to maintain a constant cerebral perfusion. Cerebral perfusion pressure is a factor of the difference between the mean arterial pressure and intracranial pressure. (CPP = MAP – ICP)[9].

Table 4: **Late sub acute (maintenance 2nd – 6th month) and Long term (chronic – 7th month onwards) care**

Activities	Complications	investigations	Treatment/prevention
Treatment	see tables 2 and 3		
Rehabilitation			
Physical support	Chronic illness	See tables 2 and 3	Physiotherapist
Social/psychological support			Occupational/speech therapist; social worker
Prevent recurrence	Recurrence		Control weight, D.M; Hypertension; regular exercise; discourage smoking, alcohol. Antiplatelets- aspirin + dipy ridamole; Clopidrogel; ticlopidine.Carotid end-arterectomy (stenosis > 70%)

Table 5: **Characteristics of Patients with Stroke who may be Eligible for Intravenous Tissue Plasminogen Activator Therapy.***

Age ≥ 18 years
Diagnosis of ischaemic stroke causing clinically apparent neurologic deficit
Onset of symptoms < 3 hr before possible beginning of treatment
No Stroke or head trauma during the preceding 3 months
No major surgery during the preceding 14 days
No history of intracranial haemorrhage
Systolic blood pressure ≤ 185mm Hg
Diastolic blood pressure ≤ 110 mm Hg
No rapidly resolving symptoms or only minor symptoms of stroke
No symptoms suggestive of subarachnoid haemorrhage
No gastrointestinal or urinary tract haemorrhage within the preceding 21 days
No arterial puncture at a non-compressible site within the preceding 7 days
No seizure at the onset of stroke
Prothrombin time ≤ 15 sec or international normalized ratio ≤ 1.7, without the use of an anticoagulant drug
Partial-thromboplastin time within the normal range, if heparin was given
during the preceding 48 hr
Platelet count ≥ 100,000/mm3
Blood glucose concentration > 50 mg/dl (2.7 mmol / liter)
No need for aggressive measures to lower blood pressure to within the above-specified limits

Labetalol; low dose of enalapril; sublingual nifedipine; isradipine and nimodipine have been tried. Nimodipine is cerebrospecific and also cytoprotective by reducing calcium influx into the cell.

The common acute complications of stroke are tabulated in Table 2.

Transtentorial herniation due to raised intracranial pressure is the commonest cause of death. The incidence peaks within 24 hours for cerebral haemorrhage and 4-5 days for cerebral infarction[31,32]. It accounts for 78% of stroke death in supratentorial lesions in the first seven days[28]. Most deaths after one week of the ictus are from preventable non-stroke related and usually preventable.

Cerebral oedema in stroke patients peaks on day 1 to 3 and several measures have been tried to ameliorate its effect with varying success[33,34,35].

Slight head-up tilt (15-30°) improves venous drainage and reduces cerebral oedema.

Limiting fluid intake to 1.5 litres / day also reduces cerebral oedema. These measures are of questionable efficacy. Controlled respiration using a mechanical ventilator or hyperventilation causes hypocapnea, which induces cerebral vasoconstriction and reduces cerebral perfusion and oedema. Hypothermia and barbiturates have also been tried. They reduce metabolic demand and cerebral perfusion. High dose of barbiturates is required for this purpose and its usage in comatose stroke patients is questionable. Its use has been abandoned. Phophodiesterase inhibitors such as pentoxyfilline, which is useful in peripheral vascular diseases have also been tried as well as Xanthine oxidase inhibitors (Allopurinol) with discouraging results. Diuretics such as acetazolamide and frusemide have recorded varying success[35].

Hypertonic / hyperosmolar agents creates an osmotic gradient with the brain acting as a modified osmometer. Glucose, sucrose, urea, mannitol, sorbitol, glycerol, dextran have all been tried with inconclusive efficacy. Glycerol improves mortality without improving functional recovery and also causes subclinical hemolysis[36]. However, of all the hypertonic agents, it has the least rebound increase in intracranial pressure since it is metabolised by the brain. Others would cause fluid drift or a shift back to the brain when the concentration of the solute in the blood becomes lower than that of the brain. Mannitol is usually given at a dose of 0.25 – 0.5g/kg over 20 minutes and could be repeated every 6 hours up to a maximum of 2g/kg.

Hypoosmolar agents such as 5% dextrose in water would cause hypoosmotic cerebral oedema and further aggravate the cytotoxic cerebral oedema. Its use should be discouraged[35]. SIADH also causes hypoosmotic cerebral oedema and occurs in 10% of stroke patient[32]. Early detection and fluid restriction are beneficial. Steroids, which have been used in most life threatening conditions, have also been tried. The rationale for its use include a) to counteract the stress factor; b) to reduce cerebral oedema; c) to reduce the intracranial pressure; d) to strengthen the blood brain barrier and e) reduce the production of inflammatory cytokines such as IL-1; TNF and prostaglandin[37].

Dexamethasone – a potent anti-inflammatory glucocorticoid with virtually no mineralocorticoid activity has been tried in high and low doses with a consensus that its use should be discouraged. Increased early mortality was recorded in patients who had high dose of steroids[38]. Its usefulness in the vasogenic cerebral oedema complicating subdural hematoma, brain tumors and cerebral abscess has been well established but not in the predominantly cytotoxic cerebral oedema in stroke.

Aspiration pneumonitis would be prevented by regular sunctioning, chest physiotherapy and antibiotics could be added as appropriate[31].

Dysphagia with aspiration occurs in 51% of conscious stroke patients leading to aspiration. Nasogastric tube feeding is encouraged in such patient[39]. Oral intake is allowed if a swallow test with about 50mls of water is tolerated.

Early subacute phase: The complications are as tabulated in Table 3.

Pulmonary embolism accounts for 9-13% of all stroke deaths[28] and 25% of late death[29] occurring after one week. This could complicate deep venous thrombosis, which occurs in 75% of hemiplegic legs[40]. 5000 units of subcutaneous heparin every 8 or 12 hours could be given after 48hrs of the ictus with caution.

Hyperglycaemia complicates 28% of stroke[41] and increases the risk of early progression. It needs to be treated with insulin. Stroke patients with normoglycaemia at the time of ictus fare better than those with hyperglycaemia. Under ischaemic conditions, glucose is metabolised anaerobically and anaerobic metabolites such as lactate are generated with their deleterious effect on neurones.

Fever should be treated as this causes vasodilatation and worsens cerebral oedema.

Intraurethral catheterisation should be avoided as much as possible to prevent urinary tract infection. Paul's tubing or condom could be used.

iii) Late subacute and chronic phase

Passive and active physiotherapy should commence within 24 hours of admission[2] .

Adequate nursing care with change of position every 2 to 4 hours or the use of special pressure mattresses to avert pressure sores should be encouraged.

Subacute and chronic care should commence after one week and patient should be rehabilitated physically, socially and psychologically. Family support is important as up to 50% of stroke patients develop depression during the course of illness[31].

The Mathew score or the NIHSS or any other stroke score could be used to monitor the progression, level of consciousness or worsening of the neurological deficit.

Prognosis

The overall stroke related case fatality is 20 – 35%[29]. However, the prognosis in each patient depends on a) the location of the infarct (posterior fossae or deep location carries a poor prognosis), b) size c) level of consciousness on admission, and d) later progression of neurological signs, haemorrhagic transformation and development of raised intracranial pressure.

Patients with cerebral infarction have a recurrence rate of 12 –17% in the first year and 7% thereafter[42].

***Prevention*:**

Regular preventive measures include the removal of the risk factors if identified. In about 12% of Nigerians below the age of 40, no risk factor was identified[15].

Hypertension and diabetes should be controlled. Smoking and alcohol should be discouraged. Normal weight should be maintained with regular exercise. Secondary prevention should commence early during the treatment of stroke[43].

Drugs used in prevention include aspirin (with 25% efficacy) at a low dose of 75 –300mg; at higher analgesic doses this anti-platelet effect is lost. Aspirin is an irreversible inhibitor of the cyclo-oxygenase pathway. At low doses, it inhibits thromboxane-A_2 synthesis (responsible for platelet aggregation and vasoconstriction) in the circulating platelet while at high doses, prostacyclin (inhibits platelet aggregation and causes vasodilatation) synthesis in the vascular endothelium is inhibited. Thus, at high doses, the initial benefit of thromoxane A_2 inhibition is counteracted by simultaneous inhibition of prostacyclin.

Other drugs include ticlopidine 250mg bd; clopidogrel (caprie with 33% efficacy as an antiplatelet). Warfarin - an oral anticoagulant has efficacy of about 66%; but when facility for effective monitoring of anticoagulant is not readily available, aspirin provides a good preventive measure[43].

Carotid end-arterectomy has been successfully tried in patients with severe carotid stenosis greater than 70% except that it worsens cerebral oedema[44].

Exchange blood transfusion in sicklers reduces the risk of stroke[15].

CONCLUSION AND RECOMMENDATION:

New horizon has been opened for more effective management of stroke to reduce mortality and improve outcome. Thrombolytic therapy appears to be the only promising strategy for routine use in patients with acute ischaemic stroke. Its application in our setting appears unfeasible in view of the time – delay, limited CT scan and neurosurgical facilities. Data on all other agents are inconclusive. Haemodilution should be avoided. Combination of thrombolytics, agents to protect against the effects of ischaemia and anti-oedema measures are likely to be required. Possible agents that might halt the ischaemic process before infarction becomes inevitable include NMDA receptor blockers, ion channel blockers such as Nimodipine, free radical scavengers (21 Aminosteroids, Vitamins C and E), caspase inhibitors and Xanthane oxidase inhibitors such as Allopurinol.

Treatment of hypertension in the first ten days of ictus should be discouraged. Management of stroke by a stroke team in defined stroke units could reduce mortality and improve morbidity. In its absence however, treatment for stroke patient may not be optimal. Blood pressure are often inappropriately treated or excessively lowered and hypotonic glucose containing fluid administered frequently.

Critical changes in the nations health care delivery system is recommended and stroke management should be re-prioritised as a time dependent urgent medical emergency, just as is currently stressed for major trauma and acute myocardial infarction. Efforts should equally be made to set up stroke units and primary prevention strengthened.

REFERENCES

1. National Stroke Association Consensus Statement. Stroke: The first six hours. J Stroke Cerebrovasc dis 1993; 3:133–144.

2. **Adams RJ, Fisher M, Furlan AJ, et al.** Acute stroke treatment trials in the United States. Rethinking stategies for success. Stroke 1995; 26: 2216–2218.

3. Adams HP, Brott TG, Olinger CP, et al. Guidelines for the management of patient with acute ischaemic stroke. Stroke 1994; 25:1901–1914.

4. The National Institute of Neurology Disorders And strokes rt-PA Stroke Study Group. Tissue plasminogen activator for acute aschemic stroke. N. Engl J. Med. 1995; 333:1581–1587.

5. **Adams H, Brott T, Crowell R, et all.** AHA Medical/scientific Statement – Guidelines for management of patients with acute ischaemic stroke. A statement for health care professionals from a special writing group of the stroke Council, American Heart Association. Stroke 1994; 25(5): 1901 – 1914.

6 **Adams H, Brott TG, Furlan AJ et al.** Guidelines for thrombolytic therapy for acute stroke: A supplement to the guidelines for the management of patients with acute ischaemic stroke. A statement for healthcare professionals from a special writing group of the stroke Council, American Heart Association. Circulation 1996; 94:1167–1174.

7. **Camarate PJ, Heros RC, and Lathow RE.** "Brain attack" The

rationale for treating stroke as medical emergency. Neurosurgery 1994; 34(1): 144–158.

8. **HESS WD.** Pathophysiology of ischaemic stroke as determined by P.E:T. STROKE 1990; 21 (1): 2–3.

9. **Powers W.** acute hypertension after stroke: The scientific basis of treatment decisions. Neurology 1993; 43:461-467.

10. **Rosemary M.Gibson.** Does apoptosis have a role in Neurodegenerations ? *BMJ. 2001* ; 322 : 1539 – 1540.

11. **Siesjo B K, Bengtsson F.** Calcium fluxes, calcium antagonist and calcium related pathology in brain ischaemia, hypgylcemia and spreeding depression: a unifying hypothesis. J. Cerber. Flow Metab. 1989; 9: 127–40.

12. **Thomas G Bratt, Clarke Harley, David E Levy, Williams Barsen.** Urgent therapy for stroke. Part 1: Pilot study of tissue plasminogen activator administered within 90 mins. Stroke 1992; 23: 30–32.

13. THE rt-PA / Acute stroke group; An open safety/efficacy trial of rt-PA in acute thromboembolic stroke. Stroke 1991; 22:153

14. **Donian GA.** Investigation of patients with stroke and TIA Lancet 1992; 399:473–477

15. **Osuntokun BO.** Stroke in the Africans Afr. J. Med. Sci. 1977; 6: 64–76.

16 **Sotaniemi KA, Pyktinen J, Myllyia VV.** Correlation of clinical and computerised tomographic findings in stroke patients. Stroke 1990; 21:1562–6.

17. **Edlow, J.A., Caplan, L.R.** Avoiding pitfalls in the diagnosis of sub arachnoid haemorrhage. NEJM 2000; 342: 1: 29–35.

18 **Adams HP, Brott TA, Crosswell RM, Furlan AJ, Gomez CR, Grotta J, Helgason CM, Marler JR, Woolson, R.F., Zivin, J.A., Feinberg, W., Mayberg, M.** Guidelines for the management of patients with acute ischaemic stroke Circulation 1994; 90(3):1588–1601.

19. **Hund E, Grau A, and Hacke W.** Neurocritical care for acute ischaemic stroke. Neurologic Critical Care. 1995; 13(3): 511–527.

20. Maniscalo PM, and Petrous ZG. New team approach to acute stroke starts with EMS. J. Emerg Med. Service 1997; 22(5): 18–20.

21. **Bratina P, Greenberg LW et all.** Current emergency department management of stroke in Houston, Texas. Stroke 1995; 26: 409–414.

22. **Odusote KA.** Management of Stroke N Medical Practitioner 1996; 32 (5/6): 54–62.

23. Italian Acute Stroke Study Group Haemodilution in acute stroke Lancet. 1988; 1: 312–21.

24. **Anderson DC, Bottini AG, Jagiela WM.** Hyperbaric Oxygen in acute ischaemic stroke. Stroke 1991; 22: 1137–42.

25. **Schmidley JW.** Free radicals in C. N. S. ischaemia. Stroke. 1990, 25: 7–12.

26. **Rhotmans SM.** Glutamate and the pathophysiology of hypoxic ischaemic brain damage AN. Neuro. 1986; 19: 105–11.

27. **Shaw SWJ, Johnson RH.** The effect of Nafridrofuryl in the metabolic response to exercise in man. Acta. Neurol. Scand. 1975; 52: 231–237.

28. **Silver FL, Norris JW, Lewis AJ, Hachinski VC.** Early mortality following sroke: A prospective review. Stroke 1984; 15 (3): 492–496.

29 **Brown M, Glassenberg M.** Mortality factors in patients with acute stroke. JAMA 1973; 224 (11): 1493–1495.

30. **Standgaard S.** Autoregulation of cerebral blood flow in hypertensive patients. Circulation. 1976; 53: 720–727.

31. **Oppenheimer, S. , Hachinski, V.** Complications of acute stroke. Lancet 1992; 339: 721–727.

32. **Bounds JV, Wiebers DO, Whisnant JP, Okazaki H.** Mechanism and timing of death from cerebral infarction. Stroke 1981; 12 (1): 474–477.

33. **Katzman, R, Closen R, Klatzo I, Meyer JS, Poppius HM, Waltz, D.G.** Brain oedema in stroke. Stroke 1977; 8 : 572–540.

34. **Canderlise L, Colombo A, Spinner H.** Therapy against brain swelling in stroke patients: A retrospective clinical study in 277 patients. Stroke 1975; 6: 353–35.

35. **McCarthy KD, Reed DJ.** The effect of acetazolemide and frusemide on csf production J. Pharm Exp. Thee. (April) 1974; 189: 194–201.

36. **Meyer JS, Fukuuchi Y, Shimazu K,** Effect of Intravenous infusions of glycerol on hemisperic blood flow and metabolism in patients with acute cerebral infarction. Stroke. (Mar – Apr.) 1972; 168–180.

37. **Fishman RA.** The pathophysiology and treatment of brain oedema. In: Mathews WB.EDS. Recent Advances in Clinicals Neurology Vol. 2 Edingburgh; Churchhill living stone 1978; 119–29.

38. **Ogun SA, Odusote KA.** Effectiveness of high dose dexamethasone in the treatment of acute stroke. West Afr. J. Med 2001; 20 (1) :1–6.

39. **Hormer J, Massey E W, Rishi JE, Lathrop D L, Chase KN.** Aspiration following stroke. Clinical correlates and outcome. Neurology 1988; 38: 1359–62.

40. **Warlow C, Ogston D, Douglas AS.** Deep venous thrombosis in legs after stroke . part 1 : incidence and Predisposing factors. B. M. J. 1976; 1178–81.

41. **MELAMED C.** Reactive hyperglycemia in stroke J. Neurol. Sci. 1976; 29: 267–75.

42. **Chung chung chang, Chien Jen chen.** Stroke saccular trend of mortality from cerebral infarction and cerebral haemorrhage in Taiwan 1974 – 1988. Stroke: 1993;24:2–23.

43. **Charles Warlow.** Secondary prevention of stroke Lancet, March 21, 1992; Vol. 339: 724–72.

44. European Carotid Surgery Trial Collaborative Group: MRC: interim results of symptomatic patients with severe (70-91% or mild (0-29%) carotid stenosis. Lancet: 1991, 337: 1235–1243.