CHAPTER

45

Transient Cerebral Ischemic Attacks

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Introduction

"Stroke" is defined as rapid onset of focal neurological deficit, resulting from diseases of the cerebral vasculature and its contents. The term "transient ischemic attacks" *(TIA) implies warning symptoms of stroke usually lasting upto 30 minutes to one hour, and complete recovery within 24 hours*. Second TIA often causes more damage than the first. Without proper treatment one out of ten subjects who have had TIA will develop a stroke within a year.[1,2]

The normal functions of the brain are dependent upon a relatively constant supply of oxygen and glucose derived from the blood perfusing it (55 to 70 ml of blood per 100 g of brain per min). The *principal source of energy is almost exclusively oxidation of glucose*. If the blood flow is critically reduced below 15 ml per 100 g per min, the resulting ischemia with hypoxia, when sufficiently prolonged, may cause death of neurons and glia.

The mean arterial blood pressure, cerebrovascular tissue resistance, local metabolic products (pH, PaO_2, $PaCO_2$), together with several known and unknown factors, help to maintain the critical threshold of blood flow for energy metabolism. Furthermore, the blood flow varies in different areas of the brain and a self-regulatory mechanism (**"***autoregulation***"**) determines the regional flow to meet local metabolic needs.

To protect the brain from ischemia several collateral pathways exist. The four major extracranial arteries (carotid and vertebral arteries) form good-caliber, low-resistance anastomoses at the base of brain (*"circle of Willis"*). In addition, extracranial anastomoses exist between the cervical branches of the ipsilateral external carotid, subclavian and vertebral arteries. Such arterial anastomoses help to maintain cerebral blood supply even with severe narrowing or occlusion of major extracranial arteries or intracerebral arteries. These *post-Willisian anastomoses* further protect the brain tissue from the effects of occlusion of single cortical branches. However, in the presence of generalized arterial disease or multiple skipped stenotic lesions (atherosclerosis), anomalous or congenital variations, these collateral pathways may prove inadequate and predispose to cerebral ischemia.

Pathophysiology of Ischemic injury[3]

Experimental studies on pathophysiological events leading to cerebral ischemia have shown that *there is a dense central core, surrounded by a less dense zone of ischemia ("penumbra") and neuronal death occurs in this central focus unless perfusion is quickly restored*. On the other hand, *cells in the zone of penumbra remain viable for about three hours* (*"therapeutic window"*) and can be salvaged by

reperfusion or neuroprotective agents. Major factors, which enhance neuronal injury, are an *increase in intracellular cytosolic calcium concentration from failure of ionic-pump functions or "leaks", changes in Na^+/K^+ gradients, acidosis, release of free radicals* and other unknown factors, which in turn *disrupt the blood-brain barrier (BBB)* and microvascular function. Energy depletion from brain hypoxia is one of the key events that fails to maintain normal concentrations of cellular adenosine triphosphate (ATP), leading to delay in resynthesis of macromolecular proteins essential for endothelial cell structure and function. Energy failures also induce proteolysis and lipolysis, production of arachidonic acid and platelet activating factors, cell adhesion molecules, nitric oxide and free radicals, post ischemic hypo-or hyper-perfusion injuries resulting in further neuronal damage (*"ischemic cascade hypothesis"*). Thus, development of prolonged cerebral ischemia with or without infarction is the end-result of several highly complex "ischemia-modifying factors." For example, exposure of vascular endothelium to raised homocysteine (> 100 µmol / L) levels leads to reduced nitric oxide, increased levels of adhesion molecules and expression of procoagulant factors (PAI-1-plasminogen activator inhibitor, tPA-tissue plasminogen activator, PC – protein C and TM – thrombomodulin), which in turn promote platelet aggregation, leukocytes adhesion and obstruction to cerebral perfusion. *Transient Ischemic Attack (TIA) implies cerebral ischemia with complete recovery of focal neurologic deficit within 24 hours, resulting from platelet-fibrin micro emboli ("embolic hypothesis") or "hemodynamic crisis".* In "subclavian steal syndrome" transient brain stem ischaemia can be induced by exercising the arm that has significant stenosis of the subclavian artery. It is postulated that blood flow is reversed in ipsilateral vertebral artery precipitating brain stem ischemia.

Symptoms

The symptoms of transient ischemia are usually located in the *carotid-middle cerebral axis* or in the *vertebro-basilar territory.*

Carotid territoryTIA syndrome

1. ***Ipsilateral*** mono-ocular visual loss ("*amaurosis fugax*");
2. ***Contralateral*** homonymous visual field defect;
3. ***Contralateral*** weakness or clumsiness of hand, arm face or leg, with or without sensory loss;
4. ***Confusional state or aphasia*** (loss of understanding meaning of words, or names of objects etc);
5. Combination of above symptoms.

Vertebro-basilar TIA syndrome

1. ***Diplopia***;
2. Binocular *visual loss* ("out of focus" vision);
3. ***Vertigo*** ("dizziness"), *incoordination* (ataxia) or both;
4. Bilateral, unilateral or *alternating paresis of limbs*;
5. Dysarthria (*slurred speech*);
6. Dysphagia (*swallowing difficulty*);
7. Memory problems (*transient amnestic syndromes*);
8. Combination of above.

The *diagnosis of TIA is based on historical information* as given by patient or reliable observers. No investigative modality can substitute for careful history. *Face-arm-speech test (FAST)* helps to recognize TIA or stroke syndrome. Here, person is asked to smile, to check for facial or mouth weakness, elevation of both limbs will detect weakness and difficulty in speaking clearly or understanding the command will point to dysarthria or aphasia. However subjects having non-dominant hemispheric ischemia may not be aware of their deficits (agnostic syndromes), whereas patients with dominant hemispheric injury may have aphasic

difficulty. The latter situations may interfere with clinical evaluation.

A typical history of *TIA is a discrete event of sudden onset* where the symptoms reach maximum severity at the onset and intensify over next few minutes. Sometimes there is progressive march of symptoms from face, arm or leg, or to another part of the body. *The symptoms may wax or wane but vague episodes are not TIA.* Accompanying neurologic deficit should resolve within an hour and disappear completely by 24 hours. *The usual duration of TIA is 5 to 30 minutes but symptoms lasting less than few seconds are usually not TIA.* When TIA persists longer than one hour, the underlying mechanism may be a micro infarct!

As described above the *symptoms of TIA, alone or in combination are usually located in specific arterial territory (carotid or vertebro-basilar).* For example subjects having episodes of *ipsilateral mono-ocular blindness* alternating with contralateral weakness or heaviness of limbs may be indicative of ipsilateral carotid stenosis with local embolism to middle cerebral territory. *Sensory symptoms* are usually described as numbness, paraesthesia or tingling and often restricted to hand, face or both. *Transient speech difficulties* like naming may indicate aphasic disturbance. Likewise transient difficulty with articulation (*dysarthria)* may be accompanied by *vertigo, ataxia or diplopia* suggestive of vertebro-basilar TIA. *Blurred vision or distorted vision* is common but blindness is rare; if accompanied by headache this visual symptoms may be suggestive of migraine. *Vertigo per se should not be attributed to vertebro-basilar ischemia* unless accompanied by other motor or sensory symptoms, dysarthria or ataxia. *However, isolated diplopia, dysarthria or dysphagia may not be TIA.* "Drop attacks" from transient quadriparesis may be TIA or a seizure. *Likewise transient global amnesia* where patient is unable to form new memories for hours without other focal neurologic signs may be an epileptic event of vascular etiology. Detailed examination of fundus may reveal fibrin- platelet, cholesterol or other type of embolic material in ipsilateral retinal vessels in patients with history of *amaurosis fugax*. It may also reveal evidence of diabetic, hypertensive retinopathy.

Risk factors [4,5,6,7]

Apart from non-modifiable risk factors like i) *age*, ii) *race*, iii) *gender*, iv) *family history*, the common controllable or treatable (modifiable) risk factors include i) *arterial hypertension*, ii) *diabetes mellitus* (poorly controlled), iii) *cardiac disease* (ischemic heart disease and cardiomyopathies of varied etiologies etc), iv) *tobacco use* (smoking or chewing), v) *lipoprotein abnormalities* (high cholesterol levels), vi) *lack of regular physical exercise* and vii) *miscellaneous factors* (e.g. oral contraceptives, alcohol consumption, high fibrinogen level, protein C and S deficiency, hyperhomocysteinemia etc) .

Poorly controlled hypertension is primary treatable risk factor for cerebral atherosclerosis and improved management leads to decline in stroke burden. It should be noted that cerebral atherosclerosis is usually accompanied by coronary, carotid and peripheral artery disease which may be symptomatic or asymptomatic. Furthermore sudden deaths from myocardial infarction are not uncommon thus proper diagnosis and management of TIA will include management of co-existing coronary artery disease as well as management of hypertension.

Cerebral atherosclerosis involves major extracranial as well as intracranial vasculature. Atheromatous plaques containing lipids are located at branches, curves and bifurcations and in presence of hypertensive and diabetic states these plaques grow in size to narrow the lumen (arterial stenosis). When stenotic lesions are of significant size (> 70%), any drop in mean arterial pressure (hypotension) will result in decrease perfusion distally and may produce transient ischemic attack (*hemodynamic theorey).* It is also documented that break in endothelial lining over a plaque surface attracts platelet adhesions / aggregations and thrombus formation; detachment of plaque-thrombus material leads to distal embolization and precipitates an ischemic attack. Thus in treatment

and prevention of TIA it would be necessary to distinguish between hemodynamic hypoperfusion events and "local embolism" episodes.

The precise role of Diabetes Mellitus in pathogenesis of cerebral atherosclerosis is not very clear. Cerebral microvascular disease is a leading cause of TIA and stroke. It is postulated that excessive glycation and oxidation, endothelial dysfunction and increased platelet aggregation may be responsible for endothelial proliferation and thickening of plasmatic membrane in small blood vessels ("lipohyalinosis") leading to cerebral ischemic injury. The role of prothrombotic state, platelet aggregability, elevated fibrinopeptide and D-dimer in pathogenesis of ischemic infarct are not certain but suppressed fibrinolytic activity is common. Of many unknown factors in pathogenesis, deficient insulin secretion, resistance to action of insulin at level of "insulin receptors", changes in counter regulatory hormones (e.g. glucagons, growth hormone etc) and decrease in hepatic sensitivity to insulin action in suppressing glucose output have received more attention. In view of complicated pathogenetic mechanisms early recognition and treatment for better glycemic control may reduce recurrent TIA's or minor strokes.

High risk group

In elderly subjects over the age of 60 years, a stroke is more likely to develop within three months of first TIA, if a) TIA lasts longer than 10 minutes; b) if symptoms include severe weakness and speech difficulty; c) if hypertension and diabetes are poorly controlled and d) if there is family history of stroke. In such subjects complete recovery within three weeks (reversible ischemic neurological deficit – RIND) is not uncommon but neuro imaging usually demonstrates small lacunar type infarction.

Diagnosis

TIA is considered a medical emergency and diagnosis should be established to prevent a major stroke. The following tests are considered most informative:

Physical examination

Physical examination including cuff pressure readings. Presence or absence or inequality of pulsations in arms and neck vessels and *ultrasound scanning of carotid arteries* for detection of significant lesions. A bounding superficial temporal or supra orbital pulse may suggest occlusion or high grade stenosis of internal carotid artery with collateral blood flow from ipsilateral external carotid artery. Auscultation may reveal high pitch carotid bruit over high grade stenotic lesion and low pitch flow murmur over collateral vessels. Transmitted cardiac murmurs in aortic stenosis or hyperdynamic flow murmurs in hyperthyroidism or arteriovenous malformation will need careful evaluation. Absence of a bruit over carotid artery in a patient of TIA does not exclude tight or occluded carotid artery lesion; sometimes bruit may be heard on the side contralateral to an occlusion. In summary neck murmurs should be interpreted with caution.

Blood tests

Blood tests (hematocrit, platelet count, prothrombin time and special tests when necessary- e.g. protein C / S deficiency, homocysteinemia). Complete lipidogram is advisable to measure cholesterol and Low Density Lipoprotein levels to initiate statin therapy when indicated.

Electrocardiogram

Electrocardiogram [8] to rule out irregular heart rhythm (atrial fibrillation) and myocardial ischemia.

Echocardiogram

Echocardiogram [9,10] (heart ultrasound) to assess cardiac function and exclude cardiomyopathies, valvular dysfunctions, mural thrombi etc.

Neuroimaging

Neuroimaging[11] - computed axial tomography (CT) to rule out stroke mimic lesions (e.g. post epileptic Todd's paresis, tumors). Magnetic Resonance imaging and angiography (MRI and MRA) may

show embolic vascular lesion but parenchymal injury is not found. However special studies like brain SPECT may show evidence of cerebral hypoperfusion.

Transcranial Doppler sonography and cerebral angiography may be required

Differential Diagnosis

The following conditions can mimic episode of TIA i) *hypoglycemia*, ii) *akinetic seizures* with transient paresis iii) *vertigo or dizziness from labyrinthine disorders*, iv) focal or visual or sensory symptoms in *migraine* patients, v) episodic confusional states in *temporal lobe lesions*. Here meticulous history and careful physical evaluation with appropriate or specific diagnostic test will prove helpful in majority.

Hypoglycemia

In a diabetic subject on oral hypoglycaemic agent and with history of having missed a meal, the episode of limb weakness associated with unconscious state may mimic TIA, particularly if evidence of vascular disease is present. Here accurate history in support of above and blood sugar levels in hypoglycemic range (below 40 mg%) as well as dramatic therapeutic response to 50 cc of 50% glucose infusion will settle the diagnosis.

Seizures

Not infrequently, a subject with history of epilepsy having missed regular medication may be found in an unconscious state with stiffness or flaccid limbs simulating paresis. The episode is usually brief and often preceded by tonic or clonic involuntary movements. Tongue bite and or urinary incontinence helps to arrive at a diagnosis.

Dizziness from labyrinthine disorders

Episodic vertigo associated with imbalance or unsteady gait and unsustained nystagmus may mimic vertebro basilar ischemia. Here, history of deafness, tinnitus, sweating without frank evidence of limb or cranial nerve paresis will prove helpful.

Migraine aura

It may be difficult to distinguish TIA from migraine, but younger age of the patient, previous history of migraine and associated headache, nausea or photophobia will be more suggestive of migraine than TIA. Above symptoms in presence of explosive headache and neck stiffness or syncope may suggest acute subarachnoid hemorrhage and specific investigations like CT scan or CSF test may help.

Treatment [12,13]

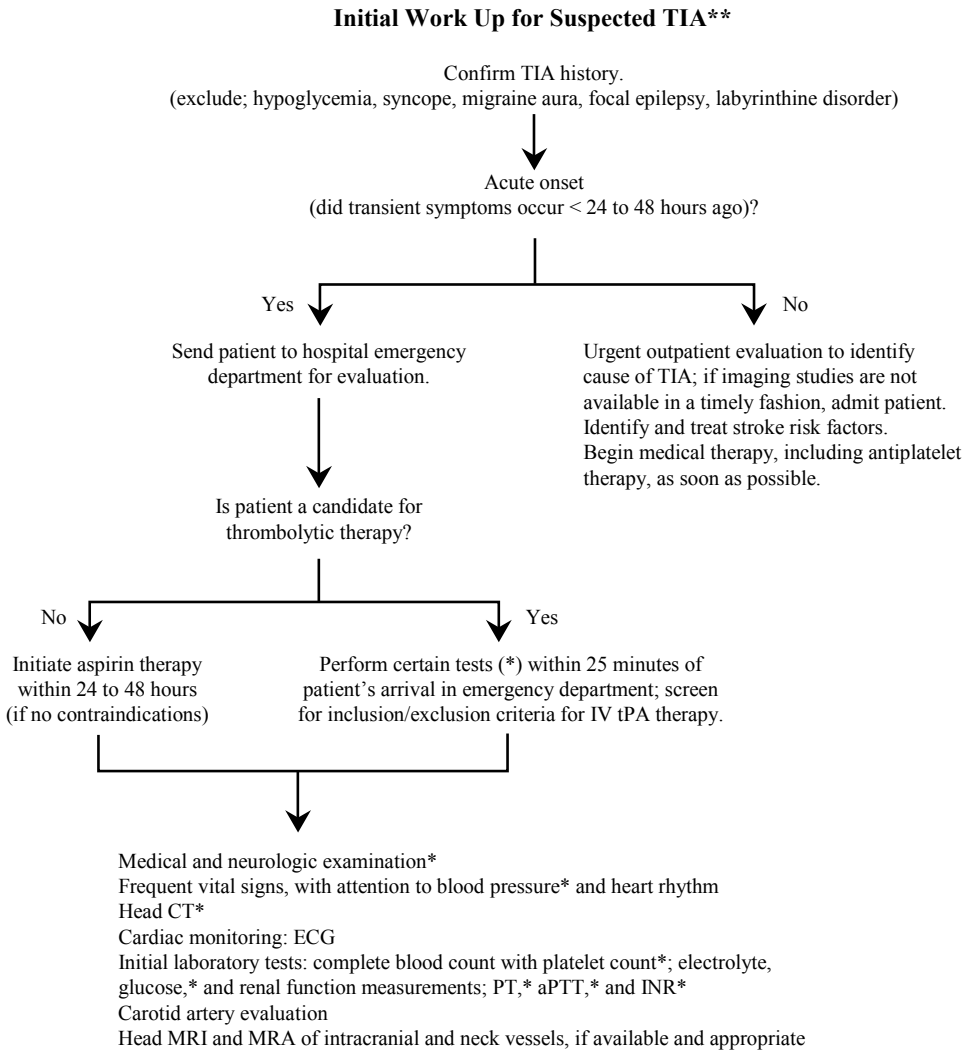
TIA is no longer considered a benign event, but a critical medical emergency which demands immediate evaluation to prevent disabling stroke. 90-day post TIA risk of stroke is estimated at 10%, and in nearly half of them stroke occurs within the first two days, particularly if TIA is related to internal carotid artery stenosis. Subjects who arrive within 180 minutes of symptoms should undergo urgent clinical evaluation and selected laboratory tests (blood count, platelet count, prothrombin time with INR , electrolytes and glucose levels) to determine if the patient is a candidate for thrombolytic therapy. CT scanning of head should be performed to exclude cerebral or subarachnoid hemorrhage or brain tumor. Thus confirmation of TIA, by clinical and diagnostic evaluation, is mandatory. The evaluation by tests should focus on ascertaining underlying etiology. The goal of therapy is to avoid development of cerebral infarction and, if already present, to restrict its progression or recurrence. Selection of therapies is case specific.

An algorithm with key points for evaluation of TIA is listed in Figure 1.

Blood Pressure

In acute stroke, "cerebral autoregulation" is lost and blood flow in the infarcted areas is solely dependent on mean arterial BP. In presence of severe hypertension (e.g. BP over 220 / 120 mm Hg) parenteral therapy with titratable agents such as I.V. labetalol or enalapril which reduce

Figure 1 : Initial work-up for the patient with possible transient ischemic attack (TIA)



(IV = intravenous; tPA = tissue-type plasminogen activator; CT = computed tomography; ECG = electrocardiography; PT = prothrombin time; aPTT = activated partial thromboplastin time; INR = International Normalized Ratio; MRI = magnetic resonance imaging; MRA = magnetic resonance angiography)

{** Solenski NJ. Transient Ischemic Attacks. American Family Physician. 2004; 69: 1665-1674}

blood pressure smoothly are recommended. Calcium channel blockers are best avoided because they produce severe drop in blood pressure in some patients. On the other hand, raised blood pressure levels in hypertensive and non-hypertensive stroke subjects often fall unpredictably within 24 hours to few days, worsening perfusion in ischemic penumbra leading to irreversible injury. Therefore, *any significant hypotensive episode should be promptly treated to prevent extension of cerebral infarction.*

Measures to Improve Cerebral Blood Flow

Hematocrit is one of the chief determinants of whole-blood viscosity. It is postulated that lowering the hematocrit value to 30 to 33 per cent with hemodilution therapy improves CBF and oxygenation of infarcted tissues. However, results of recent randomized trials have failed to show consistent beneficial effects of hemodilution therapy.

Specific Therapy[14]

Platelet Antiaggregants[15]

Antiplatelet drugs reduce risk of stroke by 25% (Antiplatelet Trialists collaboration 1994). The benefit of therapy is not influenced by age, sex and presence of hypertension or diabetes.

Acetylsalicylic acid (aspirin)

Acetylsalicylic acid (aspirin) prevents platelet aggregation by blocking production of platelet derived thromboxane-A_2 but it also suppresses release of prostacyclin from vascular endothelium. The effects of aspirin are immediate and last for 7-10 days of life of platelet. It is widely used in primary and secondary prevention of strokes. In the treatment of TIA, RIND and in secondary prevention of strokes, the optimal dose is still debated. Low-dose therapy (75-100 mg/day) is as effective as higher dose (325 mg/day or more)(ref UK TIA study Group 1991, Dutch TIA trial 1991 and Swedish Aspirin low dose trial collaborative group 1991). Other antiplatelet drugs like sulfinpyrazone or dipyridamole used alone do not offer any specific advantage. However, in female "non-responders" aspirin combined with dipyridamole (upto 200 mg twice a day) may prove more effective on account of its synergistic activity. Aspirin therapy does alter clotting of blood and thereby carries a marginal risk for intracerebral bleed. Aspirin therapy does not appear to increase the frequency of carotid-plaque hemorrhage. Soluble aspirin is often associated with side effects like epigastric pain, peptic ulcer disease and GI bleed. Use of enteric coated aspirin with ranitidine may increase safety of long term use.

Dipyridamole

Dipyridamole is vasodilator and inhibitor of platelet phosphodiesterase enzyme and a potent platelet antiaggregant. Dipyridamole in combination with aspirin is often treatment of choice in a subject with an impending stroke. Sustained release preparations of Dipyridamole (200 mg twice a day) in combination with 75 mg aspirin are often prescribed.[16]

Ticlopidine (a thienopyridine derivative)

Ticlopidine (a thienopyridine derivative) inhibits platelet aggregation by interfering with ADP – induced transformation of glycoprotein IIb / IIIa receptors on platelet membrane. It has shown more than 30% reduction in "stroke risk" when compared to aspirin therapy. It is equally beneficial to men and women. Subjects with diabetes mellitus, those on antihypertensives and those with elevated creatinine levels benefit more with ticlopidine (250 mg b.i.d.) than aspirin. However, the drug is relatively toxic (i.e. reversible neutropenia, diarrhea). *Clopidogrel* (75 mg / day) is reported to be safer than ticlopidine. In a recent trial (MATCH study), combination of clopidogrel (75 mg) and aspirin (75 mg) showed no real benefit in outcome of vascular end-points. Newer antiplatelet agents like Abciximab are potent antagonists of platelet glycoprotein IIb / IIIa receptors but hazards like symptomatic intracranial bleeding are a major concern.[17]

Anticoagulants [14,18]

Parenteral heparin and long-term oral anticoagulants have been extensively tried in acute cerebral ischemia, particularly in elderly subjects having non-rheumatic atrial fibrillation (NRAF) or from cardioembolic source. Though such treatment can prevent extension of thrombus, its value in completed stroke is doubtful and its use is often fraught with dangers. Judicious use in recurrent TIAs, thrombosis in-evolution, cardiogenic embolisation to the brain in subjects not responding to platelet antiaggregant therapy, and in patients who are not fit for carotid surgery has been suggested.

To minimize the risk of hemorrhagic complications, it is necessary that cerebral ischemia or hypoperfusion is confirmed by special investigations like Magnetic resonance imaging (perfusion weighted and diffusion weighted images). If a subject worsens under anticoagulant therapy diagnostic re-evaluation should be done and even a second CT or MRI may have to be carried out to ascertain the cause of worsening (extension of ischemic injury or intracranial bleeding).

Heparin

Heparin is heterogenous mixture of glycosaminoglycan of variable molecular weight (4000-40,000 daltons), its anticoagulation action is immediate with a half life time of 60 minutes. It prolongs activated partial thromboplastin time (aPTT), whole blood clotting time as well as activated clotting time. aPTT value of 1.5-2 times control is considered therapeutic range. Somehow heparin of bovine origin enhances platelet aggregation causing thrombocytopenia (mild in 80%). Heparin induced thrombocytopenia with recurrent thromboembolism ("white-clot syndrome") is a rare complication.

During the stage of heparinisation partial thromboplastin time (aPTT) is kept up to 2.0 times the control, and 3000 to 5000 units of heparin are often given on 6 to 8 hourly basis. In practice, an intravenous bolus of 100 units/kg body weight followed by continuous infusion (1000 units per hour for 24 hours), under constant supervision for bleeding parameters, preferably in an acute care unit is advocated. Newer synthetic short-chain (low molecular weight) heparins or heparinoids are safer and effective but expensive.

Oral anticoagulant drugs

Oral anticoagulant drugs[14] have structural similarity to vitamin K and they inhibit hepatic synthesis of clotting factors II, VII, IX and X. The therapeutic effect is delayed upto 72-96 hours after initiation of therapy. Of the many oral anticoagulant drugs, coumarin sodium (2 to 5 mg/day) is generally well tolerated. Prothrombin index (ideally INR) of 2.0 to 3.0 is usually maintained for months or longer, keeping a close watch on hemorrhagic complications (like GI or urinary tract bleed) in elderly subjects or in severely hypertensive patients. *In the presence of actively bleeding ulcers, malignant hypertension, hepatic failure and poor patient compliance, anticoagulant treatment is contraindicated.*

A recent Cochrane review (2004)[19] concluded that in patients with TIA or minor stroke, there was no significant difference in outcome of vascular events in those receiving anticoagulant versus antiplatelet drug therapy. The current evidence suggests that aspirin is treatment of choice when compared to anticoagulants for patients with non-cardioembolic stroke. However anticoagulant therapy significantly benefits high-risk patients with atrial fibrillation in the elderly subjects whereas aspirin may still be the drug of choice in stroke prevention in low risk group in the younger age. There is dire need for well planned randomized double blind controlled studies to define the role of Antithrombotic agents in "cryptogenic stroke" (PFO/ASD related) antiphospholipid antibody syndrome, arterial dissections and intraluminal clot syndromes. Furthermore, evaluation and treatment of associated risk factors in all categories needs greater emphasis.

Raised homocysteine (ThCY) level – "An Independent Risk Factor" for Vascular Disease":

Elevated levels of tHcy have been reported as significant and an "independent risk factor" for myocardial infarction and stroke, though precise mechanism linking raised tHcy to vascular disease have not been established. It has been suggested that raised tHcy harms endothelial cell functions, increases oxidative stress and thereby risk to thrombosis. Treatment with vitamins (B_6, B_{12}, Folic acid) reverses the raised levels of tHcy and thereby possibly prevents progression of vascular disease. Some studies have shown clinical benefit with higher dose of vitamin B_{12} therapy in coronary angioplasty and peripheral vascular disease. On the other hand, results of randomized controlled trials (VISP- Vitamin Intervention in Stroke Prevention; VITATOPS- Vitamins to Prevent Stroke) have not supported above hypotheses. Thus, vitamin therapy (B_6, B_{12}, Folic acid) in prevention of recurrent stroke continues to be debated.

Statins and Stroke [6,7]

Hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitors or statins, have also been considered beneficial in prophylaxis against myocardial infarction, stroke and other vascular events. The integrity and function of endothelium

depends on synthesis of nitric oxide and inhibition of smooth muscle proliferation, endothelial leukocyte adhesion and platelet aggregation. Inhibition of generation of NO by nitricoxide synthase has atherogenic effect. It has been postulated that beneficial effect of statins may have multiple mechanisms, like upregulation of eNOs and increase blood flow, reduce inflammation or it may be an independent "class effect".

Recent data from **SPARCL Study** (Stroke Prevention by Aggressive Reduction in Cholesterol Levels) suggest that statins reduce a risk of recurrence of stroke and that stroke prevention may be independent of their effects on lowering low-density lipoprotein.

Surgical Management [17,21]

Thromboendarterectomy with or without reconstructive vascular surgery within a few hours or days after an acute ischemic brain infarction is considered risky, because early reperfusion may convert pale infarct into a hemorrhagic one. However CEA has been established as a useful procedure in prevention of stroke in subjects having TIA from lesions in extracranial carotid circulation. Duplex ultrasound is non-invasive investigation of choice as a screening test to locate the plaque and measure the degree of obstruction and ulceration. Frequent embolization of platelet fibrin material from ulcerated plaque is considered an important cause of recurrent TIA. Here Real time, B-mode Duplex scanning of carotid artery provides good information on thickness of arterial wall, residual lumen and plaque characteristics. However B-mode scanning is less accurate for assessing mild degree of stenosis. Phonoangiography, periorbital directional Doppler ultrasonography, oculoplethysmography, and ophthalmodynamometry are other screening tests. MRA and CT angio images of the carotid artery demonstrate vessel wall, residual lumen, and pathological process within the plaque. It also helps in detecting dissection. At present, MR angio or CT angio has become an important noninvasive test for evaluation of lesions of intracranial and extracranial vasculature. If surgery (CEA) is planned, digital intravenous subtraction angiography (DISA) may be carried out as an alternative to conventional digital intraarterial arteriography. Demonstration of a stenotic lesion greater than 70% or presence of ulcerated plaque is considered important criteria for CEA in subjects with recurrent TIA in that territory. Perioperative morbidity and mortality under 5% is considered an acceptable risk.

Recent well-designed controlled studies (NASCET – North American Symptomatic Carotid Endarterectomy Trial [21]) have confirmed beneficial results of endarterectomy in tight cervical stenosis (70-99%). It has been observed that there is 17% absolute and 35% relative risk reduction for ipsilateral stroke and stroke death, if endarterectomy is combined with best medical care. Patients who benefit the most from surgery are those with highest risk-factors. During immediate post-operative period higher doses of aspirin and control of all risk-factors are mandatory. The benefit by carotid endarterectomy in symptomatic lesions with mild stenosis (30-69%) or in asymptomatic cases is controversial.

Stenting and Angioplasty in Symptomatic Carotid Stenosis

Though CEA appears well established in tight symptomatic carotid stenosis (> 70%), stenting with or without embolic protection devices are getting accepted as alternative mode of treatment in cases with CEA is not feasible or difficult. It has been reported that fewer complications occur with stenting as compared to CEA (e.g. neck hematoma, cranial neuropathy etc.).

The **SAPHIRE Study** (Stenting and Angioplasty with Protection at High Risk for Endarterectomy) assessed results of stenting against carotid endarterectomy (CEA) in subjects with greater than 50% symptomatic or 80% asymptomatic stenosis. It was reported that "stenting arm" had lower cumulative incidence of stroke, myocardial infarction or death at 1 year compared to those who had CAE. Recurrent intervention was less

common in the patients in the stenting group. The results indicate that carotid stenting with embolus protection is at least as good as CEA, particularly in patients with substantial comorbidity or for inaccessible lesions in elderly patients.

Summary

TIA is a serious condition and medical emergency requiring immediate evaluation and treatment to prevent a stroke. Confirmation of diagnosis is vital. Medical conditions like hypoglycemia, migraine etc which mimic TIA should be identified. TIA syndrome in carotid territory needs special evaluation by Duplex sonography to detect significant stenosis (> 70%) near bifurcation. Recurrent TIA in the same territory leaves neuro deficit and this needs prevention by appropriate therapy (platelet antiaggregants, anticoagulants, surgical intervention). Associated risk factors (e.g. high blood pressure, tobacco use, uncontrolled diabetes mellitus, high cholesterol level and obesity etc) need special emphasis. Lifestyle modification and lack of physical exercise cannot be ignored. In high risk group where TIA lasts longer than 10 minutes with significant neuro deficit in elderly subjects having diabetes or hypertension will need special attention and treatment. Diagnostic tests should include cardiovascular evaluation and ultrasound scanning of carotid arteries. Special neuroimaging tests like CT/MRI and CTA/MRA to visualize cerebral vasculature and detect asymptomatic lesions are helpful in planning long term management and prevention of stroke.

No conflict of interest

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