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Clinical practice guidelines for the management of ischemic stroke in Pakistan

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Background

Ischemic stroke represents a huge global burden, being the leading cause of physical disability and the third-leading cause of death worldwide.r Although rigorous epidemiological data from Pakistan are lacking, stroke is certainly the commonest reason for admission to a neurology ward in our part of the world, as elsewhere. Recent years have seen a number of new developments in the clinical approach to stroke, including in the areas of diagnostic work-up, acute treatment and secondary prevention. These developments enable the formulation of clinical practice guidelines for achieving standardized management of ischemic stroke, with the overall aini of improving the care of stroke patients. This article presents a set of guidelines that may be useful to clinicians involved in the care of stroke patients in Pakistan. The term 'stroke' is used here to refer exclusively to ischemic brain infarction; this paper does not address intracerebral hemorrhage.

Diagnostic Approach

The diagnostic approach to suspected stroke is summarized in the accompanying algorithm (Figure). Any sudden-onset focal neurological deficit must be considered a stroke unless proven otherwise. The first step in the evaluation of suspected stroke is medical stabilization with attention to airway, breathing and circulation. The second step is imaging of the brain, either with CT scar, if seen within 3 hours of symptom-onset, or preferably MR1 if the patient is seen later. Patients seen within 3 hours of stroke onset may be eligible for treatment with the intravenous thrombolytic agent r-t-PA (recombinant tissue plasminogen activator)'-, as noted in the accompanying algorithm; in practice, this constitutes only a very small percentage of stroke patients because most patients arrive outside the tirne window. Any patient being considered for thrombolytic treatment must undergo immediate non-contrast cranial CT scan. If the scan is normal, the thromboiysis checklist can be initiated.

All patients (whether they receive rt-PA or not) undergo a set of diagnostic tests to determine stroke subtype, which forms the basis for rational secondary prevention. This includes (i) cardiac evaluation (ECC and transthoracic echocardiogram with air-contrast); and (ii) cranio-cervical vascular evaluation (carotid duplex ultrasound for anterior circulation ischemia and MRA for posterior circulation ischernia). Additional tests including Iloiter monitoring. transesophageal echocardiography or blood hypercoaguiability profile, may be considered in cases of embolic stroke .where the initial work-up is negative. The goal of this work-up is to assign patients to one of four categories: small-vessel stroke (lacunar stroke); large-vessel stroke (atherothrornbosis in large-caliber artery such as internal carotid or bas'lar); embolic stroke (infarction in a major vascular territory such as major branches off the Circle of Willis or in the vertebro-basilar system); or unclear }

Acute thrombolysis

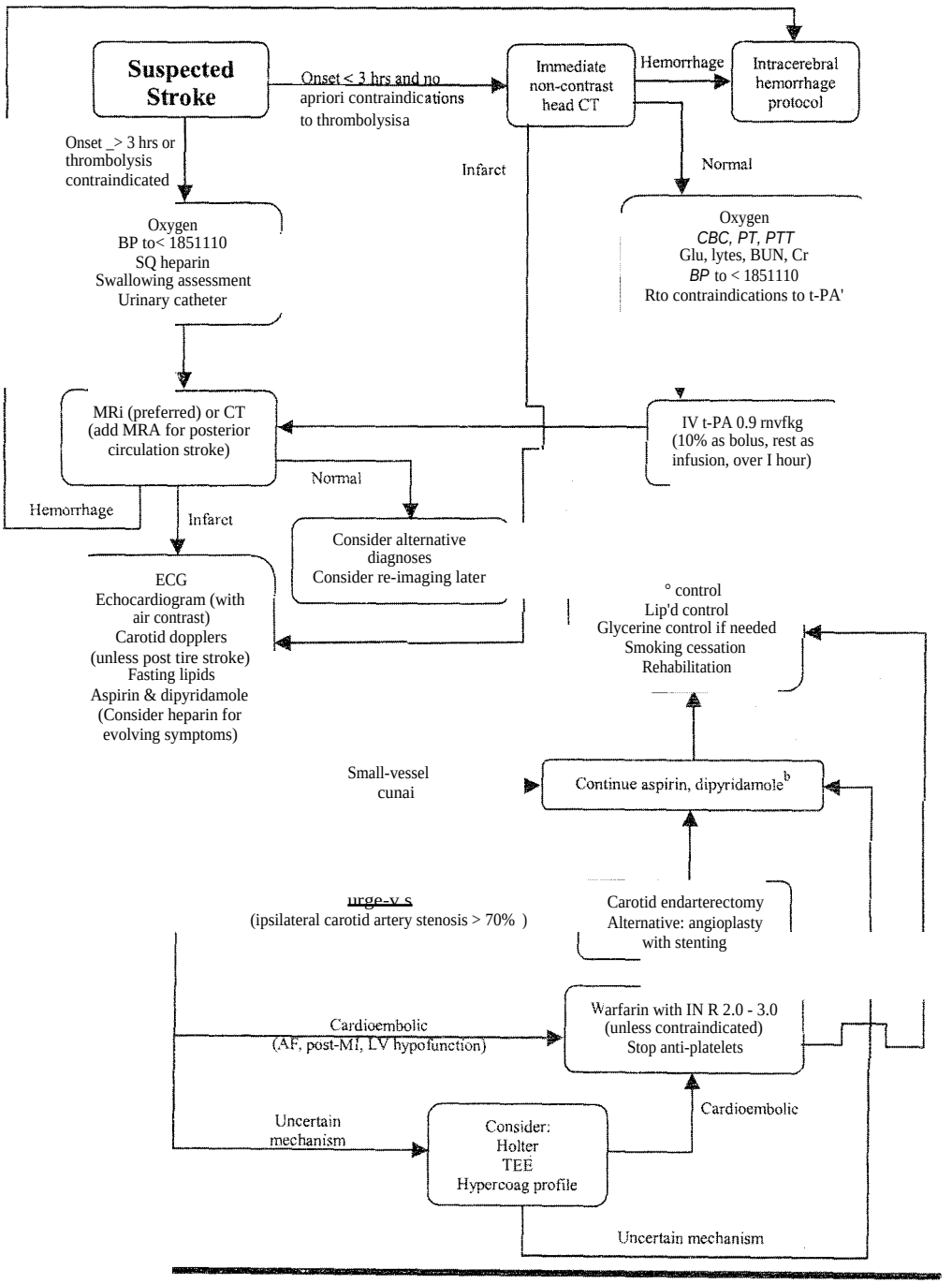
Acute treatment of the stroke patient includes intravenous rt-PA for patients seen within 3 hours of symptom-onset, as noted above. Time of onset is determined from when the patient was last seer] to be well; this is especially important for patients who wake lip with their deficit. The cost of the usual adult dose of rt-PA for stroke approaches Rs.100,000 in Pakistan. Although of proven efficacy is improving functional stroke outcome. the drug is associated with a I0-fold increase in the risk of symptomatic intracerebral hemorrhage.'- These factors underscore tile need to use rt-PA in stroke after careful clinical judgment and with detailed informed consent of patient and/or next of kin. The use of rt-PA should not be considered for patients who cannot be evaluated by a neurologist. Contraindications to the use of rt-PA are summarized in Figure.

Other acute considerations

All patients (whether they receive rt-PA or not), need careful evaluation and concurrent management of co-morbid conditions as appropriate, including diabetes mellitLIs, coronary artery disease, renal dysfunction and/or liver disease. If needed, blood pressure should be gently brought down under systolic i 85 and diastolic I I0.'-

Assessment sllouid be made with regards to swallowing. For nnild strokes, this can be done by asking the patient to swallow small sips of water while observing for cough or change it, voice. If the patient fails to swallow properly, 0€~ if stroke severity precludes swallou·ing assessment, a nasogastric tube must be maintained.

Most patients will also require urinary catheterization with a Foley catheter. In males without a history of prostate symptoms, a condom, catheter should be tried first.



[a] Contraindications to t-PA: Prior intracranial hemorrhage; history of intracranial neoplasm, aneurysm or AVM; stroke or head trauma within last 3 months; major surgery or biopsy of parenchymal organ within last 2 weeks; GI or genito-urinary bleeding within last 3 weeks; recent MI; seizure at stroke onset; disorder of hemostasis; prothrombin time > 15 seconds; use of heparin in previous 48 hours with prolonged partial thromboplastin time; use of low-molecular weight heparin during previous 48 hours; rapidly improving neurological deficit; mild, isolated neurological deficit, e.g. ataxia, dysarthria, or sensory loss alone; systolic BP => 185 or diastolic *BP > 110;* platelet count < 100,0001mm'; blood lucose < 50 mgldL or > 400 mg(dL.

[b] Dosages. aspirin 75-300 mg po daily; dipyridamole 200 mg po twice daily or 100 mg po three times a day.

P)An lormanklementot stroke

DVT prophylaxis

All patients must receive subcutaneous heparin 5,000 BID for prevention of deep-vein thrombo=is and reduction of pulmonary embolism risk.

Secondary prevention

All patients must receive targeted secondar_,

Table. secondary prevention.

Therapy	Indication	Strategy
Warfarin anticoagulation	Presence of atrial fibrillation Presence of prosthetic heart valve Embolic stroke in post-Ml period LV hypofunction (EF <35%)	Maintain INR 2.0 - 3.0 (2.5 - 3.5 for patient with prosthetic valve)
Anti-platelet agents*	All patients not requiring warfarin	Aspirin 300 nig qd in combination with either: (i? dip)ridamole 100 mg tidi or (ii) clopidogrel 75 ing qd
Carotid endarterecton°iy	Presence of internal carotid artery stenosis 70-99% ipsilateral to brain infarction in a patient with some demonstrable ftmctional recovery	Referral to an experienced vascular surgeon with proven lox; complication rate: carotid angiopiastq and scenting <,iso an option but safety and long-term efficac% unverified

* This recommendation is based on the author's best clinical judgment. Although data from randomized trials favors twice-daily Agarenox (aspirin 25 mg ,vith extended-release dipyridamole 200 ing) as the most efficacious anti-platelet regimen in secondary stroke prevention. neither Agcrcnox nor extended-release dipyridamole are available in Pakistan. The efficacy of combining regular dipyridamole with aspirin is unknown. The combination of aspirin and clopidogrel for secondary stroke prevention is currently under investigation.

prevention to reduce the risk of stroke recurrence. Options include anti-platelet therapy, oral anticoagulation with warfarin6 and carotid artery intervention.? indications for their use are summarized in Table.

Risk Factor Management

All patients must undergo aggressive management of all modifiable risk factors, including blood pressure control. glycemie control in diabetics, cessation of cigarette smoking, and reduction of serum LDL cholesterol to 100 mg/dL or less with inhibitors of HMG-CoA reductase. A number of medications are available for blood pressure reduction; some evidence suggests that angiotension-converting enzyme inhibitors and diuretics may be particularly beneficial in stroke patients.s The recommendation for serum LDL cholesterol reduction is based on trails of HMG-CoA reductase inhibitors ("statins") performed it, patients with primary cardiac disease; results from trials in stroke patients are currently awaited.

Rehabilitation

Rehabilitation requires a holistic approach that uses multiple supportive strategies to help stroke patients achieve maximum functional recovery. All patients should be offered the benefits of rehabilitation therapy, including physical, occupational and speech therapy, begun as early as feasible. Training must be administered in multiple areas, including gait, transfers and bed mobility, as well as speech/cognition and manual dexterity (occupational therapy).

Neuroprotective agents

Neuroprotective agents are drugs that inhibit the biochemical consequences of stroke at the cellular level. Although effective in animal models, so fat· no agent has proven efficacious in human clinical trials; accordingly, the use of neuroproteetive medication in ischemic stroke is not recommended at present. | 0 In Pakistan, a number of drugs are marketed with claims of neuroprotection, including= a-ents such as Hydergine (ergoioid inesYlate), Nootropil (piracetam), and Encephabol (pyritinol). The use of these and similar drugs is not supported by the available evidence.

Constraints

The above guidelines are based on evidence from randomized trials or high quality observational studies. and are internationally considered to be 'standard of care'. While economic and logistical realities may make them unfeasible for many practitioners in Pakistan, at a minimum the investigational work-up of suspected stroke must include cranial CT scanning. Clinical assessment alone cannot distinguish intracerebral hemorrhage from ischemic stroke - two coi-iditions that demand a vastly different management apprcac".

If the CT scan is normal or indicates infarction, anti-platelet therapy can be safely begun. If carotid artery intervention and the use of adjusted-dose warfarin with frequent prothroinbin time monitoring are not feasible. further work-up is unnecessary, and the anti.-platetet treatment should be used indefinitely, along with risk factor management as feasible.

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