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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. 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 aim 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 scan, if seen within 3 hours of symptom-onset, or preferably MRI if the patient is seen later. Patients seen within 3 hours of stroke onset may be eligible for treatment with the intravenous thrombolytic agent rt-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 time window. Any patient being considered for thrombolytic treatment must undergo immediate non-contrast cranial CT scan. If the scan is normal, the thrombolysis 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 ischemia). Additional tests including Iloiter monitoring, transesophageal echocardiography or blood hypercoagulability 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 (atherothrombosis in large-caliber artery such as internal carotid or basilar); 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 seen to be well; this is especially important for patients who wake up 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 in improving functional stroke outcome, the drug is associated with a 10-fold increase in the risk of symptomatic intracerebral hemorrhage. These factors underscore the 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 mellitus, 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 10.

Assessment should be made with regards to swallowing. For mild strokes, this can be done by asking the patient to swallow small sips of water while observing for cough or change in voice. If the patient fails to swallow properly, or if stroke severity precludes swallowing 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.
Consider alternative diagnoses
Consider re-imaging later
Oxygen
BP to < 185/110
SQ heparin
Swallowing assessment
Urinary catheter
ECG
Echocardiogram (with air contrast)
Carotid dopplers (unless post t/ee stroke)
Fasting lipids
Aspirin & dipyridamole (Consider heparin for evolving symptoms)
Small vessel 

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 2 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 < 100,000 mm'; blood glucose < 50 mg/dL or > 400 mg/dL.

DVT prophylaxis
All patients must receive subcutaneous heparin 5,000 BID for prevention of deep-vein thrombosis and reduction of pulmonary embolism risk.

Secondary prevention
All patients must receive targeted secondary...
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).

**Risk Factor Management**

All patients must undergo aggressive management of all modifiable risk factors, including blood pressure control, glycemic 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. The recommendation for serum LDL cholesterol reduction is based on trials of HMG-CoA reductase inhibitors ("statins") performed in 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 far no agent has proven efficacious in human clinical trials; accordingly, the use of neuroprotective medication in ischemic stroke is not recommended at present. In Pakistan, a number of drugs are marketed with claims of neuroprotection, including \( \alpha \)-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 conditions that demand a vastly different management approach.

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 prothrombin time monitoring are not feasible, further work-up is unnecessary, and the anti-platelet treatment should be used indefinitely, along with risk factor management as feasible.
Changing Patterns of Neonatal Herpes Encephalitis and Current Treatment Guidelines

Ansari

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Herpes simplex virus (HSV) infections are among the most commonly encountered infections in human beings. A pool of 30 million HSV infected patients exist in the USA. Two types of HSV infections have been identified: HSV-1, which usually causes orolabial disease, and HSV-2, which is associated more frequently with genital and newborn infections. Usually, HSV causes mild and self-limited disease of the mouth and lips or at genital sites. However, on occasion, the disease can be life threatening. Neonatal herpes infections occur in infants at a mean age of 14 days, but can happen up to six weeks after birth. Clinical manifestations of neonatal infection can be localized to the skin, eye or mouth (SEM) or to the central nervous system (CNS), such as encephalitis with or without skin lesions. They can also present as disseminated sepsis. Furthermore, in the immunocompromised host, severe infection has been encountered and is a source of morbidity. Even in the immunocompetent host, frequent recurrences, particularly those of the genital tract, can be debilitating. Because HSV does cause genital ulcerative disease, it is associated with an increased risk of acquiring a human immunodeficiency virus infection.

This article will summarize the natural history of neonatal HSV encephalitis and will describe recent developments in neonatal HSV disease management.

Epidemiology

Neonatal herpes simplex virus (HSV) infections may be caused by either herpes sin, piex virus type-1 (HSV-1) or frel;pes simplex virus type-2 (HSV-2). In the United States, HSV-2 is responsible for 75% of genital and neonatal infections, while HSV-1 causes the rest. HSV-1 more commonly affects the oropharynx, the eyes, and the central nervous system. A pool of 30 million HSV infected patients exist in the USA. With 600,000 new cases occur each year. Sero prevalence has increased steadily from 16.49% (1976–80) to 21.7% (1989–90). It is estimated that 20 to 30% of sexually active adults are seropositive for HSV. The majorit; of subjects with HSV infections host life-like symptoms. HSV infection has been encountered and is a source of morbidity. Treatment options include antiviral therapy and prophylactic antibiotics.