EMERGENCY MEDICINE CASES
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Episode 17 – Stroke

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Update on ABCD2 Score to Predict Stroke Risk after TIA

Age >60yo, Blood pressure >140/90, clinical features (1pt – speech disturbance only, 2pts – unilateral weakness), duration (1pt – 10-59min, 2pts – >60min), diabetes

Lower risk (0-3pts), moderate risk (4-5pts), high risk (6-7pts)

Recent criticism of ABCD2 score:

Ann Emerg Med. 2011;57:46-51. In population that was treated very aggressively with early carotid + brain imaging and treatment, the rate of stroke was independent of the ABCD2 stratification.

CMAJ. July 12th, 2011;183(10). Sensitivity & specificity for predicting stroke 7 and 90 days after ED visit for TIA. Found that ABCD2 score is inaccurate at any cut-point as a predictor of stroke.

Dr. Himel's conclusion: Patients in these trials were investigated and treated more aggressively compared to when the ABCD2 score was initially developed. If you investigate patients with TIA within 24-48hrs and treat aggressively, the risk of stroke drops dramatically and the ABCD2 score is less important.

ABCD2 should not be used as rigid rule, but still helpful as a rough guide in determining which patients need urgent follow-up and aggressive investigation. Some argue that every patient with a probable TIA should be worked up urgently. A low ABCD2 score does not necessarily mean that the patient is at low risk for stroke, especially if posterior circulation TIA.

Update on Carotid Imaging for TIA

Consider Carotid Doppler Ultrasound or CT Angiogram of the neck ***in the ED*** for high risk TIA patients, to determine those with carotid artery stenosis who would benefit from time-sensitive early surgical intervention with carotid endarterectomy.

Important Thrombolysis Trials for Ischemic Stroke

Prior to NINDS, thrombolytic trials showed negative results because of either higher dose of lytic or concomitant treatment with anticoagulants resulting in an unacceptable rate of ICH.

NINDS trial 1995: 2 trials of 624 patients at 0-90min and 90-180min, with NNT 7-9 for <180min and NNT 4.5 for <90min for significant functional outcome benefit, however no mortality benefit.

ATLANTIS trial 1999: trial of <5hrs but with most patients at 4-5hr mark, resulting in a negative trial – i.e. it's too late to treat when approaching 5hrs

ECASS-3 trial 2008: trial of 3-4.5hr, where patients do better than no thrombolytics, but not as good as patients treated earlier. Different exclusion criteria compared to NINDS (eg: excluded diabetics). This trial showed benefit compared to ATLANTIS because they paid more attention to excluding patients based on imaging results and because the bulk of patients were treated earlier (<4hrs).

Dr. Himel & Selchen's Conclusions: There is a linear relationship between time to treatment and improved functional outcome in carefully selected patients in a systematized protocol.

Should Elderly be excluded from lytic protocols? Dr. Himel & Selchen believe that although there have been few elderly patients in lytic trials, being elderly should not be an absolute contra-indication to thrombolytics, as registry data show improved outcomes and the notion of increased risk of ICH in the elderly with lytics has been overstated.

Should community hospitals be using lytic for stroke? If systematized protocol in place, then yes. CASES study - *Thrombolysis for acute ischemic stroke: Results of the Canadian Alteplase for Stroke Effectiveness Study. CMAJ 2005, 172(10):1307-12.* Prospective cohort study to assess effectiveness of lytic in actual practice in 60 centres. Improved clinical outcome in 37% with symptomatic ICH in 4.6%.

Volume of Infarct and Ischemic Penumbra as a factor in deciding lytic treatment: A small volume of infarct with a large surrounding ischemic penumbra is more likely to benefit from lytic compared to a large infarct with small penumbra. CT perfusion scanning or diffusion MR is used in some centres to determine size of infarct and penumbra which helps neurologists make lytic decisions in the later time window even beyond 4.5hrs, although data is not strong enough yet to make any definitive recommendations.

Intra-arterial (IA) thrombolytics: for 'late presenters' and for certain stroke types (eg: in large upper internal carotid or very proximal MCA clots seen on CT angiogram), patients don not derive benefit from IV thrombolytics, so IA t-PA is either added to IV lytic or used alone in the cath lab up to 6hrs after symptom onset for anterior circulation, and up to 12hrs for basilar occlusion. The ED doc needs to make the call to interventionist within 4hrs of symptom onset in anterior circulation strokes and within 10hrs in posterior circulation stroke for consideration of IA lyrics to allow time for transfer and cath lab activation.

Some Issues around Contraindications to thrombolytics:

> Rapidly resolving or fluctuating deficits may mean collateral circulation is temporarily perfusing brain tissue, and therefore is NOT an absolute contraindication. If a patient improves to a point where there is still a significant functional deficit they may still benefit from lytic.
>
> INR should be below 1.5-1.7 - Do you need to wait for INR result before giving lytic? If answer is "no" to the 3 following questions, one study showed 100% sensitivity for normal INR: use of warfarin? use of heparin? and hemodialysis? (also consider bleeding diathesis and liver disease)
>
> Blood work Contra-indications: platelet count <100,000, serum glucose <2.7mmol/L (risk of stroke mimic) or >22.2mmol/L (increased ICH risk). Some experts would correct a low glucose, and if stroke symptoms persists, will give lytic.

Imaging

Early signs of stroke on plain CT head (not contraindications to lytic): blurring in basal ganglia, internal capsule or insula; loss of the grey-white junction clarity, sulcal effacement (gyri edema), hyperdense MCA sign has a large differential so exercise caution in ruling in stroke based solely on hyperdense MCA sign

CT contraindications to lytic: hemorrhage (differentiate from bilateral basal ganglia calcifications), and clear evidence of large area of ischema (>1/3rd MCA territory or large part of 2 lobes)

Dr. Selchen's Tips on Informed Consent for Lytic: the patient is often not able to provide informed consent because of 'stunned brain' from the stroke, so next of kin should be contacted. Explain that t-PA is not a 'miracle drug' (i.e. doesn't work in every patient) with benefit of 13-25% that outweighs the hemorrhage risk of 6% (in the brain and the gut most likely) – if no family member available, argument for treatment with t-PA as the standard of care is possible (i.e. treat as an surgical emergency – "treat now and discuss later")

Thrombolytic Adverse Events

Consider symptomatic intracranial hemorrhage if patient develops severe headache (especially if associated with vomiting) or new neurologic symptoms – stop t-PA and obtain plain CT head, and consider giving 10u of cryoprecipitate (to replace the fibrinogen) and a pool of platelets – Recombinant Factor VIIa and Prothrombin Complex Concentrates are **not** indicated; neurosurgery does not need to be involved immediately given that an operation would be contraindicated right after giving a thrombolytic

Other ED supportive measures (as per AHA guidelines): intubation as necessary, oxygen to maintain O_2 >92%, IV fluids: normal saline to maintain euvolemia, avoid hyperglycemia (<10mmol/L) - note that there is no benefit to 'tight' glucose control (4-7mmol/l) and keep patient normothermic (tylenol PRN), Foley catheter if retention to avoid excessive hypertension, and resist urge to decrease blood pressure dramatically: goal of <220/120mmHg (or MAP <150) if not thrombolysed, and <185/110mmHg (or MAP <130) if thrombolyzed – decrease by 10-15% with IV labetalol or nicardipine

=>**3 numbers to remember for BP goal in stroke:** MAP **<150** for ischemic stroke not thrombolysed, MAP <**130** if thrombolyzed, MAP <**110** for ICH

Antiplatelets and Heparin for Ischemic Stroke

Antiplatelets: Similar to TIA; as soon as CT scan shows NO hemorrhage: ASA 160-325mg chew or crushed down NG tube or rectally, or for ASA allergy or failure, Clopidogrel (Plavix) 300mg load then 75mg daily (if allergy to or failed ASA), or Aggrenox BID (but often causes headaches)

Heparin: very unusual to give to stroke patient (except in the setting of of extra-cranial carotid/vertebral dissection, crescendo stroke), and should be discussed with neurologist

Posterior circulation stroke

NIH Stroke Score quite insensitive to posterior circulation stroke due to overreliance on motor weakness findings; CT scan also insensitive, so MRI is required

Suspect cerebellar edema and increased ICP with decreasing LOC, headache, vomiting, loss of sensation or weakness, or upgoing toes; look for decreased 4th ventricle size on CT scan –consider neurosurgery consult

Anticoagulation for Acute Stroke Patients with Atrial Fibrillation:

Expert Opinion - delay starting Warfarin for a few days after massive stroke because of high risk of hemorrhagic transformation and lower risk of repeat stroke in the first few days, but start Warfarin 5mg right away after small strokes given low risk of hemorrhagic transformation

Stroke Units

The outcome benefit from admission to a dedicated stroke unit is greater than that of lytic for stroke

Dabigatran

Oral direct thrombin inhibitor reaching peak concentration in 2hrs and no monitoring required, but no way of ensuring compliance (i.e. no monitoring strategy as aPTT increase is not linear nor reliable), contraindicated in renal failure (because 80% renaly excreted) and no antidote to reverse its effects (in the setting of half-life of 12-14hrs)

At least as good as warfarin in preventing stroke in atrial fibrillation in RCTs, with lower rate ICH, but slightly higher rate of GI bleeding (*Dabigatran vs Warfarin in Patients with Atrial Fibrillation. NEJM 2009;361:1139-1151)*

Patients already taking Warfarin with excellent INR control have little to gain by switching to Dabigatran. Where Dabigatran has an advantage is in the patient whose INR is poorly controlled within the 2-3 INR range.

Dabigatran Reversal: In the setting of life-threatening bleed, the only method to mitigate the effects of dabigatran is hemodialysis – cryoprecipitate may be of help as well as activated charcoal in acute overdose

Intracranial hemorrhage (ICH)

Mortality of ICH 3x higher than Ischemic stroke which is attributed to the mass effect of the bleed, leading to increased ICP, as apposed to Ischemic stroke mortality associated with complications of stroke such as aspiration and sepsis.

40% of patients with ICH have significant hematoma expansion in the first few hours after ICH and so the ED doc needs to do everything they can to minimize this hematoma expansion early on.

Supportive care: similar to ischemic stroke (see above), except -

1. have low threshold for early intubation as many patients deteriorate early on

2. if BP >180/105 (MAP >130) lower the pressure to 160/90 (MAP 110) and avoid hypotension

3. Elevate head of bed 30 degrees and keep neck in midline to prevent internal jugular veins compression and worsened increased ICP

4. For raised ICP consider using mannitol for clinical deterioration and gentle hyperventilation with PCO_2 down to 35mmHg only as a bridge to definitive treatment in the or O.R. with neurosurgery

5. No seizure prophylaxis required as per recent AHA guidelines

Indications for neurosurgical intervention: no clear data on this topic, but some possible indications include:

1. Ventricular drains for posterior fossa bleeds

2. Superficial bleeds within 1cm of cortical surface showed a trend toward improved outcome in the STICH trial with neurosurgical intervention compared to medical management alone (*Early surgery versus initial conservative treatment in patients with spontaneous supratentorial inctracerebral haematomas in the International Surgical Trial in Intracerebral Haemorrhage (STICH): a randomized trial. Lancet. 2005; 365(9457):387-97)*

3. Neurosurgery may be beneficial in lobar bleeds associated with cocaine, AVMs or amyloid

Recombinant Factor Vlla for treatment of ICH has been shown to significantly decrease hematoma size in RCT but has never shown an outcome benefit.

> Current Canadian Study looking at patients with a 'spot sign' on CT Angiogram (which is an indicator of high likelihood of hematoma expansion) who may be a subset of patients that do derive an outcome benefit

Warfarin-associated ICH Reversal: replace the missing clotting factors and ensure they stay up by giving Vitamin K 10mg IV (1mg per minute) and Prothrombin Complex Concentrates (PCCs) - Octaplex in Canada (fast onset in minutes and small volume of infusion – dose is 1,000u if INR <4 and body weight <90kg, or 2,000u if INR >4 or body weight >90kg) or fresh frozen plasma (which takes hours to thaw and to reverse INR plus requires large volumes, and therefore less optimal compared with PCCs)

Antiplatelet-associated ICH: consider giving a pool of platelets in the setting of ASA, but less likely to be useful for Clopidogrel