Update on Stroke and Other Neurologic Conditions

Vanja Douglas, MD, Associate Professor of Clinical Neurology, Sara and Evan Williams Foundation Endowed Neurohospitalist Chair, Department of Neurology, University of California, San Francisco, School of Medicine

Stroke

Treatment options for ischemic stroke: all acute stroke trials use aspirin; probably acceptable to use clopidogrel (similar mechanism of action), although no trials support use; best evidence-based treatment is intravenous (IV) tissue plasminogen activator (tPA) and mechanical embolectomy; majority of patients who undergo mechanical embolectomy also receive IV tPA; within 0- to 3-hr window, IV tPA standard of care (can use IV tPA ≤4.5 hr; not approved by Food and Drug Administration [FDA], but used off-label at many centers); can perform embolectomy ≤6 hr; count time from when patient last known to be normal; if IV tPA given within 0 to 3 hr, likelihood of patient having no disability 3 mo after stroke is 39% (without tPA, 26%); in trial looking at 4- to 4.5 hr-window, difference not as significant and number needed to treat higher; urgent to administer tPA as soon as possible; Embolectomy: performed only for large-vessel occlusion, which in present in ≥20% of all ischemic strokes; difference between treatment group and nontreatment group substantial for patients with large-vessel stroke; in some trials, ≤71% of patients independent after embolectomy; previously, only noncontrast computed tomography (CT) of head needed (to determine whether stroke hemorrhage or ischemic); now, CT angiography also needed, to look for large-vessel occlusion; in procedure, catheter advanced through blockage; has become effective because of use of stent retrievers; Stenting and endarterectomy: stenting appears equivalent to endarterectomy in younger patients, but in those ≥70 yr of age, seems more dangerous than endarterectomy; in older patients, consider stenting only in those at extremely high surgical risk; treatment options for carotid stenosis are endarterectomy and stenting; problem with stenting that bits of plaque can break off and cause microinfarction in brain; emboli protection devices can be deployed to catch bits that break off during stenting; in symptomatic patients with ≥70% stenosis of carotid artery, surgery more effective and safer than medical management; if stenosis 50% to 70%, surgery only slightly better; if surgical risk <6%, reasonable to consider endarterectomy if stenosis 50% to 70%; difficult to determine surgical risk, so refer to surgeon with <6% surgical morbidity rate; stenting vs surgery — meta-analysis found that stenting has increased risk for stroke or death within 30 days of procedure (odds ratio [OR] of 1.7 for increased risk for stroke); during follow-up, treatments equivalent; when patients stratified, all additional risks with stenting occurred in those ≥70 yr of age; 10-yr follow-up of recent major trials showed increased rate of stroke or death with stenting in those ≥70 yr of age.

Transient ischemic attack (TIA)

Risk for stroke after TIA: 10% of patients with TIA have stroke ≥90 days, with 50% occurring in first 2 days; TIA unstable condition and must be treated as such; ABCD2 score — age, blood pressure, clinical features, duration of TIA, and presence of diabetes; if TIA involved speech or weakness and of long in duration, risk higher; score ranges from 0 to 7; risk for stroke determined at different time points (2 days, 7 days, 30 days, and 90 days); effective for stratification; if score ≥4, probably advisable to admit patient and work up.

Modifying risk: study of 91,000 patients in United Kingdom measured baseline rate of stroke after TIA (a=10%); in phase 1, received usual care (primary care physician refers patient to TIA clinic, which provides recommendations, and patient returns to primary care physician); in phase 2, urgent referral to TIA clinic, which then manages patient; risk for stroke in phase 2 decreased significantly; researchers created TIA registry; 80% of patients in registry seen by TIA clinic ≤24 hr of event; under this urgent evaluation paradigm, rate of stroke of 3 mo 3.7%, and in 1 yr, 5%; urgent evaluation seems to have lowered global stroke rate after TIA. Dual antiplatelet therapy (DAPT) for TIA: 2013 Chinese trial — looked at combination of aspirin and clopidogrel for 21 days after TIA, followed by platelet monotherapy; found that DAPT reduced rate of stroke at 90 days.

Back Pain

Acute low back pain (LBP): naproxen evidence-based therapy; physical therapy (PT) not as effective; Cochrane review of nonsteroidal anti-inflammatory drugs (NSAIDs) and muscle relaxants found effective, compared to placebo; trials looking at combination of naproxen and muscle relaxant showed mixed results; study — randomized patients to naproxen alone, naproxen plus cyclobenzaprine, and naproxen plus opiate and acetaminophen; outcome included difference on disability questionnaire and pain; 5-point improvement in questionnaire considered clinically significant; found no difference in 3 treatment arms; more side effects in those on drugs that affect central nervous system; slightly less pain seen in opiate arm; at 1 wk, 54% of patients in naproxen arm and 65% in opiate arm.

Educational Objectives

The goal of this program is to improve the management of stroke and other common neurologic and neuro-ophthalmologic conditions. After hearing and assimilating this program, the clinician will be better able to:

1. Elaborate on the intravenous and endovascular treatment strategies for ischemic stroke.
2. Establish the importance of urgent evaluation to lower the risk for stroke after a transient ischemic attack.
3. Perform evidence-based evaluation of patients with suspected concussion.
4. Differentiate between causes of monocular and binocular transient visual loss.
5. Recognize which neuro-ophthalmologic conditions require emergent treatment.

Faculty Disclosure

In adherence to ACCME Standards for Commercial Support, Audio Digest requires all faculty and members of the planning committee to disclose relevant financial relationships within the past 12 months that might create any personal conflicts of interest. Any identified conflicts were resolved to ensure that this educational activity promotes quality in health care and not a proprietary business or commercial interest. For this program, members of the faculty and planning committee reported nothing to disclose. In his lecture, Dr. Douglas presents information that is related to the off-label or investigational use of a therapy, product, or device.
had mild or no pain; adding opiates results in additional 10% benefit in number of patients with mild or no pain; NSAIDs alone probably adequate for pain relief, and opiates may be reserved for most severe symptoms

Physical therapy (PT): study — looked at individuals with acute LBP for ≤16 days; those with chronic LBP had to have no treatment for last 6 mo, with acute exacerbation of pain for ≥2 wk to be eligible for trial; individuals with radiculopathy not included; randomized to PT for 4 wk (once weekly) or education, reassurance, and no PT for 4 wk; used Oswestry Disability Index (5-15 points often considered clinically meaningful); at 3 mo, PT group had slightly lower score (but not clinically meaningful)

Radiculopathy: Kaiser study — looked at patients with disc herniation and radicular pain; randomized to steroids (prednisone) or placebo; looked at Oswestry Disability Index at 3 wk and 1 yr; found statistically significant difference between 2 groups at 5- to 7-point range, but with no difference in pain; ≥9% of patients in each group eventually had surgery for herniated disc; concluded that steroids result in modest benefit on functional outcome, but provide no difference in pain or need for surgery; authors of study left decision of recommending steroids to individual patient and physician; speaker suggests recommending steroids for those with severe radiculopathy not immediately responsive to NSAIDs

Nontraditional modalities for treatment: study randomized patients with chronic LBP to mindfulness-based stress reduction, cognitive behavioral therapy (CBT), or usual care; used Roland Disability Questionnaire; found that at 1 yr, ≥50% of patients receiving usual care had some improvement; 68% who received mindfulness-based stress reduction and 58% who received CBT had clinically meaningful improvement; meta-analysis of trials found CBT beneficial vs usual care and guideline-based treatment

Dementia and Agitation

Treatment: antipsychotic drugs (APDs) — well-established association with increased mortality in elderly patients, especially first-generation APDs; mechanism unknown (probably cardiac); black-box warning on all; used for agitation and dementia off-label; trial — showed that cilazapram seemed effective for agitation and dementia, with tendency toward prolonged QTc in treatment arm; electrocardiographic monitoring recommended with use; no good data for valproate or donepezil; other mood stabilizers (eg, carbamazepine) also used, but no good data; dextromethorphan/quinidine — approved by FDA for treatment of pseudobulbar affect (impaired ability to regulate expression of emotion) in amyotrophic lateral sclerosis; dextromethorphan thought to work due to activity in N-methyl-D-aspartate (NMDA) receptor; phase 2 trial looked for 2.5 point-difference in index of aggression at end of trial, but found only 1.5-point difference (statistically significant, but not clearly clinically meaningful); however, improvements seen in caregiver burden and patient-related outcome; seems effective, but requires larger trial for validation; adverse events seen, but none clearly related to drug; in patients presenting with dementia and agitation, first 3 treatment options nonpharmacologic

Migraine Headaches

Prophylactic treatment: consider in patients with ≥3 severe episodes/mo to reduce frequency and severity of headaches; no randomized trials for verapamil and gabapentin to support use as prophylactic treatment; riboflavin relatively benign and has some data to support use; American Academy of Neurology has guidelines on evidence-based prophylactic treatment

Future developments: calcitonin gene-related peptide (CGRP) receptor antagonists — CGRP thought to be major mediator in migraine pain; found highly effective in randomized trials, but tended to cause fatal hepatic failure, so development stopped; CGRP antibody — monoclonal antibody; 4 subcutaneous injections once per mo; phase 2 trial comparing 2 doses vs placebo in people with episodic migraine found reduction in number of migraines over 3-wk period (wk 9-12); 6 fewer migraines occurred, compared to 4 fewer in placebo group; in participants with chronic migraine (≥15 headache-days/mo), found 6 fewer headache days, compared to 4 fewer in placebo group

Concussion

Evidence-based examination: to determine whether symptoms related to concussion, important to know patient’s condition before concussion; however, patient’s condition before concussion, especially regarding nonspecific symptoms, often unclear; perform cognitive assessment focused on concentration and memory; test sense of smell (olfactory nerve highly susceptible to injury in concussion); evaluate smooth pursuit and saccadic eye movements (as person ages, smooth pursuit tends to degenerate and become jerky); check for convergence insufficiency (in normal patients, blurry or double vision when object 6 to 10 cm from face; possible sign of concussion if blurry or double vision reported when object farther out); perform dynamic visual acuity test with Snellen chart, ie, have patient shake head back and forth twice per second; visual acuity should be same or 1 or 2 lines lower on Snellen chart; if visual acuity decreases by ≥3 lines, shows inability to maintain fixation when moving head and indicates impaired vestibulo-ocular reflex (sensitive to concussion)

Suggested Readings

Neuro-ophthalmology for the Internist
Jonathan D. Trobe, MD, Professor of Ophthalmology and Neurology, Departments of Ophthalmology and Visual Sciences, and Neurology. Director of Neuro-ophthalmology, University of Michigan Medical School, Ann Arbor

Transient visual loss: first question to test patient is whether one or both eyes affected
Monocular visual loss: papilledema is swelling due to increased intracranial pressure, and it can affect one or both eyes; may indicate impending problem with retina or optic nerve; giant
cell arteritis can lead to complete loss of vision in both eyes and should be considered in patient with chronic rheumatologic conditions who presents with transient visual loss; must be considered emergency; “remote source” (eg, cervical carotid artery stenosis; considered emergency because of threat of stroke); systemic hypotension common cause of monocular or binocular visual loss; Hollenhorst plaque is retinal vascular manifestation of remote atherosclerotic or calcific problem in neck or heart (almost always from carotid artery in neck) Binocular visual loss: clues to binocular visual loss — highly likely if patient reports episode of inability to see highway signs, read, or look at computer; migraine — scintillation that travels across field of vision almost always migraine; probably most common cause of transient visual loss; activation of occipital lobe or visual cortex from adrenergic stimulus; traveling wave of excitation is visual aura of migraine, followed by headache; TIA — involving occipital lobe or vertebrobasilar circulation or possibly cardiogenic; most often not stimulatory or scintillatory, and do not travel across visual field (helps distinguish from migraine); glioblastoma — episode of colored scintillations in periphery of field of vision that comes and goes, with development of seizures later; no cure; typical presentation with seizure usually stationary scintillation, often with colored lights

Acute persistent visual loss: immediate referral needed; retinal detachment — base on history (3Fs [flashes, floaters, field loss]); in elderly (age 60s to 80s), almost always posterior vitreous detachment; fluid from vitreous (liquefies with age) can get under retina, causing separation; considered greater emergency if patient can see than if patient cannot see (urgent to real-tach retina to prevent further dissection of retina onto fovea); polymyalgia rheumatica — in small percentage of patients, includes cephalic component; can lead to infarction of optic disc (sudden); if this has occurred in one eye, can quickly occur in other; high-dose corticosteroids useful in preventing visual loss in other eye; checking for afferent pupillary defect — shine light on one eye, then on other eye; afferent pupillary defect strongly suggestive of asymmetric or unilateral optic neuropathy or severe retinal problem; perform in dimly lighted room, with patient looking far away; cherry-red spot — indicates that retina turbid (cloudy) everywhere except in fovea; surface of retina infarcted; seen in central retinal artery occlusion, which can occur from thrombosis in situ or embolic disease; must look for source to determine whether embolic; no treatment of eye indicated; central retinal vein occlusion — arteriosclerotic disease of inflow to eye; results in stasis in veins, causing occlusion; eventually ruptures, resulting in blood throughout eye; managed medically

Diplopia: monocular diplopia “trivial,” but binocular diplopia urgent; third-nerve palsy — usually ischemic mononeuropathy that typically improves with time; usually indicates presence of vascular disease; however, may be caused by aneurysm (difficult to determine); emergent care needed

Anisocoria: not usually cause for concern; may be result of chemical in eye, old eye trauma, or trauma from surgeon during cataract surgery; tonic pupil of ciliary ganglionopathy — trivial; usually viral or postviral condition; however, consider third-nerve palsy if other symptoms or signs present (eg, double vision, ptosis); acute Horner syndrome — slight ptosis present; main cause carotid dissection; risk (<10%) for middle cerebral artery stroke in first 14 days; spontaneous or traumatic; referral to ED indicated

Ptosis: neurogenic (nerve to lid or Mueller muscle) or myogenic (muscle itself); neurogenic causes — third-nerve palsy, myasthenia gravis, and Horner syndrome

Papilledema: serious condition involving increased intracranial pressure

Suggested Readings


Acknowledgements

Dr. Douglas was recorded at the 44th Annual Advances in Internal Medicine, held May 23-27, 2016, in San Francisco, CA, and presented by the Department of Medicine, University of California, San Francisco, School of Medicine. For information about upcoming CME activities from University of California, San Francisco, School of Medicine, visit their website at www.cme.ucsf.edu. Dr. Trobe was recorded at the 4th Internal Medicine Spring Review, held May 6-7, 2016, in Plymouth, MI, and sponsored by the University of Michigan Medical School, Department of Internal Medicine. For information about upcoming CME activities from University of Michigan Medical School, Department of Internal Medicine, visit their website at www.med.umich/nttmed/cme. The Audio Digest Foundation thanks the speakers and the sponsors for their cooperation in the production of this program.
TOPICS IN NEUROLOGY

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1. The following statements about the treatment options for stroke are true, EXCEPT:
   (A) All acute stroke trials use aspirin as part of treatment
   (B) Intravenous tissue plasminogen activator is approved by the Food and Drug Administration (FDA) for use ≤4.5 hr after a stroke
   (C) Mechanical embolectomy can be performed ≤6 hr following stroke
   (D) Acceptable to use clopidogrel instead of aspirin

2. In carotid artery stenosis of 50% to 70%, surgery is ______ medical management.
   (A) Slightly better than (B) Slightly worse than (C) Equivalent to

3. A follow-up of recent major trials showed an increased rate of stroke or death with stenting (vs endarterectomy) in individuals:
   (A) ≥50 yr of age (B) ≥60 yr of age (C) ≥65 yr of age (D) ≥70 yr of age

4. Ten percent of patients with transient ischemic attack have a stroke within 90 days, with 50% occurring in the first:
   (A) 24 hr (B) 2 days (C) 5 days (D) 7 days

5. A study comparing steroids to placebo in patients with disc herniation and radicular pain concluded that steroids resulted in a modest benefit in:
   (A) Functional outcome (B) Relieving pain (C) Need for surgery (D) All the above

6. A study randomized patients with chronic low back pain to mindfulness-based stress reduction, cognitive behavioral therapy, or usual care. Which treatment modality had the greatest number of patients with clinically meaningful response?
   (A) Mindfulness-based stress reduction (B) Cognitive behavioral therapy (C) Usual care

7. Which of the following is approved by the FDA to treat pseudobulbar affect in patients with amyotrophic lateral sclerosis?
   (A) Lithium (B) Valproate (C) Dextromethorphan/quinidine (D) Carbamazepine

8. ______ is a retinal vascular manifestation of remote atherosclerotic or calcific problem in the neck or heart, while ______ is a finding in the macula of the eye seen in central retinal artery occlusion.
   (A) Hollenhorst plaque; cherry-red spot (B) Cherry-red spot; Hollenhorst plaque

9. Which of the following is NOT a characteristic sign or symptom of retinal detachment?
   (A) Floaters (B) Flashes of light (C) Anisocoria (D) Visual field loss

10. Which of the following neuro-ophthalmologic conditions usually do NOT require emergent care?
   1. Monocular diplopia
   2. Anisocoria
   3. Tonic pupil of ciliary ganglionopathy
   4. Third-nerve palsy
   (A) 1,3 (B) 2,4 (C) 1,2,3 (D) 1,2,3,4

Answers to Audio Digest Internal Medicine Volume 63, Issue 33: 1-C, 2-A, 3-B, 4-C, 5-B, 6-C, 7-A, 8-B, 9-B, 10-B