

G. Secondary Prevention of Stroke Educational Supplement

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G1. Transient Ischemic Attack

G1.1 Case Study: TIA

Case Study

A 32 year old female patient presents to the Emergency Room and tells you that something strange happened one hour ago: She couldn't see out of her left eye for 50 minutes. Although she can see fine now, she and her family want to know what might have caused this temporary blindness.

Q1. What do you think happened and what it is your recommendation?

Answers

1. TIA
2. Immediate workup (preferably by neurologist) for stroke risk.

Q2. The patient and her family want to know more about the role of TIA as a possible risk factor for Stroke. What information can you give them?

Answer

1. TIA is a significant risk factor for stroke

Q3. Which clinical features are predictive of greater stroke risk with a TIA?

Answers:

1. Age (older)
2. High blood pressure
3. Unilateral weakness
4. Speech impairment
5. Length of symptoms
6. Diabetes

G2. Hypertension

Canadian Best Practice Recommendations (2008): Recommendation 2.2 – Management of High Blood Pressure

Hypertension is the single most important modifiable risk factor for stroke. Blood pressure should be monitored in all persons at risk for stroke.

2.2a. Blood pressure assessment

- i. All persons at risk of stroke should have their blood pressure measured at each health care encounter, but no less than once annually [Evidence Level C] (CHEP, NICE, RCP).
- ii. Proper standardized techniques, as described by the Canadian Hypertension Education Program, should be followed for blood pressure measurement (CHEP).
- iii. Patients found to have elevated blood pressure should undergo thorough assessment for the diagnosis of hypertension following the current guidelines of the Canadian Hypertension Education Program [Evidence Level A] (ASA, CHEP, RCP).
- iv. Patients with hypertension or at risk for hypertension should be advised on lifestyle modifications. [Evidence Level C]. Refer to recommendation 2.1, "Lifestyle and risk factor management," for details on lifestyle modifications.

2.2b. Blood pressure management

- i. The Canadian Stroke Strategy recommends target blood pressure levels as defined by the Canadian Hypertension Education Program (CHEP) guidelines for prevention of first stroke, recurrent stroke, and other vascular events.

CHEP 2008 Recommendations for Management of Blood Pressure (excerpts used with permission; see www.hypertension.ca/chep for detailed information (Khan et al. 2008):

- For the prevention of first stroke in the general population the systolic blood pressure treatment goal is a pressure level of less than 140 mm Hg [Evidence Level C]. The diastolic blood pressure treatment goal is a pressure level of less than 90mm Hg [Evidence Level A].
- Blood pressure lowering treatment is recommended for patients who have had a stroke or transient ischemic attack to a target of less than 140/90 mm Hg [Evidence Level C].
- In patients who have had a stroke, treatment with an angiotensin-converting enzyme (ACE) inhibitor or diuretic is preferred [Evidence LevelB].
- Blood pressure lowering treatment is recommended for the prevention of first or recurrent stroke in patients with diabetes to attain systolic blood pressures of less than 130 mm Hg [Evidence Level C] and diastolic blood pressures of less than 80 mm Hg [Evidence Level A].
- Blood pressure lowering treatment is recommended for the prevention of first or recurrent stroke in patients with nondiabetic chronic kidney disease to attain a blood pressure of less than 130/80 mm Hg [Evidence Level C].

- ii. Randomized controlled trials have not defined the optimal time to initiate blood pressure lowering therapy after stroke or transient ischemic attack. It is recommended that blood pressure lowering treatment be initiated (or modified) prior to discharge from hospital. For patients with

nondisabling stroke or transient ischemic attack not requiring hospitalization, it is recommended that blood pressure lowering treatment be initiated (or modified) at the time of the first medical assessment [Evidence Level B] (EXPRESS, PROGRESS).

iii. For recommendations on specific agents and sequence of agents, please refer to the current Canadian Hypertension Education Program guidelines (Khan et al. 2008).

G2.1 Case Study: Hypertension

Case Study

A 55 year old woman is admitted to the inpatient rehabilitation unit with a lacunar infarct in the right thalamic/subcortical area. Her past medical records state that she has a history of hypertension which is not well controlled. The nurse notes that the patient's blood pressure (BP) is 145/90 mmHg and that she is not currently taking any antihypertensive medication.

Q1. What are the risk factors for this patient having a new stroke?

Answers

1. Stroke
2. Hypertension

Q2. What BP level is considered normal?

Answer

1. Less than 120/80 mmHg

Q3. The patient tells you that her current BP (145/90 mmHg) is normal for her and that she questions whether it needs to be treated because she doesn't want to have to take any "pills". What can you tell her?

Answer

1. Her BP is considered to be elevated.
2. Hypertension is a modifiable risk factor for stroke.
3. Treatment of hypertension will reduce her risk of stroke.

4. Medications are often needed as nonpharmacological methods are often unsuccessful.

Q4. After the patient agrees to be treated, the resident asks what pharmacological treatments are available for hypertension and which treatment would be most appropriate for this patient. What would be your initial treatment?

Answer

1. Diuretic alone or in combination with an ACE inhibitor

Q5. List the reasons why it is important to treat hypertension in stroke survivors?

Answers:

1. Most important treatable risk factor
2. High prevalence
3. Easily modifiable
4. Proportional risk
5. Reduction associated with decreased risk.

Q6. Two important studies looking at the treatment of hypertension post-stroke were the PROGRESS and HOPE trials. Describe both of these trials.

Answers:

1. The PROGRESS trial randomized 6105 patients (both HBP and non-HBP) with a history of ischemic stroke or TIA to either perindopril 4mg/day + indapamide versus perindopril alone versus placebo. The researchers found a 28% reduction in relative risk was associated with the combined treatment of perindopril + indapamide, as compared to perindopril alone.
2. The HOPE trial randomized 3577 diabetic patients (age 55+ and history of cardiovascular disease) to 10 mg Ramipril/day versus placebo. Ramipril lowered the risk of myocardial infarction by 22%, stroke by 33%, cardiovascular disease by 37%, and total mortality by 24%.

G2.2 Case Study: Intracerebral Hemorrhage and Hypertension

Case Study

34 year old obese male presented to hospital emergency room with aphasia, right hemiparesis and decreased level of consciousness. CT scan showed a large left intracerebral hemorrhage. BP was 236/124. Patient was admitted to the ICU.

Past medical history was a 2 year history of malignant hypertension complicated by two hypertensive crisis in the month before his stroke for which he was treated but he failed to follow through with his prescriptions. At the time of admission and in the ICU his BP proved extremely difficult to control and he was discharged from the ICU with a BP of 170/95.

Q7. What treatment options are available?

Answers

1. Thiazide diuretic (i.e. hydrochlorothiazide)
2. ACE inhibitor (i.e. Ramipril – HOPE trial; Perindopril – PROGRESS; Captopril not to be used)
3. ARB (angiotensin receptor blocker) (i.e. Losartan – LIFE trial; Candesartan; Eprosartan – MOSES trial)
4. Calcium channel blocker (i.e. Diltiazem – NORDIL; Amlodipine)
5. Beta-blocker
6. Salt restrictions

* These medications can be used in combination for resistant hypertension

Case Study (continued)

He was admitted to rehabilitation and during his rehabilitation stay his blood pressure was generally running between 120-140 systolic and 70-90 diastolic with occasional BPs of 150-160 systolic and 90-100 diastolic.

Medications for HBP while on the rehabilitation unit included Amlodipine 7.5 mg q12h, Metoprolol 150 mg q12h, Perindopril 2 mg OD, Prazosin 6 mg q6h with the suggestion of adding an additional 12.5 mg of Hydrochlorothiazide to further regulate the patient's blood pressure.

G3. Hyperlipidemia and Hypercholesterolemia

Canadian Best Practice Recommendations (2008): Recommendation 2.3 – Lipid Management

Lipid levels should be monitored in all persons at risk for stroke.

2.3a. Lipid assessment

i. Fasting lipid levels (total cholesterol, total glycerides, low-density-lipoprotein [LDL] cholesterol, high-density-lipoprotein [HDL] cholesterol) should be measured every 1 to 3 years for all men 40 years or older and for women who are postmenopausal and/or 50 years or older [Evidence Level C] (McPherson et al., VA/DoD). More frequent testing should be performed for patients with abnormal values or if treatment is initiated.

ii. Adults at any age should have their blood lipid levels measured if they have a history of diabetes, smoking, hypertension, obesity, ischemic heart disease, renal vascular disease, peripheral vascular disease, ischemic stroke, transient ischemic attack or asymptomatic carotid stenosis [Evidence Level C] (McPherson et al.).

2.3b. Lipid management

i. Ischemic stroke patients with LDL cholesterol of >2.0 mmol/L should be managed with lifestyle modification and dietary guidelines [Evidence Level A] (AU, CSQCS, McPherson et al., VA/DoD)

ii. Statin agents should be prescribed for most patients who have had an ischemic stroke or transient ischemic attack to achieve current recommended lipid levels [Evidence Level A] (AU, CSQCS, McPherson et al., VA/DoD).

G3.1 Case Study: Hyperlipidemia

Case Study

A 68 year old man was admitted into the stroke rehabilitation program with an ischemic stroke on the left ACM territory. He has a history of hyperlipidemia and the cholesterol related results from a recent blood test are as follows:

- Total cholesterol 4.1 mmol/L
- Triglycerides 0.74 mmol/L
- LDL 2.83 mmol/L
- HDL cholesterol 0.94 mmol/L
- Total cholesterol to HDL ratio 4.4

Q1. When the patient asks about the cause of his stroke, the resident tells him that high cholesterol is a major risk factor and that it is the likely cause of his stroke. Do you agree with the resident and why?

Answer

1. No
2. It is not possible at this point to say it is the most likely cause of his stroke.

Q2. After your explanation, the resident asks “if hyperlipidemia is not a major risk factor, do you still have to treat it”?

Answer

1. Yes
2. Reducing hyperlipidemia or hypercholesterolemia does reduce stroke incidence.

Q3. How would you treat the hyperlipidemia?

Answers

1. Reduce dietary intake of saturated fats and cholesterol.
2. Weight reduction
3. Increase physical activity
4. Use of statins.

Q4. What are the target values for treating hyperlipidemia following stroke?

Answer

1. Stroke patients are considered high risk patients
2. For high risk patients aim for values of LDL < 2.5 mmol/L and Total cholesterol to HDL ratio < 4.0.

Q5. Why is it important to distinguish between LDLs, HDLs and total cholesterol in high risk patients?

Answers

1. Canadian Guidelines note that LDL-C should be < 2.5 mmol/L
2. Total cholesterol to HDL ratio < 4.0.

3. Total cholesterol < 4-5 mmol/L

Q6. Describe the pharmacological treatment of hypercholesterolemia.

Answer

1. Statins, HMG-CoA reductase inhibitors, are considered the first-line treatment for hypercholesterolemia.

Q7. Describe your treatment for each of the following cases.

Patient Description	Lipid Profile	Proposed Treatment and Rationale
Case A: Post Stroke – High Risk	Total cholesterol 4.75 LDL 2.4 mmol/L HDL 1.2 mmol/L	No treatment needed. All cholesterol numbers are at target levels and total cholesterol to HDL <4.0.
Case B: Post Stroke – High Risk	Total cholesterol 5.8 LDL 3.3 mmol/L HDL 1.4 mmol/L	Treatment with statin and diet. Total cholesterol and LDL-C is high and total cholesterol to HDL > 4.0
Case C: Post Stroke – High Risk	Total cholesterol 4.72 LDL cholesterol 3.0 mmol/L HDL 1.04 mmol/L	Treatment with statin and diet. LDL-C is high and total cholesterol to HDL > 4.0.
Case D: Post Stroke – High Risk	Total cholesterol 5.2 LDL cholesterol 2.6 mmol/L HDL cholesterol 1.2 mmol/L	Treatment with statin and diet. Total cholesterol to HDL > 4.0, LDL > 2.5

G4. Diabetes

Canadian Best Practice Recommendations (2008): Recommendation 2.4 – Diabetes Management

2.4a. Diabetes Assessment

- i. All individuals in the general population should be evaluated annually for type 2 diabetes risk on the basis of demographic and clinical criteria [Evidence Level C] (CDA).
- ii. A fasting plasma glucose should be performed every 3 years in individuals > 40 years of age to screen for diabetes [Evidence Level C] (CDA). More frequent and/or earlier testing with either a fasting plasma glucose or plasma glucose sample drawn 2 hours after a 75-g oral glucose load should be considered in people with additional risk factors for diabetes [Evidence Level C] (CDA). Some of these risk factors include family history, high-risk population, vascular disease, history of gestational diabetes, hypertension, dyslipidemia, overweight, abdominal obesity, polycystic ovary syndrome.
- iii. In adults, fasting lipid levels (total cholesterol, HDL cholesterol, total glycerides and calculated LDL cholesterol) should be measured at the time of diagnosis of diabetes and then every 1 to 3 years as clinically indicated. More frequent testing should be performed if treatment for dyslipidemia is initiated [Evidence Level C] (CDA).
- iv. Blood pressure should be measured at every diabetes visit [Evidence Level C] (CDA).

2.4b. Diabetes Management

- i. Glycemic targets must be individualized; however, therapy in most patients with type 1 or type 2 diabetes should be targeted to achieve a glycated hemoglobin (Hb_{A1c}) level $\leq 7.0\%$ in order to reduce the risk of microvascular complications [Evidence Level A] (CDA) and, for individuals with type 1 diabetes, macrovascular complications. [Evidence Level C] (CDA).
- ii. To achieve an $Hb_{A1c} \leq 7.0\%$, patients with type 1 or type 2 diabetes should aim for a fasting plasma glucose or preprandial plasma glucose targets of 4.0 to 7.0 mmol/L [Evidence Level B] (CDA).
- iii. The 2-hour postprandial plasma glucose target is 5.0–10.0 mmol/L [Evidence Level B]. If Hb_{A1c} targets cannot be achieved with a postprandial target of 5.0–10.0 mmol/L, further postprandial blood glucose lowering, to 5.0–8.0 mmol/L, can be considered [Evidence Level C] (CDA).
- iv. Adults at high risk of a vascular event should be treated with a statin to achieve an LDL cholesterol ≤ 2.0 mmol/L [Evidence Level A] (CDA).
- v. Unless contraindicated, low dose acetylsalicylic acid (ASA) therapy (80 to 325 mg/day) is recommended in all patients with diabetes with evidence of cardiovascular disease, as well as for those individuals with atherosclerotic risk factors that increase their likelihood of cardiovascular events [Evidence Level A] (CDA).

G4.1 Case Study: Diabetes

Case Study

A 55 year old man was admitted into the rehabilitation unit with a right MCA ischemic stroke and he has no known history of medical problems or complications.

Q1. The nurse tells you that he has a fasting plasma glucose level of 127 mg/dL or 7.0 mmol/L. Is he diabetic?

Answer

1. Yes. Diagnosis of diabetes according to 2008 CDA Guidelines: Fasting plasma glucose 7.0 mmol/L (fasting = no caloric intake for at least 8 hours) or casual plasma glucose 11.1 mmol/L + symptoms of diabetes.

Q2. His Hemoglobin A1C level is 8.2%. What is its significance?

Answer

Hemoglobin A1c level >7% is defined as inadequate control of hyperglycemia.

Q3. Provide a classification for diabetes.

Answer

1. Prediabetes
2. Type 1 diabetes
3. Type 2 diabetes
4. Gestational diabetes
5. Other specific types – eg LADA (latent autoimmune diabetes in adults), prednisone-induced hyperglycemia

Q4. How is diabetes related to stroke?

Answers

1. Diabetics have increased susceptibility to atherosclerosis, hypertension, obesity and hyperlipidemia
2. Diabetics, in particular, have elevated levels of triglycerides, reduced levels of HDL cholesterol and increased LDLs when compared to a non-diabetic sample.
3. Glucose intolerance has been shown to double the risk of a stroke
4. Diabetes has an independent effect on stroke risk after controlling for other risk factors with relative risks ranging from 1.5-3.0.
5. Diabetes is present in 15% to 33% of patients with ischemic stroke and its treatment reduces the stroke risk.

Q5. Is glycemic control associated with secondary stroke prevention?**Answer**

1. The evidence that glycemic control reduces the risk of a second stroke has been slow to come.
2. Glycemic control is often associated more with prevention of microvascular complications (retinopathy, nephropathy, peripheral neuropathy) than macrovascular complications (stroke, myocardial infarction, peripheral vascular disease)
3. Recent data suggests that glycemic control may help prevent strokes in patients with type 2 diabetes (particularly if they are obese) but not in type 1 diabetics

Q6. List three different groups of treatments recommended for glycemic control.**Answer**

1. Diet and exercise.
2. Oral hypoglycemic drugs.
3. Insulin.

Case Study (continued)

The 55 year old man who was admitted into the rehabilitation unit with a right MCA ischemic stroke with no known history of medical problems or complications has now been diagnosed with type 2 diabetes. His fasting blood sugar is 7.0 mmol/L and his hemoglobin A1c is 8.2%. He has no other complications apart from the stroke.

Q7. Describe a glycemic control protocol for his new found Type 2 diabetes.

Answer

1. Lifestyle intervention is important (initiation of nutrition therapy and physical activity).

Case Study (continued)

Despite nutritional interventions and a structured physical activity program his Hemoglobin A1C still comes back at 8.3%.

Q8. What treatment is indicated now?

Answer

1. Because the HA1c remains elevated but <9.0% the treatment of choice is Metformin, an oral hypoglycaemic agent.

Q9. How important is BP control important in this diabetic patient post stroke?

Answer

1. It is even more important than in non-diabetic patients.

G5. Lifestyle Modification

Canadian Best Practice Recommendations (2008): Recommendation 2.1 – Lifestyle and risk factor management

Persons at risk of stroke and patients who have had a stroke should be assessed for vascular disease risk factors and lifestyle management issues (diet, sodium intake, exercise, weight, smoking and alcohol intake). They should receive information and counselling about possible strategies to modify their lifestyle and risk factors [Evidence Level B] (AU, NZ, RCP, VA/DoD). Lifestyle and risk factor interventions should include:

- i. *Healthy balanced diet:*** High in fresh fruits, vegetables, low-fat dairy products, dietary and soluble fibre, whole grains and protein from plant sources and low in saturated fat, cholesterol and sodium, in accordance with Canada's Food Guide to Healthy Eating [Evidence Level B] (ASA, CHEP, RCP).
- ii. *Sodium:*** The recommended daily sodium intake from all sources is the Adequate Intake by age. For persons 9– 50 years, the Adequate Intake is 1500 mg. Adequate Intake decreases to 1300 mg for persons 50–70 years and to 1200 mg for persons > 70 years. A daily upper consumption limit of 2300 mg should not be exceeded by any age group [Evidence Level B]. See www.sodium101.ca for sodium intake guidelines.
- iii. *Exercise:*** Moderate exercise (an accumulation of 30 to 60 minutes) of walking (ideally brisk walking), jogging, cycling, swimming or other dynamic exercise 4 to 7 days each week in addition to routine activities of daily living [Evidence Level A]. Medically supervised exercise programs are recommended for high-risk patients (e.g., those with cardiac disease) (ASA, CHEP, EBRSR, NZ).
- iv. *Weight:*** Maintain goal of a body mass index (BMI) of 18.5 to 24.9 kg/m² and a waist circumference of <88cm for women and < 102 cm for men [Evidence Level B] (ASA, CHEP, OCCPG).
- v. *Smoking:*** Smoking cessation and a smoke-free environment; nicotine replacement therapy and behavioural therapy [Evidence Level B] (ASA, CHEP, CSQCS, RCP). For nicotine replacement therapy, nortriptyline therapy, nicotine receptor partial agonist therapy and/or behavioural therapy should be considered [Evidence Level A] (ASA, AU).
- vi. *Alcohol consumption:*** Two or fewer standard drinks per day; and fewer than 14 drinks per week for men; and fewer than 9 drinks per week for women [Evidence Level C] (ASA, AU, CHEP).

G5.1 Case Study: Lifestyle Modification

Case Study

A 54 year old male patient is admitted to the rehabilitation unit. He has been a lifelong smoker and has a history of alcoholism. As well, he is overweight (with a BMI of 36kg/m²) and acknowledges that he rarely engages in physical activity.

Q1. What known modifiable risk factors does he have?

Answer

- Smoking
- Alcohol
- Obesity
- Physical activity

Q2. How can physical activity affect the risk of stroke?

Answer

1. Physical activity reduces the risk of stroke through lowering BP, decreasing weight, improving vasodilatation, improving glucose control and improving cardiovascular health.

Q3. Is the patient obese?

Answer

Yes. Obesity is defined as a body mass index (BMI) of >30 kg/m².

Q4. What can you tell the patient regarding obesity and diet in the secondary prevention of stroke?

Answer

1. Abdominal obesity, more than general obesity, is related to stroke risk.
2. Diet is important in treatment of hypertension and hyperlipidemia.

Q5. The patient does not want to stop smoking. What can you tell him regarding smoke cessation in the secondary prevention of stroke?

Answer

1. Smoking generally doubles the risk of stroke.
2. There is a dose-responsive risk.
3. The risk of stroke is reduced by quitting smoking.

Q6. The patient tells you that he is going to need help in order to avoid cigarette consumption. What can you suggest to help him?

Answer

1. Counseling, nicotine products, and oral smoking cessation medications have all been found to be effective in helping smokers to quit.

Q7. What can you tell the patient regarding alcohol consumption as a risk factor for stroke?

Answer

1. Light alcohol consumption reduces the risk of ischemic stroke.
2. Heavy drinking increases the risk of stroke.

G6. Homocysteine and Stroke

G6.1 Case Study: Homocysteine

Case Study

A 45 year old male presented with a right subcortical stroke. The neurologist feels that it was probably due to a high homocysteine levels in his blood.

Q1. What is homocysteine and what are considered normal serum levels?

Answer

1. Homocysteine is a sulphur-containing amino acid.
2. Normal serum plasma homocysteine level is 5-15 $\mu\text{mol/L}$.

Q2. Is hyperhomocystinemia associated with secondary cardiovascular events?

Answer

1. Yes

Q3. What is the relationship between folic acid, vitamin B6, and Vitamin B12 levels and plasma homocysteine levels?

Answer

1. Folic acid, vitamin B6 and vitamin B12 levels are inversely related to plasma homocysteine levels.

G7. Antiplatelet Agents

Canadian Stroke Guidelines (2008): Recommendation 2.5 – Antiplatelet therapy

All patients with ischemic stroke or transient ischemic attack should be prescribed antiplatelet therapy for secondary prevention of recurrent stroke unless there is an indication for anticoagulation [Evidence Level A] (ASA, AU, CSQCS, ESO, NZ, RCP, VA/DoD).

i. ASA, combined ASA (25 mg) and extended-release dipyridamole (200 mg), or clopidogrel may be used depending on the clinical circumstances [Evidence Level A].

ii. For adult patients on ASA, the usual maintenance dosage is 80 to 325 mg per day [Evidence Level A] (CSQCS, VA/DoD), and in children with stroke the usual maintenance dosage of ASA is 3 to 5 mg/kg per day for the prevention of recurrent stroke [Evidence Level C] (AHA-P).

iii. Long-term combinations of ASA and clopidogrel are not recommended for secondary stroke prevention [Evidence Level B] (CHARISMA, MATCH).

G7.1 Case Study: Antiplatelet Agents

Case Study

A 68 year old man with a right MCA is admitted into the rehabilitation unit. He has had a carotid ultrasound that shows a cholesterol plaque occluding 40% of the lumen of the right internal carotid vessel.

Q1. Assuming that he has had an atherothrombotic stroke, what treatment would you recommend to avoid a stroke recurrence?

Answer

1. Antiplatelet agents.

Q2. What is the major adverse side-effect of antiplatelet therapy?

Answer

1. Increased risk of bleeding.

Q3. Knowing there may be an increased risk of bleeding, would this influence your decision to use antiplatelet treatment and why?

Answer

1. No. Risk-benefit ratio is low with advantages for stroke prevention.

Q4. Describe the different types of antiplatelet therapy?

Answer

- ASA
- Thienopyridines – Clopidogrel and Ticlopidine
- Dipyridamole

Q5. If antiplatelet therapy is the treatment of choice, which drug would be the initial choice?

Answer

1. Monotherapy with low-dose ASA (81 mg/day) would be the initial choice.

Q6. The patient's family believe the patient should get at least 325 mg of Aspirin per day. How do you respond?

Answer

1. ASA 81 mg/day is just as effective as 325 mg/day with less potential side effects.

Q7. When should antiplatelet treatment be initiated and when should it be terminated?

Answer

Antiplatelet treatment should be initiated in the acute phase and is usually continued for the rest of the patient's life.

Case Study (continued)

You tell the nurse that the patient is going to begin taking 81mg of aspirin/day but the nurse tells you that the patient is allergic to ASA.

Q8. Which other treatment options are available?

Answer

1. Clopidogrel.

Q9. The nurse questions you about the difference between ASA and Clopidogrel in terms of effectiveness.

Answer

1. ASA and Clopidogrel have comparable effectiveness.

Q10. The nurse asks you why Clopidogrel is not used more often as the first line treatment.

Answer

1. Clopidogrel has more side-effects for the same efficacy.

Q11. Clopidogrel and Ticlopidine are both thienopyridines. Describe the differences between these two medications.

Answer

1. Ticlopidine has unacceptable side-effect profile, being associated with neutropenia and thrombotic thrombocytopenia purpura.

Q12. The resident asks about using combination therapy of different antiplatelet therapies.

Answers

1. The addition of aspirin to clopidogrel had little added benefit and the small demonstrated benefit when compared to Clopidogrel alone was outweighed by a higher rate of bleeding events associated with combined therapy (i.e. MATCH trial).
2. The addition of dipyridamole to ASA has a small benefit over ASA alone with a higher rate of side effects (largely headaches).
3. There does not appear to be a significant benefit to combination over single antiplatelet therapy.

G8. Atrial Fibrillation and Coumadin

Canadian Stroke Guidelines (2008): Recommendation 2.6 – Antithrombotic Therapy in Atrial Fibrillation

Patients with stroke and atrial fibrillation should be treated with warfarin at a target international normalized ratio of 2.5, range 2.0 to 3.0 (target international normalized ratio of 3.0 for mechanical cardiac valves, range 2.5 to 3.5) [Evidence Level A], if they are likely to be compliant with the required monitoring and are not at high risk for bleeding complications (ASA, AU, CSQCS, ESO, SIGN, VA/DoD).

G8.1 Atrial Fibrillation and Anticoagulation

Case Study

A 76 year old man is admitted to your rehabilitation unit with a left MCA stroke. In the emergency department atrial fibrillation was diagnosed and was thought to be the cause of the stroke.

Q1. What is the relationship between atrial fibrillation and the development of stroke?

Answer

1. AF is a powerful, independent risk factor for ischemic stroke.
2. Leads to embolic stroke, with emboli formed within the fibrillating left atrium.

Q2. What are some other cardiac disorders that could lead to an embolic stroke?

Answer

Cardiac risk factors can be divided into atrial fibrillation, myocardial disease and cardiac valve factors.

Q3. Once a patient with AF has had a stroke, what is the risk for recurrence of stroke?

Answers

1. Within the first 2 weeks following a stroke event, the risk of recurrence has been estimated to be 0.1%-1.3% per day. Conversely, the risk for AF patients with a history of prior stroke or TIA has been estimated to be 12% per annum (Devuyst and Bogousslavsky 2001).
2. The presence of AF in individuals following their first ischemic stroke has been shown to be associated with higher rates of stroke recurrence (6.9% vs 4.7%, p=0.04) (Marini et al. 2005).

Q4. Describe some contraindications for anticoagulant therapy?

Absolute Contraindications

- Subarachnoid or cerebral haemorrhage
- Malignant hypertension
- Serious active bleeding
- Recent brain, eye and spinal cord surgery
- Lack of patient compliance; ie. monitoring the PT, PTT.

Relative Contraindications

- Severe hypertension
- Major recent surgical operation
- Recent major trauma
- Active GI bleeding
- Bacterial endocarditis
- Severe renal failure
- Severe hepatic failure
- Haemorrhagic diathesis

Q5. Which drug would you use for anticoagulant therapy in this patient?

Answer

Warfarin (a vitamin K antagonist).

Q6. The patient's daughter asks you if treatment with warfarin is effective and also wants to know the optimal range of INR.

Answers

1. Warfarin has been shown to reduce the risk of recurrent stroke in appropriate patients by almost two-thirds.
2. INR should range between 2.0 and 2.5 or 3.0.

Q7. The patient's daughter asks you when treatment should be initiated.

Answer

1. Warfarin should be initiated as soon as possible.
2. A delay in initiating warfarin is appropriate for patients with large infarcts or uncontrolled hypertension.

Q8. The nurse asks you to explain to the patient any negative side effects associated with warfarin.

Answer

1. Main side effect is an increased risk of bleeding.

Q9. The resident asks why not use ASA alone as treatment for atrial fibrillation.

Answer

1. ASA therapy (300-325 mg/day) is associated with a reduction in the risk of stroke with AF.
2. Meta-analyses clearly show Coumadin to be more effective than ASA.

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G9. Patent Foramen Ovale

G9.1 Case Study: PFO

Case Study

You see a 45 year old woman in your outpatient clinic. She has had a TIA and her echocardiogram shows a patent foramen ovale (PFO).

Q1. What it is a PFO?

Answer

1. Patent foramen ovale is a congenital defect in the interarterial septum.
2. Associated with a right-left shunt.

Q2. Is PFO a stroke risk factor?

Answer

1. Studies have found an association between PFO and strokes of unknown etiology.

Q3. How can PFO be treated?

Answer

1. Antiplatelet therapy unless there is some other indication for anticoagulation.

Q4. The resident asks you if it is necessary to close the PFO.

Answer

1. Operation is not recommended unless it is a recurrent stroke despite optimal medical therapy.

G10. Carotid Artery Stenosis

Canadian Stroke Guideline (2008): Recommendation 2.7 – Carotid Intervention

2.7a Symptomatic carotid stenosis

Patients with transient ischemic attack or nondisabling stroke and ipsilateral 70%–99% internal carotid artery stenosis (measured on a catheter angiogram or by 2 concordant noninvasive imaging modalities) should be offered carotid endarterectomy within 2 weeks of the incident transient ischemic attack or stroke unless contraindicated [Evidence Level A] (ASA, AU, CSQCS, ESO, NZ, SIGN 14).

- i. Carotid endarterectomy is recommended for selected patients with moderate (50%–69%) symptomatic stenosis, and these patients should be evaluated by a physician with expertise in stroke management [Evidence Level A] (ASA, AU, CSQCS, NZ, SIGN 14).
- ii. Carotid endarterectomy should be performed by a surgeon with a known perioperative morbidity and mortality of < 6% [Evidence Level A] (ASA, CSQCS, ESO, NZ).
- iii. Carotid stenting may be considered for patients who are not operative candidates for technical, anatomic or medical reasons [Evidence Level C].
- iv. Carotid endarterectomy is contraindicated for patients with mild (< 50%) stenosis [Evidence Level A] (ASA, CSQCS, SIGN 14).

2.7b Asymptomatic carotid stenosis

Carotid endarterectomy may be considered for selected patients with asymptomatic 60%–99% carotid stenosis.

- i. Patients should be less than 75 years old with a surgical risk of < 3%, a life expectancy of > 5 years and be evaluated by a physician with expertise in stroke management [Evidence Level A] (AAN, AHA, AU, CSQCS).

G10.1 Case Study: Carotid Endarterectomy (CEA)

Case Study

A 62 year old woman was admitted to your rehabilitation unit with a left MCA ischemic stroke. 75% stenosis of the left internal carotid artery due to atherosclerotic plaque was found on carotid ultrasound.

Q1. What issues must be considered when deciding on therapeutic options?

Answers

1. Grade of occlusion (< 50%, 50-69%, >70%)
2. Cost-benefit of surgery (Risk of medical treatment, Benefit of surgery)
3. Surgical risk

Q2. In this case, what will be your recommendation and why?

Answers

1. Carotid endarterectomy
2. NASCET trial showed that >70% occlusion benefits from carotid endarterectomy.

Q3. The medical student asks you why you think carotid endarterectomy (CEA) should be used instead of carotid artery stenting (CAS).

Answer

1. CAS is a good as CAS over the short to medium term, but the risk of severe restenosis is higher.

Case Study (continued)

The radiologist revises his report; the grade of stenosis was 60%, not 75%.

Q4. Does this change your treatment decision?

Answer

1. Results of NASCET were less impressive for the 50-69% stenosis group. One must carefully calculate the risk of the intervention but CEA is still an option.

Q5. How long after the symptomatic event do you recommend performing the CEA?

Answer

1. The sooner the better.

G10.2 Case Study: Symptomatic Stenosis (<50%)

Case Study

A 62 year old woman was admitted to your rehabilitation unit with a left MCA ischemic stroke. A 40% stenosis due to atherosclerotic plaque was found on the carotid ultrasound.

Q6. What will be your recommendation in this case and why?

Answer

1. Medical treatment is the only option.
2. Not a surgical candidate.

G10.3 Case Study: Non-symptomatic Stenosis

Case Study

You see a 55 year old man in your outpatient clinic. He has an asymptomatic 55% stenosis in his right internal carotid artery.

Q7. What is the risk of stroke for this patient?

Answer

1. The one year risk of stroke in patient with ICA stenosis is 1-3%. The 10 and 15 year risk of stroke if >50% stenosed is 9.3% and 16.6% respectively.

G10.4 Case Study: Recurrent Carotid Stenosis

Case Study

You see a 52 year old man in your outpatient clinic who was treated with CEA for his symptomatic 70% stenosis of his left internal carotid artery. In his new ultrasound you find a restenosis of 80% and he is complaining about recurrent numbness in his right side

Q8. Which treatment do you recommend in this situation, carotid endarterectomy or carotid artery stenting?

Answer

1. For recurrent carotid stenosis post carotid endarterectomy, carotid artery stenting results in similar outcomes.