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Clinical Guide - Prevention of Ischemic Stroke

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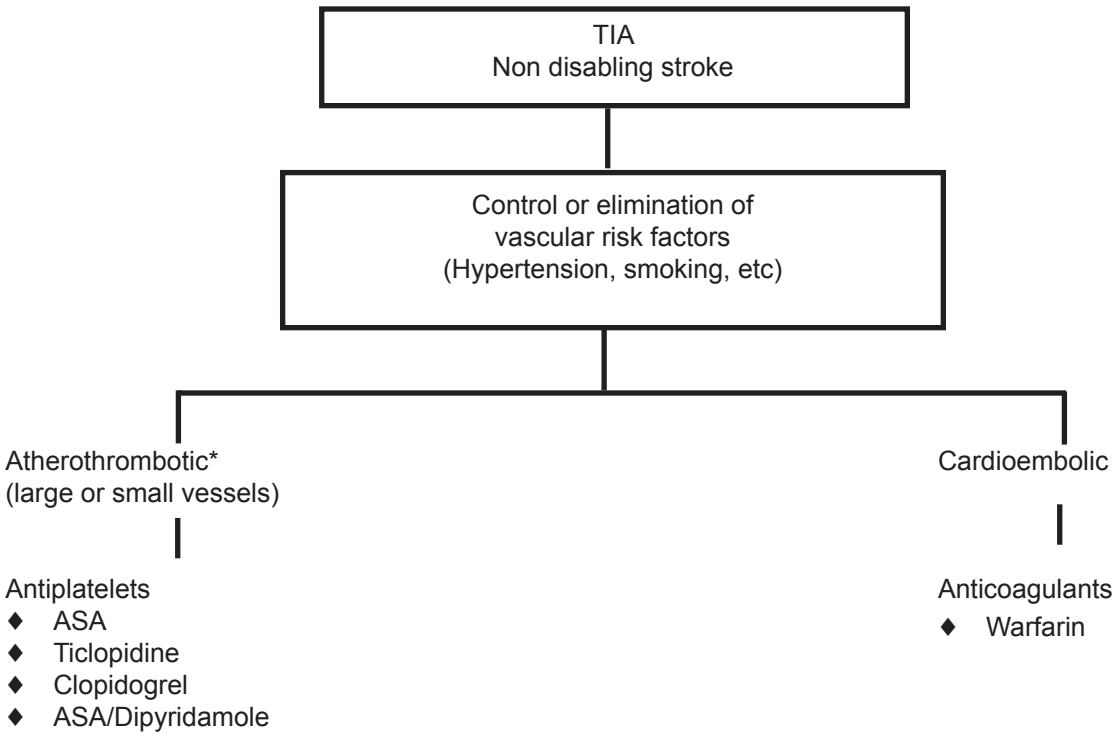
Background

Stroke constitutes a major medical problem representing one of the most common causes of mortality and disability. Although strokes can be of an hemorrhagic nature, ischemic strokes are by far the most common ones accounting for approximately 85% of all strokes.

Epidemiology

Annually, almost 50,000 new cases of stroke occur in Canada and the associated short term mortality is about 20 - 25%. Of the 200,000 stroke survivors in Canada approximately 40-50% are left with varying degrees of disability affecting activities of daily living. The prevalence of stroke increases with age and other risk factors such as hypertension, smoking, and associated cardiac conditions such as atrial fibrillation. The risk of experiencing an ischemic stroke after an initial stroke or after a transient ischemic attack (TIA) is approximately 10-20% in the first year.

Prevention of Ischemic Stroke



* If symptomatic carotid stenosis (>70%) endarterectomy indicated. Endarterectomy can also be considered in some patient with >50% symptomatic carotid stenosis.

As mentioned previously carotid endarterectomy is beneficial in selected patients, however angioplasty/stenting of the cervical/intracranial arteries is still considered investigational.Recent reviews (see references 1 and 2) have covered several aspects of stroke prevention ina more comprehensive fashion.The following focuses on the antithrombotic aspects.

- **Acetylsalicylic Acid (ASA):** Drug most commonly used for stroke prevention, recommended dosage is between 50-325 mg/day.. Side effects are mostly GI related including peptic ulcer disease.
- **Clopidogrel:** Analog of ticlopidine but with better safety profile. Comparable antiplatelet effect showing a modest advantage over ASA for prevention of ischemic events and no increased incidence of neutropenia compared to ASA. The dosage is 75 mg once a day. Clopidogrel should be used in cases where ASA has failed, is not tolerated or an allergy to ASA exists.
- **Dipyridamole:** Dipyridamole in combination with low dose ASA has been shown to be effective for stroke prevention. The combination of ASA 50 mg/day and dipyridamole slow release 400 mg/day has been shown to reduce the risk of stroke by approximately 23% compared to ASA. The most ommon side effects of dipyridamole is headache.
- **Ticlopidine:** Slightly superior to ASA for preventing stroke but less well tolerated. Dosage of ticlopidine is 250 mg b.i.d. Common side effects include diarrhea and rash. Hematological complications include severe neutropenia in 0.8% of cases. Close monitoring of neutrophil count is suggested every 2 weeks for first 3 months. Increased incidence of thrombotic thrombocytopenic purpura has also been reported.

Comparison of antiplatelet agents

The following is a semi-quantitative evaluation of antiplatelets for the prevention of stroke and other vascular events based on selected criteria and available evidence.

	Clopidogrel	ASA	Ticlopidine	ASA/DipyridamoleSR
Efficacy	+++	++	+++	++++
Tolerability	+++	+++	+	++
Routine Monitoring	No	No	Yes	No
Dosing Frequency	od	od	bid	bid
Cost	++++	+	++	+++

All of the above antiplatet agents except for Ticlopidine are acceptable for initial therapy but because of its efficacy, safety and cost, ASA should probably be used first in most circumstances for ischemic stroke prevention. Alternatives to ASA for second choice would include clopidogrel or the combination of ASA /DipyridamoleSR. The combination of ASA and Clopidogrel cannot be recommended for long term stroke prevention both because of a lack of efficacy and increased risk of intracranial hemorrhage.

- **Warfarin:** Oral anticoagulants have been shown to provide more benefit in certain conditions where the mechanism of ischemic stroke is presumed to be cardioembolic (atrial fibrillation, post MI) **[See guidelines for these specific conditions]** or in the case of cerebral sinovenous thrombosis. Recent evidence does not support it's use over ASA for the prevention of recurrent stroke after a first noncardioembolic ischemic stroke or for patients presenting a symptomatic intracranial arterial stenosis.

Childhood stroke

The incidence of pediatric ischemic stroke is 3.3/100,000 children/year. The ratio of arterial ischemic stroke to sinovenous thrombosis is approximately 4:1. Neonates make up 25-30% of pediatric ischemic stroke patients and there is a slight male predominance. Residual neurological deficits are present in 20% of sinus thrombosis and 50% of arterial ischemic stroke survivors.

- **Aspirin:** For prevention of ischemic stroke, the recommended dosage is 3-5mg/kg/day. Grouping the doses into every other day scheduling is feasible because of the prolonged effect of the medication on platelet function. Reye's syndrome has not been reported at this low dose.
- **Warfarin:** Arterial Ischemic Stroke: Major uses of warfarin treatment in children with arterial ischemic stroke include congenital or acquired heart disease, severe hypercoagulable states, arterial dissection and recurrent stroke or transient ischemic attack while on aspirin. Target International Normalized Ratio (INR) is 2.0-3.0.
- **Sinovenous Thrombosis:** Following acute anticoagulation, children with sinovenous thrombosis can be treated as is the practice in adults, with a minimum of 3-6 months of warfarin.

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