ASPIRIN DOSING FOR PREVENTION AND TREATMENT OF ISCHEMIC STROKE

Stroke represents the third leading cause of death in the United States and 1 out of every 18 deaths in 2006 occurred due to a stroke. In addition, stroke complications leads to disability, impaired functionality, and reduced quality of life. Since most of strokes are ischemic, antithrombotic agents (e.g., aspirin, clopidogrel, ticlopidine, extended-release dipyridamole, warfarin) are the gold standard for prevention of stroke. Aspirin is typically used as first-line therapy due to its affordability, lack of needed monitoring, and clinical efficacy. However, controversy exists regarding the optimal aspirin dosing for treatment and prevention of ischemic stroke. This issue of CLIPS briefly summarizes an article about appropriate dosing of aspirin in the prevention and treatment of stroke. If you need further information, please contact the Samford University Drug Information Service at (205) 726-2659.


Mechanism of action
- Aspirin prevents vascular complications by inhibiting the effects of platelets and has the ability to prevent arterial thrombosis through COX enzyme inactivation (primarily COX-1).
- Antiplatelet actions occur within 30 minutes after ingestion and are maintained throughout the lifespan of the platelet.
- Arterial thrombosis leads to vascular thrombus formation, intraluminal occlusion, and transient ischemia or infarction.

Primary Prevention
- Aspirin 100mg every other day should be considered for primary prevention in women over 45 without a history of heart or cerebrovascular disease.
- Current guidelines from the American Heart Association include a class IIa recommendation for aspirin use in high-risk women and recommend against its use in men for primary prevention of stroke.
- Despite the lack of efficacy for primary stroke prevention in men, aspirin is recommended at a minimum dose of 75 mg daily for patients at risk for CV events.

Acute Ischemic Stroke
- Aspirin 160-300 mg daily administered within 48 hours of ischemic stroke provide small reductions in death and recurrent ischemic stroke rates.
- ACCP recommends early ASA therapy (150-325 mg) for patients with acute ischemic stroke who have not received thrombolysis with TPA.
- AHA and American Stroke Association recommend ASA 325 mg.

Stroke Prevention in Atrial Fibrillation (AF)
- Aspirin is recommended by the current Chest and American College of Cardiology guidelines as an alternative to warfarin in patients with ≤1 risk factor.
- Several clinical trials failed to show a reduction in stroke rates with aspirin use. However, some meta-analyses suggest that 325 mg of aspirin daily reduces the incidence of stroke in the AF setting.
- Chest AF guidelines recommend a low dose aspirin (75-100 mg daily) in certain patient populations to decrease the risk of cardioembolic events so as to limit bleeding risk.

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Stroke Prevention in Carotid Artery Disease Following Carotid Endarterectomy
- Several studies revealed a clear benefit with aspirin following carotid endarterectomy for secondary stroke or TIA prevention, as well as a possible mortality reduction.
- Current guidelines from the AHA and American Stroke Association, regardless if carotid endarterectomy was performed, recommend aspirin doses of 50-325 mg daily.

Secondary Stroke Prevention
- ASA 30-1300 mg daily prevent strokes in patients with prior TIA or stroke; however, higher doses are associated with greater bleeding risks.
- Minimum dose needed is ASA 50 mg daily.
- AHA/American Stroke Association recommends ASA 50-325 mg daily for secondary prevention of ischemic stroke or TIA.
- Clopidogrel and extended-release dipyridamole are alternatives for patients who are unable to tolerate ASA.

Secondary Prevention of Stroke in Post-Myocardial Infarction Patients
- Data suggests that the addition of aspirin may reduce the incidence of stroke in post MI patients.
- Despite the lack of stroke prevention, post MI patients should be treated with aspirin 75 mg daily for the prevention of CV events.
- The AHA recommends indefinite oral aspirin therapy at doses of 75-162 mg daily for the secondary prevention of CV.

Dose-Related Bleeding Rates with Aspirin
- Low doses of aspirin <100mg are associated with the lowest risk of bleeding.
- Doses ≤200 mg cause fewer major bleeds when compared to doses >200 mg.

Summary:
- Aspirin has been proven to reduce the risk of stroke in a wide variety of setting but it is still not proven to be efficacious for the primary prevention of stroke in men or in post MI patients.
- There are a wide variety of applications for aspirin use. Individual guidelines and trials have a wide range of recommended doses for stroke prevention.
- The following table provides a summary of the recommendations for the use of ASA for the treatment and prevention of stroke.

<table>
<thead>
<tr>
<th>Indication</th>
<th>Minimum Daily Dose</th>
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<tbody>
<tr>
<td>Primary prevention in men</td>
<td>None identified</td>
</tr>
<tr>
<td>Primary prevention in women</td>
<td>100 mg every other day</td>
</tr>
<tr>
<td>Acute ischemic stroke</td>
<td>160 mg daily</td>
</tr>
<tr>
<td>Secondary stroke prevention</td>
<td>50 mg daily</td>
</tr>
<tr>
<td>Post-myocardial infarction</td>
<td>75 mg daily (not proven to prevent ischemic stroke)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>325 mg daily</td>
</tr>
<tr>
<td>Post-carotid endarterectomy</td>
<td>81 mg daily</td>
</tr>
</tbody>
</table>

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