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FPIN's Clinical Inquiries

Aspirin in Patients with Acute Ischemic Stroke

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Clinical Question

Does aspirin decrease morbidity or mortality in patients with acute ischemic stroke?

Evidence-Based Answer

Aspirin in a daily dose of 160 to 300 mg initiated within 48 hours of symptom onset results in a net decrease in morbidity and mortality caused by acute ischemic stroke (Strength of Recommendation [SOR]: A, based on a systematic review), regardless of the availability of computed tomography (CT). (SOR: A, based on a meta-analysis).

Aspirin is as effective as anticoagulants in this regard and causes less harm (SOR: A, based on a systematic review), but it should not be used in patients receiving thrombolytic therapy. (SOR: B, based on one randomized controlled trial [RCT]).

Ibuprofen (Motrin) may decrease aspirin's effectiveness in acute ischemic stroke. (SOR: C, based on expert opinion).

Evidence Summary

Stroke is the third leading cause of mortality worldwide, with an estimated 30-day mortality of 10 percent. Of those who survive, 50 percent will require help for activities of daily living six months later. Approximately 80 percent of strokes are ischemic in origin.¹ Despite advances in the treatment of other atherothrombotic diseases, such as acute coronary syndrome, treatment options for acute ischemic stroke remain limited.

A Cochrane systematic review summarized nine RCTs (n = 41,399) evaluating the use of aspirin in treating acute ischemic stroke.² Six of the RCTs were double-blinded and placebo-controlled. Approximately 98 percent of the data was derived from two trials, the International Stroke Trial (IST; unblinded factorial design, no placebo)³ and the Chinese Acute Stroke Trial (CAST).⁴ Patients in these trials were treated with 160 to 300 mg of aspirin daily for two to four weeks, starting within 48 hours of the onset of symptoms. At a maximum of six months follow-up, aspirin therapy resulted in decreased odds of death or dependency (odds ratio [OR] = 0.94; 95% confidence interval [CI], 0.91 to 0.98; number needed to treat [NNT] = 77; cost of \$58 per improved outcome⁵), recurrent ischemic stroke (OR = 0.77; 95% CI, 0.69 to 0.87; NNT = 143), and pulmonary embolism (OR = 0.71; 95% CI, 0.53 to 0.96; NNT = 1,000).

This Cochrane review also demonstrated increased odds of complete recovery (OR = 1.06; 95% CI, 1.01 to 1.11; NNT = 100), despite an increased risk of symptomatic intracranial hemorrhage (OR = 1.23; 95% CI, 1.00 to 1.50; number needed to harm [NNH] = 500) and major extracranial hemorrhage (OR = 1.68; 95% CI, 1.34 to 2.09; NNH = 250). Overall, the numbers needed to treat are relatively large; however, they outweigh the small but measurable risk from aspirin therapy. Clinical benefit may not be apparent to the individual physician, but it is evident on a population level.²

The Cochrane review confirmed the findings of a previous meta-analysis of the IST and CAST. This meta-analysis included subgroup analyses, which found no difference in effect of treatment based on time from onset of symptoms (zero to 48 hours), age, sex, level of consciousness, history of atrial fibrillation, heparin administration, CT findings, or previous CT scanning. Patients with a hemorrhagic stroke who were inadvertently randomized did not appear to be harmed by aspirin (16 percent death or further stroke compared with 18 percent for the control group).⁶ A double-blind, randomized, placebo-controlled trial of 441 patients evaluated the effects of aspirin 325 mg daily for five days on progression of acute ischemic stroke compared with placebo. Aspirin did not affect stroke progression during the treatment period (relative risk = 0.95; 95% CI, 0.62 to 1.45), at discharge, or at three months as measured by the Scandinavian Stroke Supervision Scale. This study was not powered to detect the size of effect reported in the Cochrane review and meta-analysis described above.⁷

Another Cochrane systematic review summarizing 15 trials (n = 16,558) compared anticoagulants (unfractionated heparin or low-molecular-weight heparin) versus aspirin in acute ischemic stroke. No significant difference was found in rates of death or dependency, recurrent stroke, neurologic deterioration, or deep venous thrombosis/pulmonary embolism. However, anticoagulants were associated with higher rates of symptomatic intracranial hemorrhage (OR = 2.27; 95% CI, 1.49 to 3.46), major extracranial hemorrhage (OR = 1.94; 95% CI, 1.20 to 3.12), and all-cause mortality (OR = 1.10; 95% CI, 1.01 to 1.29).⁸

Lastly, a posthoc analysis was performed on data from a randomized factorial trial of 622 patients with acute ischemic stroke. Patients receiving both thrombolytics and aspirin had increased mortality at three to 10 days compared with those receiving thrombolytics alone (OR = 2.1; 95% CI, 1.2 to 3.6). These deaths were more likely to be cerebral in origin (death preceded by neurologic deterioration or recurrent stroke), rather than extracerebral (OR = 2.0; 95% CI, 1.3 to 3.7), with a trend toward cerebral hemorrhage (OR = 2.2; 95% CI, 1.0 to 5.0).⁹

Recommendations from Others

The American Heart Association and the American Stroke Association Stroke Council recommend an initial aspirin dose of 325 mg within 24 to 48 hours of the onset of symptoms; however, not within 24 hours of thrombolytic therapy.¹⁰ The American College of Chest Physicians recommends aspirin 160 to 325 mg daily started within 48 hours in patients not receiving thrombolytic therapy.¹¹

The U.S. Food and Drug Administration has issued a warning about the potential for concomitant ibuprofen use to decrease the antiplatelet effect of low-dose aspirin. Although it is unknown whether clinical end points are adversely affected, this interaction may be minimized by administering ibuprofen at least eight hours before or 30 minutes after an 81-mg dose of immediate-release (not enteric-coated) aspirin. Other nonsteroidal anti-inflammatory drugs should be considered to have the same potential effects unless proven otherwise.¹²

Clinical Commentary

The data are clear—in the setting of acute ischemic stroke, aspirin reduces the risk of death and recurrent stroke. Because it is inexpensive and well tolerated, it should be used routinely in this setting (although delayed one or two days after a thrombolysis attempt). However, physicians should keep in mind that other common clinical interventions, including blood pressure control, statin use, and smoking cessation, are each about three times more effective than aspirin at preventing future stroke. All these interventions must be integrated into the care of the patient with stroke for optimal long-term outcomes.

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