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ATHEROSCLEROTIC CARDIOVASCULAR DISEASE PRIMARY PREVENTION WITH ASPIRIN

The primary cause of death in the United States is due to cardiovascular issues. Although there has been a decline in death rates over the past decades, these improvements, are in part due to smoking cessation, reduction in untreated cholesterol and blood pressure, and use of antiplatelets (e.g., aspirin [ASA]), statins, antihypertensives and others. The purpose of this review is to discuss advances in treatment that promote the use of aspirin for primary prevention of cardiovascular disease. If you need further information, please contact the Center for Healthcare Innovation and Patient Outcomes Research (CHIPOR) at CHIPOR@samford.edu.

Mora S, Manson JE. Aspirin for primary prevention of atherosclerotic cardiovascular disease. *JAMA Intern Med.* 2016;176:1195-1204.

Randomized clinical trials and meta-analyses with aspirin in primary prevention of cardiovascular disease

- The use of aspirin should be carefully evaluated in patients without clinical atherosclerotic cardiovascular disease (ASCVD) because the ASCVD risk is lower than that of patients with ASCVD. Aspirin use in patients without ASCVD may be associated with an increased risk of bleeding.
- Evidence from the 2016 United States Preventive Services Task Force (USPSTF) systematic review indicated that aspirin primary prevention trials (n=11 trials, n=118,445 patients) were associated with a significant reduction in nonfatal myocardial infarction (MI; 22%), cardiovascular mortality (6%), and all-cause mortality (6%).
- Aspirin doses ≤100 mg were associated with a significant reduction in nonfatal MI (17%) and nonfatal stroke (14%).
- In four additional randomized trials, aspirin and other agents (e.g., statins) were evaluated to determine if a significant reduction in total ASCVD (nonfatal and fatal events) were observed and aspirin use did not significantly reduce these endpoints.

Cardiovascular mortality

- Patients without ASCVD experience little or no benefit from the use of aspirin therapy.
- Lack of reduction in CV mortality may be due to a variety of reasons including: advances in treatment options and interventions (e.g., revascularizations and thrombolysis) for MI and stroke; cross-contamination by cross over to active aspirin therapy after a nonfatal ASCVD event occurs; lower mortality rates in primary vs. secondary prevention populations; and significant reductions in nonfatal ASCVD events with aspirin in primary prevention populations.

Baseline ASCVD risk

- The appropriate use of ASA in patients without ASCVD has not been determined due to the risks associated with ASA therapy.
- Primary prevention trials have included patients with low or very low estimated baseline ASCVD risk (10-year risk <10%).
- The benefit:risk profile of aspirin is largely dependent on baseline ASCVD risk.
- If a patient's baseline calculated 10-year ASCVD risk is at least 10%, the estimated ASA benefit was 1%- 2% for reducing ASCVD risk over 5 years.
- Additional clinical trials are needed to determine the ASCVD risk in patients with a 10-year risk of ≥ 10%.

Age

- Age is a major determinant of ASCVD risk.

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Age (continued)

- In one meta-analysis (2009 Antithrombotic Trialists [ATT]), similar reductions with ASA were observed between those younger or older than 65 years.
- However, in the Women's Health Study (WHS), ASA use was associated with a reduction in both MI and ischemic stroke. Women aged 45-64 years had no reduction in ASCVD events.
- 2016 USPSTF recommendations deemed the evidence insufficient to recommend ASA for patients ≥70 years or for those <50 years.

Differences by Gender

- Clinical trials that evaluated ASA efficacy in women and men with ASCVD found similar results.
- Primary prevention trials between genders have revealed some differences. ASA was shown to reduce the risk of MI, but not ischemic stroke in men and in women, the risk of ischemic stroke, but not MI were reduced.
- The 2016 USPSTF recommendations state that ASA use in primary prevention does not differ by sex.

Appropriate ASA dose and formulation

- Mixed recommendations have been made regarding the appropriate ASA dose (up to 325 mg/d).
- ASA doses between 75 and 162 mg/day appear to be as effective as higher doses without the bleeding risk.
- Enteric coated or buffered ASA do not appear to improve ASA safety.
- Up to 28% of patients treated with ASA has displayed resistance to therapy.
- In addition, genetic testing should not be used for targeting the appropriate ASA dose.

Colorectal Cancer

- The 2016 USPSTF recommendations include taking a low-dose aspirin product daily for at least 10 years in patients with a life expectancy of at least 10 years for both colorectal cancer and cardiovascular benefit.
- A relative risk reduction of 40% for aspirin use of at least 10 years for colorectal cancer was observed.

Gastrointestinal (GI) bleeding

- Risk factors can increase the risk of GI bleeding including: *Helicobacter pylori* infection; a history of an upper GI disorder; age >60 years; male sex; concomitant use of NSADs; or other medications; excess alcohol; and renal or liver disease.

GI prophylaxis

- Proton pump inhibitor (PPI) use may reduce the risk of upper GI bleeding by half in patients receiving aspirin.
- PPI use is recommended for reducing GI bleeding risk in patients with multiple risk factors who require ASA.

Summary

- Decisions to initiate ASA therapy should be highly individualized. Risk:benefit profile should be discussed prior to initiating long-term treatment.
- ASCVD risk assessment, GI bleeding risk factors, and age/sex based factors should be addressed.

Prepared by: Maisha Kelly Freeman, Pharm.D., MS, BCPS, FASCP

Atherosclerotic cardiovascular disease primary prevention with aspirin. *CLIPs- Current Literature and Information for Pharmacists.* 2016 September 5;20(9):1-2.