Long-Term Care Updates

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Effects of Low-Dose Aspirin on the Incidence of Anemia in Elderly Patients

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Introduction

Aspirin is a nonsteroidal anti-inflammatory drug (NSAID) indicated to reduce the risk of death and myocardial infarction in patients with coronary artery disease and to reduce the risk of death and recurrent stroke in patients who have had an ischemic stroke or transient ischemic attack. Aspirin exerts its antithrombotic effects through irreversible inhibition of cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2), which results in decreased formation of prostaglandin precursors and platelet aggregation. COX-1 exerts gastroprotective effects through increased bicarbonate and mucus secretion. The inhibition of this enzyme in conjunction with aspirin's platelet inhibiting properties increases the risk of gastrointestinal bleeding. Intracranial bleeds have also been reported with its use.[1]

The Aspirin in Reducing Events in the Elderly (ASPREE) trial was designed to assess whether treatment with 100 mg of enteric-coated aspirin, compared to placebo, extended the duration of disability-free life in healthy participants ≥ 70 years or ≥ 65 years and older if they were Black or Hispanic. The authors concluded that although low-dose aspirin is recommended as secondary prevention in patients with a history of cardiovascular events, its use in geriatric patients for primary prevention is no longer recommended due to the lack of evident benefits and the increased risk of major bleeding.[2]

A secondary review of the ASPREE trial data analyzed aspirin's effect on the incidence of anemia, hemoglobin concentrations, and ferritin levels. Anemia is associated with functional decline in geriatric patients, including increased fatigue, depressive symptoms, slowed cognition, and increased mortality. This post-hoc analysis of the original ASPREE trial is designed to assess the effect of daily low-dose aspirin on the incidence of anemia in a generally healthy older population.[3]

The purpose of this newsletter is to review the results of the post-hoc analysis and provide insight into the effects of low-dose aspirin on the incidence of anemia in the elderly.

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Results

A total of 18,153 participants were included in the post-hoc analysis. The primary outcome for this analysis was incident anemia, defined by the World Health Organization as hemoglobin <130 g/L for men and <120 g/L for women. The secondary outcomes for this analysis were changes in hemoglobin concentration and ferritin levels, which are indicators of iron deficiency.[3]

Effects of aspirin on incidence of anemia

The incidence of anemia was 51 events per 1000 person-years in the aspirin group compared with 43 events per 1000 person-years in the placebo group. The estimated probability of experiencing anemia within 5 years was 23.5% (95% CI, 22.4% to 24.6%) in the aspirin group and 20.3% (95% CI, 19.3% to 21.4%) in the placebo group. Treatment with aspirin resulted in a 20% increased risk for anemia (HR 1.20, CI 1.12 to 1.29). The effect of aspirin on incident anemia was consistent across subgroups including age, sex, CKD, DM, smoking, alcohol use, and concomitant NSAID or PPI use.[3]

Effects of aspirin on hemoglobin concentration

Participants randomly assigned to placebo had hemoglobin levels decline by a mean 3.6 g/L per 5 years. Those randomly assigned to aspirin had an estimated lower mean baseline of 0.4 g/L (CI 0.1 to 0.7 g/L) and experienced a steeper decline in hemoglobin over time by 0.6 g/dL (CI 0.3 to 1.0 g/L) compared with placebo.[3]

Effects of aspirin on ferritin

Out of the 8295 participants that had their serum ferritin levels measured either before random assignment or within 4 weeks of beginning the intervention, 7139 participants had their levels re-measured 3 years later. Participants in the aspirin group were more likely to have serum ferritin less than 45 μ/L and less than 100 μ/L at year 3. Serum ferritin levels declined by an average of 16% in the aspirin group and 3% in the placebo group after 3 years. After adjusting for baseline levels, the average decrease in ferritin levels at year 3 was found to be 11.5% greater in the aspirin group compared with placebo.[3]

Conclusion

Upon reviewing the collected data, the risk of developing anemia for patients taking aspirin was determined to be 23.5%, an incidence rate 20% higher than patients assigned placebo. Even when major bleeding was censored in the statistical analysis, participants in the aspirin group are more likely to experience incident anemia, changes to hemoglobin concentrations, and ferritin levels. While only a minority of participants are likely to experience major bleeding, aspirin still exerts an increased risk for anemia likely due to lesser degrees of bleeding and occult blood loss.

Between 2011 and 2018, approximately half of all US adults aged 60 years and older were taking aspirin for primary prevention of cardiovascular disease (CVD); however, recent guideline changes may decrease the use of aspirin for primary CVD prevention. In April 2022, the U.S. Preventive Services Task Force (USPSTF) released a statement recommending the initiation of low-dose aspirin for the primary prevention of CVD in adults 40 to 59 years old who have a 10% or greater 10-year CVD risk should be decided on an individual basis. Aspirin initiation is not recommended in adults 60 years and older. Current evidence is inadequate regarding CVD or mortality reduction.[4]

Ultimately, the decision of whether or not to initiate aspirin therapy for primary prevention of CVD should be a conversation between patient and provider within the established clinical guidelines. Benefits should be weighed against the risks for optimal therapy.

References

1. Clinical Pharmacology. Tampa, FL: Gold Standard, Inc; 2015 https://www.clinicalkey.com/pharmacology/monograph/44. Updated December 17, 2019.
2. McNeil JJ, Nelson MR, Woods RL, et al. Effect of Aspirin on All-Cause Mortality in the Healthy Elderly. N Engl J Med. 2018;379(16):1519-1528.
3. McQuilten ZK, Thao LTP, Pasricha SR, et al. Effect of Low-Dose Aspirin Versus Placebo on Incidence of Anemia in the Elderly : A Secondary Analysis of the Aspirin in Reducing Events in the Elderly Trial. Ann Intern Med. 2023;176(7):913-921.
4. Aspirin Use to Prevent Cardiovascular Disease: Preventive Medication | United States Preventive Services Task-force. U.S. Preventative Services Task Force. April 2022. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/aspirin-to-prevent-cardiovascular-disease-preventive-medication