

Aspirin use in elderly for primary prevention of Cardiovascular Disease: Double edged sword?

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Title: Major GI bleeding in older persons using aspirin: incidence and risk factors in ASPREE randomized trial.

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Summary

As the aging population increases globally, adopting cost-effective preventive measures to maintain a healthy and active lifestyle in this demographic is a challenge. The major causes of disability in the older population can be due to atherosclerotic cardiovascular disease, cancer and dementia. Aspirin as a primary preventive strategy may be effective against atherosclerotic vascular diseases, cancer and dementia.^{1,2,3}

Efficacy of Aspirin in secondary prevention of atherosclerotic cardiovascular events is well established.⁴ Recently, aspirin as a primary prophylaxis against cardiovascular diseases has been studied in three major trials ARRIVE, ASCEND, and ASPREE5.^{6,7} In the ARRIVE trial, Aspirin was used in patients with moderate to high cardiovascular risk. In the ASCEND trial, aspirin was used in patients with diabetes mellitus (DM) and in the ASPREE trial elderly patients were enrolled. Of these three studies, only the ASCEND trial has shown a significant reduction in the rate of major adverse cardiovascular events and this was accompanied by a significant increase in major bleeding. The ASPREE trial was designed to address the composite primary end point termed “disability free life”, resulting from cardiovascular disease events, cancer and dementia. Unfortunately, the study was prematurely ended due to lack of efficacy for the primary endpoint.

In general, Aspirin usage is associated with increased risk of bleeding including gastrointestinal tract⁸. Robust data is lacking on significant gastrointestinal bleeding with the low dose aspirin being used as a primary preventative strategy

in the older population. Mahady et al studied major GI bleeding in older people using aspirin: Incidence and risk factors in the ASPREE randomized control trial⁹. ASPREE trial was a double blind trail which enrolled 19,114 apparently healthy Australian and US adults over 70-years-old or Black and Hispanic adults over 65 year old in US were recruited. Participants were randomised and given either 100 mg per day of enteric coated Aspirin or a placebo. There were 137 upper gastrointestinal bleeds (89 in the aspirin group and 54 in the placebo group) and 127 lower GI bleeds (73 in the aspirin group and 54 in the placebo group), representing a 60% increase in incidence of bleeding during the study period. There were two fatal bleeds in the placebo group. On multivariate analyses, age, smoking, hypertension, chronic kidney disease and obesity were associated with increased risk of bleeding. The absolute 5-year risk of bleeding was only 0.25% for a 70-year-old without aspirin compared to 5.03% for an 80 year old taking aspirin with additional risk factors. The study concluded that 5-year absolute risk of overall GI bleeding up by 60%, compared to healthy younger individuals.

Opinion

There has been a significant increase in the aging population in the last few decades due to improvement in life expectancy resulting from major healthcare advances. Risk of atherosclerotic cardiovascular disease doubles with each decade of life beyond traditional risk factors¹⁰. In the older population, usage of over the counter medications - especially nonsteroidal anti-inflammatory drugs (NSAIDs) due to chronic pain along with multiple comorbidity – increases the risk of

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gastrointestinal bleeding both by mucosal irritation and by potentiating aspirin's antiplatelet effect.

In view of serious adverse events including bleeding, other primary preventive strategies should be the first line against atherosclerotic cardiovascular diseases in the elderly. The usage of aspirin should be tailored to individuals after assessing risk and benefit.¹¹ Bleeding risk in the elderly is determined by multiple factors such as prior history of GI bleeding, liver and renal disease, fall risk, frailty and concomitant usage of other drugs like NSAIDs. Further, it is advisable to use low dose aspirin alone, if aspirin usage is deemed necessary. To reduce the risk of GI bleeding, usage of enteric coated aspirin along with proton pump inhibitor may also be considered. Caution must be practised when prescribing aspirin in elderly patients who are obese, have a history of significant smoking, history of renal dysfunction or chronic liver disease, due to increased risk of bleeding. Other questions regarding aspirin use still exist. Should older people undergo an upper GI endoscopy to rule out H. Pylori gastritis and gastroduodenal ulcers before starting aspirin?

Does the eradication of H. Pylori infection decrease the risk of upper GI bleeding? Should adults who are taking aspirin for primary prevention of cardiovascular disease without any adverse effects, continue to use this medication after 70 years of age? Should individuals who are doing well with aspirin for secondary prevention after indexed cardiovascular events, continue this as life-long therapy after over 70 years of age? At present we do not have the answers to these questions. Additionally, these results cannot be extrapolated to the older population of other ethnic and geographical groups. We know that with increase in age, the risk of clinically significant GI bleeding increases. There is a need to balance the benefit of aspirin in reducing the risk of morbidity and mortality associated with atherosclerotic cardiovascular with risk of GI bleeding. Future studies should assess these points to find a solution. To summarise, aspirin is not a magic bullet as a primary preventive strategy against atherosclerotic cardiovascular disease, cancer and dementia in the older population. These individuals need to be educated about the risk of complications with "over the counter" usage of aspirin for primary prevention. **!**

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