

Antiplatelet therapy in peripheral artery disease - A brief overview

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In this brief communication, I intend to provide an overview of evolution of antiplatelet therapies for peripheral arterial disease supported by the major clinical trials. Many trials have evaluated the potential benefit of anti-platelet agents in reducing the incidence of clinical thrombotic events. The evidence from antiplatelet trialists' collaboration, which included an analysis of 145 randomized trials with about 70,000 high risk patients including those with peripheral arterial disease (A total of 2621 patients) showed a significant reduction in the combined end point of non fatal myocardial infarction, non fatal stroke and vascular death. The most widely tested antiplatelet regimen was medium dose aspirin (75-325 mg) in this meta-analysis [1]. This established aspirin as the most widely used antiplatelet agent for peripheral arterial disease. In three later studies that compared aspirin and ticlopidine, the odds ratio although favored ticlopidine, still was not statistically significant to be considered a superior antiplatelet agent [2]. Clopidogrel, which was available subsequently is a thienopyridine derivative, chemically related to ticlopidine (which had a favorable odds ratio in earlier trials) had a greater effect on thrombosis in animal models. The presumed superiority of clopidogrel resulted in the next trial comparing aspirin and clopidogrel. Clopidogrel (75 mg once daily) was shown to be superior to aspirin (325 mg once daily) in a randomized blinded trial in reducing the composite end point of ischemic stroke, myocardial infarction or vascular death, without any significant increase in adverse events [2]. The effect of combining aspirin with clopidogrel compared to aspirin alone was then tested. Overall, clopidogrel plus aspirin was not found to be significantly more effective than aspirin alone in reducing the rate of myocardial infarction, stroke, or death from cardiovascular causes [3]. Ticagrelor, an inhibitor of P2Y₁₂ receptor is newer antiplatelet agent that was

discovered subsequently. This agent was shown to be beneficial in patients with acute coronary syndrome and stable coronary disease, as defined by a history of myocardial infarction. In a clinical trial, patients with concomitant history of myocardial infarction and peripheral artery disease had a higher risk of cardiovascular events and a greater absolute risk reduction with ticagrelor than patients with history of myocardial infarction alone [4,5]. These promising data led to the next randomized trial comparing ticagrelor and clopidogrel. However, in this randomized, double blind clinical trial of 13,885 patients with symptomatic peripheral arterial disease, ticagrelor monotherapy (90 mg twice a day) was not superior to clopidogrel (75 mg once a day) in reducing the composite end point of adjudicated cardiovascular death, myocardial infarction, or ischemic stroke. Major bleeding occurred at similar rates among the patients in the two trial groups.

References

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