Effect of chronic treatment with acetylsalicylic acid and clopidogrel on atheroprogression and atherothrombosis in ApoE-deficient mice in vivo.

Acetylsalicylic acid (ASA) and the thienopyridine clopidogrel are established anti-platelet drugs that significantly reduce secondary cardiovascular events in patients with manifest atherosclerosis. However, their impact on atherosclerotic lesion development remains controversial. Four-week-old ApoE-deficient mice were randomly assigned to four groups receiving a cholesterol diet together with either ASA (5 mg/kg), or clopidogrel (25 mg/kg), or a combination of both ASA and clopidogrel, or vehicle for 8-12 weeks. Using intravital microscopy we found that daily administration of ASA in combination with clopidogrel reduces platelet thrombus formation following rupture of atherosclerotic plaque in vivo by approximately 50%. However, therapy with ASA or clopidogrel alone, or in combination for a period of 8-12 weeks had no significant effect on adhesion of platelets to dysfunctional endothelial cells or on atherosclerotic lesion formation in the aortic root or the carotid artery. In conclusion, anti-platelet therapy is effective in reducing platelet adhesion and subsequent thrombus formation following rupture of atherosclerotic plaque in vivo. However, our data do not support a role of either drug in the primary prevention of atherosclerosis in ApoE-deficient mice.