CLOPIDOGREL ALTERS THROMBUS QUANTITY AND QUALITY IN PATIENTS WITH TYPE II DIABETES MELLITUS AND STABLE CORONARY ARTERY DISEASE

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Recurrent thrombotic events are higher despite current secondary prevention therapy in patients with type 2 diabetes mellitus (T2DM) and coronary artery disease (CAD). Addition of clopidogrel to aspirin is proven beneficial after an acute event, but its benefits in stable CAD are unknown.

Methods: We hypothesised that clopidogrel improves thrombus quantity and quality in T2DM with proven stable CAD. Sixty six individuals with T2DM and CAD, (age 64±7 years, duration diabetes 9±5 years, BMI 33.0±5.5 kg/m2, HbA1c 58±8.5 mmol/mol) received ACC/AHA recommended secondary prevention therapy including aspirin 75mg od. In this randomised, double blinded, placebo controlled trial, participants received one week therapy with clopidogrel 75mg od or placebo (n=33 each). Thrombus area was quantified by the Badimon chamber and visco-elastic properties by thromboelastography (TEG). In 20 randomly identified participants, thrombus ultrastructure was assessed by quantitative scanning electron microscopy (SEM).

Results: Thrombus area was reduced after clopidogrel (14014±5230 vs 11025±4050 μ2/mm2, p=0.001), but not after placebo (13250±5501 vs 13723±5693 μ2/mm2, p=0.266). SEM showed platelet content of thrombus was lower with clopidogrel (84.4 vs 76.4 %, mean difference 8.0 (95%CI 1.5-14.5), p=0.022). Fibrin diameter increased with clopidogrel (171±11.7 vs 187±14.1 μ, p=0.016). Density of fibrin fibres also increased with clopidogrel (32.2±4.8 vs 41.0±10.2 n/μ2, p=0.023). All parameters remain unchanged after placebo therapy. Fibrin fibre diameter correlated negatively with TEG- measured shear elastic force of the thrombus (rho -0.609, p=0.007) and maximum amplitude of the visco-elastic force after ADP stimulation (rho -0.491, p=0.033).Thrombus lysis parameter, correlated positively to fibrin fibre diameter (rho 0.461, p=0.047).

Conclusions: In T2DM with proven stable CAD, addition of clopidogrel decreased platelet incorporation into thrombus, resulting in increased fibrin fibre diameter and fibre number density. This reduced the shear elastic strength of thrombus and promoted thrombus lysis. The clinical benefits of this strategy remain to be proven by large scale studies.