Background: It is not known whether further suppression of platelet function can be achieved with clopidogrel beyond that provided by currently recommended loading and maintenance doses. We performed a comparative assessment of the antiplatelet effects of a 600-mg loading dose of clopidogrel given to patients with and without chronic clopidogrel therapy.

Methods and Results: Those eligible for this prospective study were aspirin-treated patients with suspected or documented coronary artery disease admitted to hospital for coronary angiography. Two series of 20 consecutive patients each were assessed in this study. The first series included patients who had never received clopidogrel (first-use group); the second series included patients on chronic therapy with a daily dose of 75 mg clopidogrel for > or =1 month (chronic therapy group).

Blood samples were drawn before and 6 hours after oral administration of 600 mg clopidogrel for aggregometry and flow cytometry studies. In the first-use group, loading with 600 mg clopidogrel inhibited ADP 5 micromol/L-induced platelet aggregation from 90 +/- 9% to 51 +/- 19% (P<0.001). In the chronic therapy group, loading with 600 mg clopidogrel yielded further inhibition of ADP 5 micromol/L-induced platelet aggregation in addition to that achieved by the maintenance dose of 75 mg/d, from 52 +/- 14% to 33 +/- 12% (P<0.001). In both groups, 600 mg...
clopidogrel loading significantly inhibited ADP-induced expression of glycoprotein IIb/IIIa and P-selectin receptors. CONCLUSIONS: Further platelet inhibition can be achieved with clopidogrel in addition to that provided by currently recommended loading and maintenance doses. Higher doses may be warranted after assessment of their clinical efficacy and safety.