Evaluation of prolonged antithrombotic pretreatment ("cooling-off" strategy) before intervention in patients with unstable coronary syndromes: a randomized controlled trial.

Abstract:

CONTEXT: In unstable coronary syndromes, catheter intervention is frequently preceded by antithrombotic treatment to reduce periprocedural risk; however, evidence from clinical trials to support antithrombotic pretreatment is sparse. OBJECTIVE: To test the hypothesis that prolonged antithrombotic pretreatment improves the outcome of catheter intervention in patients with acute unstable coronary syndromes compared with early intervention. DESIGN, SETTING, AND PATIENTS: Randomized controlled trial conducted from February 27, 2000, to April 8, 2002, and including patients admitted to 2 German tertiary care centers with symptoms of unstable angina plus either ST-segment depression or elevation of cardiac troponin T levels. INTERVENTIONS: Patients were randomly allocated to antithrombotic pretreatment for 3 to 5 days or to early intervention after pretreatment for less than 6 hours. In both groups, antithrombotic pretreatment consisted of intravenous unfractionated heparin (60-U/kg bolus followed by infusion adjusted to maintain partial thromboplastin time of 60 to 85 seconds), aspirin (500-mg intravenous bolus followed by 100-mg twice-daily oral dose), oral clopidogrel (600-mg loading dose followed by 75-mg twice-daily dose), and intravenous
tiroliban (10- microg/kg bolus followed by continuous infusion of 0.10 microg/kg per min). MAIN OUTCOME MEASURE: Composite 30-day incidence of large nonfatal myocardial infarction or death from any cause. RESULTS: Of the 410 patients enrolled, 207 were allocated to receive prolonged antithrombotic pretreatment and 203 to receive early intervention. Elevated levels of cardiac troponin T were present in 274 patients (67%), while 268 (65%) had ST-segment depression. The antithrombotic pretreatment and the early intervention groups were well matched with respect to major baseline characteristics and definitive treatment (catheter revascularization: 133 [64.3%] vs 143 [70.4%], respectively; coronary artery bypass graft surgery: 16 [7.7%] vs 16 [7.9%]). The primary end point was reached in 11.6% (3 deaths, 21 infarctions) of the group receiving prolonged antithrombotic pretreatment and in 5.9% (no deaths, 12 infarctions) of the group receiving early intervention (relative risk, 1.96 [95% confidence interval, 1.01-3.82]; P =.04). This outcome was attributable to events occurring before catheterization; after catheterization, both groups incurred 11 events each (P =.92). CONCLUSION: In patients with unstable coronary syndromes, deferral of intervention for prolonged antithrombotic pretreatment does not improve the outcome compared with immediate intervention accompanied by intense antiplatelet treatment.