Clopidogrel was effective in patients who have MI with ST segment elevation receiving aspirin and fibrinolytic therapy


Clinical impact ratings Internal medicine ****** Cardioiology ******

In patients who have myocardial infarction (MI) with ST segment elevation and are receiving aspirin and standard fibrinolytic therapy, is the addition of clopidogrel beneficial?

METHODS

Design: randomised controlled trial (Clopidogrel as Adjunct Reperfusion Therapy [CLARITY]-Thrombolysis in Myocardial Infarction [TIMI] 28 Study).

Allocation: concealed.

Blinding: blinded (patients and healthcare providers).

Follow up period: to the start of coronary angiography (median 3.5 d), or in patients not having angiography, to hospital discharge or day 8, whichever came first.

Setting: 319 sites in 23 countries.

Patients: 3491 patients who were 18–75 years (mean age 57 y, 80% men); presented within 12 hours after the onset of ischaemic discomfort at rest lasting ≥20 minutes; had ST segment elevation of ≥0.1 mV in ≥2 contiguous limb leads, ST segment elevation of ≥0.2 mV in ≥2 contiguous precordial leads, or left bundle branch block that was not known to be old; and were scheduled to receive a fibrinolytic agent, aspirin, and heparin if a fibrin specific lytic agent was prescribed. Exclusion criteria included clopidogrel use in the previous 7 days, planned clopidogrel or glycoprotein IIb/IIIa inhibitor treatment before angiography, cardiogenic shock, and previous coronary artery bypass grafting.

Intervention: clopidogrel, 300 mg loading dose and then 75 mg once daily (n = 1752), or placebo (n = 1739), up to and including the day of coronary angiography (48–192 h after the start of study medication). Patients not having angiography had the study medication for 8 days or until hospital discharge.

Outcomes: primary outcome was composite of an occluded infarct related artery (TIMI flow grade 0 or 1), recurrent MI before angiography, or all cause mortality before angiography could be achieved benefit without any clinically relevant excess bleeding.

In fact, early hospital mortality was <3%, so the population was quite low risk. The trial excluded patients >75 years of age; thus the population most at risk and vulnerable to haemorrhage was not studied.

CONCLUSION

In patients with ST-segment elevation MI, recent efforts to improve upon a regimen of aspirin, thrombolysis, and heparin have met with frustration because aggressive antiplatelet strategies, primarily with glycoprotein IIb/IIIa receptor antagonists, have caused unacceptably high rates of haemorrhage. The CLARITY-TIMI 28 Investigators used the simple and elegant addition of clopidogrel to the triple therapy and achieved benefit without any clinically relevant excess bleeding. Unfortunately, the trial excluded patients >75 years of age; thus the population most at risk and vulnerable to haemorrhage was not studied.

Given the safety and clear benefit on coronary patency, the CLARITY-TIMI 28 trial appears to show that the addition of clopidogrel to aspirin, heparin, and thrombolytic therapy is an appropriate standard of care for younger patients who may have delayed catheterisation by several days. Because urgent angiography and primary angioplasty remain unavailable to a large number of patients worldwide and in the US with ST-segment elevation, thrombolysis will continue to be used, now with a safe, beneficial, and inexpensive adjunct.

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Abbreviations defined in glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article.

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