THERAPEUTICS

Clopidogrel before percutaneous coronary intervention reduced cardiovascular outcome in ST-elevation myocardial infarction

Sabatine MS, Cannon CP, Gibson CM, et al. **Effect of clopidogrel pretreatment before percutaneous coronary intervention in patients with ST-elevation myocardial infarction treated with fibrinolytics: the PCI-CLARITY study.** JAMA. 2005;294:1224-32.

Clinical impact ratings: Emergency Med ★★★★★★☆ Hospitalists ★★★★★★★ Cardiology ★★★★★☆☆

QUESTION

In patients with ST-elevation myocardial infarction (STEMI) treated with fibrinolytics, does clopidogrel pretreatment before percutaneous coronary intervention (PCI) reduce cardiovascular death, recurrent MI, or stroke?

METHODS

Design: Planned subanalysis of a randomized placebo-controlled trial (PCI-Clopidogrel as Adjunctive Reperfusion Therapy [CLARITY]-Thrombolysis in Myocardial Infarction [TIMI] 28 trial [CLARITY-TIMI 28]).

Allocation: {Concealed}†.*

Blinding: Blinded (clinicians, patients, {data collectors, clinical events committee, and data analysts}†).*

Follow-up period: 30 days.

Setting: 319 sites in 23 countries.

Patients: 1863 patients 18 to 75 years of age (mean age 57 y, 82% men) with onset of ischemic discomfort at rest ≤ 12 hours and lasting ≥ 20 minutes; ST-segment elevation ≥ 0.1 mV in ≥ 2 contiguous limb leads, ≥ 0.2 mV in ≥ 2 contiguous precordial leads, or new left bundle-branch block; and planned treatment with a fibrinolytic, anticoagulant, and aspirin. Exclusion criteria were clopidogrel in the previous 7 days, clopidogrel or glycoprotein IIb/IIIa inhibitor planned before angiography, contraindication to fibrinolysis, angiography planned within 48 hours, cardiogenic shock, previous coronary artery bypass grafting, or bolus of any heparin at greater than standard doses.

Intervention: Clopidogrel, 300 mg followed by 75 mg/d (n = 933) or placebo (n = 930) up to the time of angiography. All patients received aspirin, 150 to 325 mg followed by 75 to 162 mg/d, or unfractionated heparin for 48 hours (60 U/kg intravenous bolus [maximum 4000 U] followed by an infusion of 12 U/kg per h [maximum 1000 U/h]), and coronary angiography 2 to 8 days after starting medication. It was recommended that patients having PCI receive open-label clopidogrel with a loading dose at the time of PCI.

Outcomes: Composite endpoint of cardiovascular death, recurrent MI, or stroke from PCI to 30 days after randomization. Secondary outcomes were recurrent MI or stroke before PCI, the composite endpoint from randomization to 30 days, and TIMI major or minor bleeding.

Patient follow-up: 99.9% (intention-to-treat analysis).

MAIN RESULTS

Patients in the clopidogrel group had lower rates of the composite endpoint from PCI to 30 days after randomization, recurrent MI or stroke before PCI, and the composite endpoint from randomization to 30 days than placebo-group patients (Table). Groups did not differ for TIMI major or minor bleeding.

CONCLUSION

In patients with ST-elevation myocardial infarction treated with fibrinolytics, clopidogrel pretreatment before percutaneous coronary intervention reduced cardiovascular death, recurrent myocardial infarction, and stroke.

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*See Glossary.

†Information provided by author.

Clopidogrel pretreatment before percutaneous coronary intervention (PCI) vs placebo in ST-segment myocardial infarction (MI)‡

Outcomes	Clopidogrel	Placebo	Adjusted odds ratio (OR) (95% CI)	RRR (CI)	NNT (CI)
Composite endpoint§ from PCI to 30 d	3.6% (34/933)	6.2% (58/930)	0.54 (0.35 to 0.85)	44% (14 to 64)	37 (26 to 113)
MI or stroke 2 to 8 d before PCI	4.0%	6.2%	0.62 (0.40 to 0.95)	37% (4.7 to 58)	44 (28 to 341)
Composite endpoint from randomization to 30 d	7.5%	12%	0.59 (0.43 to 0.81)	38% (17 to 54)	22 (16 to 49)

‡Abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from adjusted OR in article.

§Composite endpoint = cardiovascular death (1.4% vs 2.6%), recurrent MI (1.9% vs 3.1%), or stroke (0.4% vs 1.2%).

COMMENTARY

The subanalysis of the CLARITY-TIMI 28 study reinforces the importance of clopidogrel in patients with acute STEMI. The composite primary endpoint (cardiovascular death, recurrent MI, or stroke) and each component were reduced by clopidogrel both before and after PCI and without any significant increase in bleeding.

Clopidogrel is similarly supported by positive large trials in several settings: after non-STEMI (1, 2), after STEMI (1, 3), and before and after angioplasty (4, 5). A large trial of clopidogrel taken long-term for secondary and high-risk primary prevention, CHARISMA, is under way. Taken together, we know that clopidogrel is useful early in the course of hospitalization, is best when started several days before PCI and continued for months afterward, and adds little to the bleeding risk of aspirin (especially when aspirin dose is < 100 mg/d).

The dosages of clopidogrel, including the rebolus of 300 mg in the catheterization laboratory for all patients in PCI-CLARITY, are still not completely worked out. The benefits of clopidogrel are still tangible, although much more modest, when the catheterization laboratory is unavailable or far away (1).

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References

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