Aspirin is a life-saving drug for patients with acute myocardial infarction

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TITLE	Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2.
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In-hospital mortality of patients with acute myocardial infarction (AMI) has decreased from about 30% in the 1960s to about 6-7% nowadays, mostly as a consequence of improvements in patients' management. In the 1960s, the first coronary care units were organized in which continuous monitoring of patients' cardiac rhythm allow prompt detection and treatment of frequent, potentially lethal abrupt arrhythmias, almost halving in-hospital mortality. A further dramatic improvement was obtained by treating patients with drugs interfering with the hemostatic system, which plays a central role in the pathogenesis of the thrombi occluding coronary arteries that precipitate tissue infarction. Early coronary recanalization, achieved by lysis of fibrin in coronary thrombi, can rescue myocardial cells before

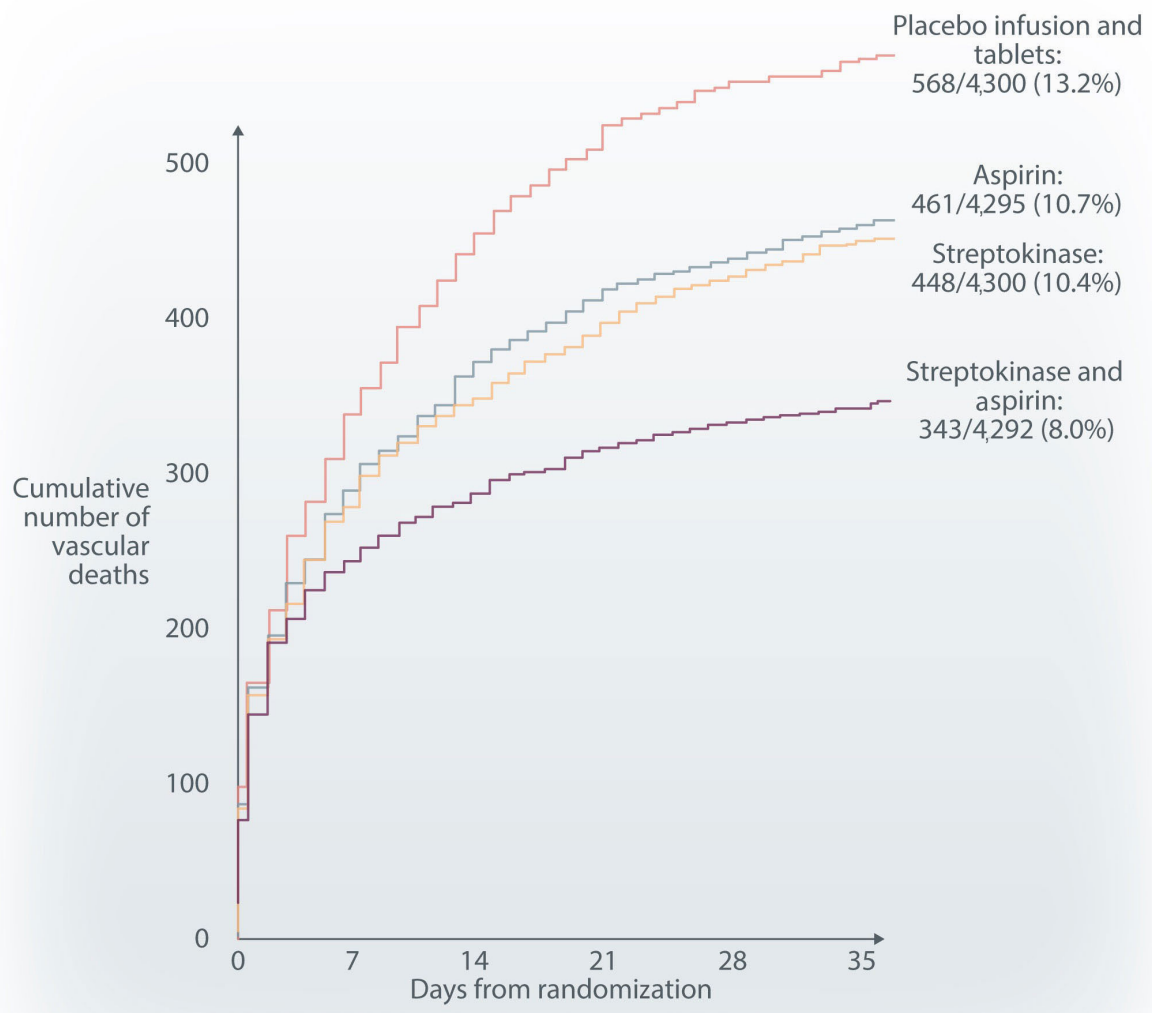

Figure 1. Cumulative vascular mortality in days 0-35 among 17,187 patients with suspected acute myocardial infarction in the ISIS-2 study. A 2x2 factorial study design was used: patients were randomized to treatment with (i) placebo infusion plus placebo tablets, (ii) streptokinase infusion (1.5 MU over 1 hour) plus placebo tablets, (iii) placebo infusion plus aspirin tablets 162.5 mg daily for 30 days, or (iv) streptokinase infusion plus aspirin tablets. Figure adapted, with permission, from *The Lancet*.[2]

irreversible damage and, possibly, improve prognosis. The *Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto miocardico (GISSI)* trial showed that the 21-day mortality in 11,806 AMI patients was reduced from 13% to 10.7% (-18%) by intravenous infusion of the thrombolytic agent streptokinase within 12 h of the onset of symptoms.[1] The extent of the beneficial effect was a function of time from onset of symptoms to streptokinase infusion, with the maximal effect at 0-3 h. The *Second Study of Infarct Survival (ISIS-2)*, with a 2x2 factorial design, explored not only the effect of thrombolysis, but also of platelet function inhibition by aspirin in 17,187 patients with suspected AMI, randomized within 24 h of symptom onset.[2] Aspirin was given at a dose of 162.5 mg daily for 1 month, with the first dose crushed, sucked or chewed to allow rapid drug absorption. The impressive and perhaps somewhat unexpected finding of ISIS-2 was that the extent of reduction of 35-day vascular mortality attained by aspirin or streptokinase as monotherapy was very similar for both strategies: from 13.2% to 10.7% (-19%) with aspirin and to 10.4% (-21%) with streptokinase (Figure 1). The combined administration of aspirin and streptokinase displayed additive effects, further reducing mortality to 8% (-39.4%). Contrary to streptokinase, aspirin did not increase the incidence of major and intracranial bleeding. The great importance of the landmark ISIS-2 study[2] is twofold. From a pathophysiological standpoint, it provided evidence that thromboxane A2-dependent platelet activation plays critical roles in both initiating and propagating coronary thrombi during the acute phase of myocardial infarction. Most importantly, from pragmatic and clinical standpoints, ISIS-2 revealed the impressive life-saving effects of aspirin, which has many important advantages over other drugs and therapeutic interventions. Aspirin is among the cheapest and safest drugs available. Moreover, aspirin can be easily and promptly administered to patients at the moment of first medical intervention, at home or during transportation to a hospital. Therefore, for patients with suspected AMI who cannot reach specialized centers in time to be treated with thrombolytics or with percutaneous coronary intervention (which is now the preferred method for coronary revascularization), prompt administration of aspirin can provide safe protection from vascular death. To further decrease time to treatment, patients could be instructed to self-prescribe aspirin when symptoms evocative of AMI arise: a recent study calculated that self-administration of aspirin could save up to about 13,000 deaths annually in the USA.[3]

Disclosures

No conflicts of interest to disclose.

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