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COMPARISON OF INTRAVENOUS ANISOYLATED PLASMINOGEN STREPTOKINASE ACTIVATOR COMPLEX (APSAC) AND INTRACORONARY STREPTOKINASE IN ACUTE MYOCARDIAL INFARCTION. J. Anderson (1), R. Rothbard (2), R. Hackworthy (1), S. Sorensen (1), P. Fitzpatrick (2), V. Marder (2), for the APSAC Multicenter Study Investigators, The University of Utah, Salt Lake City, UT (1), and The University of Rochester, Rochester, NY, USA (2).

To compare the reperfusion potential of intravenous anisoylated plasminogen streptokinase activator complex (APSAC) a new thrombolytic, and standard therapy with intracoronary streptokinase in acute myocardial infarction (AMI), a randomized multicenter reperfusion trial was performed. Consenting patients with clinical signs of AMI and documented coronary occlusion (flow grade 0 or 1) were randomized to treatment within 6 hours of symptoms (mean, 3.4h) with intravenous APSAC (30 U in 2-4 min) or intracoronary streptokinase (bolus, then 2,000 U/min x 60 min). Reperfusion success was defined as grade 2 or 3 flow at 60 min for intracoronary and 90 min for intravenous therapy. A total of 189 patients (pt) were randomized and 179 pt were evaluable for efficacy. Reperfusion was similar for the two treatments: 52% (49/94) for APSAC and 61% (52/85) for streptokinase ($p \leq 0.2$). Success was dependent on initial occlusion grade ($p \leq 0.001$): 49% (65/133) for grade 0 (APSAC= 45%, streptokinase=54%), but 78% for grade 1 (APSAC=80%, streptokinase=77%). The success of intravenous (APSAC) therapy was also dependent on time to treatment: 59% for $\leq$4h, versus 36% after 4h ($p<0.04$). APSAC was well tolerated, the change in mean blood pressure after bolus injection being modest (-11 mmHg). Systemic fibrinolysis was somewhat greater after APSAC than low dose streptokinase: fibrinogen levels averaged 39 $\pm$ 4% (SE) of control at 90 minutes after APSAC, versus 64 $\pm$ 5% after streptokinase ($p<0.01$) in the subgroup tested. The rate of bleeding complications was acceptable for both regimens, and other adverse reactions were comparable. Rates of early occlusion were low in both treatment groups, and evolution of ECG and enzymatic indicators were similar. Thus, APSAC provides approximately similar reperfusion results as intracoronary streptokinase, especially when given within 4h, but is easier to administer and is well tolerated.

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ACYL PLASMINOGEN STREPTOKINASE VERSUS HEPARIN IN RECENT ACUTE MYOCARDIAL INFARCTION. PRELIMINARY REPORT OF A FRENCH INTERUNIVERSITY TRIAL

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One hundred and twenty seven patients (pts) suffering from a first acute myocardial infarction (AMI) were included in a multicenter trial involving three University Hospitals and 22 community Hospitals without catheterization facilities. Patients were randomly allocated within 5 hours following the onset of symptoms either to acyl plasminogen streptokinase (APSAC) 30 IU within 5 min followed 4 hours later by heparin at a dose of 500 IU/kg/day or to conventional Heparin (H) therapy 500 IU/kg/day. 63 pts received APSAC and 64 received H. Both APSAC and H groups were similar in age, location of AMI, Killip class and time of randomization. After initial therapy Pts were referred to the University Hospitals and submitted between Day 1 and Day 7 to a selective coronary angiography and immediate percutaneous transluminal angioplasty (PTCA) of the infarct-related artery if suitable for the procedure. 4 APSAC pts and 2 H pts died during the hospital course (NS). The arterial patency rate determined on average 3.4 $\pm$ 1.2 days after the onset of symptoms was 88% in APSAC and 42% in H ($P < .001$). 15 APSAC pts and 7 H pts were submitted to PTCA with one failure in each group. LVEF and akinetic score (AK) were determined from left ventricular angiography :

	Overall		Anterior AMI		Inferior AMI	
LVEF	.50$\pm$.15	.46$\pm$.13	.45$\pm$.16	.37$\pm$.16	.54$\pm$.12	.51$\pm$.09
AK	10.9$\pm$7.0	13.2$\pm$7.0	14.2$\pm$8.5	19.2$\pm$7.5*	7.0$\pm$4.4	9.5$\pm$4.4
	APSAC	H	APSAC	H	APSAC	H

*P < .05

On Day 14, pts were submitted to Ti 201 scan and to radionuclide angiography (RNA). Results are not yet available.

Our results showed that early infusion of APSAC in AMI produced a high short term patency-rate of the IRA with a tendancy toward improvement of the left ventricular systolic function which failed to reach statistical significance because of the relatively small size of the cohort.

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RANDOMIZED FACTORIAL TRIAL OF HIGH-DOSE INTRAVENOUS STREPTOKINASE, OF ORAL ASPIRIN, AND OF INTRAVENOUS HEPARIN IN ACUTE MYOCARDIAL INFARCTION. R. Collins - for the ISIS Collaborative Group. ISIS, Radcliffe Infirmary, Oxford, UK.

619 patients with suspected acute myocardial infarction (MI) were randomized to receive either a high-dose short-term intravenous infusion of streptokinase (1.5 MU over one hour) or placebo. In addition, using a "2x2x2 factorial" design, patients were also randomized to receive either oral aspirin (325 mg on alternate days for 28 days) or placebo, and separately randomized to receive either intravenous heparin (1,000 IU/hour for 48 hours) or no heparin. Streptokinase (SK) was associated with a non-significant decrease in hospital mortality (7.7% allocated SK vs 9.2% allocated placebo) and increase in non-fatal reinfarction (3.6% vs 2.9%). There were significantly more minor adverse events after SK (e.g. hypotension, allergies, bruises or minor bleeds), but no excess of strokes or of anaphylactic shock. Aspirin was associated with fewer reinfarctions (2.9% allocated aspirin vs 3.9% allocated placebo; NS), deaths (6.1% vs 10.5%; 2P<0.04) and strokes (0.3% vs 2.0%; 2P<0.1). Heparin was associated with a decrease in reinfarction (1.9% allocated heparin vs 4.9% allocated no heparin; 2P<0.04), though not in mortality (8.3% vs 8.2%; NS), and with a trend towards more strokes (1.6% vs 0.7%; NS) and more bruising and bleeding (14% vs 11%; NS). To assess reliably the effects of SK and aspirin on major endpoints, several hundred hospitals are now collaborating in a large (about 20,000 patients planned) randomized trial (ISIS-2).

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EFFECTIVENESS OF INTRAVENOUS THROMBOLYTIC TREATMENT IN ACUTE MYOCARDIAL INFARCTION:SHORT AND MEDIUM TERM PROGNOSIS

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An unblinded trial of intravenous stretokinase in early acute myocardial infarction was planned to study wheter the drug produces a clinically relevant benefit in terms of reduction of in-hospital and one year mortality.

11806 pts in one hundred and seventy six coronary care units were enrolled over 17 months.Patients admitted within 12 h after onset of symptons and with no contraindications to SK were randomized to receive SK in addition to usual treatment and complete data were obtained in 11712 for what concerns in hospital prognosis.At 21 days overall hospital mortality was 10.7% in SK recipients versus 13%,in controls,an 18% reduction($p=0.0002$,relative risk 0.81).The extent of beneficial effect appears to be a function of time from onset of pain to SK infusion(relative risk 0.74,0.80, 0.87 and 1.19 for the 0-3,3-6,6-9 and 9-12 h subgroups).The data of 1-year follow-up concerning 11605 pts(95.3% of the whole population)were available up to December the 31st.1987.4333 pts out of the SK-treated group(74.0%)and 4219 out of the control one (72.1%)were alive,with a significant difference.These results document that the benefit produced by SK in the hospital period remains substantially unchanged.The differences in mortality in favour of SK vs.C remain highly significant specifically for the 0-3 and 3-6 hrs subgroups and is dramatic for patients treated between one hour from onset of symptoms. 503 out of the 637 treated with SK were alive at 1-year follow-up versus 443 out of 641 control group pts:the amplitude of the benefit seems to be further increased in this particular subgroup.The GISSI results document conclusively that an acute thrombolytic treatment with SK in AMI is effective in reducing mortality not only over the short,but also over the medium period.