1002-44A Collaborative Angiographic Patency Trial of Recombinant Staphylokinase (CAPTORS II)

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Our primary objective was to compare bolus dose(s) of PEGylated staphylokinase (PEG-Sak) to rt-PA as assessed by culprit infarct vessel patency at 60 minutes. Additional objectives were to examine the safety profile of PEG-Sak, net clinical benefit and conventional 30-day clinical sequelae of acute myocardial infarction. We used a randomized, parallel-group, sequential design clinical trial comparing a novel potent highly fibrin specific fibrinolytic agent, single bolus PEG-Sak with conventional front-loaded recombinant tissue plasminogen activator (rt-PA). Both treatment arms employed unfractionated heparin according to ACC/AHA guidelines. The table below shows 60 minute TIMI 3, combined TIMI 2/3 patency (mean with 95% confidence intervals) and median frame counts for TIMI 2/3 patients for those randomized to PEG-Sak in a single-bolus, weight-adjusted, dose-finding strategy ranging from 0.01 mg/kg to 0.15 mg/kg as compared with conventional weight-adjusted, front-loaded rt-PA. Patients studied were those presenting with acute ST elevation myocardial infarction within six hours of symptom onset. Angiographic patency was assessed by a blinded core angiographic laboratory system.
Conclusion: These data support pharmacologic efficacy for PEGylated staphylokinase as compared with rt-PA across a wide range of doses with some attenuation of efficacy at 0.01 mg/kg.

PEG-Sak dose mg/kg	n=sample size	TIMI 3 (95% C.I.)	TIMI 2/3 (95% C.I.)	Frame count from TIMI 2/3 (n=pts)	ICH - # pts
.01	19	37 (16-62)	53 (29-76)	22 (10)	
.01875	96	33 (24-44)	63 (52-72)	26 (60)	1
.025	110	35 (26-44)	62 (52-71)	29 (68)	
.0375	103	34 (25-44)	66 (56-75)	28 (68)	1
.05	23	43 (23-66)	74 (52-90)	29 (17)	2
rt-PA	112	42 (33-52)	70 (60-78)	28 (78)	1

1002-45 Intravenous Adenosine Diphosphate P2T Platelet Receptor Antagonism as an Adjunct to Fibrinolysis for Acute Myocardial Infarction

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Background: Oral adenosine diphoshate (ADP) platelet receptor antagonists have shown benefit during acute coronary syndromes. Our aim was to investigate a novel intravenous ADP_{P2T} platelet receptor antagonist during fibrinolysis for acute myocardial infarction (AMI).
Methods: Patients presenting within 6 hours of AMI were randomized to receive 35-, 140-, or 280 µg/min AR-C69931MX along with 50 mg t-PA administered over 60 minutes, 280 µg/min AR-C69931MX alone, or standard dose t-PA in the Safety, Tolerability and Effect on Patency in Acute Myocardial Infarction (STEP-AMI) trial. All patients underwent 60-minute angiography and rescue intervention if necessary. Patients were followed through 30 days. The primary endpoint was thrombolysis in myocardial infarction (TIMI) grade flow at 60 minutes by independent core laboratory analysis.
Results: The trial was stopped after 101 of 240 planned patients were enrolled. Of 81 evaluable films, complete reperfusion was achieved in 57% of patients receiving combination therapy compared with 50% with t-PA alone, p=NS (see table). Major adverse clinical events (MACE) and bleeding complications were comparable between combination therapy and standard dose t-PA groups (20% and 17% non-CABG related TIMI major bleeding rates, respectively). No intracranial hemorrhage was observed.
Conclusion: Early experience with intravenous ADP_{P2T} platelet receptor antagonism suggests feasibility and possible improvements in reperfusion during fibrinolysis for AMI.

	t-PA alone	t-PA + P2T (35 µg/min)	t-PA + P2T(140 µg/min)	t-PA + P2T(280 µg/min)	P2T alone (280 µg/min)
TIMI grade 3 flow	3 (50%)	10 (53%)	11 (61%)	12 (55%)	3 (19%)
TIMI frame count	58±46	53±32	49±30	54±42	78±31
ST-segment recovery>70%	1 (14%)	4 (24%)	5 (28%)	5 (33%)	2 (13%)
30-day MACE	0 (0%)	4 (17%)	3 (13%)	3 (12%)	0 (0%)
Non-CABG TIMI major bleed	1 (17%)	3 (18%)	8 (33%)	3 (13%)	2 (11%)

1002-46 Aging of Intracoronary Thrombus Due to Delayed Time-to-Reperfusion Increases Ischemic and Angiographic Complications in Acute Myocardial Infarction

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BACKGROUND: Progressive cross-linking of fibrin produces temporal change in Thrombus (*T*) composition making an aged *T* firmer, lysis-resistant and more likely to result in distal flow and ischemic complication than fresh *T*. We hypothesized that in myocardial infarction(AMI), both delay in "time to reperfusion" and *T* are associated with flow and ischemic complications with an interaction between the two.
METHODS: We analyzed AMI pts from TIMI 4, 10, & 14 trials (n=2321) who presented <12 hr of symptom and received fibrinolysis. Total ischemia time (symptom onset to needle) was delayed if > 4 hr. *T* was assessed with quantitative angiography.
RESULTS: *T* pts were more likely to have TIMI flow <3 (72% vs 26%), 90-min infarct vessel occlusion (54% vs 3%), prolonged TIMI frame count (CTFC: 42±27 vs 35±21), pulmonary edema (4% vs 2%), pump failure (6% vs 3%), severe ischemia (55% vs 19%), rescue PTCA (41% vs 1%), and death (6% vs 3%) [all p<0.01].
Pts with delayed presentation were more likely to have vessel occlusion at 90-min (25% vs 18%, p<0.001), TIMI flow <3 (44% vs 40%, p=0.07), pump failure (2% vs 1%, p=0.05), and death (6% vs 3%, p=0.007). In multivariate analysis, *T* and "*T* & total ischemia time interaction" were predictive of angiographic antegrade flow variables and >=70% ST segment resolution. (**TABLE**)
CONCLUSION: Interaction is such that *T* results in more flow and ischemic complications with delayed perfusion time. Rescue PTCA in the setting of *T* and delayed presentation may require alternative strategy to reduce *T* burden.

Multivariable predictors	Odds Ratio	95% C.I.	p value
Predictors of >=70% ST segment resolution			
Absence of coronary thrombus	0.40	0.26 – 0.62	0.0001
Thrombus & total-ischemia-time Interaction	0.57	0.38 – 0.86	0.007
Predictors of 90-minute TIMI 3 antegrade flow			
Absence of coronary thrombus	0.17	0.14 – 0.22	0.0001
Thrombus & total-ischemia-time Interaction	0.45	0.29 – 0.72	0.001
Predictors of 90 minute Corrected TIMI Frame Count			
Presence of coronary thrombus	34.51	31.68 – 37.34	0.0001
Thrombus & total-ischemia-time Interaction	13.08	7.93 – 18.23	0.0001

POSTER SESSION

1003 Cardiopulmonary Resuscitation/ Emergency Cardiac Care

Sunday, March 17, 2002, 9:00 a.m.-11:00 a.m.
Georgia World Congress Center, Hall G
Presentation Hour: 10:00 a.m.-11:00 a.m.

1003-31 Magnesium Reduces Free Radicals Generated by Direct Current Shocks and Prevents Left Ventricular Dysfunction in an In Vivo Swine Model

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Background: Oxygen free radicals are generated by myocardial ischemia-reperfusion sequences or by direct current countershocks for the termination of ventricular fibrillation. We have previously shown that magnesium reduces free radicals in a coronary occlusion-reperfusion model. The purpose of this study was to determine if magnesium reduces free radicals generated by direct current countershocks.
Methods: Eight swine weighing 18 to 27 kg underwent a midline sternotomy. Using electron paramagnetic resonance, we continuously monitored the coronary sinus concentration of ascorbate free radical ($Asc^{\bullet-}$), a measure of free radical generation (total oxidative flux). A 30 Joule epicardial shock using a truncated exponential biphasic waveform (5/5 msec) was administered to generate free radicals. Each animal received 2 shocks. No-magnesium shocks were given while the animals were receiving intravenous saline infusion. Magnesium shocks were given while the animals received magnesium (80 mg/min) beginning 10 min before the shock and continuing to 15 min after the shock. Left ventricular fractional area shortening was determined by 2-dimensional (2-D) echocardiography.
Results: Magnesium pre-treatment significantly ($p<0.05$) reduced $Asc^{\bullet-}$ concentration after biphasic shocks. The peak increase in $Asc^{\bullet-}$ concentration was 18% (no-magnesium shocks) vs. 5% (magnesium shocks); the total radical flux after shocks was reduced by 72% by magnesium pre-treatment. Using 2-D echo, the fractional area shortening at baseline (before shocks) was 69 ± SE 3%; after no-magnesium shocks, the percent fractional area shortening fell to 41 ± 3% ($p<0.001$), whereas shocks given after pretreatment with magnesium resulted in fractional area shortening of 61 ± 4% (p=NS vs. baseline).
Conclusions: Magnesium pre-treatment reduces oxygen free radicals generated by biphasic shocks and prevents left ventricular dysfunction. Magnesium may be cardioprotective during defibrillation.