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THE COMBINED EFFECT OF u-PA AND t-PA ON A CANINE CORONARY THROMBUS MODEL. M. Nobuhara (1), Y. Ashida (1), K. Kato (1), Y. Horisawa (1), H. Kubota (1), T. Yajima (1) and S. Shiraki (1). The Research Laboratories for Cell Science, Mochida Pharmaceutical Co., Ltd., Tokyo, Japan (1).

The combination experiments of both PAs have been performed in in vitro and in vivo to know whether they act synergistically or not.

In in vitro experiments the additive combined effects of u-PA and t-PA were observed on human plasma clot lysis. In in vivo experiments, on a canine coronary thrombus model with a thrombin thrombus in LAD, the combined administration of u-PA and t-PA (1 x 10^4 IU/kg/30') gave significant thrombolysis without enhancing the reduction of Fbg, Plg and α2-PI.

Group	Dose ($x10^{-3}$ IU/kg)	Reperfusion rate
Control	0	0%
t-PA	10	20
u-PA	10	20
Combined	10+10	80

In order to study the mechanism of in vivo synergistic thrombolysis, changes of plasma and blood dynamic viscosities by administration of u-PA and t-PA were investigated. Whole blood dynamic viscosity decreased significantly in both u-PA and the combination groups, while plasma viscosity was not changed. This lowered blood viscosity was rather notable at the lower shear rate condition than at the higher shear rate.

From these results it can be expected that u-PA could suppress the elevation of blood dynamic viscosity under the condition of retained blood flow, while t-PA might provide a thrombus specific lysis without any bleeding complications. And the synergism of u-PA and t-PA demonstrated here have a greate advantage on not only thrombolysis but also on lowering of blood viscosity in the coronary artery.

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PREHOSPITAL CORONARY THROMBOLYSIS: A NEW STRATEGY IN ACUTE MYOCARDIAL INFARCTION. A. Teddy Weiss, David G. Fine, David Applebaum, Sima Welber, Dan Sapoznikov, Chaim Lotan, Morris Mosseri, Yonathan Hasin, Mervyn S. Gotsman. Hadassah University Hospital, Jerusalem, Israel.

Thirty-four patients with acute myocardial infarction were treated prospectively using a new strategy of pre-hospital intravenous streptokinase given by a physician-operated mobile intensive care unit. Pre-hospital treated patients who had experienced no previous myocardial infarction were compared to a similar group treated with streptokinase in-hospital. All patients underwent cardiac catheterization on day 6.

Patients receiving streptokinase in the pre-hospital phase of acute myocardial infarction had smaller infarcts and better residual myocardial function than the group given streptokinase in-hospital in terms of peak creatine phosphokinase (900 v.1298 IU, p=0.023), ejection fraction (62 v. 55%, p=0.004), computer-derived dysfunction index (427 v. 727, p=0.003), and electrocardiographic QRS score (4.1 v. 6.4, p=0.001). The only difference between these groups at baseline was the duration of pain prior to initiation of streptokinase therapy (1.0 ± 0.4 hours vs. 1.9 ± 0.9 hours). There were no major complications related to pre-hospital administration of streptokinase.

Pre-hospital stretokinase infusion is feasible, safe and practical. It reduces ischemia time because treatment is not delayed until hospital arrival and therapy limits infarct size. Thrombolytic therapy for acute myocardial infarction can be initiated at home and should not be limited to hospitalized patients.

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PEAKING TIME OF CK-MB IN PATIENTS TREATED WITH THROMBOLYTIC AGENTS DURING MYOCARDIAL INFARCTION: IS IT REALLY A CLUE TO REPERFUSION? C. Brunelli, P. Spallarossa, G. Ghigliotti, M. Iannetti, S. Caponnetto. Dept. of Cardiology, University of Genova, Genova, Italy.

Aim of the study is to evaluate the relevance of CK-MB peaking time as a marker of reperfusion in patients (pts) treated with thrombolytic agent. 150 pts were recruited in 4 centers and randomized into two treatment groups: Group A = conventional therapy + urokinase (2.000.000 U i.v.),Group B = conventional therapy. Interval between onset of symptoms and beginning of therapy was 3.50 ± 1.25 hrs in group A and 3.45±1.20 hrs in group B. Serum cardiac enzyme determination was performed every 4 hrs for 48 hrs. On day 20 all pts underwent coronary angiography and ventriculography. Clinical and angiographic data were not significantly different in the two groups. Patency of infart related artery (IRA) was evident in 51% of pts of group A vs 38% of pts in group B ($p<0.05$). In 119 pts both IRA status and complete CK-MB curve were known. Mean time to peak CK-MB in pts with patent and occluded IRA was 18.7±1.6 hrs and 24.4±1.4 hrs respectively ($p<0.02$); 15 hrs from onset of symptoms was considered as the boundary between early and late peak.

	GROUP A		p	GROUP B		p
	occluded	patent		occluded	patent	
Early peak < 15 hrs	3/18(17%)	15/18(83%)	<0.01	5/13(38%)	8/13(62%)	NS
Late peak >15 hrs	24/40(60%)	16/40(40%)		34/48(71%)	14/48(29%)	

11 pts died in hospital: 3 in group A and 8 in group B.
Conclusion: 1) CK-MB peak time is significantly different in pts with patent and occluded vessels. 2) From a clinical point of view in conventionally treated pts IRA status is not predicted by CK-MB peaking time, while in urokinase treated pts IRA status is predicted only by early peaking.

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THROMBOLYSIS AND ACUTE MYOCARDIAL INFARCTION (A.M.I.) D.Villemant(1), P. Barriot(2), P. Bodenan(2), Ph.Lafay, JF MONSALLIER(1) ICU Cochin Hospital PARIS, SAMU-SP Paris France.

AMI is a major cause of morbidity and mortality in modern society. Conventional treatment has no benefic effect on the size of infarct, alteration of left ventricular (LV) function and mortality. Intravenous (IV) thrombolysis reduces in-hospital mortality by 23 % if infused within 3 hours of ischemia,47 % if within 1 hour. It reduces the size of infarct by 51 % if reperfusion occurs within 1 hour of ischemia, 31 % if between 1 and 2 hours and 13 % if between 2 and 4 hours. The preservation of LV function is of 28 to 42%. These benefic effects, thanks to IV thrombolysis, can be obtained only if reperfusion occurs within 3 or 4 hours of ischemia. Unfortunately, a french prospective study "ENIM 84" estimates that the mean delay between onset of chest pain and arrival at hospital is 10,3 hours.Goals of the study were to show that "at home" thrombolysis:1) is a feasible and a safe technique, 2) is responsible of a significant saving of time, 3) preserves LV function according to the precocity of treatment.Two groups of patients (pts) are compared : group A : 62 pts had "at home" thrombolysis by a trained medical staff aboard a mobile emergency care unit. Group B : 53 pts had thrombolysis at arrival at CCU. Protocol is simular in both groups : An IV infusion of 1 5 M iu of streptokinase over 45 to 60 min after an IV bolus of 100 mg Hydrocortisone. Criteriae and contra-indications are those usually used for thrombolysis. Radionuclide angiography was performed 4 days and 1 month after AMI to evaluate global and regional ejection fraction (EF). Only 1 hemorrhagic complication (a mild melaena) and 2 reversible ventricular fibrillations were reported. Reperfusion arrythmias were frequent (55 %) but do not need treatment. The number of candidates for thrombolysis is then increased. The saving of time is 73 min. Difference between the 4 days and 1 month EF is not significant in pts with conventional treatment or if reperfusion occurs after 4 hours of ischemia 48 ± 11 % vs 51 ± 13 %.But it is significant if before 4 hours 49 ± 11 % vs 56 ± 12 % and highly significant if before 2 hours 48 ± 12 % vs 59 ± 10 %.

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