CORONARY THROMBOLYSIS: SINGLE-CHAIN UROKINASE-TYPE PLASMINOGEN ACTIVATOR

THE Efficacy and Relative Fibrin Selectivity of Prourokinase in Patients with Acute Myocardial Infarction. J. Loscalzo for the Prourokinase in Myocardial Infarction Study Group, Boston, MA, USA.

The use of thrombolytic agents in acute myocardial infarction has gained widespread acceptance as an important early therapeutic option. Acute coronary thrombosis has been found in approximately 80% of patients with acute infarction and the use of standard thrombolytic agents often produces only a modest improvement in most cases. Unfortunately, in many individuals standard agents also produce a systemic lytic state with its attendant hemorrhagic complications. Prourokinase (PUK) has been shown to be a relative fibrin selective thrombolytic agent in vitro owing to its localization to the clot surface. Because of this desirable property, we studied the efficacy and selectivity of PUK in vivo in 19 patients with acute myocardial infarction. Each of these patients was documented by angiography to have a totally occluded infarct-related artery. Each patient was treated within six hours (range: 2 to 5.8 hours) of the onset of symptoms with 62.5 mg of PUK derived from the human kidney cell line, LLC and administered intravenously at a dose of 4000 IU/kg/min. Angiographically confirmed thrombolysis occurred after 30 minutes. The thrombolysis by PUK was accompanied by bleeding from all surgical wounds and consumption of plasminogen, alpha-2-antiplasmin and fibrinogen. Rec-pro-UUK was administered to six other dogs in a PUK-UUK-equivalent dose. Thrombolysis was achieved after 30 minutes in all six cases without inducing a systemic lytic state. Neither in the PUK group nor in the group treated with rec-pro-UUK intracerebral bleeding complications were observed on cerebral plates examined autopsically. Our findings indicate that intravenous administration of rec-pro-UUK is safe and efficient in the treatment of occluded cerebral arteries in acute stroke.

Influence of recombinant pro-urokinase on the hemostatic system in patients with acute myocardial infarction. U. Schmitz-Huebner (1), H. Dettmann (2), D. G. Mathay (2), J. Schofer (2), H. Diefensbach (3) and R. Ebel (3). Dept. of Internal Medicine, Univ. of Hamburg, FRG (2) and 2. Dept. of Internal Medicine, Univ. of Mainz, FRG (3).

Recombinant unglycosylated pro-urokinase (recombinant single chain urokinase-type plasminogen activator, rSCU-PA) was studied in twelve patients with acute myocardial infarction as a 20 mg bolus followed by a 50 mg intravenous infusion (iv. inf.) over 1 hour and a 12 mg bolus followed by a 3 mg iv. inf. over 1 hour. Reperfusion was angiographically confirmed in 9/12 pts. with the higher dose and in 6/12 pts. who obtained the lower dose. Different parameters of hemostasis were determined before and after administration, 30 min after the beginning of inf. at the end of inf., 60 min thereafter and 6-12 hours afterwards.

The most significant systemic changes were observed 60 min after the end of inf. when the following mean values ± SEM were determined (pre-inf. values in brackets):

- Fibrinogen (mg/dl): 40 mg: 207.9 ± 14.1 (333.1 ± 39.1) 80 mg: 179.8 ± 33.0 (291.7 ± 21.5)
- Plasminogen (%): 40 mg: 65.6 ± 9.8 (115.7 ± 4.0) 80 mg: 51.9 ± 1.5
- Antiplasmin (%): 40 mg: 36.6 ± 6.8 (103.2 ± 3.4) 80 mg: 13.9 ± 4.9 (85.9 ± 5.2)
- Fibrinogen Split Products (μg/ml): 40 mg: 112.5 ± 46.1 (140.0) 80 mg: 112.5 ± 46.1 (140.0)

Fibrinolytic activity in plasma determined on fibrin plates was highest in both groups 30 min after the beginning of inf. and hardly measurable 60 min after the end of inf. No bleeding complications were observed. Based on these results, a randomized, double-blind multicenter trial was started to study the effects of 80 mg CG4509 versus 1.5 million U streptokinase iv.


Seventeen patients with acute myocardial infarction were treated with heparin combined with intravenous single-chain urokinase-type plasminogen activator (scu-PA), obtained from transformed human kidney cells LG4509, infused intravenously over 90 minutes. Complete vessel patency was achieved in nine patients within 61 ± 19 minutes of the start of the infusion without apparent hemorrhagic complications. We evaluated the effect of PUK on fibrinogen, on specific fibrinogen degradation products (FDP) and on fibrinogen/fibrin I peptide (FIP) 1,4-2, as well as on the specific fibrinogen degradation products (FDP) and on fibrinogen/fibrin I peptide (FIP) 14-2. Values for these parameters measured before and at the end of the 90-minute infusion of PUK were determined as the mean ± SEM.

![Table data]

Fibrinogen (mg/dl) 207 ± 19 270 ± 19
FDP (μg/ml) 1.62 ± 0.76 60.2 ± 26.0
XOP (μg/ml) 0.21 ± 0.01 3.09 ± 1.40
syspl-14-2 (μg/ml) 9.82 ± 1.36 22.29 ± 5.96
β 15-42 (μg/ml) 7.15 ± 1.81 17.78 ± 4.20

Conclusion: PUK is a thrombolytic agent with which to achieve coronary thrombolysis and that at the doses used in this study, it appears to be relatively fibrin selective.