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FIBRINOLYTIC THERAPY IN ACUTE VERTEBROBASILAR STROKE. G. J. del Zoppo (1,2), H. Bruckmann (1), A. Ferbert (1), R. Drummen (1), W. Hacke (1,2) and H. Zeumer (2,3), Klinikum, RWTH, Aachen, FRG (1), Scripps Clinic and Research Foundation, La Jolla, CA, USA (2) and University of Hamburg, Hamburg, FRG (3).

Local intra-arterial administration of fibrinolytic agents has been successfully used to achieve recanalization in acute thrombotic stroke patients (Zeumer, H., J Neurol 231:287-294, 1985). 65 consecutive patients with clinical signs of severe brainstem ischemia and angiographically demonstrated vertebrobasilar (VB) thrombotic occlusion were treated with antithrombotic therapy.
22 patients (Group A) received antiplatelet/anticoagulant treatment. 43 patients (Group B) received local intra-arterial infusion of streptokinase or urokinase proximal to the thrombotic occlusion. In 19 patients of Group B (Group B_1) arterial recanalization was achieved as demonstrated angiographically; in 24 patients (Group B_2) the arterial occlusion could not be resolved. None of the patients in Group B_2 survived.

GROUP	NUMBER	SURVIVORS	DEMISES	p*	HEMORRHAGE
A	22	3	19	0.0005	0
B_1	19	14	5	0.0001	2
B_2	24	0	24		2
B	43	14	29		4

* exact 6 table test, X^2 test; applied to survival data (B_1 vs A, B_1 vs B_2).

When clinically favorable (minimal/moderate deficit) and unfavorable (severe deficit/demise) outcomes are compared, the results are highly significant (B_1 vs A; $p < 0.007$; B_1 vs B_2; $p < 0.0003$).
It was possible to describe the vascular conditions associated with angiographically unsuccessful fibrinolytic therapy (Group B_2) and to identify the clinical conditions associated with an unfavorable clinical outcome in patients with successful lysis (Group B_1). These data indicate that successful fibrinolytic therapy is associated with a beneficial clinical effect in VB thrombotic stroke.

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INTRA-ARTERIAL THROMBOLYTIC THERAPY IN ACUTE MIDDLE CEREBRAL ARTERY STROKE. G. J. del Zoppo (1,2), S. M. Otis (1), J. Zyroff (1), W. Hacke (1,2), H. Zeumer (2,3) and L. A. Harker (1). Scripps Clinic and Research Foundation, La Jolla, CA, USA (1), Klinikum, RWTH, Aachen, FRG (2) and University of Hamburg, Hamburg, FRG (3).

18 patients presenting with acute carotid territory stroke, secondary to angiographically demonstrated occlusion of the middle cerebral artery (MCA), have been treated within 8 hours of the onset of acute symptoms by local intra-arterial infusion of urokinase or streptokinase. All patients were screened by baseline CT cerebral scan to exclude intracerebral hemorrhage as a cause of the acute stroke. 14 patients demonstrated complete, 2 partial, and 2 no recanalization (reopening) of the previously occluded artery following a 1 to 2 hour infusion of the fibrinolytic agent. 10 of the 14 patients displaying complete recanalization had complete neurological recovery or improvement with residual neurological deficits, while the 2 patients who did not display recanalization did not improve clinically. No clinical improvement was observed in the absence of recanalization.
Hemorrhagic transformation of cerebral ischemic areas may be classified as hemorrhagic infarction (minimal hemorrhage, no clinical deterioraton) and parenchymatous hemorrhage (mass effect, clinical deterioration). Minor infarction-related hemorrhages without detectable neurological sequelae (hemorrhagic infarctions) were found by CT scan in 4 patients; all displayed complete recanalization; and all hemorrhagic infarctions resolved.

RECANALIZATION	HEMORRHAGE	IMPROVED	UNCHANGED	DEMISE
COMPLETE 14	4	3	1	0
PARTIAL 2	0	-	-	-
NIL 2	0	-	-	-

This uncontrolled prospective clinical experience suggests that early local infusion of thrombolytic agents in selected patients may be efficacious and safe.

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FEMORO-POPLITEAL ARTERY THROMBOLYSIS WITH INTRA-ARTERIAL INFUSION OF RECOMBINANT TISSUE-TYPE PLASMINOGEN ACTIVATOR (rt-PA). R. Verhaeghe (1), G. Wilms (2), P. Mombaerts (1), J. Vermylen (1), A. Baert (2) and M. Verstraete (1). Centre for Thrombosis and Vascular Research (1) and Department of Radiology (2), University of Leuven, Leuven, Belgium.

The efficacy and tolerance of intra-arterial rt-PA infusion was tested in 27 patients with a thrombotic occlusion of the femoro-popliteal artery. The mean length of the occluding thrombus was 10 cm (range : 2-25 cm). The occlusion was recent (< 1 week old) in 7 patients; in 2 it existed for more than 6 months. The rt-PA solution was infused through an angiographic catheter embedded into the thrombus at a rate of 10 mg/hr in the first 11 patients, 5 mg/hr in the next 11 and 3 mg/hr in the last 5. The maximal dose foreseen in the protocol was 50 mg; the mean dose infused was 42 mg. Heparin (400 IU/hr) was infused concomitantly. Thrombolysis occurred in all 27 patients. Angiographic restoration of patency was obtained in 25 (93%); it first appeared after a mean dose of 27 mg rt-PA (range : 10 to 50 mg). In 21 patients, a percutaneous transluminal angioplasty was needed to dilate a residual stenotic lesion or remaining mural thrombi. This secondary procedure initiated reocclusion in 2 patients by causing a distal embolus and a subintimal dissection, respectively. Early rethrombosis occurred spontaneously in 3 other patients. Thus, 20 (74%) patients had a clinical improvement at discharge from the hospital.
rt-PA infusion was complicated by bleeding in 10 (37%) patients: a groin hematoma at the catheter entry site occurred in 9 patients, a hematoma from a previous venous puncture in 2 and gingival oozing in 3. None required blood transfusion. Premature interruption of the infusion because of local hematoma formation was the cause of failure in one patient.
This pilot trial confirms the feasibility of thrombolysis with local infusion of rt-PA in peripheral arterial thrombosis. The early clinical results and the incidence of bleeding complications appear similar to those observed with local low-dose streptokinase, although initial patency seems easier to restore with rt-PA. A prospective trial comparing rt-PA to streptokinase in this condition is thus warranted.

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TREATMENT OF ACUTE MASSIVE PULMONARY EMBOLISM WITH INTRAVENOUS VS. INTRAPULMONARY ARTERY ADMINISTERED RECOMBINANT TISSUE-TYPE PLASMINOGEN ACTIVATOR. M. Verstraete. Center for Thrombosis and Vascular Research, University of Leuven, Belgium. Spokesman for a European Group.

Recombinant tissue-type plasminogen activator (rt-PA) was given to 34 patients with acute massive pulmonary embolism of less than five days and with an angiographic Miller index greater than 15. The regimen was 50 mg rt-PA over 2 hours followed by repeat angiography, and, if the Miller index was judged still to be above 15, by an additional dose of 50 mg over 5 hours. Heparin was given in a bolus of 5000 IU followed by 1000 IU per hour. The rt-PA preparation (Boehringer Ingelheim GmbH, G 11021) contained mainly two-chain rt-PA. The infusion route was at random in a peripheral vein (IV) or in the pulmonary artery (PA). Pulmonary angiographs were assessed blindly by a panel of five radiologists according to the protocol developed by Miller (Br Med J 1971). 19 patients were given rt-PA via the pulmonary artery, 15 patients received rt-PA intravenously. Eleven patients were postoperative (PA 9, mean 13 ± 11 SD days, IV 4, 7 ± 3 days).
Sixteen patients (66%) received two infusions (PA 14; IV 8). The Miller index decreased from 25 ± 3 to 22 ± 6 (-12%) in the PA group and from 26 ± 2 to 22 ± 5 (-15%) in the IV group after the first infusion. In the patients who received a second infusion, the Miller index decreased to 16 ± 6 (-38%) after 100 mg in the PA group and to 16 ± 6 (-38%) in the IV group. The mean pulmonary artery pressure decreased from 30 ± 7 to 22 ± 6 (-27%) and further to 14 ± 5 (-53%) in the PA group and from 29 ± 7 to 22 ± 9 (-24%) after 50 mg and to 13 ± 5 (-55%) after 100 mg in the IV group. All these differences are significant ($p < 0.01$).
Fibrinogen levels dropped 46% from baseline after 50 mg and 66% from baseline after 100 mg. Bleeding occurred in 16 patients, 5 of whom had recent surgery (mean 8 days, range 2-13).
This pilot trial indicates that a prolonged infusion of rt-PA over 7 hours (100 mg) is superior to a single infusion over 2 hours (50 mg) and that infusion in the pulmonary artery does not offer a significant clinical benefit over the intravenous route. In case of life-threatening massive pulmonary embolism, treatment with rt-PA could be envisaged as early as from the third day after major surgery.