Local intraarterial thrombolysis in vertebrobasilar thromboembolic disease.

H Zeumer, W Hacke and E B Ringelstein

AJNR Am J Neuroradiol 1983, 4 (3) 401-404
http://www.ajnr.org/content/4/3/401

Local Intraarterial Thrombolysis in Vertebrobasilar Thromboembolic Disease

H. Zeumer,[1] W. Hacke,[2] and E. B. Ringelstein[2]

The poor prognosis of basilar artery occlusion is well known. Systemic anticoagulation rarely prevents a lethal outcome. A new therapeutic approach involves selective perfusion of streptokinase through the vertebrobasilar artery via a coaxial catheter system. Three of five reported cases demonstrated successful vascular recanalization with clinical improvement.

Between 1976 and 1981, 17 patients with angiographically diagnosed basilar artery thrombosis were treated at our clinic. Ten patients died within 2 weeks, while six patients survived more than 6 weeks but less than 3 months. Only one patient survived a 1 year period. All the patients had severe neurologic deficits and died from secondary complications such as pulmonary thromboembolism, myocardial infarction, or pneumonia. These results parallel the experiences of others [1–4] in documenting the poor prognosis of basilar artery thrombosis. In our view, the standard regimen using heparin and other anticoagulants offered no proven therapeutic advantage. With this in mind, we felt challenged to develop a new therapy, despite the possible dangers involved.

The systemic administration of the fibrinolytic agent streptokinase in doses of 2,500,000 IU/day is reported to be hazardous and fraught with complications [5]. Moreover, this therapy cannot be applied soon after angiography because of the certainty of local bleeding. However, cardiologists [6–8] have demonstrated that in patients with coronary artery thrombosis, the local use of fibrinolytic agents is superior to systemic application and that even in high local concentrations, the systemic effect is minimal. Our approach involved selective perfusion of streptokinase through the vertebrobasilar artery by means of a coaxial catheter system. Results of the treatment in five cases are reported.

Methods

The technique used to perform local fibrinolysis in the vertebrobasilar system is relatively simple: A 6 French Torcon catheter (William Cook Europe, DK-2860 Söborg, Denmark) is introduced via a femoral sheath into the vertebral arteries and angiography is performed. The same catheter is then used to guide a 3 French Teflon catheter (which completely occludes the lumen of the Torcon catheter) into the vertebral artery chosen for perfusion. The tip of this catheter is placed just below the atlas loop and the guiding catheter is then removed to the descending aorta. The drug is administered with a high-accuracy infusion pump.

The dose of streptokinase (200,000 IU) used in our first four cases was comparable to doses used by cardiologists; however, we administered the drug more slowly. When performing coronary artery thrombolysis, one must take into consideration the great loss of streptokinase to the aortic arch. In comparison, the leakage that takes place in the vertebrobasilar system is less significant. In view of our recent experience using lower doses (50,000 IU) of streptokinase, we are no longer sure that the initial dose of 200,000 IU over a period of 2 hr is either the optimal amount or the best time course for administration of the drug. The fibrinolytic therapy is accompanied by low-dose heparin treatment calculated to prolong thrombin time by a factor of 2 or 3.

Case Reports

Case 1

A 27-year-old woman, after an initial transient hemihypesthesia and hemiataxia, experienced deterioration. Symptoms included somnolence, tetraparesis, and multiple complicated oculomotor disturbances. The details have been described elsewhere [9]. An upper basilar occlusion was found (fig. 1A) in conjunction with intracranial vertebral artery occlusion. After administration of 200,000 IU streptokinase, recanalization was angiographically demonstrated. Further angiographic improvement was noted the next day and normalization was achieved after a second administration of 70,000 IU streptokinase (fig. 1B). We believe an embolus from the stump of the occluded vertebral artery was dissolved before further thrombosis occurred in the basilar artery. The patient was discharged at 8 weeks with minimal motor disturbances of the hands and was reported to be well at 11 months posttreatment.

Case 2

A 62-year-old woman showed minimal recanalization of the basilar artery after administration of 200,000 IU streptokinase. However, a complete reocclusion occurred at 12 hr posttreatment concomitant with a severe deterioration in general condition. The patient died a few hours later.

Case 3

A 57-year-old woman, initially comatose and suffering from occlusion of the lower and middle basilar artery, was treated with

[1] Neuroradiological Service, Klinikum der Rheinisch-Westfälischen, Technischen Hochschule, Goethestr. 27–29, 5100 Aachen, West Germany. Address reprint requests to H. Zeumer.

[2] Department of Neurology, Klinikum der Rheinisch-Westfälischen, 5100 Aachen, West Germany.

AJNR 4:401–404, May/June 1983 0195-6108/83/0403-0401 $00.00

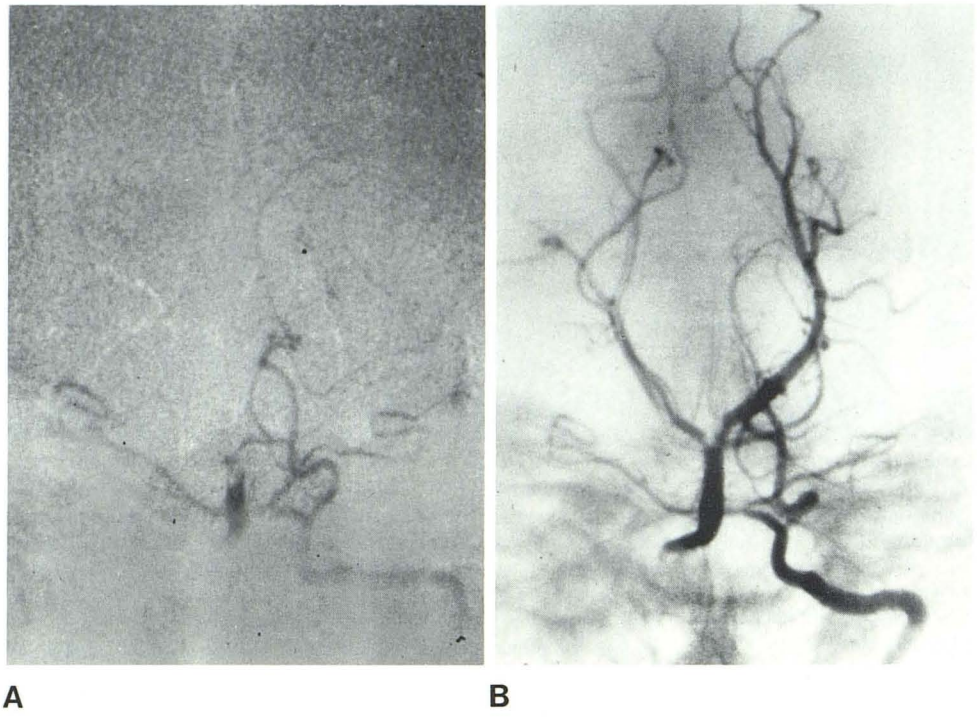

Fig. 1.—Case 1. **A,** Subtotal upper basilar artery occlusion. **B,** Recanalization after local intraarterial fibrinolysis.

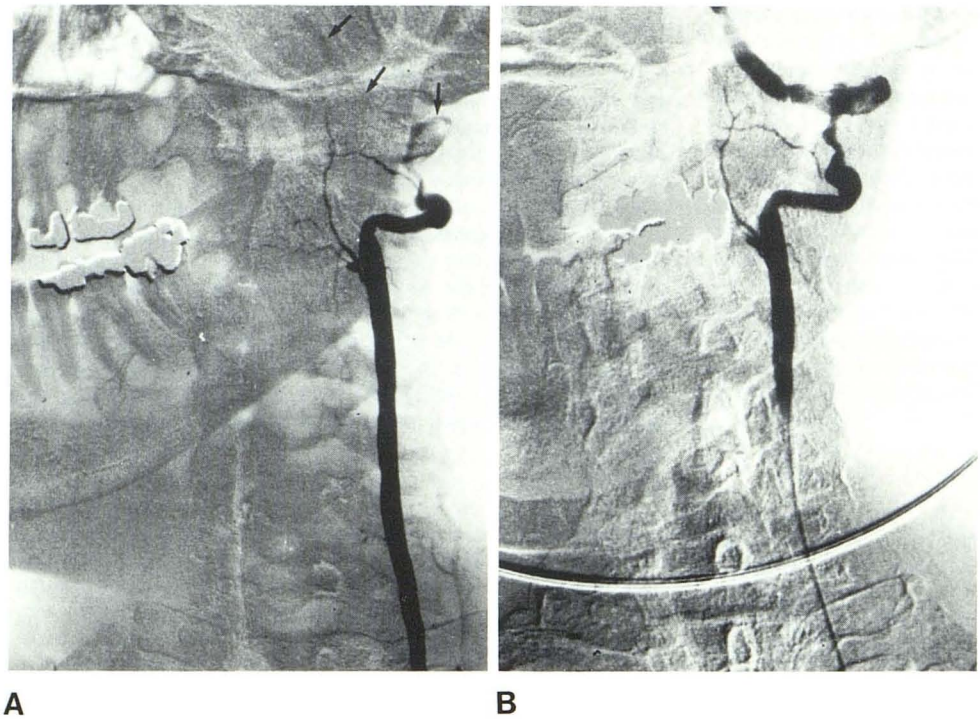

Fig. 2.—Case 4. **A,** Left vertebral angiogram (oblique projection). Subtotal stenosis of upper segments of left vertebral artery (*arrows*). **B,** Recanlization after local intraarterial fibrinolysis.

200,000 IU streptokinase. Recanalization was not achieved. In this case, we decided against repeat thrombolysis because 36 hr after the clinical onset a hypodense lesion of the pons had been detected by computed tomography (CT). This patient survived for 3 months in a state of "locked-in" syndrome. Later CT scans showed an increase in the size of the hypodense lesion of the pons.

Case 4

A 54-year-old woman with a 5 year history of quadrantanopsia complained of intermittent exacerbation of her visual defects and developed complete cortical blindness 48 hr later. Immediate angiography demonstrated normal blood flow in the right vertebral

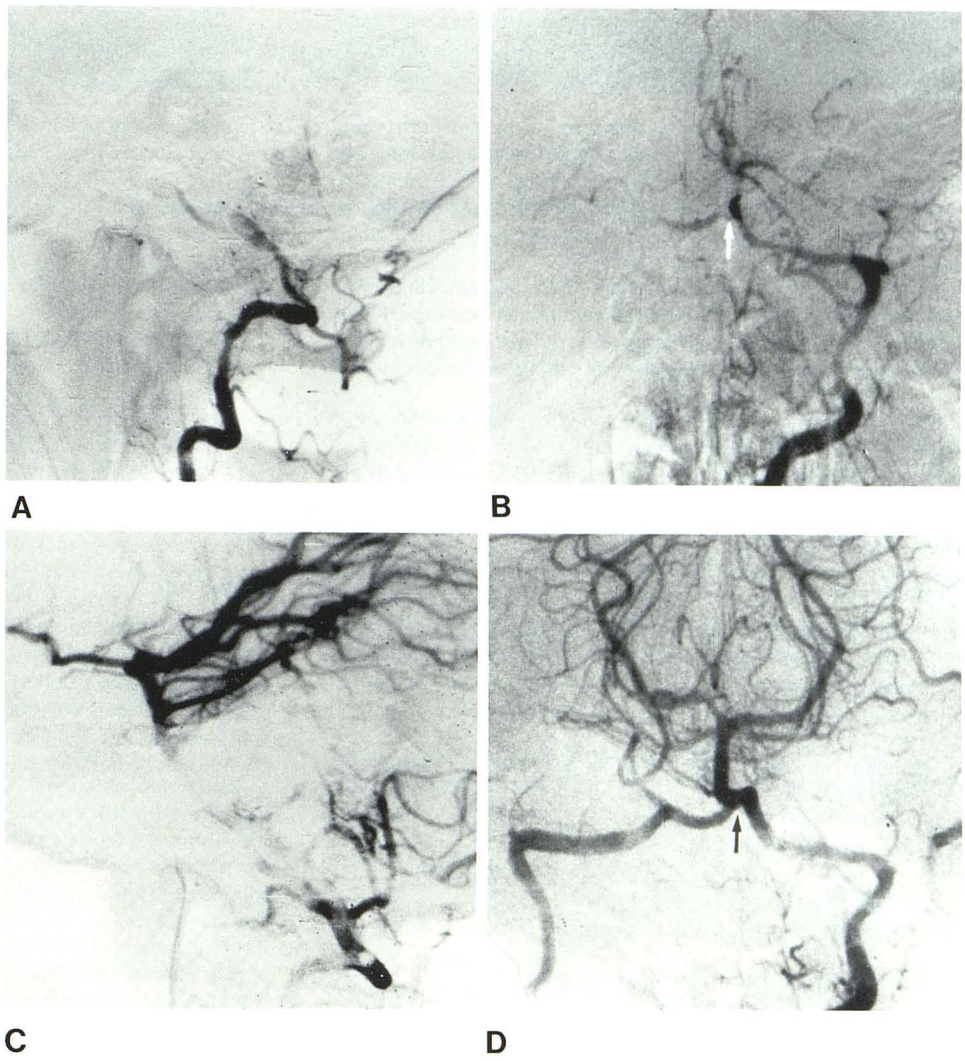

Fig. 3.—Case 5. Initial angiograms show bilateral stenoses of the intracranial vertebral arteries (**A**) with lower basilar artery occlusion (**B,** *arrow*). Posttreatment angiograms demonstrate normal flow in both vertebral arteries (**C**) and in basilar artery (**D,** *arrow*).

artery, the basilar artery, and the major branches of the posterior cerebral arteries. The left vertebral artery showed subtotal stenosis at the loop above the atlas (fig. 2A) and in the intracranial segment. Because of the possibility of further embolization from the left vertebral artery, it was decided to apply local fibrinolysis. The procedure was successful in effecting recanalization after 2 hr (fig. 2B). The patient's blindness rapidly vanished and no further brainstem or visual symptoms have since occurred.

Case 5

A 33-year-old woman with a history of transient hemihypesthesia suffered a brainstem infarction 7 days before admission with severe right hemiparesis, a left-sided Babinski reflex, impaired horizontal eye movements, dysarthria, and dysphagia. Angiography demonstrated severe bilateral stenoses of both intracranial vertebral artery segments with lower basilar artery occlusion (figs. 3A and 3B). It was decided to administer a lower dose of streptokinase over an extended period of therapy. At 12 hr intervals, the right and left vertebral arteries were alternately perfused, each for a 1 hr period, with 50,000 IU of streptokinase. Recanalization was achieved after 25 hr. The Teflon catheter was subsequently left in place in the left vertebral artery, and an infusion of 15,000 IU/hr of streptokinase was administered over 12 hr. The increasing flow in both vertebral arteries was monitored by Doppler sonography. The final results of therapy are shown in figures 3C and 3D. With normalization of flow a slight worsening of hemiparesis was noted, but this condition resolved within 1 week. The patient was able to walk with assistance after 3 weeks. The oculomotor disturbances were minimal at this time.

Discussion

In our first patient, who initially suffered from severe neurologic deficits, early implementation of therapy was very important in promoting clinical recovery. However, the value of early commencement of therapy should not be overestimated. Neurons will die if exposed to 10 min total ischemia. Such neuronal death is impossible to treat, since no available therapy can be initiated quickly enough to salvage these neurons. Clinical symptoms in stroke-prone patients may be caused not only by cell death, but also by reversible functional disturbances. Neurons in the so-called ischemic penumbra may be resuscitated and regain normal function after restoration of blood flow. Clinically, it is impossible to tell whether a clinical neurologic deficit is caused by cell death or functional insufficiency. Ischemic arterial walls are penetrated by red blood cells after a few hours. The clinical experience in our last patient, who had transient

deterioration, suggests hemorrhage into an existing necrotic lesion with surrounding edema. No bleeding was demonstrated by CT. Nevertheless we are always concerned about the possibility of secondary bleeding.

In all five cases, our main intention was to prevent further progression of local thrombosis in the vertebrobasilar system with resultant clinical deterioration. In three of our five patients, improvement of functional disturbances as well as the prevention of further ischemic necrosis was achieved. Of course preexisting neurologic deficits are not influenced by thrombolysis.

At present, we advise using small quantities of streptokinase with long administration times. It is suggested that continuous perfusion of about 10,000–15,000 IU/hr will provide optimal lysis and minimal risk, but the optimum dose and time course are still under evaluation.

It seems desirable to reduce the number of angiograms obtained during therapy. Doppler sonography of the vertebral arteries was used in all our patients, and results compared favorably with angiography. In our experience, Doppler-sonographic flow studies provide a highly reliable way of monitoring the effects of therapy.

REFERENCES

1. Kubik CS, Adams RD. Occlusion of the basilar artery—a clinical and pathological study. *Brain* **1946**;69:73–121
2. McDowell F, Potes H, Grosch S. The natural history of internal carotid and vertebral-basilar artery occlusion. *Neurology* (NY) **1961**;11:153–160
3. Dorndorf W, Gänshirt H. Die Klinik der arteriellen zerebralen Verschlüsse. In: Gänshirt H, ed. *Der Hirnkreislauf.* Stuttgart: Thieme, **1972**
4. Archer CR, Horenstein S. Basilar artery occlusion. Clinical and radiological correlation. *Stroke* **1977**;8:383–390
5. Brogden LN, Speight TM, Avery GS. Streptokinase. A review of its clinical pharmacology, mechanism of action, and therapeutic use. *Drug* **1973**;5:357–365
6. Rentrop KP, Blanke H, Karsch KR, et al. Wiedereröffnung des Infarktgefässes durch transluminale Rekanalisation und intracoronare Steptokinase-Applikation. *Dtsch Med Wochenschr* **1979**;104:1438–1440
7. Rentrop KP, Blanke B, Rahlf G, Leitz K. Infarktgrößenbegrenzung durch nicht-chirurgische Rekanalisation der Koronararterien. *Dtsch Med Wochenschr* **1981**;106:765–770
8. Merx W, Dörr R, Rentrop P, et al. Evaluation of the effectiveness of intracoronary streptokinase infusion in acute myocardial infarction: Postprocedure management and hospital course in 204 patients. *Am Heart J* **1981**;102:1181–1187
9. Zeumer H, Hacke W, Kolmann HL, Poeck K. Lokale Fibrinolyse-Therapie bei Basilaris Thrombose. *Dtsch Med Wochenschr* **1982**;107:728–731

Addendum

Recent experience has shown that an intermittent application of streptokinase is superior to a continuous perfusion. Starting with bolus injections of 4,000 IU streptokinase every 15 min, the dosage should be reduced to 2,000 IU/injection, when the plasma fibrinogen level has fallen to half the initial level. Using this regimen, therapy can be performed over a period of 12–24 hr in an intensive care unit.