those frequencies the signal is apt to be masked by mechanical noise due to handling of the detector and body movements, and so sound detection might be difficult. If we can overcome this difficulty, we may have more direct information about the cranial vascular system.

When bruit is clearly recorded at different points on the head surface simultaneously, it is possible to determine the position of an affected part in a manner similar to that of seismic center detections. So far, however, the cross-correlation method, a technique of measuring the slight time difference between the bruit recordings, is not perfect because of the multi-path effect and the existence of skull resonance. For improving the resolution and reliability of the determination technique, it is necessary to lessen the influence of resonance, which would be done in a manner similar to the diagnostic use of the acoustic emission in metal materials, and to stabilize the transmission characteristics of the interface between the detectors and the head.

Acknowledgements

The authors are grateful to Dr. Y. Higo of the Tokyo Institute of Technology for his useful discussions on resonance elimination technology, and to Mr. H. Takahashi and Mr. A. Ando, students of the Institute, for their assistance in the data processing.

References

5. Richardson C, Kofman O: Cranial Bruit with Intracranial Saccular Aneurysms. Trans Am Neurol Assoc 76: 151-154, 1951

Evaluation of the Risk of Immediate Anticoagulant Treatment in Patients with Embolic Stroke of Cardiac Origin

J. LODDER AND P.J.M. VAN DER LUGT

SUMMARY We evaluated immediate anticoagulation of embolic stroke. Of 39 patients suffering a focal cerebral ischemia caused by a cardiac embolus, 38 were submitted to CT within 24 hours after onset. Twenty-one patients received direct full anticoagulation and, in 10 patients, treatment was delayed because of hemorrhagic infarction on initial CT (3 cases), cardiac cause 24 hours or more after stroke onset, or treatment delay without specific reason (6 cases). Eight patients with severe deficit were not anticoagulated because of hemorrhagic signs on initial CT, impaired consciousness, or general contra-indications to such treatment. Twenty-one follow-up CT-scans were performed under full anticoagulation, and in only 2 cases hemorrhagic infarction was noticed without clinical deterioration. No clinical worsening attributable to anticoagulant treatment was observed during the three week observation period. It is concluded that direct anticoagulation therapy does neither induce hemorrhagic infarction nor cerebral hemorrhage in patients with embolic stroke nor does it cause clinical deterioration.

Stroke, Vol 14, No 1, 1983

ANTICOAGULATION TREATMENT IN patients with cerebral ischemic events caused by cardiac emboli is no longer a matter of debate. The problem is when to start. Because of a recurrence rate of 15 to 20% in the first few weeks after the initial event, direct anticoagulation by means of intravenous heparin followed by oral anticoagulants seems to be indicated. However, in pathological studies, a high incidence of hemorrhagic infarction was seen in cases with embolic stroke, although such hemorrhage into ischemic brain areas in patients with embolic stroke, although...
the few available clinical studies lent no support to this view. Since hemorrhagic infarction is seldom seen on CT even in cases with embolic stroke, we assumed that clinical findings differ from the outcome of pathology and experimental studies. Therefore we prospectively studied the risk of early anticoagulant treatment (started within 24 hours after the embolic stroke) during the early phase (three weeks) in patients with an embolic stroke.

**Patients and Methods**

Included in the study from March 1981 until April 1982 were all patients with a non-septic embolic focal neurological deficit caused by a supra-tentorial brain infarction which had lasted longer than 24 hours, provided a plain CT-scan had been performed within 24 hours after onset. The patients had been admitted to the neurological department and were attended to by one of the staff neurologists. Five patients were initially seen on the coronary care unit. Embolus was diagnosed on the following clinical grounds: paroxysmal or chronic atrial fibrillation, rheumatic heart disease, aortic or mitral valve stenosis or prosthesis, and myocardial infarction in the preceding two weeks. The deficit should have an acute onset and its maximum at the start. All patients had a full physical and neurological examination on admission. Blood pressure, routine blood cell count and blood chemistries, ECG and chest X-rays were recorded. Echocardiogram and 24-hours Holter monitoring were done on some patients. All patients were seen at least once by a cardiologist and anticoagulant (AC) treatment was never started without his consent. The degree of neurological deficit at onset was divided into three categories according to Pessin et al: mild, moderate, or severe. However, aphasia alone was not regarded as 'severe' and the degree of (un)consciousness was not implicated in dividing the deficit into these categories. The type and timing of the AC treatment was always left to the attending neurologist. Before AC treatment, partial activated thrombin time (APTT) or the thrombostest percentage (TT) was measured once and then repeatedly during treatment. Immediate AC treatment consisted of a standard regimen: a bolus of 5000 IU heparin and maintained uneventfully. ED was done mainly to look for bleeding under AC treatment. Since it was the objective of this study to investigate the risk of early AC treatment, all patients were followed for three weeks after the initial ischemic event.

**Results**

Depending on when therapeutic anticoagulation was achieved, the patients were divided into three groups: 1) therapeutic AC within 24 hours after stroke onset, 2) full AC later than 24 hours after stroke onset and 3) no AC treatment.

**Group 1**

Group 1 included 11 males and 10 females aged 71 (59–86) (median with range). Table 1 shows the presumed cardiac source of embolus. The degree of neurological deficit and the number of cases with HI on the initial CT are given in table 2. Fifteen patients were started on heparin and 6 had therapeutic OAC on admission. In one case, heparin was started without prior CT-scan. In 8 cases hypodense areas were seen on CT which were multiple in 3. In spite of HI on the initial CT, heparin was started and maintained uneventfully in one patient, and repeated CT showed disappearance of HI on day 18. AC was stopped on day 12 in one patient who was to be discharged, but AC was considered dangerous with regard to his mental state. Thirteen repeated CT-scans were performed on various days (2–10) after the initial event in 10 patients under full AC treatment. In one case, HI was seen on day 10. However, AC was continued uneventfully. Although one patient had a BP of 240/120 mm Hg and signs of mass effect on CT, no HI was seen on a repeated CT on day 3. Two patients suffered decreased consciousness on day 3 and 4 respectively. Because repeated CT revealed no HI, AC treatment was continued and both patients gradually regained full consciousness some
days later. In spite of therapeutic OAC treatment, one patient suffered a recurrent embolus in the opposite hemisphere on day 10. Repeated CT could not be performed. Postmortem examination showed ischemic necrosis in both cerebral hemispheres without microscopic signs of HI. One patient died of pulmonary embolus on day 5 under full OAC. Repeated CT was not performed. Postmortem examination showed no signs of HI. One patient with mitral stenosis suffered multiple cerebral infarctions while she was on 24,000 IU heparin daily because of suspected pulmonary embolus. CT showed multiple hypodense areas in both hemispheres and lumbar puncture, performed while AC treatment was shortly arrested, revealed no signs of hemorrhage. The patient had an impaired consciousness but AC treatment was continued because this was considered of vital importance regarding possible pulmonary embolus. Four days later she died of respiratory insufficiency although there were some clinical signs of early central herniation. Postmortem examination showed vast bilateral pulmonary infection and brain autopsy did not reveal any sign of raised intracranial pressure or brain herniation. Multiple ischemic and partial hemorrhagic infarcted areas were noticed in both hemispheres. Pathological diagnosis was multiple brain emboli.

No further recurrences of emboli were observed in this group and no clinical deterioration attributable to AC treatment was noticed.

Group 2

Group 2 included 5 males and 5 females, aged 68 (47–86) (median with range). Table 1 shows the presumed cardiac source. The degree of neurological deficit and the number of cases with HI on the initial CT are shown in table 2. Echocardiography in the patient with myocardial infarction showed the presence of a left ventricle thrombus. Therapeutic AC treatment was achieved in 5 (2–14) (median with range) days. CT showed hypodense areas in 7 cases with multiple hypodensities in 3. In 3 patients HI was seen on admission and had disappeared on day 4, 8 and 13. Five repeated CT-scans were performed. CT in 2 patients under full AC did not reveal HI. The various reasons for postponing AC were as follows: HI on the initial CT in 3 cases, in one case intermittent atrial fibrillation was discovered afterwards by 24-hours Holter monitoring, and in 4 patients OAC was started immediately but consequently therapeutic TT was achieved several days later. Two cases had treatment delay without specific reason. No recurrent embolic event nor clinical deterioration attributable to AC treatment was observed in this group.

Group 3

Group 3 included 6 males and 2 females, aged 73 (54–86) (median with range). Table 1 shows the embolic source. The degree of neurological deficit and the number of cases with HI on the initial CT are depicted in table 2. Hypodense areas were noticed on CT in 5 cases, with multiple hypodensities in 3 of them. HI was seen in one case with severe deficit. The various reasons for refraining from AC treatment in this group were: HI on initial CT, impaired consciousness, and high age. Three patients died of central herniation on day 2, 3 and 8. Postmortem examination in 2 of them showed HI in the central nuclei and the posterior artery territory on the same side as the ischemic event in one case, and HI in the posterior cerebral artery territory in the other. On the initial CT no HI was observed in either case. Postmortem examination was not allowed in the third patient.

Discussion

The frequency of embolic cerebral infarction varies from 20 to 50 percent in recent studies. The recurrence rate is high, especially during the first 3 weeks after the initial event and therefore AC treatment is indicated. A matter of debate has been when to start such treatment. In pathology studies a high frequency of small petechial hemorrhages, mainly in gray matter, was observed in cases with cerebral embolic infarction. Fragmentation of the embolus with reperfusion through the distal affected vessels was supposed to be the responsible mechanism for such hemorrhagic infarction. This finding plus incidental clinical data led to the fear of a bleeding tendency if AC treatment should be started immediately after cerebral embolic ischemia. Moreover, experimental studies showed an increase in HI and clinical deterioration in animals under AC treatment after reperfusion of temporarily occluded cerebral arteries. Therefore some authors advised to wait a period ranging from a few days to weeks before initiating AC treatment. However, the few available clinical studies although not meeting today's methodological criteria, lent no support to this view. Since the feared dangerous complication of direct AC treatment in embolic stroke has never been confirmed in clinical studies, others advised to start immediate AC treatment by means of intravenous heparin to prevent early recurrences. An exception was made for cases with massive neurological deficit and cerebral bleeding had to be excluded by lumbar puncture. Immediate AC treatment after lumbar puncture, however, increases the risk of spinal haematoma. Although Söderström and Buruma et al. suggested that spectophotometry of spinal fluid was superior to CT in detecting HI, no clear evidence was offered. On the contrary, Lee et al. could not separate HI from ischemic infarction by CSF analysis. Others found CT superior to lumbar puncture and therefore sufficient when direct AC treatment is considered.

Davis found HI in 12 patients with embolic stroke with increasing deficit and he concluded that clinical worsening had been caused by HI. However, in only 2 patients was prior CT performed, so that the supposed causal relation between HI and increasing neurological deficit was not based on clear evidence.

In the present study CT was performed in 38/39 patients with suspected cerebral embolus. No clinical
deterioration attributable to AC treatment was observed in 21 patients treated immediately and in 10 patients with delayed treatment. Clinical worsening in 3 patients under AC was probably due to cerebral edema; no signs of HI were seen on CT and the patients recovered to the previous level while AC treatment was continued. Twenty-two CT-scans were performed under full AC and in 2 cases HI was seen without worsening of symptoms although AC was continued for two more days in one patient and was not stopped at all in the other. Two of the 21 patients (group I) had a recurrent embolic event while on therapeutic oral anticoagulants. However, this figure is as yet too small to make firm conclusions about the early recurrence rate despite anticoagulation. Further data will be gathered in the future. Whether the risk of re-embolisation is related to the type and source of the embolus is not known.

The low frequency of HI on CT in the present study (5/38) is in accordance with the findings of the others.20-23 This contrasts with the findings in pathology series in which in about two thirds of the cases with embolic stroke HI was found.6,7 This could be explained by a possible bias in pathology series, especially when death is primarily caused by structural brain impairment in cases with brain herniation. On the other hand the possibility remains that in clinical studies HI goes undetected in a large number of cases because the seize of the petechial bleedings lies under the resolution capacity of the CT scanner.22,41 Even if this should be the case, the present study and the study of Furlan et al.4 and that of Koller9 offer no support to the view that immediate AC treatment is dangerous in patients with embolic cerebral ischemia. On the contrary, we find direct AC treatment indicated unless there are signs of bleeding or HI on CT or unless the patient’s consciousness is decreased, since this could be the beginning of central herniation with possible consequent structural cerebral damage when herniation advances.42 Moreover, patients with general contra-indication to AC should of course be excluded.

Thus, considering CT findings and clinical data, a well defined group of patients with embolic stroke with varying degrees of neurological deficit can safely be anticoagulated directly. This should be done by continuous intravenous heparin administration followed by an oral anticoagulant. Heparin should be stopped as soon as therapeutic anticoagulation is achieved by the latter.

The pathology of the patient (group I) who died on day 5 of a pulmonary embolus in spite of full OAC showed no signs of HI. The pathology of the other patient (group I) who died of recurrent embolus in spite of full OAC revealed no signs of HI. Postmortem examination of the two patients without anticoagulation in group III showed clear HI. Initial CT in these cases was without HI and therefore it is possible that HI was caused during brain herniation.

The patient with respiratory insufficiency (group I) did not die of brain herniation but nevertheless HI was found at autopsy. HI was missed by CT or developed afterwards. Whether CT misses HI or HI is caused by brain herniation remains an important question in respect of the clinical consequences. A comparative study of CT and postmortem findings could give insight in this matter. Such a study is currently being carried out at our institution.

References
Effect of Mannitol on rCBF in Canine Thalamic Ischemia — An Experimental Study

HIROBUMI SEKI, M.D., TAKASHI YOSHIKAWA, M.D., AKIRA OGAWA, M.D., AND JIRO SUZUKI, M.D.

SUMMARY Using the canine thalamic infarction model, we have investigated the effects of 10 ml/kg of 20% mannitol on the brains of animals with severe ischemic foci. Increases were statistically significant in the animals with moderate ischemia. Increases in rCBF due to mannitol administration lasted for about 1 hour, as did the rise in serum osmolarity. The actual relationship between these two parameters remains unclear.

EXPERIENCE With a case in which direct surgery on a cerebral aneurysm was performed under northerma and normotension, and long occlusion of cerebral vessels was unavoidable, led to the idea that mannitol may have a suppressive effect on the development of cerebral infarction. Since then, various animal experiments to test this idea have been undertaken and reported extensively.1-9

Mannitol has been widely used to decrease cerebral volume and it has been demonstrated by various investigators that it increases cerebral blood flow.4, 10, 11 and that such increases are unrelated to changes in blood pressure.10, 12 Unfortunately, little work has been done to determine whether or not mannitol has the ability to increase cerebral blood flow in pathological states, such as brain ischemia.

The present paper reports an investigation on the effects of administration of mannitol on the region.

From the Division of Neurosurgery, Institute of Brain Diseases, Tohoku University School of Medicine, Sendai, Japan.
Address correspondence to: Hirobumi Seki, M.D., Division of Neurosurgery, Institute of Brain Diseases, Tohoku University School of Medicine, 5-13-1 Nagamachi, Sendai, 982 Japan.
Received May 6, 1982; revision accepted August 10, 1982.

35. Ruff RL, Dougherty JH: Evaluation of acute cerebral ischemia for anticoagulant therapy: Computed tomography or lumbar puncture.

Evaluation of the risk of immediate anticoagulant treatment in patients with embolic stroke of cardiac origin.
J Lodder and P J van der Lugt

Stroke. 1983;14:42-46
doi: 10.1161/01.STR.14.1.42

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/14/1/42

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/