Almost half a century has elapsed since the original descriptions of cerebral vasospasm after aneurysmal subarachnoid hemorrhage (SAH), but despite intense research into the causes, pharmacological treatment, and prevention of vasospasm, only very modest gains have been made. Nimodipine is the only drug used worldwide to prevent delayed ischemic neurological deficits (DINDs) resulting from vasospasm. A number of other drugs have been proven ineffective in clinical trials or had unacceptable side effects. Because of the inadequacy of pharmacological treatment described previously for experimental vasospasm, the authors conducted a pilot trial in humans to assess the safety and efficacy of TBA performed within 3 days of SAH.

Methods. The study group consisted of 13 patients with Fisher Grade 3 SAH who had a very high probability of developing vasospasm. In all patients, regardless of the site of the ruptured aneurysm, target vessels for prophylactic TBA were as follows: the internal carotid artery, A1 segment, M1 segment, and P1 segment bilaterally; the basilar artery; and one vertebral artery. Prophylactic TBA was considered satisfactory when it could be performed in at least two of the three parts of the intracranial circulation (right and/or left carotid system and/or vertebrobasilar system), and included the aneurysm-bearing part of the circulation. Of the 13 patients, none developed a DIND or more than mild vasospasm according to transcranial Doppler ultrasonography criteria. At 3 months posttreatment eight patients had made a good recovery, two were moderately disabled, and three had died; one patient died because of a vessel rupture during TBA and two elderly individuals died of medical complications associated with poor clinical condition on admission.

Conclusions. Compared with large series of patients with aneurysmal SAH reported in the literature, the results of this pilot study indicate an extremely low incidence of vasospasm and DIND after treatment with prophylactic TBA. A larger randomized study is required to determine whether prophylactic TBA is efficacious enough to justify the risks, and which vessels need to be dilated prophylactically.

Keywords: subarachnoid hemorrhage • cerebral vasospasm • transluminal balloon angioplasty • aneurysm
Experiments in which a dog model of vasospasm was used have shown that TBA performed on Day 0 totally prevents the development of arterial narrowing on Day 7, which was ascribed to the blood vessels becoming unresponsive to a large number of constrictive (as well as to dilating) agents.35 Because preventive TBA was more effective in experimental vasospasm than any previously described pharmacological treatment and because this procedure can be performed in patients before secondary insults become important, we have advocated an investigation of this treatment in patients with aneurysmal SAH.12 Thus, a pilot trial was conducted for preliminary assessment of the safety and efficacy of TBA performed within 3 days of the onset of aneurysmal SAH. A relationship between the amount and distribution of subarachnoid blood detected on computerized tomography (CT) scanning and the subsequent development of cerebral vasospasm was found by Fisher and colleagues.12 They found that in the presence of subarachnoid blood clots larger than 5 × 3 mm (measured on the reproduced images) or layers of blood 1-mm thick or more in fissures and basal cisterns (Fisher Grade 3), severe spasm followed almost invariably. Transluminal balloon angioplasty is a risky, invasive procedure. Therefore, we believed that a pilot study of prophylactic TBA should include only patients at greatest risk to develop vasospasm (that is, those with Fisher Grade 3 SAH).

Clinical Material and Methods

The Human Subjects Review Committee at the medical center of the University of California Davis approved this study. The experimental nature of the treatment was explained to the patients and/or their families and informed consent was obtained before we performed the preventive TBA.

Enrollment Criteria

All patients considered for enrollment had presented with SAH from a ruptured aneurysm, and in each diffuse, thick clots in the basal cisterns or hemispheric fissures (Fisher Grade 3)12 were revealed on CT scans obtained within the first 2 days post-SAHI. Patients were only included after undergoing surgical treatment of the ruptured aneurysm and any incidental unruptured aneurysm and when preventive TBA could be performed within 3 days of bleeding. Patients included in our study had no angiographically demonstrated evidence of vasospasm prior to the TBA treatment. There were no age limits for inclusion; pregnancy was not a reason for exclusion. Patients in whom vasospasm was confirmed on the postsurgical angiogram also underwent TBA, but were not considered part of the prophylactic treatment group. Also, for a patient to be included in the study group, TBA had to be performed in at least two of the three parts of the intracranial circulation (right and/or left carotid system, and/or verteobasilar system), including the arteries leading directly to the clipped ruptured aneurysm.

Surgical and Medical Management

Within 2 days of rupture, all patients underwent clipping of their aneurysms performed by the senior author (J.P.M.) via the classic transsylvian approach as described in Yasargil and Fox.52 All operations were performed at the first opportunity, day or night. Perivascular blood was cleared only from the cisterns, which were easily accessible (usually around the ipsilateral internal carotid artery [ICA]), M1 and A1 segments, and also around the contralateral A1 for an anterior communicating artery (ACoA) aneurysm, whereas Liliequist’s membrane was opened in practically all cases to reach the tip of the basilar artery (BA). Papaverine was not used, and no cisternal drains were left in place. All patients received nimodipine postoperatively (60 mg every 4 hours or 30 mg every 2 hours). Magnesium supplementation to obtain plasma levels of approximately 2.2 mg/L was also considered standard.51 Other drugs were given only for a specific indication. Each patient’s hematocrit level was kept between 30% and 35% by either hemodilution or infusion of packed red blood cells. Ample fluids, including 500 ml of albumin over 24 hours, were infused for prophylactic hyperdynamic therapy.40 No other plasma expanders were used. For hypertensive therapy, 30 to 300 μg/minute of phenylephrine was used as necessary in case of DIND.

Transluminal Balloon Angioplasty

After surgery the first nine patients in the series were allowed to wake up to check for any new neurological deficits, and the last four patients remained intubated for TBA immediately postsurgery. Patients were then taken for angiographic studies. In all patients arterial access was gained via a No. 6 French sheath (Pinnacle; Meditech, Watertown, MA) placed percutaneously in the femoral artery. A 100-cm, No. 5.8 French thin-wall guide catheter (model P5.8-NT-100-M-NS-0; Cook, Inc., Bloomington, IN) was then advanced into the ICA and the vertebral artery (VA). A diagnostic transfemoral angiogram was obtained to check for adequate clipping, patency of the parent vessel, and the presence of early vasospasm. After diagnostic angiography a 4 × 10–mm 0.1-ml occlusion type balloon angioplasty catheter (model NDSB 8501/20002; Interventional Therapeutics Corp., Fremont, CA) was coaxially advanced through a No. 6 French guide catheter and into the intracerebral circulation. Angioplasty target goals for the carotid circulation were the A1 segment of the anterior cerebral artery (ACA), the M1 segment of the middle cerebral artery (MCA), and the supraclinoid ICA. Target goals in the VA were the P1 segment of the posterior cerebral artery (PCA) bilaterally, the BA, and the ipsilateral distal VA. All angioplasty balloon manipulations were performed using systemic heparinization and the roadmapping technique. A single 5000–U bolus of heparin was administered immediately prior to balloon introduction, and no further heparin doses were adminis-

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**TABLE 1**

Grading of cerebral vasospasm using TCD

<table>
<thead>
<tr>
<th>Mean Blood Flow Velocity (cm/sec)</th>
<th>Severity of Vasospasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>150–200</td>
<td>mild</td>
</tr>
<tr>
<td>200–250</td>
<td>moderate</td>
</tr>
<tr>
<td>&gt;250</td>
<td>severe</td>
</tr>
</tbody>
</table>
tered after the initial bolus. Angioplasty balloons were inflated to the vessel diameter, with approximately 1 mm of balloon elongation. Each inflation continued for 5 seconds. No arteries were expanded beyond their normal diameter during angioplasty. The type of angioplasty balloon used ruptures at approximately 6 atm, and no balloon ruptures were encountered during the treatment of the patients. Therefore, in all treated arteries the radial pressures were less than 6 atm. All target arteries that could be entered with the flow direction technique were treated along their entire lengths. A postangioplasty angiogram was obtained in all cases to evaluate the change in vessel caliber and the presence of any vessel damage.

Diagnosis of Vasospasm and DINDs

For 10 to 14 days after onset of SAH, transcranial Doppler (TCD) ultrasonography was performed on all vessels comprising the circle of Willis. Cerebral vasospasm was graded according to peak mean velocities, referring to the scale shown in Table 1. The DINDs were assumed to be caused by vasospasm if they occurred between Days 3 and 14 post-SAH in a vascular distribution judged to be at risk (criteria included focal deficits for all vessels and/or a decline in the Glasgow Coma Scale score of 2 or more points for midline vessels), and when there was no other discernible cause of deterioration such as postoperative hematoma, hydrocephalus, seizure, or metabolic derangement. In patients with suspected DINDs the protocol specified angiographic evaluation and, if indicated, repeated TBA. Outcome was assessed at 3 months (± 2 weeks) by using the Glasgow Outcome Scale (GOS) by an experienced assessor in a blinded fashion. The outcome rating was assigned by the operating surgeon only in cases of early, unequivocal good outcome (that is, patient returned to former employment before the 3-month window).

Results

The patient characteristics and results are outlined in Tables 2 and 3. Representative CT scans obtained in patients who fulfilled enrollment criteria and were treated with TBA during the study period are shown in Fig. 1. Within a period of 20 months (June 1997 to January 1999), a total of 13 patients were enrolled and underwent TBA as planned (study group; Table 2 and Fig. 1). During the same period, seven patients presented with Fisher Grade 3 SAH on CT scans but were not included in our treatment group for various reasons (excluded group, Table 3). The 13 patients in the study group consisted of four men and nine women ranging in age from 29 to 75 years (mean age 48 years). Patients presented with the following Hunt and Hess grades: Grade II (three patients), Grade III (five patients), Grade IV (four patients), and Grade V (one patient). The ruptured aneurysms were located as follows: ACoA (eight patients), MCA (one patient), posterior communicating artery (PCoA) three patients), and BA tip (one patient). One patient (Case 10007) had multiple aneurysms, including a ruptured BA aneurysm and an unruptured PCA aneurysm. One patient (Case 10005) was 37 weeks pregnant at the time of her SAH. After intensive discussion with physicians in the obstetric department, who were actively involved in managing her care, it was decided to allow her to continue her pregnancy and facilitate normal vaginal delivery after her aneurysm had been surgically treated. Two days after surgery and TBA, continuous fetal monitoring revealed late deceleration, and an uneventful cesarean section was performed, resulting in the birth of a healthy infant.

TABLE 2

Characteristics of 13 patients with Fisher Grade 3 SAH treated with prophylactic TBA*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Hunt &amp; Hess Grade</th>
<th>Site of Aneurysm</th>
<th>Peak Mean TCD Vel (cm/sec) Day Post-SAH</th>
<th>Peak Mean TCD Vel (cm/sec) Day Post-SAH</th>
<th>Symptomatic</th>
<th>Angiographic</th>
<th>GOS Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>10001†</td>
<td>41, F</td>
<td>IV II</td>
<td>ACoA</td>
<td>196 5</td>
<td>132 10</td>
<td>no</td>
<td>NA</td>
<td>GR</td>
</tr>
<tr>
<td>10002†</td>
<td>32, M</td>
<td>IV III</td>
<td>ACoA</td>
<td>176 9</td>
<td>90 9</td>
<td>no</td>
<td>NA</td>
<td>GR</td>
</tr>
<tr>
<td>10003†</td>
<td>38, M</td>
<td>III III</td>
<td>ACoA</td>
<td>146 8</td>
<td>70 7</td>
<td>no</td>
<td>NA</td>
<td>MD</td>
</tr>
<tr>
<td>10004†</td>
<td>44, F</td>
<td>III III</td>
<td>ACoA</td>
<td>165 9</td>
<td>106 3</td>
<td>no</td>
<td>NA</td>
<td>GR</td>
</tr>
<tr>
<td>10005†</td>
<td>29, F</td>
<td>II II</td>
<td>ACoA</td>
<td>172 6</td>
<td>102 3</td>
<td>no</td>
<td>NA</td>
<td>GR</td>
</tr>
<tr>
<td>10006†</td>
<td>43, M</td>
<td>IV IV</td>
<td>PCoA</td>
<td>90 9</td>
<td>122 8</td>
<td>no</td>
<td>NA</td>
<td>MD</td>
</tr>
<tr>
<td>10007†</td>
<td>47, F</td>
<td>III III</td>
<td>BA</td>
<td>115 8</td>
<td>143 7</td>
<td>no</td>
<td>NA</td>
<td>D</td>
</tr>
<tr>
<td>10009†</td>
<td>43, F</td>
<td>II II</td>
<td>PCoA</td>
<td>127 9</td>
<td>179 12</td>
<td>no</td>
<td>NA</td>
<td>D</td>
</tr>
<tr>
<td>10010†</td>
<td>64, F</td>
<td>V IV</td>
<td>ACoA</td>
<td>83 9</td>
<td>85 9</td>
<td>no</td>
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<td>GR</td>
</tr>
<tr>
<td>10011‡</td>
<td>73, F</td>
<td>III III</td>
<td>PCoA</td>
<td>119 6</td>
<td>62 3</td>
<td>no</td>
<td>NA</td>
<td>GR</td>
</tr>
<tr>
<td>10012‡</td>
<td>45, M</td>
<td>III III</td>
<td>ACoA</td>
<td>112 11</td>
<td>22 10</td>
<td>no</td>
<td>NA</td>
<td>GR</td>
</tr>
</tbody>
</table>

* D = dead; GR = good recovery; MD = moderate disability; NA = not applicable; vel = velocity.
† Patients also having marked intraventricular hematoma (Fisher Grades 3 and 4).
§ TCD probe broken.
§§ Unable to obtain TCD velocities due to patient’s early death.
\[Untreated.\]
During the study period we found two patients (Cases 14001 and 14002) who were unable to undergo prophylactic TBA because severe atherosclerotic and tortuous arteries precluded the procedure. These patients were 78 and 71 years old, respectively. Two other patients (Cases 14003 and 14005) received prophylactic TBA in only one part of the intracranial circulation, mostly because of severe atherosclerotic changes and vascular abnormalities. These patients were 74 and 72 years old, respectively, indicating that this treatment may not be feasible for some patients in the older age range. Three patients presented to our hospital several days after their SAH. These individuals were either found unresponsive at home or had a delayed referral from another facility. Angiography demonstrated evidence of vasospasm just before angioplasty in one of the patients represented in Table 3 (Case 14004). This excluded her from the preventive/prophylactic treatment group. One patient (Case 14007) refused to be included in the study. The patient characteristics and outcomes in this excluded group are outlined in Table 3.

Findings on TCD Ultrasonography

In the study group TCD velocities of between 150 and 200 cm/second were recorded in four patients, which was graded as mild vasospasm. There were no velocities in excess of 200 cm/second (moderate-to-severe vasospasm). In the exclusion group, one patient had mild and one patient had moderate vasospasm. Due to a temporarily broken probe a complete TCD examination could not be obtained in all patients.

Transluminal Balloon Angioplasty

As mentioned earlier, four patients had to be excluded.
Prophylactic transluminal angioplasty: pilot study

ed from the study group because atherosclerotic changes made angioplasty partially or totally impossible. Dilatation was obtained in 40% of the A1, all M1, and in 35% of the P, segments. The balloon was introduced and inflated in 80% of the supraclinoidal ICA segments and 60% of the BAs. Unilateral catheterization of a VA was successful in 70% of the cases. One patient (Case 10009) died of a rupture in the posterior inferior cerebellar artery (PICA) during TBA.

Delayed Ischemic Neurological Deficits and Outcome

No patient in the study group developed DINDs. In the exclusion group symptomatic vasospasm occurred in at least two cases.

Outcome assessment in the study group revealed eight patients with good recovery and two with moderate disability, for a favorable outcome rate of 77%. Three patients died, one because of a vessel rupture during TBA. Two older patients, 75 and 64 years of age, were in very poor clinical condition preoperatively (Hunt and Hess Grades IV–V). Both improved to the level of following commands and spontaneous eye opening on approximately Day 10, indicating that there had been no occurrence of clinical vasospasm or DIND, but they later died of pulmonary complications. The moderate disability in the patient in Case 10003 was caused by nearly complete kinking of a right A1, segment of the ACA by the aneurysm clip, as confirmed on postoperative angiographic studies. This caused the patient to experience a predominantly left-sided lower-extremity hemiparesis immediately postoperatively, from which he did not completely recover. Preoperatively this vessel was already extremely narrow; yet by 6 months the patient made a full recovery. The patient in Case 10002, a police officer, underwent neuropsychological testing at his work 8 weeks post-SAH and was found to be fit to resume his former job.

In the exclusion group two patients had a good recovery, one patient remained vegetative, and four died. One patient (Case 14001) died in a nursing facility because of pulmonary complications and another patient (Case 14003), who had an extensive medical history of congestive heart failure and rhythm disturbances, died of respiratory failure in the course of her hospital stay. Two patients died and one remained vegetative because of vasospasm (Cases 14002, 14006, and 14004, respectively).

Discussion

Preventive postoperative TBA, performed within 3 days after SAH from a ruptured berry aneurysm, proved to be feasible in this pilot study of 13 patients. Angioplasty for symptomatic vasospasm has been performed at various institutions with promising results. In a 10-year review of 224 clinically good grade patients treated for aneurysmal SAH by Le Roux, et al., 39 patients (17.4%) experienced symptomatic vasospasm, of whom 22 were treated with angioplasty and 17 without (technique not available). Comparison of these two groups revealed a favorable outcome in 95.5% of the patients treated with angioplasty, whereas in those not treated, 76.5% had a favorable outcome. Immediate postoperative TBA was described earlier by Le Roux and colleagues, 38 but this was not prophylactic because their patients already had severe angiographically confirmed vasospasm.

In a similar study with the same enrollment criteria and the same criteria for TCD assessment of vasospasm, a study in which cyclosporine A was used as preventive therapy, moderate-to-severe spasm was detected on TCD ultrasonography in seven (77%) of nine patients.39 Five patients (56%) developed a DIND; five (56%) had a good recovery or moderate disability. Three patients (33%) died; all had DINDs, and severe diffuse vasospasm was demonstrated on angiographic studies. In another recent study in which nicardipine was used to prevent vasospasm, 13% of patients receiving placebos were seen to have moderate-to-severe spasm on TCD studies, DINDs were seen in 46%, and 56% made a good recovery, 12% had moderate disability, and 18% died. Vasospasm was identified as the primary cause of death in 4% of the placebo-treated patients. Overall, 11% of the placebo-treated patients in this study had a poor outcome because of vasospasm.17,18 The percentages of patient groups with SAH in each of the Fisher grades cannot be determined from these publications; however, our study included only patients with extensive SAH. In our pilot study no patient had moderate-to-severe vasospasm documented on TCD ultrasonography or developed a DIND. Ten patients (77%) had a good recovery or a moderate disability and three patients (23%) died, one because of a vessel rupture during TBA and two patients presumably because of the combination of severe initial damage and older age. It has been speculated that the aging brain might have a less optimal response to the initial bleeding.29 When the data for the 13 patients in the study were compared with the last 12 characteristic-matched patients who also underwent operation by the senior author, were managed in a very similar fashion but did not undergo angioplasty, and for whom a good concurrently gathered database was present, the following data were obtained (Table 4): four (33%) of 12 patients developed DINDs, eight (67%) made a good recovery or had moderate disability, and four (25%) had poor outcomes. Of these four, one patient remained vegetative and three died. Of the patients with DINDs, two made a good recovery, one definitely died of

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Hunt &amp; Hess Grade</th>
<th>Symptom- atic Vaso- spasm</th>
<th>Fisher Grade</th>
<th>Site of Aneurysm</th>
<th>GOS Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>20001</td>
<td>34, M IV IV IV</td>
<td>ICA yes</td>
<td>GR</td>
<td>F II II</td>
<td>ACoA &amp; PCoA</td>
<td>yes GR</td>
</tr>
<tr>
<td>20002</td>
<td>34, M II II BA</td>
<td>no</td>
<td>GR</td>
<td>F II II</td>
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</tr>
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<td>F II II</td>
<td>ACoA</td>
<td>yes GR</td>
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<tr>
<td>20004</td>
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<td>no MD</td>
<td>GR</td>
<td>F II II</td>
<td>PCoA</td>
<td>no MD</td>
</tr>
<tr>
<td>20005</td>
<td>32, F II II ICA</td>
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<td>F II II</td>
<td>PCoA</td>
<td>no MD</td>
</tr>
<tr>
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<td>57, M V V V</td>
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<td>D</td>
<td>F II II</td>
<td>ACoA &amp; PCoA</td>
<td>no D</td>
</tr>
<tr>
<td>20007</td>
<td>40, M II II ACoA &amp; PCoA</td>
<td>no GR</td>
<td>GR</td>
<td>F II II</td>
<td>pericallosal artery</td>
<td>no GR</td>
</tr>
<tr>
<td>20008</td>
<td>37, F II II pericallosal artery</td>
<td>no GR</td>
<td>GR</td>
<td>F II II</td>
<td>PCoA</td>
<td>no MD</td>
</tr>
<tr>
<td>20009</td>
<td>44, F II III ACoA &amp; PCoA</td>
<td>no D</td>
<td>GR</td>
<td>F III III</td>
<td>BA no</td>
<td>no GR</td>
</tr>
<tr>
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<td>51, F III III BA</td>
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<td>GR</td>
<td>F III III</td>
<td>PCoA &amp; MCA</td>
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</tr>
<tr>
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<td>yes V</td>
<td>GR</td>
<td>F III III</td>
<td>PCoA</td>
<td>yes V</td>
</tr>
</tbody>
</table>

* No TCD data available.
vasospasm, and one remained vegetative; two (17%) of 12 had an unfavorable outcome caused by vasospasm.

Comparison of the data in the previously published studies and our own characteristic-matched patients with those from this pilot study indicates a much lower incidence of vasospasm in the study group (Table 5). However, it cannot be determined from this small sample size whether prophylactic TBA is more effective than TBA for symptomatic vasospasm in providing a better outcome.

The time window and best technique (degree and duration of dilation) for preventive TBA to be effective cannot be established from our study. In the experimental study by Megyesi, et al.,35 the vessels were dilated to a mean of 166% of baseline (range 148–200%) just before the placement of the blood clot, and on Day 7 the vessels were still at 164% of baseline. In our study TBA was performed much later. It should be noted that all arteries that underwent angioplasty in this study were not dilated beyond their normal anatomical confines (with the exception of the single PICA that ruptured). A force was definitely applied to the intima of these arteries, because there was a 1- to 2-mm elongation of balloon length once the balloon diameter matched the normal artery diameter. Moreover, in the experimental study each segment was dilated twice for 10 seconds, whereas we dilated the vessel only once for 5 seconds as we usually do for the treatment of clinical vasospasm.14 Any of these technical differences, alone or in combination, could be responsible for our finding of a certain degree of increase in TCD velocity occurring in most patients between Days 5 and 10 post-SAH, whereas the experimental study of Megyesi, et al.,35 dilation well above baseline was maintained. Species differences or the lesser severity of the experimental SAH compared with clinical, aneurysmal SAH could also account for the seemingly better efficacy under experimental conditions (none of the dogs with untreated vessels with a diameter of 69% of baseline on Day 7 developed neurological deficits).

We aimed at performing TBA in no less than 10 vessels (one VA, the BA, both P1 segments of the PCA, bilateral ICAs, M1 segments of the MCAs, and A1 segments of the ACAs), but this goal was not achieved in a single case. Short duration of cerebral angiographic procedures is associated with increased safety.52 Because there was no proven therapeutic utility for prophylactic angioplasty while our study data were collected, we favored a shorter procedure duration with angioplasty of fewer vessels over a longer procedure duration with more target vessels treated. Given the large number of target vessels (10), a 5-minute limit was placed on the manipulation time allowed to introduce the angioplasty balloon into each target vessel. If the flow-guided angioplasty balloon could be navigated into the target vessel in 5 minutes or less of diligent effort, then that vessel would undergo angioplasty; otherwise the angioplasty balloon would be moved to the next target vessel. To add to standardization of the methods, only a single flow-guided angioplasty balloon was used for each procedure. No guidewires or over-the-wire angioplasty balloon systems were used. If a longer procedural duration had been accepted and if a greater array of devices had been used, then more target vessels in each patient could have been treated with angioplasty.

Another problem we frequently encountered was severe atherosclerosis or vessel tortuosity in older patients, which precluded navigating the balloon into more than one (sometimes none) of the three parts of the intracranial circulation specified by our protocol. In view of the preliminary character of our study, we did not believe that becoming overly aggressive with our attempts to dilate the intracranial vessels was justified. Considering the encouraging results of this study and the high incidence of poor outcome caused by vasospasm in the elderly,21,37 a more persistent approach seems warranted.

The most severe and clinically relevant vasospasm seems to occur in the vessel system containing the ruptured aneurysm.14 Thus, it might be sufficient only to dilate the right ICA and right M1 segment for a ruptured right-sided MCA aneurysm, or the right ICA, A1 segment for an ACoA aneurysm with a dominant right A2, or only the vertebrobasilar artery system for posterior circulation aneurysms, and so forth. In five of the patients in our study who had ACoA aneurysms, both of their A1 segments filled from a single A2 segment via the ACoA preoperatively. In one case we did not use the ACoA with the clip on the aneurysm in situ, despite observing a certain degree of movement of the clip during this maneuver. In this case the operating surgeon believed that the clip was placed securely enough not to jeopardize the patient, but whether this is necessary can only be determined in a much larger study.

Schwartz and Lellouch44 have proposed a distinction between “pragmatic” (does the therapy under investigation improve outcome?) and “explanatory” trials (does the therapy under investigation do what it is supposed to do?). In this sense, ours is an explanatory study, as we aimed to research whether prophylactic TBA could prevent DINDs and lead to diminished vasospasm by TCD criteria. With the data available, this question cannot be answered as yet. Probably the best way to assess the effect of prophylactic TBA on TCD velocities would be to compare TCD data in left- and right-sided “mirror vessels,” in which TBA has been performed on one side only. However, in practically all cases the A1 segments were of such different calibers to begin with that angioplasty could only be performed on the dominant side, making comparisons between treated and untreated vessels meaningless. Furthermore, the P1 segments could not be insonated bilaterally in most cases. This left only the ICA and M1 segments for bilateral comparison. However, there were only two patients treated with unilateral TBA in whom reliable bilateral TCD data

<table>
<thead>
<tr>
<th>Group &amp; Study</th>
<th>No. of Patients</th>
<th>Patients Included</th>
<th>% W/ DIND</th>
<th>% W/ Favorable Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBA group, this study</td>
<td>13</td>
<td>III, III &amp; IV</td>
<td>0</td>
<td>77</td>
</tr>
<tr>
<td>exclusion group, this study</td>
<td>7</td>
<td>III, III &amp; IV</td>
<td>43</td>
<td>29</td>
</tr>
<tr>
<td>nicardipine; Haley, et al., 1993</td>
<td>457</td>
<td>all</td>
<td>46</td>
<td>56</td>
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<tr>
<td>cyclosporine; Manno, et al., 1997</td>
<td>9</td>
<td>III</td>
<td>56</td>
<td>56</td>
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<tr>
<td>matched controls, this study</td>
<td>12</td>
<td>III, III &amp; IV</td>
<td>33</td>
<td>67</td>
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* Roman numerals represent the Fisher grades in patients reported in the arms of the studies cited.
Prophylactic transluminal angioplasty: pilot study

were available. In both cases velocities in the treated vessels were consistently higher than on the untreated side, with the largest differences being 156 compared with 115 m/second (Day 4, Case 10002) and 147 compared with 75 m/second (Day 5, Case 14003). Because we did not measure the Lindegaard index or cerebral blood flow at the time of this study, it is impossible to tell whether the higher velocities in the treated arteries were due to narrowing of the conductance vessels or to less spasm in the medium and small resistance vessels, leading to a better runoff. This would be an important question to answer, because it could shed light on the mechanism by which prophylactic TBA prevents DINDs; if the runoff were better one might assume that prophylactic TBA prevents the release of some (endothelium-derived?) constriction factor into the downstream circulation, which in turn would make the internal manipulation of the blood vessels more important than dilation per se. In this respect it is interesting to note that, in contrast with the animal study on which this clinical pilot study was based, we did not actually dilate the vessels beyond their original (nonspastic) diameter, and we still did not see DINDs. Therefore, in future studies we plan both pragmatic and explanatory endpoints.

The single intraoperative death that occurred during TBA warrants particular attention, because TBA poses risks both from the angiographic technique and from the actual dilation. From a retrospective study of 597 diagnostic angiograms obtained after aneurysm surgery it was concluded that postoperative angiography is safe and should be routinely performed. Only a few complications were encountered in this large series of patients and included groin hematoma, catheter-related spasm, and vessel dissection. The highest quoted mortality rate from TBA associated with vessel rupture is 4%, and is derived from a large series of patients. The initial protocol (used in the first nine patients in the study) called for treating the patients who underwent angioplasty exactly as they would have been if angioplasty had not been performed. This decision was made to avoid confounding variables and theoretically to avoid excess morbidity related to prolonged or repeated intubation. Because the standard (nonangioplasty) therapy used by the senior author called for immediate extubation to permit neurological evaluation, angioplasty was initially performed in extubated patients, who thus could not be paralyzed for the procedure. In the first eight patients angioplasty was successfully performed with minimal or no sedation. In the ninth patient, roadmap misregistration due to patient movement resulted in unintended entry of the angioplasty balloon into the PICA, with subsequent rupture of that vessel resulting in death. The protocol was immediately modified so that patients remained intubated until angioplasty was performed, permitting paralysis to be induced during angioplasty and ensuring adequate roadmapping. All subsequent patients have been intubated and paralyzed during their angioplasty procedures. An additional advantage of TBA immediately post-surgery is that we can use the femoral sheath, which can be left in place from the preoperative angiogram.

Despite the aforementioned complication, the results described here are encouraging. Whether prophylactic TBA is effective enough to justify the risks and whether the costs of this treatment in all patients are offset by great savings in some, can only be determined in a much larger randomized study of patients with Fisher Grades 2 and 3 SAH. Such a study is presently being designed.

References

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