Effect of STA-MCA Anastomosis On the Course of Experimental Acute MCA Embolic Occlusion

ROBERT LEVINTHAL, M.D., JOHN I. MOSELEY, M.S., M.D., W. JANN BROWN, M.D., AND W. EUGENE STERN, M.D.

SUMMARY The experiments in this report were designed to evaluate the effect of superficial temporal-middle cerebral artery (STA-MCA) anastomosis on the course of middle cerebral artery (MCA) occlusion by emboli while avoiding a vessel clipping technique as well as the use of long-acting barbiturate anesthesia. Dogs were divided into 3 general groups: A) embolus placement 1 hr following anastomosis; B) embolus placement 5 h prior to anastomosis; C) control group without anastomosis. Anastomosis prior to MCA occlusion has a favorable clinical effect and reduces the size of an infarction. Anastomosis 5 h after embolus placement is deleterious unless other therapeutic modalities can be shown to delay the course of infarction.

SINCE the superficial temporal to middle cerebral artery anastomosis (STA-MCA) was first described a decade ago, the indications for the procedure have remained controversial. The effect of a superficial temporal to middle cerebral artery by-pass on the course of acute occlusion of the middle cerebral artery is of considerable importance in the prevention and early therapy of stroke. Revascularization by carotid endarterectomy in patients with acute stroke has generally produced poor clinical results. In the limited number of reports on extracranial to intracranial by-pass following early vessel occlusion, the outcome has also been discouraging. Previous laboratory studies have utilized vessel clipping methods to produce occlusions or have failed to direct their attention specifically to extracranial-intracranial revascularization procedures.

This study was designed to evaluate the effect of an extracranial to intracranial anastomosis on the course of an acute embolic occlusion of the middle cerebral artery, while avoiding clipping the vessel as well as avoiding the use of long-acting barbiturate anesthesia.

Clinical Material and Methods

Thirty-one mongrel dogs underwent operative procedures, but only 17 were available for this report, owing to aberrant emboli or other unforeseen problems. Anesthesia was induced in all animals with thiopental (20 mg/kg intravenous push). They were maintained on methoxyfluorethane inhalation anesthesia. The femoral artery was exposed and cannulated for continuous blood pressure recording and random blood gas sampling. Three operative groups were selected as follows:

Group A — STA-MCA followed in 1 hr by embolic occlusion of the middle cerebral artery.
Group B — STA-MCA performed 5 hr after embolic occlusion of the MCA.
Group C — MCA embolus to the MCA with or without control craniectomy.

The technique previously described by Molinari was utilized for embolization (fig. 1). A silicon rubber cylinder (1.8 X 8 mm) was inserted into an 18-gauge medicut cannula and injected into the isolated internal carotid artery. The cannula was removed and the ICA ligated. An extracranial-intracranial anastomosis (EC-IC) was performed between the STA, which was 1.0-1.4 mm in diameter, and a MCA cortical branch 0.8-1.0 mm in diameter (fig. 2).

On the day following surgery, the animals were clinically graded and this was continued daily until sacrifice 2 to 5 days after operation (table 1). Grading of all animals was done by 2 observers separately. Immediately prior to death, the dogs received 50 milliliters of 2% Evans blue intravenously. In all animals who had anastomosis, vessel patency was evaluated by 2 methods: 1) observation of rapid Evans blue discoloration of the STA and 2) cutting the STA and observing blood flow.

The animals were killed by aortic perfusion with gluteraldehyde or formalin. The brains were im-
FIGURE 1. A) Silicone rubber cylinder 1.8 X 8 mm with 18-gauge polyethylene cannula. B) Silk sutures around origin of the internal carotid artery. Cannula containing the silicone rubber cylinder is placed into internal carotid artery and injected into intracranial circulation.

immediately removed and placed in the appropriate fixative. Two weeks after perfusion, the brains were examined and photographed. Beginning immediately anterior to the distribution of the MCA in the brain, 1 cm coronal sections were made. The 1 cm thick slices were photographed and then the 20th and 220th sections of each slice were stained with H & E and Luxor blue. The slides were projected a fixed distance with a photographic enlarger and the hemispheric and infarcted areas were traced from their projected images, after which the traced images were examined with a compensating planimeter and the ratios of infarcted area to the whole hemisphere were computed for each slice. The amount of infarction present in each cut was averaged and that figure was accepted as the percent infarction for that animal.

Clinical Observations

The following results were obtained: arterial blood gas (ABG), blood pressure (BP) and operative times did not differ significantly among 3 groups. The

TABLE 1 Clinical Grades

A Strength
1. stands with no weakness—no dysfunction
2. stands well but with slight weakness—mild dysfunction
3. marked weakness and/or unable to stand—marked dysfunction

B Gait
1. walks with no deficit—no dysfunction
2. mild limp—mild dysfunction
3. marked limp or unable to walk—marked dysfunction

C Sensation
1. withdraws briskly to pain—no dysfunction
2. slow withdrawal—mild dysfunction
3. no withdrawal—marked dysfunction

D Level of consciousness
1. awake, active—no dysfunction
2. lethargic—mild dysfunction
3. comatose—marked dysfunction

E Field cut
absent —
marked +
The anastomosis was patent in all animals in Groups A and B. All group A & B dogs had emboli lodged in the proximal MCA.

The Group A animals (STA-MCA prior to embolus placement), in 4 out of 5 dogs, demonstrated no abnormality of strength, gait, sensation or level of consciousness. But all of these dogs had evidence of a visual field deficit. The one animal which had evidence of marked dysfunction in all clinical categories had an intracerebral hemorrhage (the only animal to demonstrate gross hemorrhage).

The Group B dogs (embolus placement 5 h prior to anastomosis) fared less well, and had either mild or marked dysfunction in each clinical neurologic category tested. Visual field cuts were consistently demonstrated in all animals.

Group C animals (embolus only in the MCA) fell into 2 separate clinical groups. Three animals with emboli resting in the proximal MCA had mild visual field defects. Two animals with emboli in the peripheral MCA had no neurologic deficit (table 2).

On postmortem examination, 4 of the 5 Group A dogs had scattered microscopic hemorrhage; the one with intracerebral hematoma was the exception. The percentage of infarction was 33.3. In Group B animals all had gross evidence of hemorrhage and 77.2% had cerebral infarction, and the Group C dogs had slight hemorrhage with 55.2% infarction (fig. 3).

There was a significant deleterious effect of arterial anastomosis on the percent of infarction in animals that had an operation 5 h after embolization ($p < 0.01$) (Student's $t$-test).

**Discussion**

Dujovnoy and associates showed that embolectomy in dogs is safe if performed up to and including 5 h subsequent to MCA embolization. After 5 h the animals developed massive cerebral infarction with gross neurologic impairment. Crowell and Olsson demonstrated a favorable effect of EC-IC bypass performed 2 h after MCA clip occlusion in the dog. Sundt and co-workers have reported that reinstituting MCA flow by clip removal in cats and monkeys within 6 h of clip placement will prevent significant infarction. Utilizing a similar technique in monkeys, Crowell and co-workers could demonstrate moderate to severe deficits after 6 to 8 h of clipping. Occlusion for 2 h after clipping produced mild neurologic deficits or none at all, and 4 h after clip occlusion produced results that were intermediate between these extremes. Although these reports have contributed to our understanding of the course of ischemic infarction, other variables need to be considered in their interpretation. Recent experimental work suggests a beneficial effect of barbiturates on the course of infarction and anatomic studies introduce a consideration of the activity of autonomic nerve supply to the cerebral vessels. These variables were examined more closely.

Except for Dujovnoy, the investigators used a vessel-clipping technique which might affect the vascular autonomic supply and which produces only a "point" occlusion of blood flow in contrast to an embolus in a segment of vessel. All of the animals in the reported series were anesthetized for the entire experiment with medium- or long-acting barbiturates. Only in a study by Crowell and Olsson was the effect of revascularization through an EC-IC bypass evaluated (performed 2 h subsequent to MCA clipping).

Our experimental design utilizing an embolization technique and incorporating only short-acting barbiturate induction has shown that anastomosis between the STA and MCA 5 h after an embolus is deleterious both clinically and pathologically.

For a revascularization procedure to be beneficial during an acute ischemic period, it must be performed before irreversible brain damage takes place. Our experiment indicates that this is earlier than 5 h after vascular occlusion. Because of the small number of animals involved, no significant difference could be demonstrated between the percent of infarction in control dogs and those that had a STA-MCA performed 1 h prior to embolization. However, clinically and by gross pathologic examination, there appeared to be a reproducible and consistent beneficial effect of

**Table 2 Clinical Results**

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FIGURE 3. A) Coronal serial sections of animal with embolus placement 1 h after extracranial-intracranial anastomosis. Small area of visible hemorrhage and edema. B) Coronal serial sections of animal with embolus placement 5 h before extracranial-intracranial anastomosis. Marked areas of hemorrhage and edema are visible. C) Coronal serial sections of animal with embolus placement only. Moderate hemorrhage is visible.

Revascularization when performed as soon as 1 h before embolic MCA occlusion. This experimental model may lend itself to further evaluation of the effects of various therapeutic modalities on the course of acute infarction. If therapy could be shown to delay the course of infarction and thereby lengthen the grace period in which a bypass procedure could be done, it might substantially improve the treatment of acute vascular occlusion.

References


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Role of Adrenergic Nerves in Blood-Induced Cerebral Vasospasm

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SUMMARY Cerebral arteries have an abundant supply of adrenergic nerve fibers which are believed to release vasoactive substances responsible for the induction of cerebral vasospasm. To assess the importance of adrenergic nerves in this phenomenon, high doses (600 μg/ml) of 6-hydroxydopamine (6-OHDA) were used to produce in vitro chemical sympathectomy in bovine middle cerebral artery. 6-OHDA reduced catecholamine fluorescence to undetectable limits. H3-norepinephrine re-uptake was reduced to 1.5% of intact controls. Arterial norepinephrine content was reduced by 92%.

Contractile responses to norepinephrine, serotonin, and fresh human whole blood were modestly reduced after denervation. This reduction was probably due to alpha receptor inactivation by 6-OHDA, because after protection of the alpha receptors with phentolamine the vessel response was the same as in untreated controls. Contraction in response to aged human whole blood were modestly reduced after denervation. This reduction was probably due to alpha receptor inactivation by 6-OHDA, because after protection of the alpha receptors with phentolamine the vessel response was the same as in untreated controls.

Contraction in response to aged human whole blood were not affected by denervation. The results suggest that the endogenous release of catecholamines does not play a major role in the initiation or spread of blood-induced vasospasm in large cerebral arteries.

THE PHENOMENON of cerebral vasospasm following aneurysm rupture and the clinical problems associated with it are well documented.1-4 (Study of the responses of bovine middle cerebral artery has been made in vitro to define some of the underlying mechanisms of the phenomenon of vasospasm in previous work from this laboratory.)5 The results implicated serotonin (5-HT), released from whole blood, as a primary agent responsible for the initiation of early (first phase) vessel contraction. Studies reported recently indicated that breakdown products of erythrocytes in aged whole blood6 are important factors in prolongation of spasm and the initiation of delayed spasm (second phase). An event not readily explicable by a vasoactive agent released in whole blood is the occurrence of diffuse spasm remote from the local accumulation of blood. One explanation is that the adrenergic innervation of these larger cerebral vessels plays a role in the pathogenesis and spread of spasm, that a spasmogenic agent or agents trigger release of the catecholamine (CA) norepinephrine (NE) from adrenergic nerves, or that the adrenergic nerves may spontaneously release NE which initiates the spasm. The presence of adrenergic nerve terminals in the cerebral artery of many species is well documented.9-11 By using 6-hydroxydopamine (6-OHDA), a substance known to produce functional...
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