Implanted Device for Middle Cerebral Artery Occlusion in Conscious Cats

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SUMMARY  A simple implantable device was applied to the left middle cerebral artery of adult cats. One week later the artery was occluded acutely while the animals were conscious. Forced circising and tonic deviation of the head and neck toward the left were noted within seconds of occlusion. A right hemiparesis developed one to two minutes later. Cerebral angiography confirmed the presence of the middle cerebral artery occlusion when the occluding stylet was inserted. Removal of the stylet resulted in reopening of the artery. Light microscopic examination of the brains revealed severe acute ischemic changes in a large left cortical and subcortical area. Partial loss of endothelial lining and thinning of the media were demonstrated in the compressed segment of the middle cerebral artery.

HAYAKAWA AND WALTZ produced large cerebral infarcts in cats by applying traction to a ligature which had been attached previously to a middle cerebral artery. This technique allowed them to study the effects of acute focal ischemia in conscious animals with an intact cranium.

One important disadvantage of the ligature method is the inability to reopen the artery after it has been occluded. This prevents the study of transient artery occlusion and the adequate perfusion of the ischemic tissue with fixative or other agents. The object of this investigation has been to develop a simple implantable device which produces reversible occlusion of an intracranial artery in a conscious animal with an intact cranium.

Methods

Construction of Occluding Device

The components of the occluding device are shown in figure 1. Construction of the device was relatively simple and sophisticated tools not required. The slotted housing was made from a 4.5 cm, thin-walled, 16 gauge, stainless steel tube. The distal end was flattened slightly and a 1.5 mm hole drilled. A 1 mm slot was made thereby converting the distal end into a “hook-like” process. A small amount of solder (lead-free and cadmium-free) was used to fill the narrow space between the distal limbs of the hook and small files were used to smooth the rough edges. A short side-arm made from piano wire was attached approximately at the mid-shaft position and directed 180° from the opening of the distal slot. The side-arm prevented movement of the housing in the epoxy cement (see below). A piano wire handle directed 90° to the opening of the distal slot was soldered into place at the proximal end. One end of the handle was left slightly shorter than the other. A slight crimp in the slotted housing prevented the stylets from slipping out.

The occluding stylet was made from thin-walled, 18 gauge, stainless steel tubing. The distal end of the occluding stylet following insertion into the slotted housing (fig. 1B). The bevelled contour of the distal end of the occluding stylet prevented rotation within the slotted housing.

The short stylet, approximately 4 cm in length, was constructed from thin-walled, 18 gauge, stainless steel tubing. Its distal end was filled with solder. It was inserted in order to prevent leakage of cerebrospinal fluid prior to occlusion of the middle cerebral artery.

Implantation of Occluding Device

Six adult cats with a mean weight of 3,000 gm were anesthetized with sodium pentobarbital (30 mgm/kg intraperitoneally). The head was shaved and fixed in a head holder which allowed unobstructed access to the left orbit. A 2 cm curved incision was then made below and lateral to the palpebral fissure. The orbital contents were evacuated and a small 4 mm craniectomy continuous with the superolateral margin of the optic foramen was performed using a high speed drill and the operating microscope. The dura and arachnoid were opened with sharp dissection and the proximal segment of the middle cerebral artery was mobilized carefully.

The end of the occluding device (fig. 1) was inserted above the proximal segment of the middle cerebral artery with the bevel parallel to the vessel. A 90° rotation of the device allowed the artery to slip into the slot. A small piece of gelfoam and some thin silastic sheeting were used to close the craniectomy. The orbit was sprayed with neosporin aerosol and then filled with rapidly hardening epoxy cement. The short stylet was inserted to prevent leakage of cerebrospinal fluid. The incision and the palpebral fissure were closed with continuous “3-0” silk suture. The end of the implanted device protruded approximately 1 to 2 mm through the closed incision. An occlusive dressing was applied.

Prophylactic Antibiotics

Each animal received chloramphenicol (30 mgm IM) immediately before the insertion of the device and again on the following day.

Occlusion of the Middle Cerebral Artery

One week following implantation of the device, the short stylet was removed and the occluding stylet inserted.
Cerebral Angiography

Three hours following occlusion the animals were anesthetized with pentobarbital (30 mgm/kg intraperitoneally). The left lingual artery was exposed through a small incision and a small silastic catheter inserted. Three injections of 60% hypaque (1 cc/injection) were performed: 1) with the occluding stylet inserted; 2) with the occluding stylet withdrawn 3-4 mm; and 3) with the occluding stylet reinserted.

Fixation Technique

The animals were perfused through a cannula in the ascending aorta 4 hours following the initial occlusion of the middle cerebral artery. The occluding stylet was removed immediately prior to perfusion. The animals were initially perfused with 50 ml of isotonic saline followed by a mixture of colloidal carbon (200 ml) and phosphate-buffered 4% paraformaldehyde solution (200 ml).

Tissue Preparation

The brains were removed one hour following perfusion and placed in the phosphate-buffered 4% paraformaldehyde solution. One week later the brains were cut into 5 mm coronal slices. Thin (10μ and 25μ) coronal sections were prepared from paraffin-embedded slices of both hemispheres and stained with hematoxylin and eosin. The segment of the middle cerebral artery which had been occluded was removed and embedded in paraffin. Serial sections of the vessel were cut and stained with hematoxylin and eosin.

Results

Neurological Findings

Within a few seconds of the insertion of the occluding stylet, the animals began to walk in circles toward the side of the occluded vessel. The head, neck and trunk were tonically deviated in the same direction. Weakness of the right limbs was noted within one to two minutes and was more severe in the forelimbs. Forced ambulation persisted for 10 to 20 minutes following which the animals lay quietly. The severity of the hemiparesis was seen to increase slightly over the following 3 hours.

Cerebral Angiography

Cerebral angiography demonstrated occlusion of the middle cerebral artery with the occluding stylet inserted. Withdrawal of theoccluding stylet was followed by prompt filling of the major left middle cerebral artery branches with the contrast media (fig. 2).

Macroscopic Examination

The left middle cerebral artery and its major branches contained carbon. In two animals there was some flattening.

FIGURE 2. Lateral roentgenograms of cat head. A. The slot (large arrow) is obliterated by the occluding stylet. The branches of the middle cerebral artery are not visualized. B. The slot (large arrow) can be seen when the occluding stylet is withdrawn 3 to 4 mm. Major branches of the left middle cerebral artery (small arrow-heads) contain hypaque.
angiography and again at the time of perfusion. Each animal was shown to be conscious. Cerebral angiography confirmed occlusion with the vessel being patent. A large cortical and subcortical area of each brain in the distribution of the left middle cerebral artery was poorly stained with carbon (fig. 3). The left hemispheres appeared slightly swollen. The tissue appeared to be well fixed.

Microscopic Examination

Light microscopic examination confirmed the presence of severe acute ischemic changes in the distribution of the left middle cerebral artery corresponding with the zone of pallor observed grossly. Previous experience has suggested that morphologic alterations of this severity are probably irreversible.2-4 The capillary channels were narrowed, presumably the result of compression by swollen pericapillary astrocytic processes. In one brain there was a small infarct in the left basal ganglia which appeared to be subacute in nature. It was thought to be related to the interruption of a small lenticulostriate artery at the time of insertion of the occluding device. There appeared to be some loss of endothelium in the previously occluded segment of the middle cerebral artery but no evidence of clot formation. The media was thinned slightly and there was some loss of smooth muscle detail in the region.

Discussion

A device was applied to the left middle cerebral artery of 6 adult cats using a transorbital approach. One week later the vessel was occluded acutely while the animals were conscious. Cerebral angiography confirmed occlusion with the occluding stylet inserted. As well, the artery was shown to open when the occluding stylet was removed at the time of angiography and again at the time of perfusion. Each animal developed a large left cortical and subcortical infarct following 4 hours of left middle cerebral artery occlusion.

This model provides the opportunity to study acute focal cerebral ischemia in an awake animal without the associated, often confusing, effects of various pharmacologic agents. Unlike most models of acute focal ischemia, the cranium is intact and there is no leakage of cerebrospinal fluid. This is especially important as the increase in local tissue pressure and intracranial pressure which invariably accompany acute cerebral ischemia may be significant with regard to capillary circulation and consequent tissue viability.4 These factors may be partly responsible for the more reliable production of large cerebral infarcts in 10 conscious cats described by Hayakawa and Waltz1 as compared with smaller, less reliable infarcts which followed acute middle cerebral artery occlusion in anesthetized cats with open craniectomies.4,5 The results of this investigation appear to confirm the findings of Hayakawa and Waltz.1

The advantages of using the device described in this investigation include: 1) ease of application; 2) ability to control vessel occlusion more precisely; and, 3) potential to remove the occluding stylet following a short period of occlusion in order to study the effect of reversible vessel obstruction or to allow perfusion of the ischemic tissue with fixative or other agents.

Potential disadvantages of the device include: 1) the interruption of lenticulostriate arteries during application (this occurred in one animal); 2) possible kinking or stenosis of the artery during or following application; and, 3) infection. The use of prophylactic antibiotics appears to be helpful in minimizing the incidence of infection as none of the animals in our series developed a wound infection.

The occluding device has now been used successfully in more than 20 cats. It is presently being employed in an investigation of the treatment of acute focal ischemia.

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