Basilar Artery Occlusion in Rats

Joan C. Wojak, MD; Vincent DeCrescito, PhD; and Wise Young, PhD, MD

The basilar artery is one of the three major sources of blood supply to the circle of Willis. To investigate the effects of basilar artery occlusion, we surgically exposed and coagulated the basilar artery in 25 rats. Basilar artery occlusion at any single point between the foramen magnum and the circle of Willis in 11 rats did not produce histologically detectable infarcts in the brain at 12–24 hours. Two-point occlusions of the basilar artery in 12 rats produced variable infarcts between the occlusion sites but no ischemic lesions elsewhere. After either single- or double-point occlusions, the proximal basilar artery refilled within 2–3 minutes. When the basilar artery was occluded above and below the origins of the anterior inferior cerebellar arteries, the artery segments between the occlusion points initially collapsed but refilled within 2–3 minutes in two rats. Basilar artery occlusions invariably suppressed cortical somatosensory evoked potentials by >50%. Regardless of whether a brain stem infarct developed, somatosensory evoked potential amplitudes recovered to greater than baseline levels by 4 hours in seven of 17 rats and returned to baseline levels by 24 hours in every rat tested. We conclude that the occluded basilar artery receives extensive retrograde collateral blood flow and that somatosensory evoked potentials are exquisitely sensitive to basilar artery occlusion but are insensitive to whether brain stem infarcts develop. (Stroke 1991;22:247-252)
In 11 rats, the basilar artery was occluded by radiofrequency thermocoagulation applied with fine forceps to the artery at a single point along its length. A second group of 12 rats underwent occlusion at two points 3 mm apart at various sites along the length of the basilar artery. Four rats underwent no further manipulation after opening of the dura and arachnoid; these served as controls.

In the remaining two rats, we placed silk snare around both carotid arteries. After occluding the basilar artery just caudal to the anterior inferior cerebellar arteries in one rat and just rostral to them in the other rat, we then occluded the carotid arteries and observed the pattern of blood flow in the anterior inferior cerebellar arteries and basilar artery. A second occlusion was then placed above the anterior inferior cerebellar arteries, and the changes in blood flow were again observed.

The SEPs were recorded differentially between the midline frontal electrode and the electrode placed over the primary somatosensory cortex; 50–100 amplified (500 µV full scale) and filtered (0.02–20 Hz) responses were averaged. A Tracor 3500 evoked potential system (Tracor Analytic, Milwaukee, Wis.) was used to acquire, average, and store the data. To activate the SEPs, we stimulated the sciatic nerve with constant-current pulses (3 mA amplitude, 0.1 msec duration, 2.3 Hz) delivered with stainless steel needles inserted next to the nerve. SEPs were recorded before and 1, 5, 10, 15, and 30 minutes and 1, 2, 4, 6, and 24 hours after basilar artery occlusion in all rats. In two rats, we also unilaterally stimulated the ventral brain stem rostral to the occlusion with constant-current pulses (1 mA amplitude, 0.1 msec duration, 2.3 Hz) delivered with paired silver ball electrodes placed directly on the ventral brain stem surface. Responses were recorded from the contralateral cortex before and 5, 15, and 30 minutes after basilar artery occlusion.

All rats, except for two that had carotid occlusions and eight that were kept for 6–8 weeks after surgery, were observed and euthanized 12–24 hours postoperatively. In all rats, at the end of the surgery the anterior cervical muscles were reapproximated with absorbable sutures. The tracheostomy tube, if present, was brought out through the skin incision, which was then closed. A dose of cephalosporin antibiotic (20 mg ceftazidime) was administered intramuscularly. Upon awakening from anesthesia, each rat received a second dose of atropine and the tracheal tube and oropharynx were cleared of secretions by suction. The tube was then removed, and the rat was allowed to recover from anesthesia.

At 24 hours after surgery, eight rats receiving single-point occlusions, nine rats receiving two-point occlusions, and two control rats were given an overdose of pentobarbital (75 mg/kg) and then perfused intra-arterially with normal saline followed by 10% buffered formalin. The brains were immersion-fixed in 10% buffered formalin for several days, embedded in paraffin, serially sectioned, and stained with he-
matoxylin and eosin. The sections were inspected for evidence of infarction.

Results

All rats tolerated the surgery well and awoke from anesthesia without neurologic deficits except for a right ptosis in one rat in which we exposed the pituitary fossa. However, at survival periods of >12 hours, 10 of 17 rats with tracheostomies had respiratory difficulties related to tracheal occlusion. All rats with tracheostomies were euthanized. In contrast, all 12 rats with orotracheal intubations made uneventful recoveries.

All rats had mean arterial systolic and diastolic blood pressures of 110 and 70 mm Hg, respectively, after induction of anesthesia. The pressures remained stable except when the arachnoid was opened. Diastolic pressure increased by 10–20 mm Hg at that time, while systolic pressures increased by 20–30 mm Hg. Irrigation of the brain stem with room-temperature normal saline lowered the pressures for several minutes. Basilar artery occlusion did not alter the pressures.

In four rats, we exposed the basilar artery from the foramen magnum to the circle of Willis. The vertebral arteries were visible at the foramen magnum. The rat basilar artery branching pattern resembled that in humans. Paired arteries analogous to the anterior inferior cerebellar arteries were present, along with several perforating branches. In one rat, the right posterior inferior cerebellar artery arose from the basilar artery immediately below the origin of the anterior inferior cerebellar arteries and then descended toward the foramen magnum. Venous structures also corresponded to those of the human posterior fossa. These structures included the anterior pontomesencephalic vein, the paired transverse pontine veins, and the lateral mesencephalic veins. When the dissection was carried rostrally to the level of the pituitary fossa, the base of the cerebral peduncles could be identified with overlying peduncular veins.

In 11 rats, single-point occlusion of the basilar artery rapidly deflated branches rostral to the occlusion. In all cases, retrograde blood flow from the circle of Willis and/or anterior inferior cerebellar arteries refilled the branches within 2–3 minutes. In five rats, a second occlusion was placed 3 mm rostral to an initial occlusion just rostral to the anterior inferior cerebellar arteries. In all these animals, the basilar artery rostral to the upper occlusion remained filled by the previously established retrograde blood flow, while the basilar segment between the occlusions collapsed and did not refill. In five rats, a second occlusion was placed 3 mm caudal to an initial occlusion just caudal to the anterior inferior cerebellar arteries. In all these animals, the basilar artery rostral to the upper occlusion remained filled by the previously established retrograde blood flow, while the basilar segment between the occlusions collapsed and did not refill. After placement of a second occlusion on the other side of the anterior inferior cerebellar arteries, the rostral basilar artery collapsed and did not refill.

Before basilar artery occlusion, sciatic nerve stimulation produced stereotypical responses in the contralateral cortex, with a typical positive-negative-positive waveform (Figure 2). The latency of the initial positivity averaged 13±2 msec (n=38) in 19 rats. SEP amplitude and latency were unaffected by exposure of
the brain stem. Occasionally, cortical SEP amplitude increased by approximately 10% after opening of the arachnoid. In these instances, a K-wire thermoprobe (model BAT-12, Physitemp Inc., Clifton, N.J.) placed on the surface of the exposed brain stem revealed a temperature of 33–34°C despite a core temperature of 35–37°C. SEP amplitude returned to baseline upon irrigation of the operative field with 37°C normal saline.

In all of 17 rats, basilar artery occlusion, whether single-point or two-point, reduced peak-to-peak amplitude of the cortical SEPs by >50% within 15 minutes. The SEPs gradually recovered over 3–4 hours, and the response amplitudes exceeded baseline values in seven of the 17 rats by 4 hours after occlusion. By 24 hours after basilar artery occlusion, amplitudes and latencies returned to baseline values (mean 13.5±3 msec, n=30 in 15 animals). Typical preocclusion and postocclusion SEPs are shown in Figure 2. The cortical responses to brain stem stimulation rostral to the occlusion did not change after basilar artery occlusion.

Microscopic examination of transverse brain and brain stem sections stained with hematoxylin and eosin revealed no infarct in any rat with single-point basilar artery occlusion. Two-point occlusion straddling the anterior inferior cerebellar artery origins likewise was not associated with any infarcts. However, two-point occlusion above or below the anterior inferior cerebellar arteries produced brain stem infarcts under the occluded segment. The lesions were 1.0–1.5 mm wide and along the midline. Both rats with two-point basilar artery occlusion below the anterior inferior cerebellar arteries developed infarcts extending longitudinally the full thickness of the brain stem (Figure 3, left). Both rats with occlusions above the anterior inferior cerebellar arteries developed infarcts only 1–2 mm deep that contained small areas of hemorrhage (Figure 3, right).

Discussion

Our experience suggests that wide exposure and occlusion of the basilar artery in rats are technically
feasible and well tolerated. Tracheostomies led to delayed respiratory difficulties, and we recommend orotracheal intubation if the rats are to be maintained for >12 hours postoperatively. Basilar artery occlusion can thus be carried out some time before other procedures, such as carotid artery ligation, for global cerebral ischemia studies.

Single-point occlusion anywhere along the length of the basilar artery did not produce histologically evident infarction in the brain stem, cortex, or subcortical structures rostral to the occlusion. This is consistent with our observation of rapid establishment of retrograde blood flow in the basilar artery proximal to the occlusion. The absence of infarction in rats with two-point basilar artery occlusion straddling the anterior inferior cerebellar artery origins is consistent with the blood flow reversal observed in these vessels and the subsequent refilling of the basilar artery segment between the occlusions. Such flow reversal indicates that the anterior inferior cerebellar arteries have access to arterial blood sources that are not compromised by basilar artery occlusion. The basilar artery is clearly protected by an extensive arterial network that can redistribute blood flow, similar to the middle cerebral artery.8

The infarcts produced by two-point basilar artery occlusion caudal to the anterior inferior cerebellar arteries suggest that the lower brain stem depends on blood supplied by perforating branches of the basilar artery. The small infarcts due to two-point basilar artery occlusion rostral to the anterior inferior cerebellar arteries suggests that the upper brain stem receives collateral blood supply from other sources.

In the three-vessel model of transient global cerebral ischemia, the basilar artery is occluded just caudal to the anterior inferior cerebellar arteries.1 Our observations suggest that occlusion at this point may not reliably produce global cerebral ischemia because retrograde blood flow through the anterior inferior cerebellar arteries will refill the rostral basilar artery. Residual blood flow was also seen after single-point basilar artery occlusion rostral to the anterior inferior cerebellar arteries. Two-point basilar artery occlusion straddling the anterior inferior cerebellar arteries, however, abolished this residual blood flow and should result in more consistent global cerebral ischemia. These findings also suggest that the anterior inferior cerebellar arteries have access to arterial blood both rostral and caudal to occlusions close to the anterior inferior cerebellar arteries.

Single- and two-point basilar artery occlusion completely suppressed SEPs for several hours. SEP amplitudes 4 hours after occlusion often exceeded pre-occlusion amplitudes, returning to normal within 24 hours. We examined cortical responses activated by upper brain stem pyramidal tract stimulation in two rats and found the responses to be unaffected by basilar artery occlusion, whereas sciatic nerve-evoked SEPs were suppressed by basilar artery occlusion, suggesting that the suppression occurred in the lower brain stem or spinal cord. The time course and severity of SEP depression did not correlate with the presence or absence of histologically evident brain stem infarction. We hypothesize that basilar artery occlusion causes transient ischemia in the brain stem, resulting in a release of K+ that transiently suppresses SEP conduction in the brain stem. At the level of the occlusion, the somatosensory tracts are situated approximately 1 mm beneath the pyramidal tracts in the medial lemniscus. Diffusion of the released K+ should depolarize these tracts. At high levels extracellular K+ would suppress axonal conduction, but low levels may potentiate axonal conduction by bringing cell membranes closer to threshold.

The sensitivity of SEPs to the occlusion of a ventral brain stem artery corroborates our clinical experience in patients undergoing vertebrobasilar or spinal angiography, often in conjunction with attempted embolization procedures.9 Balloon occlusion or injection of radiographic dye into the anterior spinal artery or basilar artery transiently suppresses SEPs.10 This effect is so reliable that we routinely use SEPs to verify catheter placement during these clinical studies. In patients, as in rats, SEP amplitude gradually returns to baseline values.

We conclude that two-point basilar artery occlusion can produce brain stem infarction. The size and nature of the infarct (hemorrhagic versus bland) depends on the rostral–caudal position of the occlusion. Although cortical SEPs are very sensitive to occlusion of the basilar artery, they invariably recovered within 24 hours despite the presence of brain stem infarcts in several rats. The three-vessel occlusion model of transient global cerebral ischemia, combining bilateral carotid artery occlusion with single-point basilar artery occlusion caudal to the anterior inferior cerebellar arteries, did not completely abolish the blood supply to the circle of Willis. However, two-point basilar artery occlusion straddling the anterior inferior cerebellar arteries combined with bilateral carotid artery occlusion did.

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References


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