Intracranial Pressure Gradients Caused by Experimental Cerebral Ischemia and Edema

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Abstract:

To assess the development and resolution of ischemic cerebral edema and brain swelling, measurements of intracranial pressure (ICP) were made in cats after the transorbital occlusion of one middle cerebral artery. Measurement of ICP gradients was difficult: epidural, subdural and intraventricular catheters caused brain damage or failed to function; the accuracy of a miniature strain gauge could not be determined after implantation; and absolute values for intradural pressures could not be obtained with epidural devices. However, variable increases of ICP were recorded on the sides of occlusion from three cats, and were directly related to the severity of the neurological deficits. On the sides opposite occlusion ICP increased slightly or not at all. Several days after occlusion ICP decreased and gradients could not be demonstrated with certainty. Thus, measurements of ICP gradients can be used to assess ischemic cerebral edema and brain swelling, but the usefulness of such measurements is limited at present by methodological problems.

Additional Key Words
cerebral infarction epidural pressure middle cerebral artery occlusion

Intracranial pressure gradients developing after cerebral infarction in humans can cause shifts of midline structures, increasing neurological deficits, transtentorial herniation, and death. The presumed cause of postinfarction pressure gradients is focal brain swelling due to ischemic cerebral edema. An assessment of the development and resolution of ischemic cerebral edema is important for the evaluation of therapeutic measures designed to prevent or minimize impairment of neuronal function and neurological disability. As a preliminary to a study of brain swelling and edema in an experimental model of cerebral ischemia and infarction, intracranial pressures (ICP) were measured in cats after occlusion of one middle cerebral artery (MCA).

Methods

MEASUREMENTS OF ICP

Unselected adult cats were anesthetized with phencyclidine hydrochloride, 1 mg per kilogram injected intramuscularly, and sodium pentobarbital, 25 mg per kilogram injected intraperitoneally. ICP was measured by one or more of the following methods.

(1) A crenelated, open-ended polyethylene catheter was filled with physiological saline solution (PSS) and introduced into one lateral ventricle through a needle. The catheter was connected to a calibrated pressure transducer for recording on a polygraph.

(2) Crenelated, open-ended polyethylene catheters were placed epidurally or subdurally in the parietal regions bilaterally through burr holes and connected to calibrated pressure transducers.

(3) A miniature strain gauge of the Wheatstone bridge type, 7 mm in diameter and 1 mm thick, was cemented into a burr hole over the dura in the parietal region of the skull on one side. Before implantation, the strain gauge was immersed in PSS for several days and calibrated in a pressure box with a manometer. Measurements were recorded on a polygraph.

(4) Flaccid latex membranes were secured to shallow stainless steel cylinders, 8.5 mm in diameter and 2 mm thick, which had thin tubes extending from their tops to provide access to the pressure chambers (fig. 1). One of these balloon devices was implanted in each parietal region with or without prior removal of the dura. After implantation the volume of each pressure chamber was determined by evacuation with suction and measurement of the amount of PSS that would restore the device to atmospheric pressure. Volumes ranged from 8 to 25 μl. To measure ICP, the same amount of PSS plus an additional 2 μl was instilled, so that the chamber was filled without distending the...
Balloon devices for recording ICP. Flaccid latex membranes were secured to the rims of the pressure chambers with a metal sleeve before implantation.

membrane. The device then was connected to a calibrated pressure transducer for recording on a polygraph. For each ICP measurement several observations were made, and the measurement was considered reliable only if the same ICP value was obtained for three consecutive observations. In one animal measurements of ICP were made with different volumes of PSS in the chamber; measurements were repeated in a pressure box after removal of the device from the animal.

(5) A needle was placed in the cisterna magna and connected to a calibrated pressure transducer and polygraph. Measurements of cisternal pressure were used only for comparison with other ICP measurements.

**Results**

**MEASUREMENTS OF ICP**

Reliable ICP measurements were obtained only with difficulty.

(1) The successful introduction of catheters into the lateral ventricles of the relatively small brains of cats caused considerable structural damage, so that ICP changes could not be related specifically to cerebral ischemia. Because of this and evidence that ventricular cannulation alone can cause increases of ICP, the procedure was abandoned.

(2) Despite crenelation of the open ends, catheters implanted in the epidural or subdural spaces became obstructed with fibrin and debris within a few hours. Occasionally, ICP measurements could be obtained after flushing the catheters, but the values were questionable because of the resulting instillation of PSS into the relatively small spaces.

(3) Preliminary measurements made with the miniature strain gauge appeared reasonable; later, it was noted that the values for ICP were erratic and occasionally unrealistic. Therefore, the strain gauge was placed in PSS in a pressure box and calibrated against a manometer for 15 days. Even after correction for fluctuations of atmospheric pressure there was an unpredictable and unacceptable baseline drift of 2 to 5 mm Hg per day. No data obtained with the instrument were used.

(4) Implantation of the balloon devices over brain tissue exposed by removal of dura caused damage to the underlying cortical surface. When implanted epidurally, the balloon devices recorded changes of pressure due to vascular pulsation, respiration, and abdominal compression that were similar to those recorded from the cisterna magna (fig. 2). However, the absolute values for ICP varied with the amounts of PSS used to fill the chambers. Values recorded from a pressure box outside the head were not as dependent on volume (fig. 3). Because of volume dependence, the first ICP measurement made after implantation was considered the basal value, and subsequent ICP measurements were expressed as mm Hg above this base.

(5) Cisternal pressure could be measured easily and reliably, but ICP gradients could not be detected with this technique.

There were additional problems that interfered with the successful long-term measurement of ICP. These included: loosening of the pressure devices after implantation, tissue reaction, bone resorption, infection, and the failure of an animal to recover from multiple anesthetic procedures. ICP measurements were attempted in 27 cats, but reliable measurements for prolonged periods after MCA occlusion were obtained only with difficulty.

**EVALUATION OF THE NEUROLOGICAL DEFICIT**

After preliminary measurements of ICP were obtained, MCA occlusion either was undertaken immediately or measurements were made for several additional days before occlusion. For occlusion, the cat was anesthetized with phencyclidine hydrochloride and sodium pentobarbital. The left MCA was exposed through the orbit by enlargement of the optic foramen; no additional craniectomy was done. The MCA then was mobilized by dissection of the arachnoid, held free from the brain, and occluded at its origin with a bipolar coagulator. The optic foramen was sealed so that pressure gradients could develop inside an intact cranium. ICP measurements were made before enlargement and after sealing the optic foramen, and at intervals up to seven days after MCA occlusion.
occlusion were obtainable only with the balloon devices, and from only three cats.

**Effects of Ischemia**

After implantation of the balloon devices in a cat, no changes or gradients of ICP were observed until the MCA was occluded. In one cat with a severe neurological deficit, epidural ICP on the ischemic side was 74 mm Hg above the basal pressure 15 hours after occlusion (fig. 4); in this animal, there was also an increase of ICP on the opposite side. In another cat with a minimal neurological deficit, ICP on the side of occlusion was 21 mm Hg above the base at eight hours, but ICP of the opposite side appeared to decrease (fig. 5). A third cat with a moderate neurological deficit had an epidural ICP recorded at 37 mm Hg above the base on the side of occlusion and 5 mm Hg on the opposite side at 21 hours. In each animal, epidural ICP decreased on the side of occlusion as the neurological deficit lessened. ICP values were similar on the two sides after the first two to three days (figs. 4 and 5).
Discussion

MEASUREMENTS OF ICP

The flaccid latex membranes attached to the balloon devices assured relative coplanarity with the underlying dura, and the rigid metal rings surrounding the membranes prevented "tenting" of the dura on the recording surface; these features are said to be essential for accurate recording, through the dura, of the pressures to which the brain itself is subjected. However, despite these features the pressures recorded after epidural implantation were dependent on the amounts of PSS used to fill the chambers of the balloon devices. Although epidural pressures were recorded by filling the balloon devices with the same amount of fluid each time, the relatively dense dura affected and distorted the transmission of intradural pressures to the extradural space. Comparisons with measurements of cisternal pressure indicated that changes of epidural ICP reflected changes of intradural ICP, but the measurements of epidural ICP did not provide absolute values for intradural ICP.

Methodological problems encountered in attempts to measure ICP were severe, particularly when long-term recordings were desired. Because the extent and degree of cerebral ischemia and infarction occurring after experimental MCA occlusion are variable, studies of therapeutic measures require comparisons and statistical analyses of results from many animals observed for relatively long times. At present, problems of methodology limit the usefulness of ICP measurements for such studies of experimental models of cerebral ischemia and infarction.

ISCHEMIA AND ICP GRADIENTS

The data reported here show that focal cerebral ischemia can cause ICP gradients, with the greater pressures on the side of ischemia. Similar results have been obtained with a less satisfactory model of experimental cerebral ischemia, and the occurrence of postinfarction ICP gradients in humans can be inferred from clinical experience. Considerations of intracranial hydrodynamics might lead to the expectation that the cerebrospinal fluid (CSF) would dissipate pressure differences as they develop after infarction, or restrict ICP gradients to transient events. There are at least three possible explanations for the persisting gradients that have been observed:

1. The free communication of CSF and of pressure throughout the cranium may become blocked at dural margins by brain swelling.

2. Local pressures in brain tissue are opposed by intravascular pressures and by the tension and resistance of supporting and tethering structures; not all intracerebral pressures are transmitted directly to the CSF. CSF and cerebral surfaces in contact must have the same pressure; but if swollen brain displaces CSF and touches the dura, a gradient caused by a focal increase of intracerebral pressure could be detected.

3. If the rate of change of intracerebral pressure is rapid, dissipation of the change of tissue pressure through the brain substance and the CSF may lag because of supporting and tethering structures; persisting gradients may be recorded until the rate of change decreases.

Unfortunately, no comment about the duration of postinfarction ICP gradients can be made from the data reported here. Although slightly different values for ICP were obtained from the two sides of the head as long as seven days after MCA occlusion, the values were relative, not absolute, and it is likely that a true gradient did not exist.

ICP, EDEMA, AND THE NEUROLOGICAL DEFICIT

In animals breathing spontaneously, hypoventilation and acidosis after anesthesia and MCA occlusion may cause increases of carbon dioxide tension and decreases of oxygen tension of arterial blood, and secondary intracranial vascular dilatation might contribute to increases of ICP. However, hypoventilation and acidosis by themselves could not produce postinfarction ICP gradients; these most likely are related to edema and swelling around the cerebral infarcts.

Increases of ICP and local tissue pressure may cause focal increases of vascular resistance and further decreases of an already decreased regional blood flow, particularly if ischemic vessels are unable to dilate. In this way, ischemic cerebral edema and increases of ICP could contribute to the development or worsening of a neurological deficit. It is likely that the markedly increased ICP measured on the side of MCA occlusion in one cat (74 mm Hg above the basal pressure) would have
interfered with cerebral perfusion; this cat had the most severe neurological deficit of those studied. Measurements of intracerebral oxygen availability and electrocorticographical potentials after MCA occlusion also have shown that increased ICP is associated with evidence of severe ischemia. Thus, studies of experimental models of cerebral ischemia and infarction support the assumption, based on clinical experience, that ischemic cerebral edema can be harmful to neuronal function and contribute to a neurological deficit.

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References
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