Increased Intracranial Pressure and Pulmonary Edema

Part 2: The Hemodynamic Response of Dogs and Monkeys to Increased Intracranial Pressure

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The reflex elevation of arterial blood pressure which follows any increased intracranial pressure was first demonstrated in 1881 in Germany and later confirmed in 1901 in America by Cushing. This pressor response, in which the systemic diastolic blood pressure tends to stabilize at a level slightly above that of the raised intracranial pressure, became known as the Cushing reflex or the central nervous system ischemic response. While the systemic hemodynamic changes have been thoroughly studied, the role of the pulmonary circulation in this reflex has received virtually no attention.

In Part 1 we reported a series of clinical cases in which increased intracranial pressure alone apparently produced pulmonary edema. This suggested that the relationship between intracranial pressure and the pulmonary circulation may be more specific than previously realized. Accordingly, the present studies were designed to study pulmonary hemodynamics during experimental elevation of the intracranial pressure in dogs and monkeys.*

Materials and Methods

Twelve animals were divided into three experimental groups:

Group 1. In seven dogs, weighing 13 to 21 kg, intracranial pressure was raised by increments to 150 mm Hg by the infusion of saline into the subarachnoid space through catheters placed in the cerebrospinal fluid pathways either in the cisterna magna or over the convexity. To reduce the amount of saline required to maintain elevated pressures, 5 ml of blood were first infused to block the absorption channels of the cerebrospinal fluid. Less than 30 ml of saline were required per animal per experiment.

Group 2. In eight dogs, weighing 15 to 26 kg, intracranial pressure was raised by inflation of an epidural balloon over the convexity of the parietal lobe. The intracranial pressure was maintained between 125 and 150 mm Hg as measured via the middle fossa catheter ipsilaterally.

Group 3. In five Rhesus monkeys (Macaca mulatta), weighing 2.6 to 4.6 kg, intracranial pressure was raised by the inflation of an epidural balloon placed over the convexity. The intracranial pressure was maintained at approximately 150 mm Hg during the recording of the hemodynamic response. In Monkey 2, after the animal had recovered from a typical response, the cervical cord was transected through a low cervical laminectomy. The epidural balloon was then reinflated. In Monkeys 3 and 4, bilateral cervical vagotomies were performed during the experiment.

Methods

All animals were anesthetized with intravenous pentobarbital 30 mg/kg, and endotracheal tubes were passed to assure a patent airway. Hemodynamic parameters were monitored via pressure transducers connected to appropriate preamplifiers and an amplified recording system (Sanborn 150 Recorder). Polyethylene catheters were placed in the abdominal aorta, thoracic vena cava, and pulmonary artery through the femoral and jugular vessels. In Groups 2 and 3, following thoracotomy, a catheter was threaded into the main pulmonary vein via the left atrium. The chest was then closed to allow resumption of normal spontaneous respiration in most of the studies. The heart rate was taken from an electrocardiographic tracing. The respirations were determined from fluctuations apparent in the continuous venous pressure tracings. Intracranial pressure was monitored through a catheter in the subarachnoid space placed near the floor of the middle cranial fossa. Arterial blood samples were drawn anaero-
bically into heparinized syringes for the determination of arterial pO₂, pCO₂, and pH. These determinations were performed on pH/Gas Analyzer (Instrumentation Laboratories, Inc.). If respirations slowed significantly they were supported by a constant volume ventilator (Harvard Apparatus) via the endotracheal tube at rates and volumes adequate to maintain oxygenation.

All surviving animals were sacrificed at the conclusion of the experiment. Autopsies were performed. Specimens were weighed, fixed in buffered formalin (10%), embedded in paraffin, and sectioned at 6 μ. Hematoxylin and eosin staining was routinely used. To evaluate the degree of pulmonary edema that resulted from intracranial pressure elevation, seven normal dogs and six normal monkeys were sacrificed. Normal organ/body weight ratios could then be computed.

Results

Effect of subarachnoid infusion on the hemodynamic response in dogs (Group 1). A carefully controlled subarachnoid infusion of blood and saline resulted in a stepwise elevation of the intracranial pressure to about 150 mm Hg. In response, both systemic and pulmonary arterial pressures rose without significant change in the central venous pressure (Fig. 1). In this series of experiments, alterations in the pulmonary pressure appeared prior to and were proportionately greater than alteration of the systemic pressure. The central venous pressure showed little change except for occasional 4 to 8 mm Hg transient increase for a few seconds at the onset of a change in intracranial pressure. A secondary rise appeared terminally if the animal died with cerebral herniation. The pulse frequently slowed once the intracranial pressure had risen significantly; but changes in the heart rate did not occur in every animal and appeared to be independent of the alterations in the pulmonary and systemic arterial and venous pressures. Although respirations usually slowed, the prompt institution of positive-pressure artificial ventilation avoided any hypoxia. In one of the seven animals, maintenance of the intracranial pressure at 150 mm Hg resulted in a dramatic elevation of pulmonary artery pressure to 55/25 mm Hg. Within 20 minutes the animal died with pulmonary edema; the lungs weighed 284 gm, compared to 155 ± 14 gm in the control dogs.

Effect of epidural balloon inflation on the hemodynamic response in dogs (Group 2). The eight animals in which intracranial pressure was elevated by inflation of an epidural balloon demonstrated responses similar to that in Group 1 (Fig. 1). In addition to the immediate systemic vascular pressor response, the pulmonary venous pressure rose followed by the pulmonary artery pressure. The cardiac rate slowed and in several animals the electrocardiographic tracings showed various degrees of supraventricular conduction block. The respirations were also depressed by the elevated intracranial pressure and respiratory assistance was frequently necessary. However, both cardiac and respiratory rate depressions were independent of, and did not contribute to, the changes in hemodynamic pressures. The central venous pressure did not rise significantly except for terminal changes. One of the eight dogs studied had maintained pulmonary hypertension and died with gross pulmonary edema, the lungs weighing 235 gm.

![Fig. 1. Hemodynamic response of dogs and monkeys to elevations of intracranial pressure (125-150 mm Hg) induced by subarachnoid infusion of blood and saline or inflation of an epidural balloon. Results are expressed as the mean systolic and diastolic pressures of all observations with 95% confidence limits. (Twice the standard error of the mean).](image-url)