Effect of Elevated Intracranial Pressure on Gastric Acid Secretion, Mucosal Blood Flow and Mucosal Injury

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Head injury is frequently accompanied by an increase in intracranial pressure and gastric lesion formation. We used a model of controlled intracranial pressure to investigate the effect of elevated intracranial pressure on gastric acid secretion and mucosal blood flow and on the susceptibility of the gastric mucosa to lesion formation. With increasing intracranial pressure, there was a corresponding increase in gastric acid output but no significant change in gastric mucosal blood flow. This imbalance between acid secretion and blood flow could be a factor in the pathogenesis of the gastric lesions seen with head injury. Susceptibility to gastric mucosal injury then was studied in a model that is independent of the acid secretory state—exogenous intragastric HCl plus ethanol. Elevated intracranial pressure did render the gastric mucosa more susceptible to injury in this model, but there was no impairment of the increased gastric mucosal blood flow response to the increased acid back-diffusion. In this situation, factors other than altered overall blood flow appear to be responsible for the increased lesion formation.

KEY WORDS: elevated intracranial pressure; gastric mucosal blood flow; gastric acid output; HCl + ethanol-induced gastric lesions.
effect of EICP first on gastric acid secretion and mucosal blood flow and then on blood flow and the susceptibility to gastric lesion formation in a model that is independent of acid secretion, namely intra-gastric perfusion of 0.15 N HCl plus a "barrier-breaking" concentration of ethanol.

MATERIALS AND METHODS

Animal Preparation. Male Sprague-Dawley rats, weighing 240–320 g and fasted for 24 hr but allowed free access to water, were anesthetized with urethane (1.5 g/kg subcutaneously). Tracheostomy was performed and a PE 260 cannula was inserted to ensure a patent airway and for administration of hydrogen gas. A cannula (PE 50) was inserted into the right carotid artery for monitoring blood pressure, and a needle was inserted into the femoral vein for the infusion of saline and 30 mg/kg bethanecol per hour at the rate of 1.5 ml/hr to maintain hydration and to offset the inhibitory effect of the anesthetic agent on acid secretion (10). A preliminary study showed that this dose of bethanecol was a subthreshold dose for gastric acid secretion. Body temperature was monitored by a rectal thermometer and kept at 36–37°C by an external heat lamp.

Elevating Intracranial Pressure. After exposure of the skull, a small hole was made through the skull 1.5 mm caudal and 2.0 mm lateral to the bregma. A cannula (PE 50) connected to a syringe filled with saline was inserted into the cerebral ventricle (3.5–4.0 mm deep to the bregma) through the hole (11). The cannula was fixed to the skull with cyanoacrylate glue (Krazy Glue, Itasca, Illinois). The syringe was elevated to different levels, and the height of the top of the column of saline above the animal’s head was noted as the measure of the intracranial pressure in centimeters of water (12).

Gastric Acid Output (GAO) Measurement. After exposure of the stomach by a midline laparotomy, a cannula (PE 90) was inserted into the stomach through a forestomach incision for infusion of saline, or HCl plus ethanol in gastric lesion formation experiments, at the rate of 7–8 ml/15 min. Via an incision in the proximal duodenum, another cannula was passed through the pylorus and into the stomach for drainage, and the pylorus was ligated around it. The gastric effluent was collected at 15-min intervals. Acid output (in microequivalents per 15 min) was determined by titration of the perfusate with 0.1 N NaOH to pH 7.0 using an automatic titrator (Radiometer, Copenhagen, Denmark).

Gastric Mucosal Blood Flow (GMBF) Measurement. GMBF was measured by the hydrogen gas clearance technique (13–15). Briefly, a platinum needle electrode was inserted from the serosa into the basal portion of the gastric mucosa and positioned just beneath the muscularis mucosae (16). A reference electrode (Ag–AgCl) was placed inside the peritoneal cavity. As the rat breathes the 3% hydrogen in air administered through the tracheal tube, a current is generated at the surface of the platinum electrode by dissociation of molecular hydrogen into hydrogen ions and electrons. This current is proportional to the hydrogen tension gradient at the platinum electrode and is measured by a polarographic and amplifying unit (Val Tech. Electronic, Sherman Oaks, California) connected to a recorder (Gilson, Middleton, Wisconsin). When the experimental animal breathes hydrogen, the current tracing rises and reaches a plateau as all the tissue is saturated with hydrogen (saturation). After the external hydrogen source is removed, the current tracing gradually falls due to removal of hydrogen by blood flow (desaturation). Tissue blood flow is determined from the rate of clearance of hydrogen. The experimental protocol involved alternating 15-min periods of saturation and desaturation of the tissue with hydrogen gas. A computerized monoexponential direct curve–fitting program was used for the analysis of the mucosal hydrogen gas clearance as described previously (17). GMBF was expressed in milliliters per minute per 100 g.

Gastric Lesion Measurement. Immediately after the experiment, the animal was killed by bilateral thoracotomy, and the stomach was removed, opened along the greater curvature, pinned out on cardboard, photographed, and fixed in formalin. Photographs of the fixed specimens were taken, and the area of the corpus and corpus mucosal lesions were traced on transparent paper and measured using an image analyzer by a person who was unaware of the group from which the animal came. The lesion area was expressed as a percent of the total corpus area, hereafter referred to as lesion area (%).

Experimental Protocol. After the rat was prepared as described above, at least 45 min was allowed for stabilization of gastric acid secretion and mucosal blood flow. Two sets of experiments were performed. In the first set of experiments, the effect of EICP on GAO and GMBF was studied. The experimental protocol involved five GMBF determinations (five alternating 15-min periods of saturation and desaturation of the tissue with hydrogen gas). After measuring baseline mucosal blood flow, the intracranial pressure was raised to 10, 20, 30, and 40 cm H2O, respectively, at the beginning of the second, third, fourth, and fifth saturation periods. Heart rate (HR), respiratory rate (RR), and mean blood pressure (MBP), GAO, and GMBF were measured during each desaturation period. The control group was treated in the same manner except without EICP, i.e., the syringe remained at the baseline intracranial pressure level throughout the study. In the second set of experiments, the effect of EICP on gastric mucosal susceptibility to injury was evaluated. After measuring the basal GMBF, the intracranial pressure was raised to, and maintained at, 30 cm of water, and the stomach was perfused with 0.15 N HCl plus 15% ethanol (to disrupt the gastric mucosal barrier to acid back-diffusion). Fifteen minutes later, hydrogen administration was begun for GMBF determination. In the control group, the procedure was the same, but without EICP. The stomachs were removed for lesion measurements at the end of the study. Arterial blood pressure was recorded continuously throughout each study.

Analysis of Data. All data are presented as means ± SEM. One-way analysis of variance, followed by Dunnett’s test for individual comparison, was performed to determine the significance of changes in HR, RR, MBP, GAO, and GMBF in the first set of experiments. The unpaired t test was performed to determine the signific-