Mechanism of Inhibition of Gastric Acid Secretion by Hypertonic Solutions and Vasopressin

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Summary. An experiment was performed in female rats in order to assess the influence and mechanism underlying the effects of hyperglycemia, hypertonic saline and vasopressin upon the gastric acid secretion and mucosal blood flow (MBF). Infusion of isotonic saline did not alter acid output and gastric clearance of plasma aminopyrine whereas hypertonic solutions (20% glucose or 3% NaCl) significantly increased plasma osmolality and decreased the acid secretion within 30 min and recovered to normal levels after 2 h. Vasopressin also effectively inhibited acid secretion. Both hypertonic solutions and vasopressin decreased the mucosal blood flow. However, the ratio (R) of MBF to gastric secretory rate which is a helpful guide to the mechanism of secretory inhibition did not significantly change in either case. We concluded that all three agents probably had a direct action on secretion rather than decreasing MBF. The mechanism of inhibition of acid secretion and its relationship to MBF was suggested and discussed.

Key words: Gastric secretion — Hypertonic solutions — Vasopressin — Mucosal blood flow.

INTRODUCTION

It has been recognized that the coincidence of peptic ulcer in diabetes mellitus is rare (Dotevall, 1959). Perhaps, the incidence of “Gastritis” which is associated with diabetes causes gastric hyposecretion. However, there are few studies showing that glucose, whether administered intravenously or orally, inhibits gastric secretory activity (Babkin, 1950; Dotevall and Muren, 1961; Moore, 1973; Solomon and Spiro, 1959). Some investigators cite evidence which demonstrated that hyperglycemia inhibited gastric secretion at the vagal center (Adamkiewicz and Saera, 1966; Babkin, 1950), while others believe that the inhibition was due to the inherent osmotic effect (Thorsoe, 1971). These various investigators, however, made no reference to the possible effect of endogenously released vasopressin, which has been shown to reduce gastric secretion (Dodds and Noble, 1937; Lawson and Dragstedt, 1964). In at least two studies, no inhibition of gastric secretion was found after intravenous injections of posterior pituitary extract to dogs (Atkinson and Ivy, 1938; Tandon et al., 1965).

On the basis of such uncertainty, experiments were designed to reassess the influence and the inter-relationship of hyperglycemia, hypertonicity and antidiuretic hormones upon the gastric acid secretion in the rat. It is also the purpose of this work to correlate the in vivo gastric secretory change induced by the above manipulations and agents with any possible changes in gastric mucosal blood flow, thereby indicating the likely mechanism of inhibition of gastric secretion.

METHODS

Operative Technique. The 24 h fasted female rats (Fischer’s Strain) weighing 200—250 g were anesthetized with nembutal sodium and tracheotomized with esophagus and pylorus ligated. Through a gastric fistula which was installed at the squamous part of the stomach, the gastric juice was drained directly into the collecting tubes. The anterior facial vein was cannulated for a continuous infusion of gastric secretagogue (pentagastrin 5 ug/100 g/h) and warm 0.9% saline at a rate of 2 ml/h to maintain a steady submaximal acid secretion and to replace the loss of body fluid during the experiment. A single dose of a test solution (0.6 ml/100 g of either 0.9% NaCl, 3% NaCl, 20% glucose or various concentrations of vasopressin) was given via femoral vein cannula. The original vasopressin purchased from Sigma Chemicals Company is 20 IU/ml; dilutions were made from this solution. The femoral artery was cannulated for the measurement of systemic blood pressure and collection of blood samples. The rectal temperature of the rats was monitored and maintained at normal level throughout the experiment by a thermostatically control heating lamp.
Analysis of Gastric Juice. The volume of gastric samples were recorded every 15 min both before and after the administration of test solution. Hydrochloric acid content was determined by titration with 0.01 N NaOH to pH 5.0. The amount of free acid and acid concentration were expressed in μEq/g stomach/15 min and μEq/ml respectively. Plasma osmolality was also determined at intervals using the Osmette osmometer (Precision Systems Company).

Measurement of Gastric Mucosal Blood Flow. Gastric mucosal blood flow was assessed by the technique of aminopyrine clearance introduced by Jacobson et al. (1966). This technique has been established as a valid method for measurement of gastric mucosal blood flow (Harper et al., 1968; Jacobson et al., 1968; Schapiro et al., 1966; Tandon et al., 1965) and other techniques have not contraindicated the results so obtained (Curwain and Holton, 1973). A loading dose of aminopyrine (2 mg/100 g) was infused via femoral vein followed by a continuous infusion of 1 mg/100 g/h aminopyrine concentration. 0.3 ml of arterial blood samples was collected at intervals both before and after the administration of the test solution (3% NaCl, 20% glucose, etc.), simultaneously with the collection of gastric juice samples. Aminopyrine in both plasma and gastric juice was then determined by the methods of Brodie and Axelrod (1950).

RESULTS

Inhibition of Gastric Secretion by Glucose and Hypertonic Saline

The constant infusion of aminopyrine and pentagastrin together with 0.9% NaCl was noted to maintain the plasma aminopyrine concentration (5.2 ± 1.0 μg/0.1 ml), gastric clearance (5.6 ± 1.8 ml/15 min), H⁺ secretory rate (35 ± 4 μEq H⁺/g stomach/15 min) and arterial blood pressure at stable levels for at least 3½ h. When a single intravenous injection of 0.6 ml/100 g of 20% glucose solution (Fig. 1) was administered to the rats the gastric volume, free HCl and HCl concentration were significantly reduced (when the control values were compared with the values obtained within 30 min after the injections) from 0.28 ± 0.01 to 0.18 ± 0.02 ml/15 min (P < 0.001), 38.0 ± 2.5 to 19.2 ± 2.1 μEq/g stomach/15 min (P < 0.001), and 135 ± 4 to 111 ± 7 μEq/ml (P < 0.01), respectively. The 0.6 ml/100 g of 3% NaCl, which is isoosmotic with 20% glucose, also caused a significant reduction of gastric volume, free HCl and of HCl concentration from 0.33 ± 0.01 to 0.16 ± 0.01 ml/15 min (P < 0.001), 37.6 ± 1.9 to 18.2 ± 1.6 μEq/g stomach/15 min (P < 0.001), and 129 ± 1 to 120 ± 3 μEq/ml (P < 0.01), respectively, as typically shown in Figure 2. In general, the inhibitory effects on acid output lasted for about 1 h and the recovery of the secretory rate was usually completed within 3 h after the injection of the test solution. The acid concentration showed a temporary reduction at the peak of inhibition (within 30 min after test solutions) and quickly to control values even before the secretory volume was recovered. All rats receiving glucose or 3% NaCl had an increase of plasma osmolality from 305 ± 2 to 321 ± 1 mOsm (P < 0.001), and, in the case of glucose administration, the plasma glucose increased from 110 ± 9 to 380 ± 25 mg% (P < 0.001) within the first 5 min after the injection. The increases in plasma osmolality and glucose slowly declined to normal levels within 2 h, typified by results of one rat shown in Figure 3.