Pergamon

Biochemical Pharmacology, Vol. 48, No. 1, pp. 205–206, 1994.

0006-2952/94 $7.00 + 0.00

0006-2952(94)E0107-V

Enhanced gastric acid secretion induced by gastrin can be suppressed by glucose injected into the portal vein in rats

(*Received* 11 *October* 1993; *accepted* 24 *February* 1994)

Abstract—Gastric acid secretion induced by tetragastrin was examined after glucose injection into the portal vein in rats. The enhancement of acid secretion caused by gastrin was inhibited by glucose injection into the portal vein, and the acid response was dose dependent. The acid response due to portal glucose injection was not reproduced when the hepatic vagal branch was sectioned. These findings suggest that the portal glucose signal modulates gastric acid secretion controlled by gastrin.

Key words: liver; stomach; tetragastrin; vagal nerve

It has been well documented that gastrin enhances gastric acid secretion by stimulating the gastrin-sensitive cells in the brain only when administered directly into the corresponding regions or the parietal cells in the stomach [1–3]. Moreover, it has been shown that enhanced acid secretion induced by tetragastrin can be suppressed in the dog by systemic administration of glucose [4, 5]. Recently it was also found that the medullary nuclei are one site of interaction between glucose and gastrin [6]. However, there exists a mechanism sensitive to glucose in the portal vein area [7–9].

The present study was designed to investigate whether glucose injected into the portal vein influences gastric acid secretion associated with gastrin in rats.

Materials and Methods

Twenty-eight male Wistar rats weighing about 250 g were used. The rats were deprived of food for 22 hr before the experiments. The animals were anesthetized with pentobarbital sodium (45 mg/kg, i.p.), and were adrenalectomized bilaterally 30 min before the experiment to reduce scatter in plasma concentrations of glucose and insulin [10]. A cannula was inserted into the trachea to allow adequate ventilation.

Evaluation of the gastric acid output was made by the methods described earlier [7, 8]. Briefly, a polyethylene tube was introduced into the stomach through the esophagus and was tied in position with a ligature around the esophagus in the neck. Another cannula was then inserted into the pyloroduodenal junction and passed up into the stomach. The stomach was perfused with physiological saline (154 mM NaCl) at 36.0°, and titratable acidity (end point pH 7.0) was determined with 10 mM NaOH. The acid output was calculated every 3 min. Portal glucose injection was conducted 20–90 min after starting the gastric perfusion. The anal temperature was maintained at 36.0 ± 0.5° with a heating lamp.

Tetragastrin (4 μg/kg/hr, i.v.) was administered with a pump. D-Glucose (glucose) or L-glucose, dissolved in distilled water kept at 36.0°, was injected into the portal vein. Twenty-five microliters were injected each time, over a period of 10 sec, with an infusion pump. Blood for glucose estimation (20 μL) was drawn off through the right jugular catheter. The plasma concentration of glucose was measured by the method described previously [7].

A control response to 154 mM NaCl and an experimental response to glucose were obtained in the same animal. Data for the 1st and 2nd response of each animal to a specific solution were collected and ANOVA analysed. Then the specific values were evaluated by Duncan's multiple range test.

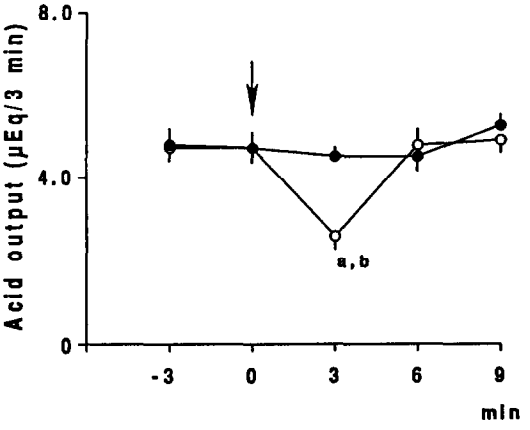

Fig. 1. Changes in gastric acid output following glucose injection into the portal vein. Ten millimolar glucose (○) or 154 mM NaCl (●) was injected. An arrow indicates the time of the injection. Values are means ± SE (N = 6). $^{a}P < 0.01$ vs the value before injection. $^{b}P < 0.01$ vs NaCl.

Results

Changes in gastric acid outputs after portal injection of glucose (10 mM, 25 μL) or NaCl (154 mM, 25 μL) in rats with tetragastrin are shown in Fig. 1. The analysis indicated that the infusion factor (glucose vs NaCl into the portal vein) was significant ($F = 43.67$, $P < 0.002$), the time factor (0 min pre- and 9 min post-infusion) was significant ($F = 14.95$, $P < 0.002$) and the interaction term (infusions by time) was significant ($F = 10.92$, $P < 0.002$). It was noted that portal injection of glucose decreased the acid output; the reduction in the response reached its maximum 3 min after injection, and then returned to the control level within another 3 min (Fig. 1). Plasma concentrations of glucose (means ±SE) before and 3 min after glucose (20 mM) injections were 3.54 ± 0.05 and 3.60 ± 0.05 mM (N = 6), respectively. The portal injection of glucose did not affect the glucose concentration in the blood.

Three different concentrations of glucose (5, 10 and 20 mM), 20 mM L-glucose and 154 mM NaCl were injected into the portal vein (Fig. 2). When the acid outputs 3 min after glucose injection were compared, the analysis indicated that the infusion factor (glucose vs NaCl and L-glucose into the portal vein) was significant ($F = 30.14$, $P < 0.01$) (Fig. 2): the inhibitory acid response was seen when 10 or 20 mM glucose was injected. The acid response

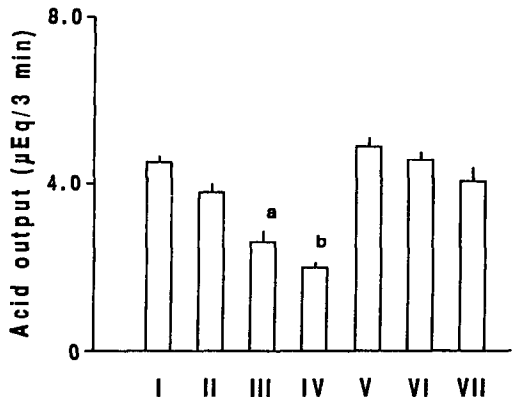

Fig. 2. Gastric acid output 3 min after glucose injection into the portal vein. Different concentrations of glucose (II, 5 mM; III, 10 mM; IV, 20 mM; V, 10 mM glucose with hepatic branch vagotomy) were injected. NaCl (I, 154 mM), L-glucose (VI, 20 mM) and hepatic branch vagotomy (VII) was used as the control. Values are means ± SE (N = 6). $^{a}P < 0.01$ vs I, II, V, VI and VII. $^{b}P < 0.01$ vs III.

due to 10 mM glucose was not reproduced after hepatic branch vagotomy. Neither L-glucose nor hepatic branch vagotomy changed the acid output.

Discussion

The finding that gastric acid output enhanced by tetragastrin was substantially suppressed by glucose injected into the portal vein (Figs 1 and 2) is consistent with the report that gastrin-induced acid secretion can be inhibited in the dog by systemic injection of glucose [4, 5].

Gastrin increases gastric acid secretion by activating not only the parietal cells of the stomach [1] but also the central mechanism sensitive to gastrin [2, 3]. However, the central mechanism is not involved in the stimulation of gastric acid secretion by i.v. tetragastrin in this study, because gastrin enhances acid secretion by stimulating gastrin-sensitive cells only when administered directly in the corresponding brain regions [2, 3]. Glucose has been shown to inhibit gastric acid secretion through a change in vagal activity in the brain or in the portal vein [8, 9, 11–13]. In the present study gastric acid output enhanced by gastrin could be depressed by glucose injection into the portal vein (Fig. 2). This could mean that the origin of neural signals responsible for the acid secretion is located in the portal vein area, and an interaction between glucose and gastrin takes place in this area. However, interactions between gastrin and glucose may also occur at the parietal cell or gastric mucosa level via gastrin–vagal interactions. Moreover, it should also be remembered that because mechanisms sensitive to glucose or gastrin have been identified in several nuclei in the hypothalamus [3, 11, 14, 15], the acid response may originate in such nuclei, and the portal glucose signal may serve as a modulator.

Gastric acid response following central administration of glucose or gastrin has been shown to be inhibited by atropin sulfate or vagotomy [2, 7]. It is likely that parasympathetic and cholinergic fibers are involved in the response observed.

Gastrin is released into the stomach or into the systemic circulation immediately after food ingestion, and the glucose concentration in the blood also increases soon after food digestion [4, 5]. The acid response found may therefore explain the part played by the fine control of reciprocal gastric acid secretion associated with feeding.

These observations suggest that portal glucose signals modulate gastric acid secretion controlled by gastrin.

Acknowledgements—The authors are greatly indebted to Mr K. Kunihara (Dept of Physiology) for his assistance. This study was supported by Grant No. 05670063 from the Ministry of Education, Science and Culture, Japan.

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