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# Effect of Intraduodenal Sodium Bicarbonate in Rat and Rabbit Exocrine Pancreatic Secretion

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The effect of intraduodenal sodium bicarbonate, 0.1 M, on exocrine pancreatic secretion and the release of two peptides, secretin and VIP, was studied in anesthetized rats and rabbits, two species largely used in the gastroenterology laboratories. In the rabbit, intraduodenal sodium bicarbonate perfusion had no effect either on exocrine pancreatic secretion or on portal plasma levels of secretin and VIP. By contrast, in the rat, intraduodenal sodium bicarbonate perfusion significantly increased hydroelectrolyte exocrine pancreatic secretion and portal plasma secretin levels. A clear interspecific difference reflecting the different gastrointestinal physiology of both species is observed.

Key words: Pancreatic juice, Intraduodenal sodium bicarbonate, Rat, Rabbit.

Many studies on the control of exocrine pancreatic secretion have focused on the effects of naturally occurring intraduodenal stimulants, such as acids, digestion products of fats and proteins and bile constituents. However, only a few studies have been undertaken to elucidate the effect of bicarbonate, which is a natural intraduodenal substance coming from the duodenum, the bile or the pancreatic juice, on exocrine pancreatic secretion. FARRELL (4), in dogs, reported that intraduodenal bicarbonate elicited a more prolonged response to exogenous secretin while TAKESHIMA *et al.* (15), also in the dog, described a slight increase of protein secretion after intraduodenal bicarbonate. More recently, the response of exocrine pancreatic secretion to alkaline solutions has been reported in the rat (7, 10).

There is a considerable difference in the income of $HCO_3^-$ to the duodenum of the rat and the rabbit, two species largely used in the gastroenterology laboratories. Thus, surface $HCO_3^-$ epithelial transport in rat duodenum is about 15 times less

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than that in rabbit duodenum (5) and practically the same occurs with bicarbonate output from exocrine pancreas (6, 12) and the liver (9, 13) of both species. This prompted us to investigate the response of exocrine pancreatic secretion to intraduodenal sodium bicarbonate in both animal species.

## Materials and Methods

*Animals and surgical technique.* — Male adult New Zealand rabbits weighing 2-2.5 kg and male adult Wistar rats weighing 300-350 g were fasted for 24 h with free access to water. The animals were anesthetized with sodium pentobarbital (30 mg/kg BW) and tracheotomized. After median laparotomy, intraduodenal perfusion was carried out by means of two cannulae, one placed at the beginning of the duodenum through the pylorus (ligating the pylorus to prevent reflux) and the other at the end of duodenum. The bile duct was cannulated to deviate bile flow to the exterior and the pancreatic duct was cannulated to collect the pancreatic juice. Blood samples were taken from the portal vein, replacing the volume withdrawn by the same volume of dextran-saline (Baxdextran saline, Braum).

Animals remained anaesthetized throughout the experiment and a heating pad was used to maintain temperature at 37 ± 1 °C as measured by a rectal thermometer.

*Experimental design.* — Intraduodenal perfusion was performed with a peristaltic pump using phosphate-buffered saline (PBS), pH = 7.4, or a solution of sodium bicarbonate 0.1 M, pH = 8.3, made isoosmotic with plasma by the addition of NaCl.

The experimental protocol used with rats has been previously described in detail (7). Briefly, an equilibration period of 30 min was followed by a 30 min basal period; during these two periods the duodenal lumen was perfused with PBS. Then followed by a 10 min stimulation period during which the perfusate was PBS (control group) or sodium bicarbonate (12 mmol/h), after which there was a 50 min recovery period during which PBS was again infused.

In rabbits the experimental protocol used, previously described (6), was as follows: An equilibration period of 30 min was followed by a 30 min basal period; during these two periods the duodenal lumen was perfused with PBS. Then followed by a 30 min stimulation period during which the perfusate was PBS (control group) or sodium bicarbonate (18 mmol/h), after which there was a 30 min recovery period during which PBS was again infused.

In both animal species pancreatic juice was collected during the 30 min basal period and over 10 min intervals throughout the stimulation and recovery periods, and a sample of portal venous blood was drawn at 5 min before the end of basal period and at the midpoint of each 10 min interval. Aliquots of pancreatic juice were collected in Eppendorf tubes and blood samples in heparinized tubes containing 500 Kallikrein inhibitory units (KIU)/ml of aprotinin (Trasylol, Bayer). Blood samples were immediately centrifuged and the plasma stored at − 30 °C.

*Analytical methods.* — Pancreatic juice output was determined by weighing the juice samples on an electronic balance (Type H-35, Mettler, Switzerland) assuming the density of the juice to be 1.0. Total protein concentration were measured by the Coomassie blue binding method (1).

Secretin and VIP plasma levels were measured by RIA methods (6, 7).

*Data Analysis.* — Values of a given parameter (Mean ± SEM) are expressed as percent of basal measurements. The integrated percentage response (IPR) was cal-

culated from the individual percentage increase compared with mean basal values of 100 %. Data were compared by the U Mann-Whitney test. Differences were considered significant at $p < 0.05$.

## Results

*Control group.* — Intraduodenal perfusion of phosphate buffered saline, pH 7.4, had no effect on flow rate from the pancreas, nor on portal secretin and VIP concentrations, remaining these parameters constant throughout the experiment in both, rats and rabbits.

Protein output, in rabbits and rats, decreased throughout the experiment until 48 % of basal values in rats and 40 % of basal values in rabbits at the end of the experiment (S7).

*Effect of sodium bicarbonate perfusion.* — Basal values (mean ± SEM) of the different parameters are shown in table I.

In rats, intraduodenal perfusion of 0.1 M sodium bicarbonate, pH 8.3, significantly increased pancreatic flow rate to a maximum of 183 ± 23 % of the basal value (fig. 1) and protein output to a maximum of 196 ± 36 % of the basal value (fig. 1). Significant increases in plasma se-

Table I. *Basal values of the pancreatic flow rate and protein output and secretin and VIP plasma levels from the bicarbonate group in rat and rabbit.* Data are expressed as mean ± SEM.

| | Rat (n = 7) | Rabbit (n = 5) |
|---|---|---|
| Flow (µl/min) | 0.37±0.04 | 7.51±1.03 |
| Protein output (µl/min) | 13.5±2.49 | 100.6±5.80 |
| Secretin (fmol/ml) | 3.69±0.39 | 4.60±0.87 |
| VIP (fmol/ml) | 4.38±0.96 | 7.80±1.50 |

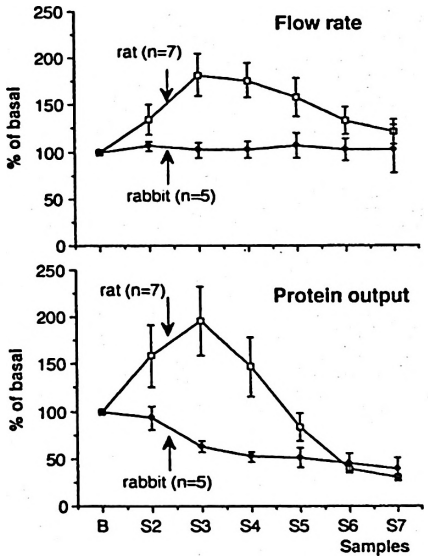


Fig. 1. *Pancreatic flow rate and protein output after intraduodenal perfusion of sodium bicarbonate in both rats and rabbits.*
Each sample point is the mean ± SEM, expressed as percent of basal values (B: basal period; S2-S7 successive 10 min periods after the basal); n is the number of animals.

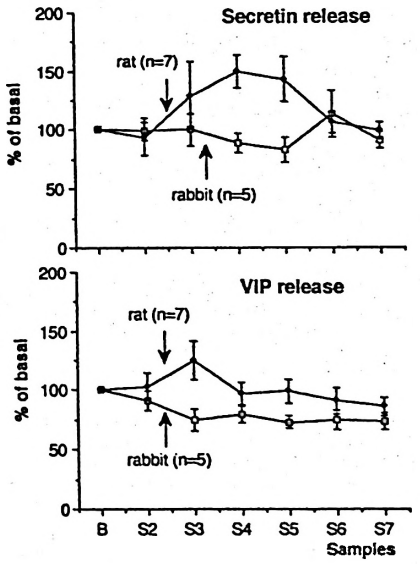


Fig. 2. *Secretin and VIP release to plasma after intraduodenal perfusion of sodium bicarbonate in both rats and rabbits.*
Legend as in fig. 1.

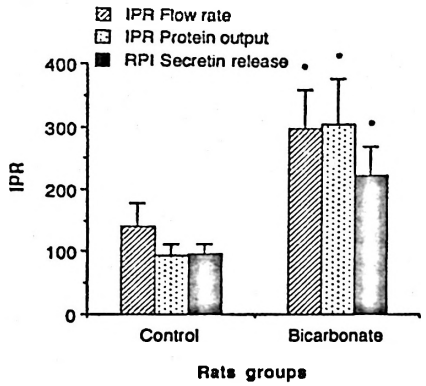


Fig. 3. *Integrated percentage response (IPR) of pancreatic flow rate, protein output and secretin release after intraduodenal perfusion of phosphate-buffered saline (control group) and sodium bicarbonate (bicarbonate group) in rats.*
Each bar graph is the mean ± SEM from the individual percentage compared with basal values of 100 %. • Significant differences ($p < 0.05$) *vs* control group.

cretin levels, with a maximum of 150 ± 15 % compared with the basal value, were also observed (fig. 2). Concerning plasma VIP levels, a lower increase, only in the S3 sample, of 125 ± 15 %, was observed (fig. 2).

In rabbits the intraduodenal perfusion of 0.1 M sodium bicarbonate, pH 8.3, had no effect on any parameters controlled by us (figs. 1 and 2).

The IPR of flow rate, protein output and plasma secretin levels were significantly higher in rats perfused with sodium bicarbonate than in the control group (fig. 3).

## Discussion

In the present work it has been shown that, in the rabbit, intraduodenal sodium bicarbonate perfusion has no effect either on exocrine pancreatic secretion or on the plasma levels of secretin and VIP. By contrast, in the rat, intraduodenal sodium bicarbonate perfusion produced significant increases in hydroelectrolyte and enzyme pancreatic secretion and plasma secretin levels. The increase in plasma secretin levels may account for the increase in flow rate, however, the earlier increase observed in flow rate and protein output may be ascribed to a nervous (cholinergic) factor.

The different behaviour of the pancreatic response observed in the rat and in the rabbit may reflect their respective gastrointestinal physiological differences. Thus, basal bicarbonate secretion from duodenum is 151 ± 21 μmol/cm × h in the rabbit, whereas in the rat this basal secretion is only 10.0 ± 0.8 μmol/cm × h (5). The same occurred with basal bile bicarbonate secretion: 8.0 ± 0.3 μmol/min in the rabbit (13), while in the rat it is 0.43 ± 0.015 μmol/min (9). Furthermore, basal bicarbonate secretion from exocrine pancreas is also higher in the rabbit, 0.4 ± 0.02 μmol/min (6) than in the rat, 0.03 ± 0.01 μmol/min (12). This is in agreement with previous results showing the relatively high hydroelectrolyte pancreatic secretion in the rabbit both *in vivo* (11) and *in vitro* (14).

Moreover, pancreatic exocrine response to better characterized duodenal stimuli such as HCl seems to confirm the lesser response of rabbit pancreas since higher intraduodenal HCl loads are needed to obtain a clear pancreatic response in the rabbit (6) compared with the rat (8) and dog (2).

A possible explanation could be related to different kinds of feeding and digestion by both species. In the rabbit it is assumed that the transit of food through the stomach is slow (3) and probably slower than in the rat, this means a more constant incoming of food from the stomach to the duodenum. In the rat the low basal bicarbonate secretion from the duodenum, liver and pancreas is accompanied by a higher capacity of response to intraduodenal stimuli; moreover, a positive feedback

mechanism mediated by bicarbonate, similar to that suggested in the dog (4, 15) could exist. However, in the rabbit, since a constant income of nutrients to the duodenum occurs, basal bicarbonate secretion should be higher, with no participation of bicarbonate in the control of pancreatic secretion.

Intraduodenal bicarbonate stimulates exocrine pancreatic secretion in the rat and this can be ascribed, at least partially, to the effect of secretin, whose release has been reported. On the other hand, this kind of control on exocrine pancreas function does not exist in the rabbit. A clear interspecific difference occurs which reflects the different gastrointestinal functions of both species.

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## Resumen

Se estudia en ratas y conejos anestesiados el efecto de la perfusión intraduodenal de bicarbonato sódico, 0,1 M, sobre la secreción pancreática exocrina y los niveles plasmáticos de secretina y VIP, péptidos que intervienen en su regulación. Los resultados en conejo no presentan ningún efecto sobre la secreción pancreática exocrina, ni sobre los niveles plasmáticos de secretina y VIP. Sin embargo, en rata, aumentan significativamente la secreción pancreática exocrina y los niveles plasmáticos de secretina. Se concluye que existe una clara diferencia interespecífica en la respuesta a la perfusión intraduodenal de bicarbonato sódico, que puede ser reflejo de la diferente fisiología gastrointestinal observada en ambas especies.

Palabras clave: Jugo pancreático, Bicarbonato sódico intraduodenal, Rata, Conejo.

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