EFFECTS OF SHORT-CHAIN FATTY ACIDS ON PANCREATIC ELECTROLYTE SECRETION IN SHEEP

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Introduction

Short-chain fatty acids, major end products of microbial fermentation in the rumen, stimulate A-cells (Bassett, 1972) and B-cells (Sasaki et al., 1977) of endocrine pancreas and acinar cells (Harada and Kato, 1983; Katoh and Tsuda, 1984) of exocrine pancreas in sheep. However, it is not clear whether these fatty acids stimulate the pancreatic duct system, another functional unit of exocrine pancreas responsible for the secretion of water and electrolytes. The present study was carried out to investigate the effects of short-chain fatty acids on pancreatic electrolyte secretion in sheep.

Materials and Methods

Six Suffolk wethers, weighing 46-68 kg, were chronically cannulated with silastic tubing (4 mm O.D., 2 mm I.D.) inserted into the common bile duct at two places, one near the duodenum for collection of pancreatic juice and the other near the gall bladder for collection of bile. The common bile duct was ligated immediately distal to both catheter insertions. A third catheter was inserted into the duodenum for the return of pancreatic juice and bile. In addition, an indwelling catheter was chronically inserted into the posterior vena cava to administer experimental solutions. The animals were kept in individual crates and fed orchard-grass hay (200g) and lucerne pellets (2.5% of body weight) once daily at 19:00. Water was available ad libitum. With a peristaltic pump the collected pancreatic juice and bile were continuously returned to the duodenum of each sheep at about the rate of production. The rate of pancreatic juice flow was measured every 10 min from 9:30 to 11:00 a.m. and an aliquot of 100 μl was taken for analyses of the concentrations of Na^+, K^+, Cl^- and HCO_3^-. Acetate, propionate and butyrate, major short-chain fatty acids produced in the rumen, and cholecystokinin octapeptide (CCK-8) and secretin were administered intravenously at 10:00 a.m. The rates of administration were 1.2 mmol/kg, short-chain fatty acids; 875 pmol/kg, CCK-8; and 4.6 pmol/kg, secretin. With the exception of acetate and propionate, the doses of the secretagogues were calculated as amounts expected to stimulate pancreatic flow in comparable amounts. The student's t-test was used in all statistical analyses.

Results and Discussion

Butyrate elicited an increase in juice flow and in the concentrations of Na^+, K^+ and HCO_3^- in pancreatic juice but significantly lowered the Cl^- concentration, as noted in table 1. After administrations of propionate and acetate, similar results were observed, though not all were significant. The effect of butyrate was measurably the greatest and that of acetate was the least, with the single exception that propionate raised the concentrations of Cl^- and HCO_3^- more than butyrate did. CCK-8 increased juice flow and the concentrations of K^+ and HCO_3^- but lowered the concentration of Cl^- significantly. Secretin increased juice flow and HCO_3^- but decreased Cl^- significantly. CCK-8 is known to act on the acinar cells to cause the secretion of pancreatic juice rich in digestive enzymes, whereas secretin acts on the duct system of exocrine pancreas to stimulate an isotonic secretion rich in HCO_3-. The concentrations of HCO_3^- and Cl^- in pancreatic juice are influenced by the rate of secretion of pancreatic juice (Case, 1979). Although butyrate, CCK-8 and secretin induced similar flow rates, the responses of Cl^- and HCO_3^- concentrations to secretin were significantly ($P < 0.01$) greater than those of butyrate and CCK-8, indicating that secretin acted on cells of the duct system. Significant changes in Cl^- and HCO_3^- concentrations elicited by CCK-8 might be caused by the potentiating effect of CCK-8 on the action of endogenous secretin. Pancreatic electrolyte secretion elicited by buty-

TABLE 1. EFFECTS OF INTRAVENOUS ADMINISTRATIONS OF SHORT-CHAIN FATTY ACIDS, CCK-8 AND SECRETIN ON PANCREATIC JUICE FLOW AND ELECTROLYTE CONCENTRATION (MEAN ± SEM)

Secretagogues		Flow (ml/10min)	Electrolytes (mEq/l)			
			Na^+	K^+	Cl^-	HCO_3^-
		(3.39±0.16)[a]	(142.6±0.8)	(6.1±0.1)	(142.4±0.7)	(24.5±0.6)
Acetate	(1.2 mmol/kg)[b]	0.30±0.21[c]	3.5±1.1	0.8±0.2*	−2.5±1.6	1.7±1.0
Propionate	(1.2 mmol/kg)	0.42±0.17	4.1±1.2	2.1±0.5**	−10.6±1.7**	9.2±1.4**
Butyrate	(1.2 mmol/kg)	1.84±0.22*	5.3±0.8**	2.8±0.8**	−6.7±1.1**	8.0±0.8**
CCK-8	(875 pmol/kg)	1.72±0.33*	−0.2±1.1	2.0±0.5**	−10.6±2.4**	11.0±1.0**
Secretin	(4.6 pmol/kg)	2.04±0.37**	3.6±1.6	0.4±0.1	−30.3±3.6**	28.0±3.4**

[a]Initial level, n=30 (6 sheep x 5 secretagogues).
[b]Rate of intravenous administration.
[c]Value subtracting the initial level from the level after administration of secretagogue, n=6.
*,**Significant change from the initial level, $p < 0.05$ and $p < 0.01$, respectively.

rate correlated closely with that of CCK-8 except for the concentration of Na^+. These results demonstrate that the short-chain fatty acids acted specifically on the acinar cells rather than on both functional units of exocrine pancreas in general.

(Key Words: Short-chain Fatty Acids, Pancreatic Electrolytes, Sheep)

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