State-of-the-Art

Development and Regulation of Porcine Pancreatic Function

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Summary

A surgical and experimental procedure was developed to enable the collection of pure and inactivated pancreatic juice during the growth of the pig. Studies have shown that, during the suckling period, both the basal and the secretory responses to suckling are low, if present at all. After weaning, basal levels of the total exocrine secretion, total protein, amylase, and trypsin, respectively, increase slightly, while the postprandial levels of total protein, amylase, trypsin, lipase, colipase, and carboxylester lipase, respectively, increase markedly. The pancreatic juice enzyme composition changes qualitatively and the antibacterial activity of the pancreatic juice also significantly increases. Piglet age appeared to be of minor importance, since weaning at either 4 or 6 wk of age gave the same results. Secretin and CCK administered together in supraphysiological doses only significantly affect exocrine function from 3–4 wk of age. However, CCK may also affect the exocrine pancreas indirectly via reflexes initiated intraduodenally. Milk consumption in the suckling pig leads to a postprandial increase in glucose levels but not insulin. Milk appears to be able to regulate the exocrine pancreas to produce only the amount and type of enzymes required for digestion. Thus, milk components or digestive products may affect pancreas function regulation. Studies show that enterostatin, the procolipase activation peptide, may inhibit pancreatic secretion mediated indirectly through the GI tract. Pancreastatin, an endocrine peptide, inhibits both insulin secretion and protein and trypsin secretion to pancreatic juice. In hypoinsulinemic (alloxan + streptozotocin diabetes) pigs (15–20 kg), no postprandial pancreatic juice response is seen, although CCK 33 + secretin can stimulate pancreatic secretion. Hypoinsulinemic pigs have a reduced capacity for glucose tissue utilization, suggesting that tissue metabolism and exocrine pancreas secretion are related.

Key Words: Pig; pancreas; weaning; insulin; CCK; secretin; milk; antibacterial activity.

Abbreviations: cAMP, cyclic adenosine 5'-monophosphate; CCK, cholecystokinin; CEL, carboxyl ester lipase; GI, gastrointestinal; GIP, gastric inhibitory polypeptide; id, inside diameter; i.d., intraduodenal; iv, intravenous; mU, milli unit; μU, micro unit; od, outside diameter; PP, pancreatic polypeptide; PYY, peptide YY; SBTI, soya bean trypsin inhibitor; VIP, vasoactive intestinal peptide; VPDP, valine-proline-aspartic acid-proline-asparagine = enterostatin.

Introduction

The function and regulation of the digestive system play a central role in normal development, growth, and health of humans, animals and experimental/laboratory animals. The digestive tract undergoes profound changes during ontogeny, especially after birth when enteral feeding starts, and after weaning when maternal milk is replaced by solid food. During these periods, disturbances within the digestive system (e.g., the GI-tract and its accessory
Glands) in morphology and/or function will result in growth retardation, increased morbidity (often manifested as diarrhea), and eventual death. The pancreas plays a central role in the digestive system by its synthesis and secretion of specific digestive enzymes, and has an integrative role for the absorption and metabolism of nutrients in the organism.

The studies were expected to provide new basic knowledge about digestive function of the growing pigs, to be used for nutritional and management considerations around weaning, and when new food and management techniques are introduced. Furthermore, the project was also expected to provide new knowledge in the areas of integrative physiology at the level of the organism and to highlight the pig as a useful omnivorous model in biomedical research.

In the adult pig, the exocrine pancreas produces pancreatic juice, which contains enzymes, non-enzymatic proteins, and salts. These substances usually reach the duodenum via a single pancreatic duct in the pig, although occasionally an accessory duct may be found, as reported by Kidder and Manners (1). Enzymes able to digest proteins, carbohydrates, lipids, and nucleic acids, respectively, are produced in the acinar cells of the exocrine pancreas (2,3). Electrolytes capable of neutralizing the acidic stomach contents and establishing the proper pH for enzymatic action are produced mainly in the intra-acinar and ductal cells (4). The islet cells of the endocrine pancreas produce hormones (e.g., insulin, glucagon) that regulate the utilization of the absorbed digestion products (5-8).

Exocrine pancreas function has previously been studied in weaned growing pigs (9-11), using different models for the long-term collection of pancreatic juice. However, newborn, suckling, and newly weaned pigs have not been investigated until the studies carried out by our research group. In order to do this, a surgical and experimental procedure has been developed to enable the collection of pure and inactivated pancreatic juice during the growth of the pancreatic and other GI tissues in the very young pig. This method does not appear to interfere with the normal physiological responses to feeding or hormonal stimulation (12).

The following report presents a brief description of the methods and results showing the development of exocrine and, to some extent, endocrine function.

### Materials and Methods

#### Animals

Purebred Swedish Landrace pigs (Sus scrofa) were used, ranging in age from 1 to 14 wk.

#### Surgical Procedures

For details of the chronic pancreatic duct catheterization and blood vessels catheterization, see Pierzynowski et al. (12-14,35).

#### Pancreatic Surgery

Sedation was carried out using azoperone (Stresnil, LEO, Sweden; 2 mg/kg body wt); anesthesia before weaning was done using an iv injection of metomidate (Hypnodil, LEO, Sweden; 4 mg/kg body wt), and after weaning using benzethone chloride (Ketalar, Parke-Davis, Spain; 10-20 mg/kg body wt) and pentobarbital natrium (Mebumal, NordVacc, Sweden; 5-10 mg/kg body wt).

For pigs operated on before weaning, a silicone catheter (Silastic, Down Corning, Belgium; id 0.3, od 0.64 mm) was implanted in the pancreatic duct and exteriorized via an abdominal cannula (Silastic) placed between the peritoneum and muscle layers in the first right intercostal space. The ductal catheter was connected to a perforated T-cannula placed in the jejunum, thus maintaining a constant re-entrant flow of juice (12). The pancreatic duct catheter was replaced, if necessary, at 3 wk of age under sedation with Stresnil (2.0 mg/kg body wt) and with the local anesthetic mepivacaine hydrochloride (Carbocaine, Astra, Sweden; 3.0-5.0 mL/animal) by a larger catheter (id 0.64, od 1.19 mm) and a silicone ring was placed between the muscle layers and peritoneum at the site of the removed abdominal cannula (14).

For pigs operated on after weaning, the method (12,14) was modified as follows: The perforated T-cannula was replaced by a nonperforated one; and a protective abdominal cannula was not used. Instead, two silastic cuffs were glued onto the pancreatic catheter (id 0.64 mm, od 1.19 mm) 2 to 3 cm apart, and a silastic ring was placed within this distance.

After a right-side paracostal laparotomy, the pancreatic catheter was implanted in the pancreatic duct and exteriorized through the first right intercostal space. During the closing of the surgical wound, the silastic ring was placed between the muscle layer...