

Null Results in Brief

Cholecystokinin and Gastrin Levels Are Not Elevated in Human Pancreatic Adenocarcinoma

David S. Weinberg,¹ Gregory J. Heyt, Mary Cavanagh, David Pitchon, Katherine A. McGlynn, and W. Thomas London

Division of Gastroenterology and Hepatology, Department of Medicine, Jefferson Medical College, Philadelphia, Pennsylvania 19107 [D. S. W., G. J. H., M. C.]; Department of Medicine, University of Cincinnati, Cincinnati, Ohio [D. P.]; Epidemiology Branch, NIH, Bethesda, Maryland 20892 [K. A. M.]; and Division of Population Science, Fox Chase Cancer Center, Philadelphia, Pennsylvania [W. T. L.]

Introduction

Despite numerous epidemiological studies of pancreatic adenocarcinoma, the identification of substantive associations between exposure and disease has been elusive. Tobacco use, age, and male gender are established risk factors. CCK² and gastrin, two gastrointestinal hormones, have also been implicated (1). The influence of endogenous hormones is well described for several human cancers. Generally, the hormones implicated are important in both the health and disease of the target organ. CCK modulates pancreatic digestive secretion, mediates satiety, and stimulates normal pancreatic growth, whereas gastrin is primarily responsible for gastric acid secretion. CCK and gastrin bind, with different affinities, to the CCK-A and CCK-B receptors located throughout the gastrointestinal tract including the pancreas.

In animal models, experimental hypercholecystokininemia induced by pancreaticobiliary diversion or administration of supraphysiological doses of CCK stimulated pancreatic growth and induced pancreatic hypertrophy, hyperplasia, and dysplasia. Exogenous CCK has stimulated the growth of pancreatic cancers in animal models, human pancreatic cancer cell lines, and xenografted human tumors (2). Gastrin enhances tumor growth of various types. Autocrine gastrin production has been implicated in human pancreatic adenocarcinoma (3).

Despite provocative animal and preclinical data, definitive studies in humans are limited. Demonstrating elevated endogenous levels of CCK or gastrin among patients with pancreatic adenocarcinoma would support a role for these hormones in pancreatic carcinogenesis. Therefore, we conducted a case-control study to assess whether serum levels of CCK or gastrin were significantly altered in patients with pancreatic adenocarcinoma compared with healthy controls.

Materials and Methods

Patients with pancreatic adenocarcinoma were identified from two academic medical centers in metropolitan Philadelphia (University of Pennsylvania and Thomas Jefferson University) between 1997 and 1999. All patients had histologically confirmed pancreatic adenocarcinoma diagnosed within 1 week of sample collection. Controls were enrolled over the same time period from two outpatient cataract and glaucoma clinics at the same centers. The controls were chosen from these clinics because they approximated the overall demographics of persons at risk for pancreatic cancer. Risk factors for these diseases have little known overlap with pancreatic cancer. All controls were scheduled for elective surgery, reflecting their overall good health.

Fasting blood samples were obtained from all participants, placed directly in ice, and subjected to centrifugation within 1 h. Separated serum was stored at -80°C until analysis. All hormone radioimmunoassays were performed in a single laboratory as described previously (4).

Student's *t* test was used to compare mean serum levels.

Results

A total of 56 cases and 87 controls provided fasting blood samples for serum CCK assay. Of these, sufficient blood was also available to measure gastrin levels in 28 cases and 73 controls (Table 1). The average age of the pancreatic cancer patients and controls participants was 65.8 and 70.4 years, respectively. Fifty-three percent of cases were male, and 47% were female. Of the controls, 47% were male, and 53% were female. Over 80% of both cases and controls were white.

The mean CCK levels were 10.71 ± 6.01 pg/ml for cases and 9.43 ± 7.22 pg/ml for controls ($P = 0.13$). Mean gastrin levels measured were 29.87 ± 18.79 pg/ml for cases and 35.94 ± 33.64 pg/ml for controls ($P = 0.087$).

Levels of neither hormone varied significantly in cases or controls when stratified by gender, race, or self-reported alcohol or tobacco use. For cases, neither CCK nor gastrin levels varied markedly relative to tumor position within the pancreas or pancreatic cancer stage at diagnosis, although numbers were small for some strata, limiting power to detect smaller differences (data not shown).

Discussion

Pancreatic adenocarcinoma has a very poor prognosis with 5-year survival rates of less than 10%. The absence of a reliable screening test, a nonspecific clinical presentation that delays diagnosis, and the lack of effective therapy contribute to this dismal outcome. Animal studies have demonstrated that CCK or gastrin enhances normal and malignant pancreatic growth. These changes can be reduced or blocked by specific antagonists for the CCK-A or CCK-B receptor. Unfortunately, the only published clinical trial of a CCK receptor antagonist failed to demonstrate benefit (5).

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¹ To whom requests for reprints should be addressed, at Division of Gastroenterology and Hepatology, Jefferson Medical College, 480 Main Building, 132 South 10th Street, Philadelphia, PA 19107. Phone: (215) 955-8900; Fax: (215) 923-3447; E-mail: david.weinberg@mail.tju.edu.

² The abbreviation used is: CCK, cholecystokinin.

Table 1 Cholecystokinin and gastrin levels in patients with pancreatic adenocarcinoma versus controls (all values are in pg/ml)

	N	Mean value	SD
CCK controls	87	9.425	±7.22
CCK cases	56	10.709	±6.01
Gastrin controls	73	35.94	±33.64
Gastrin cases	28	29.87	±18.79

In the current study, we did not observe any difference in the serum hormone levels of adenocarcinoma cases versus controls. Potential limitations include the study's limited power to detect modest differences in serum levels, given the relatively small number of participants. However, cases and controls were similar demographically, and there is little reason to expect that ascertainment bias is an important issue in newly diagnosed pancreatic cancer.

The absence of detectable differences in CCK or gastrin levels suggests that if these peptides play a role in carcinogenesis, it is likely at the level of the local tissue environment (6). Serum CCK or gastrin levels may vary if measured before the development of pancreatic cancer as compared with diagnosis. The present inadequate methods to identify persons at higher risk for pancreatic cancer limit the opportunity to address this

possibility. Because serum levels of both hormones were similar regardless of tumor stage, it suggests that serum CCK or gastrin is neither a valuable screening technique to improve early cancer detection nor a valuable diagnostic tool. Finally, these results would not support the therapeutic use of specific CCK receptor antagonists for hormonal modulation in the absence of new information.

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