*Pancreas*
Vol. 21, No. 3, pp. 262–265


# Synthetic Porcine Secretin Is Highly Accurate in Pancreatic Function Testing in Individuals with Chronic Pancreatitis

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**Summary:** The secretin stimulation test is the most sensitive and specific test for pancreatic function. It is usually performed using biologically derived porcine secretin. Several shortages of biologic porcine secretin have occurred in the past few years. The aim of this study was to compare synthetic porcine secretin to biologic porcine secretin in pancreatic function testing in subjects with chronic pancreatitis. Twelve patients with a previously abnormal secretin stimulation test were enrolled. After an overnight fast, each patient underwent a secretin stimulation test on 2 consecutive days using 1 CU/kg biologic porcine secretin or 0.2 μg/kg synthetic porcine secretin in a randomized fashion. The peak bicarbonate concentration in duodenal juice was used as a measure of pancreatic function. The peak bicarbonate concentration (mean ± SD) obtained by using biologic porcine secretin and synthetic porcine secretin were 70 ± 25 mEq/L and 68 ± 31 mEq/L, respectively ($p = 0.58$, paired $t$ test; $R = 0.964$). The accuracy of synthetic porcine secretin in diagnosing pancreatic insufficiency was 100% when compared with biologic porcine secretin. We conclude that synthetic porcine secretin is highly accurate and safe in pancreatic function testing. The 100% purity, excellent diagnostic accuracy, and ready availability make synthetic porcine secretin an attractive choice for secretin stimulation testing. **Key Words:** Secretin—Chronic pancreatitis—Diagnosis.

The diagnosis of chronic pancreatitis remains challenging despite the use of sophisticated imaging modalities like computed tomography (CT) scanning, ultrasound and endoscopic retrograde cholangiopancreatography (ERCP) (1). A number of noninvasive pancreatic function tests, also known as tubeless tests, have been developed but proved to be inferior to hormone stimulation testing, which remains the test of choice for diagnosing chronic pancreatitis (2–4). The secretin stimulation test is the gold standard for diagnosis of chronic pancreatitis, with excellent sensitivity and specificity when compared with pancreatic histology (5). The secretin test comprises double-lumen duodenal tube placement, collection of duodenal contents by continuous suction before and after pancreatic stimulation with intravenous secretin, and finally, the assessment of pancreatic function by measuring the quantity and concentration of the pancreatic fluid (6). Of all parameters evaluated during the secretin stimulation test, maximal bicarbonate concentration was shown to be the most discriminatory parameter, with a smallest coefficient of variation of 13% (5). The most likely explanation for the less satisfactory performance of total volume and total $HCO_3$ output as measures of pancreatic function lies in the fact that during the secretin test, no marker is perfused, and therefore the recovered volume represents only a fraction of the total duodenal secretions. The secretin stimulation test is routinely performed using biologically derived porcine secretin. Because of limited supply, several shortages of biologic porcine secretin have occurred in the recent past, with a severe shortage now because of an unprecedented demand for secretin, for use in autism. Synthetic porcine secretin would be an excellent alternative to biologic porcine secretin for use in pancreatic function testing. The idea of using synthetic secretin is not a recent one. It has been used in Europe for research protocols for >20 years (7,8). Several studies on healthy volunteers demonstrated comparable efficacy of biologic porcine secretin and synthetic porcine secretin during the secretin stimulation test (9,10), but we have not found any data on direct comparison of the two forms of secretin in patients with known chronic pancreatitis. We

Manuscript received July 6, 1999; revised manuscript accepted February 3, 2000.
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undertook this study to compare a newly prepared synthetic porcine secretin to biologic porcine secretin in pancreatic function testing in patients with a known history of chronic pancreatitis.

## MATERIALS AND METHODS

### Patients

The research protocol was reviewed and approved by the University of Florida Institutional Review Board. After informed consent, 12 patients with chronic pancreatitis and a previously abnormal secretin stimulation test were enrolled. In addition to the secretin stimulation test, the diagnosis of chronic pancreatitis was supported by at least one other test, including biochemical markers, ultrasound, CT scan, or ERCP in all patients. The historic peak bicarbonate of this group was 57 ± 20 mEq/L (mean ± SD), with a range of 12–77 mEq/L. The mean and median age of patients was 56 years, with a range of 37–69 years. The male-to-female ratio was 4:8. Two patients were African American, and 10 were white. Seven patients had alcohol-induced disease; the remaining five patients had idiopathic chronic pancreatitis.

### Peptides

Biologic porcine secretin was purchased from Ferring Laboratories (Suffern, NY, U.S.A.). Synthetic porcine secretin was provided by ChiRhoClin (Silver Springs, MD, U.S.A.). Synthetic porcine secretin was prepared in FDA-inspected facilities conforming to the highest standard of GMP. It is >96% pure and has a 27-amino-acid sequence identical to that of biologic porcine secretin. No toxic effects were noted in acute toxicology studies in mice and rabbits using 100 times the human dose (ChiRhoClin; data on file). The specific activity of synthetic porcine secretin in a study of 12 normal people was 5 CU/μg, and in a cat bioassay system, it was 4.92 CU/μg (ChiRhoClin; data on file).

### Secretin stimulation test

After an overnight fast, each patient underwent a secretin stimulation test on 2 consecutive days using 1 CU/kg biologic porcine secretin or 0.2 μg/kg synthetic porcine secretin in a randomized fashion. The secretin stimulation test was performed in the following way. The patient's throat was sprayed with 20% benzocaine and swabbed with 4% lidocaine. A double-lumen Dreiling tube was passed, under fluoroscopic control. The tip was positioned into the third part of the duodenum, just proximal to the ligament of Treitz, so the distal lateral openings were in the second and third portions of duodenum and the proximal openings in the stomach. The test was performed with the patient in a sitting position. During the test, the Dreiling tube was intermittently flushed with air to prevent clogging of the ports by duodenal mucosa. Although minor fluid losses will occur with this method, no marker substance was used because the principal parameter, peak bicarbonate concentration, is independent of total volume. Basal samples were collected for 15 minutes from both the stomach and the duodenum using a suction pump. After basal collections, secretin (0.2 μg/kg of synthetic porcine secretin or 1 CU/kg of biologic porcine secretin) was administered intravenously. Duodenal collections at 15-minutes intervals were made for a total of 1 hour, labeled, and kept covered for pH and bicarbonate determinations. The total volume of gastric and duodenal basal secretion as well as pH on all duodenal specimens was recorded. The duodenal pH should be >7.00; a lower value would indicate contamination with gastric juice and invalidate the test. During this study, there were no such cases. All duodenal specimens were back-titrated for bicarbonate concentration. Other parameters measured include total volume, volume per kilogram of body weight, and total bicarbonate output. In our laboratory, with extensive clinical experience with the secretin test, the normal values are (a) peak bicarbonate concentration, >80 mEq/L, (b) volume per weight, >1.5 mL/kg, and (c) total bicarbonate output, >10.1 mEq/h.

### Statistical methods

Paired *t* test, means, standard deviation, and correlation were calculated using the StatView software (Version 4.57; Abacus Concepts Inc., Berkeley, CA, U.S.A.).

## RESULTS

The peak bicarbonate concentration (mean ± SD) obtained by using biologic porcine secretin and synthetic porcine secretin were 70 ± 25 mEq/L and 68 ± 31 mEq/L, respectively ($p = 0.58$, paired *t* test; Table 1). There was no significant difference between any other parameters measured as presented in Table 1. There was an excellent correlation between the results obtained with synthetic porcine secretin and biologic porcine secretin [$R = 0.964$; Slope: Peak Bicarbonate-SPS (mEq/L) = −12.703 + 1.16 × Peak Bicarbonate-BPS (mEq/L); Fig. 1]. Using a cutoff value for peak bicarbonate concentration of 80 mEq/L, the accuracy of synthetic porcine secretin in diagnosing pancreatic exocrine insufficiency was 100% when compared with biologic porcine secretin. Substituting the cutoff value of 80 mEq/L for Peak Bicarbonate-BPS in this equation yields a corresponding cutoff value for Peak Bicarbonate-BPS of 80.097. There-

**TABLE 1.** *Comparison of results of secretin stimulation testing obtained with biologic porcine secretin and synthetic porcine secretin*

| | Preparation | | *p* Value |
|---|---|---|---|
| | BPS | SPS | (paired *t* test) |
| Peak bicarbonate (mEq/L) | 70 ± 25 | 68 ± 31 | 0.58 |
| Total volume (ml) | 166 ± 103 | 163 ± 122 | 0.88 |
| Volume/Weight (ml/kg) | 2.41 ± 1.56 | 2.33 ± 1.70 | 0.72 |
| Total bicarbonate output (mEq/h) | 10.46 ± 10.37 | 10.86 ± 11.36 | 0.70 |

Results are expressed as mean ± SD.
[a] BPS, biologic porcine secretin; SPS, synthetic porcine secretin.

fore the cutoff value of 80 can be used safely with both forms of secretin. No side effects resulted from the use of either form of secretin.

## DISCUSSION

This study demonstrates the reliability of a newly prepared synthetic porcine secretin in pancreatic function testing in individuals with history of chronic pancreatitis. Synthetic secretin has been shown to be reliable for pancreatic function testing in healthy volunteers (9,10); however, to the best of our knowledge, this is the first study demonstrating a high correlation of secretin test results obtained by using biologic porcine secretin and synthetic porcine secretin in individuals with previously documented chronic pancreatitis. Two recent reports implicated CFTR mutations in idiopathic pancreatitis (11,12). The exact effect of these mutations on bicarbonate secretion is not known; however, one can speculate that decreased $HCO_3$ secretion may result, thus helping early detection. Lankisch and Creutzfeldt (9) found a significantly higher volume and total bicarbonate with synthetic secretin. No such difference was seen either in our study or in Hoppe et al. (10) study. The most likely explanation for this discrepancy could be differences in the purity and potency of different secretin preparations. From the practical standpoint, peak bicarbonate concentration is widely accepted as the best measure of pancreatic function (2–4). This and other studies comparing biologic porcine secretin with synthetic porcine secretin demonstrated a high degree of correlation of peak bicarbonate concentration (9,10). Based on previously published experience and on our results, we conclude that synthetic porcine secretin is highly reliable in pancreatic function testing in both healthy individuals and patients with chronic pancreatitis. Our results demonstrate that, at a dose of 0.2 μg/kg, synthetic porcine secretin yields equal results as 1 CU/kg of biologic porcine secretin in pancreatic function testing and the two preparations at these doses are interchangeable. It is expected that synthetic secretin is soon going to be widely available.

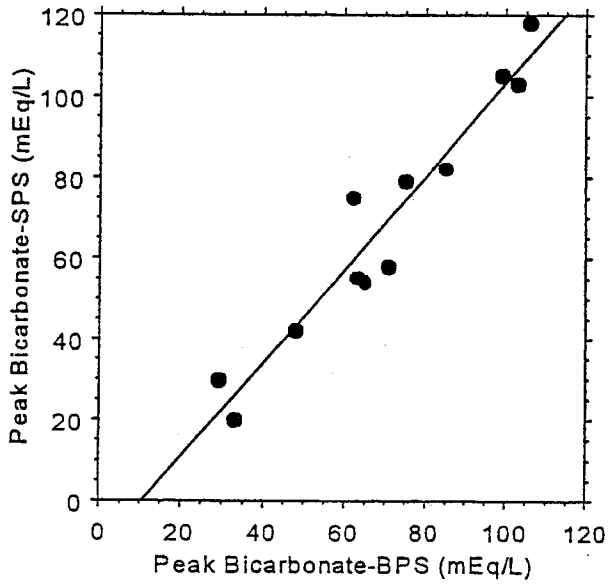


**FIG. 1.** Correlation of peak bicarbonate concentrations during secretin stimulation test using biologic and synthetic porcine secretin (BPS, biologic porcine secretin; SPS, synthetic porcine secretin).

**Acknowledgment:** This research was supported in part by ChiRhoClin Inc.

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