Human Secretin for Injection

INDICATIONS AND USAGE

1. STIMULATION OF PANCREATIC SECRETIONS, INCLUDING BICARBONATE TO AID IN THE DIAGNOSIS OF EXOCRINE PANCREATIC DYSFUNCTION:

ChiRhoSTM administered intravenously stimulates the exocrine pancreas to increase the volume and bicarbonate content of secreted pancreatic juices, which can assist in the diagnosis of exocrine pancreatic dysfunction. Normal ranges for pancreatic secretory response to intravenous secretin stimulation testing have been shown to vary. One source of variation is related to the inter-investigator differences in operative technique.

In two crossover studies (CRC98-2 and CRC99-9), a total of 18 patients with a documented history of chronic pancreatitis were given sHS, sPS and bPS. The results of correlations with sPS for both SHS and SPS were 0.02 mg (mEq/L) or SPS corresponding to 0.1 CU (mEq/L). The biological activity of SHS and SPS was approximately 5000 CU per mg as opposed to 3000 CU per mg for bPS.

This test has been used for the evaluation of synthetic human secretin. The standard unit of activity used for the biological activity of synthetic human secretin is 5000 CU per mg and the volume of distribution is approximately 5000 CU per mg as opposed to 3000 CU per mg for bPS.

There is no known instance of drug-drug interaction with synthetic human secretin. It is also not known whether drug interactions caused by synthetic human secretin will be the same as those caused by bPS.

Pharmacokinetics:
The PK profile for human secretin is as follows:

- Following an intravenous bolus administration of 0.4 mcg/kg of synthetic human secretin, the peak concentration occurred within 50 to 120 minutes.
- The elimination half-life of synthetic human secretin is 45 minutes. The clearance of synthetic human secretin is 260 ± 51 L/min and the volume of distribution is 2.7 L.

FIGURE 1

FIGURE 2

The values obtained for Figures 1 and 2 were performed by investigators skilled in performing secretin stimulation testing and are to be used only as guidelines. These results should not be generated to results of secretin stimulation testing conducted in other laboratories. Non-responders are defined by the absence of: positive bicarbonate concentration of less than 80 mEq/L, and a bicarbonate output of less than 0.2 L/kg/hr are consistent with impaired pancreatic function.

A physician or institution planning to perform secretin stimulation testing as an aid to the diagnosis of pancreatic disease should begin by assessing enough normal patients and patients with disease to develop proper techniques and to generate normal response ranges for the commonly assessed parameters for pancreatic exocrine function to ChiRhoSTM.

In three crossover studies (CRC98-1, CRC98-2, and CRC99-9) evaluating 21 different patients with a documented history of chronic pancreatitis, ChiRhoSTM was compared to synthetic porcine secretin (SPS) and biologically derived secretin (bPS). All of the patients, treated with these drugs, had peak bicarbonate concentrations of ≥ 80 mEq/L.

Pancreatic secretory response to intravenous synthetic human secretin in 35 normal healthy subjects demonstrated a mean peak bicarbonate concentration of 100 mEq/L and a mean total volume over one hour of 200 mL. All 35 subjects had peak bicarbonate concentrations ≥ 80 mEq/L.

Stimulation of gastric secretion to aid in the diagnosis of gastrinoma:

ChiRhoSTM administered intravenously stimulates gastric secretion in patients with Zollinger-Ellison Syndrome, regardless of age or small children, in gastrin secretion concentrations in normal subjects and in patients with duodenal ulcer disease. Doses, as established for the high sensitivity and specificity of the secretin stimulation test to aid in the diagnosis of gastrinoma and found using discriminant analysis that they maximize the separation of response groups by changing positive and negative tests. This gastric response is the basis for the use of synthetic human secretin as a provocative test in the evaluation of patients in whom gastrinoma is a diagnostic consideration.

In a three-way crossover study of 6 patients with tissue diagnosis gastrinoma, there was agreement among human synthetic secretin (ChiRhoSTM), synthetic porcine secretin and biologically derived secretin regarding gastric secretion. Seinoma serum gastrin levels were reported to be ≥ 110 pg/mL for all 6 patients tested after stimulation with 0.4 mcg/kg secretin. Testing of ChiRhoSTM in 12 healthy volunteers demonstrated completely negative results for gastrinoma.

Facilitation of identification of the ampulla of Vater and the accessory papilla during ERCP to assist in cannulation:

In a randomized, placebo controlled crossover study in 24 patients with pancreas divisum undergoing ERCP stimulation at a dose of 0.2 mcg/kg resulted in 16 of 24 successful cannulations of the minor duct compared to 2 of 24 for placebo.

INDICATIONS AND USAGE

ChiRhoSTM is indicated for:

- Stimulation of pancreatic secretions, including bicarbonate, to aid in the diagnosis of pancreatic exocrine dysfunction,
- Stimulation of gastric secretion to aid in the diagnosis of gastrinoma,
- Stimulation of pancreatic secretions to facilitate the identification of the ampulla of Vater and the accessory papilla during ERCP, to aid in cannulation of the minor duct.

CONTRAINDICATIONS

Patients suffering from acute pancreatitis should not receive ChiRhoSTM until the acute episode has subsided.

WARNINGS

Because of a potential allergic reaction to ChiRhoSTM patients should receive an intravenous test dose of 0.2 mg/kg. If no allergic reaction noted after 1 minute, the recommended dose may be injected slowly over 1 minute. A test dose is not recommended for patients with a history of allergy to any agent or allergic asthma. Appropriate measures for the treatment of acute hypersensitivity reactions should be immediately available. Appropriate measures for the treatment of acute hypersensitivity reactions should be immediately available. Appropriate measures for the treatment of acute hypersensitivity reactions should be immediately available.

PRECAUTIONS

General:

- Patients who have undergone vagotomy, or who are receiving anti-histaminic agents at the time of stimulation testing, or who have inflamed bowel disease may be hyporesponsive to secretin stimulation. The response does not indicate pancreatic disease.
- A greater than normal volume response to secretin stimulation, which may mask coexisting pancreatic disease, is occasionally encountered in patients with alcoholic or other liver disease.

Drug/Laboratory Test Interaction:

- The concomitant use of anti-thrombotic agents may make patients hyporesponsive, i.e., may produce a false positive result.
- Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies in animals have not been performed to evaluate the carcinogenic potential of synthetic human secretin. Studies to evaluate the potential for impairment of fertility or mutagenicity of synthetic human secretin have not been performed.

Pregnancy, Teratogenic Effects, Pregnancy Category C:

Animal reproduction studies have not been conducted. It is not known whether human secretin can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Synthetic human secretin should be given to a pregnant woman only if clearly needed.

Nursing Mothers:

It is not known whether synthetic human secretin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when synthetic human secretin is administered to a nursing woman.

Pediatric Use:

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use:

Among the 533 patients who have received ChiRhoSTM, two blood samples are drawn for determination of fasting serum gastrin levels (baseline value). Subsequently, a test dose of ChiRhoSTM 0.2 mcg/kg is injected intravenously to test for possible allergic. After one minute, if there are no untoward reactions, ChiRhoSTM at a dose of 0.2 mcg/kg of body weight is injected intravenously over 1 minute. Duodenal fluid is collected for 60 minutes thereafter. The aspirate is divided into four collection periods of 15 minutes each. The duodenal lumen of the tube is cleared with an injection of air after each collection of duodenal fluid. While wide variation in volume of the aspirate is indicative of incomplete collection. Each sample of duodenal fluid is to be chilled and subsequently analyzed for volume and bicarbonate concentration. Exocrine pancreas dysfunction typically associated with chronic pancreatitis is indicated if the peak bicarbonate concentration for any sample is < 60 mEq/L.

2. STIMULATION OF GASTRIN TO AID IN THE DIAGNOSIS OF GASTRINOMA:

The patient should have fasted for at least 12 hours prior to beginning the test. Prior to injection of ChiRhoSTM, two blood samples are drawn for determination of fasting serum gastrin levels (baseline value). Subsequently, a test dose of ChiRhoSTM 0.2 mcg/kg is injected intravenously to test for possible allergic. A dose of 0.2 mcg/kg of body weight is injected intravenously over 1 minute. The concomitant use of anticholinergic agents may make patients hyporesponsive, i.e., may produce a false positive result.

STORAGE:
The uncontrolled product should be stored at: 20°C (68°F). Exposure to light does not affect the stability of the product.

HOW SUPPLIED

ChiRhoSTM is supplied in a lyophilized sterile powder in vials containing 10 mg per vial.

REFERENCES


ChiRhoSTM is a registered trademark of ChiRhoClin, Inc.

Manufactured for:

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Butte, MT 59701-6129

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